Comparative Effectiveness Review
Number 209

Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review

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Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review

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Key Messages

Purpose of Review
To assess which noninvasive nonpharmacological treatments for common chronic pain conditions improve function and pain for at least 1 month after treatment.

Key Messages

- Interventions that improved function and/or pain for at least 1 month when used for—
  - **Chronic low back pain:** Exercise, psychological therapies (primarily cognitive behavioral therapy [CBT]), spinal manipulation, low-level laser therapy, massage, mindfulness-based stress reduction, yoga, acupuncture, multidisciplinary rehabilitation (MDR).
  - **Chronic neck pain:** Exercise, low-level laser, Alexander Technique, acupuncture.
  - **Knee osteoarthritis:** Exercise, ultrasound.
  - **Hip osteoarthritis**: Exercise, manual therapies.
  - **Fibromyalgia:** Exercise, CBT, myofascial release massage, tai chi, qigong, acupuncture, MDR.
  - **Chronic tension headache:** Spinal manipulation.
- Most effects were small. Long-term evidence was sparse.
- There was no evidence suggesting serious harms from any of the interventions studied; data on harms were limited.

This report is based on research conducted by the Pacific Northwest Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2015-00009-I). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report may periodically be assessed for the currency of conclusions. If an assessment is done, the resulting surveillance report describing the methodology and findings will be found on the Effective Health Care Program Web site at www.effectivehealthcare.ahrq.gov. Search on the title of the report.

Persons using assistive technology may not be able to fully access information in this report. For assistance contact EffectiveHealthCare@ahrq.hhs.gov.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The Centers for Disease Control and Prevention and the Office of the Assistant Secretary for Planning and Evaluation requested this report from the EPC Program at AHRQ. AHRQ assigned this report to the following EPC: Pacific Northwest Evidence-based Practice Center (Contract Number: 290-2015-00009-I).

The reports and assessments provide organizations with comprehensive, evidence-based information on common medical conditions and new health care technologies and strategies. They also identify research gaps in the selected scientific area, identify methodological and scientific weaknesses, suggest research needs, and move the field forward through an unbiased, evidence-based assessment of the available literature. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review and public comment prior to their release as a final report.

AHRQ expects that the EPC evidence reports and technology assessments, when appropriate, will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

If you have comments on this evidence report, they may be sent by mail to the Task Order Officers named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

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Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review

Structured Abstract

Objectives. Many interventions are available to manage chronic pain; understanding the durability of treatment effects may assist with treatment selection. We sought to assess which noninvasive nonpharmacological treatments for selected chronic pain conditions are associated with persistent improvement in function and pain outcomes at least 1 month after the completion of treatment.

Data sources. Electronic databases (Ovid MEDLINE®, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews) through November 2017, reference lists, and ClinicalTrials.gov.

Review methods. Using predefined criteria, we selected randomized controlled trials of noninvasive nonpharmacological treatments for five common chronic pain conditions (chronic low back pain; chronic neck pain; osteoarthritis of the knee, hip, or hand; fibromyalgia; and tension headache) that addressed efficacy or harms compared with usual care, no treatment, waitlist, placebo, or sham intervention; compared with pharmacological therapy; or compared with exercise. Study quality was assessed, data extracted, and results summarized for function and pain. Only trials reporting results for at least 1 month post-intervention were included. We focused on the persistence of effects at short term (1 to <6 months following treatment completion), intermediate term (≥6 to <12 months), and long term (≥12 months).

Results. Two hundred eighteen publications (202 trials) were included. Many included trials were small. Evidence on outcomes beyond 1 year after treatment completion was sparse. Most trials enrolled patients with moderate baseline pain intensity (e.g., >5 on a 0 to 10 point numeric rating scale) and duration of symptoms ranging from 3 months to >15 years. The most common comparison was against usual care.

Chronic low back pain: At short term, massage, yoga, and psychological therapies (primarily CBT) (strength of evidence [SOE]: moderate) and exercise, acupuncture, spinal manipulation, and multidisciplinary rehabilitation (SOE: low) were associated with slight improvements in function compared with usual care or inactive controls. Except for spinal manipulation, these interventions also improved pain.

Effects on intermediate-term function were sustained for yoga, spinal manipulation, multidisciplinary rehabilitation (SOE: low), and psychological therapies (SOE: moderate). Improvements in pain continued into intermediate term for exercise, massage, and yoga (moderate effect, SOE: low); mindfulness-based stress reduction (small effect, SOE: low); spinal manipulation, psychological therapies, and multidisciplinary rehabilitation (small effects, SOE: moderate). For acupuncture, there was no difference in pain at intermediate term, but a slight improvement at long term (SOE: low). Psychological therapies were associated with slightly greater improvement than usual care or an attention control on both function and pain at short-term, intermediate-term, and long-term followup (SOE: moderate). At short and intermediate term, multidisciplinary rehabilitation slightly improved pain compared with exercise (SOE:

moderate). High-intensity multidisciplinary rehabilitation (≥20 hours/week or >80 hours total) was not clearly better than non–high-intensity programs.

Chronic neck pain: At short and intermediate terms, acupuncture and Alexander Technique were associated with slightly improved function compared with usual care (both interventions), sham acupuncture, or sham laser (SOE: low), but no improvement in pain was seen at any time (SOE: llow). Short-term low-level laser therapy was associated with moderate improvement in function and pain (SOE: moderate). Combination exercise (any 3 of the following: muscle performance, mobility, muscle re-education, aerobic) demonstrated a slight improvement in pain and function short and long term (SOE: low).

Osteoarthritis: For ***knee osteoarthritis,*** exercise and ultrasound demonstrated small short-term improvements in function compared with usual care, an attention control, or sham procedure (SOE: moderate for exercise, low for ultrasound), which persisted into the intermediate term only for exercise (SOE: low). Exercise was also associated with moderate improvement in pain (SOE: low). Long term, the small improvement in function seen with exercise persisted, but there was no clear effect on pain (SOE: low). Evidence was sparse on interventions for ***hip and hand osteoarthritis***. Exercise for hip osteoarthritis was associated with slightly greater function and pain improvement than usual care short term (SOE: low). The effect on function was sustained intermediate term (SOE: low).

Fibromyalgia: In the short term, acupuncture (SOE: moderate), CBT, tai chi, qigong, and exercise (SOE: low) were associated with slight improvements in function compared with an attention control, sham, no treatment, or usual care. Exercise (SOE: moderate) and CBT improved pain slightly, and tai chi and qigong (SOE: low) improved pain moderately in the short term. At intermediate term for exercise (SOE: moderate), acupuncture, and CBT (SOE: low), slight functional improvements persisted; they were also seen for myofascial release massage and multidisciplinary rehabilitation (SOE: low); pain was improved slightly with multidisciplinary rehabilitation in the intermediate term (SOE: low). In the long term, small improvements in function continued for multidisciplinary rehabilitation but not for exercise or massage (SOE: low for all); massage (SOE: low) improved long-term pain slightly, but no clear impact on pain for exercise (SOE: moderate) or multidisciplinary rehabilitation (SOE: low) was seen. Short-term CBT was associated with a slight improvement in function but not pain compared with pregabalin.

Chronic tension headache: Evidence was sparse and the majority of trials were of poor quality. Spinal manipulation slightly improved function and moderately improved pain short term versus usual care, and laser acupuncture was associated with slight pain improvement short term compared with sham (SOE: low).

There was no evidence suggesting increased risk for serious treatment-related harms for any of the interventions, although data on harms were limited.

Conclusions. Exercise, multidisciplinary rehabilitation, acupuncture, CBT, and mind-body practices were most consistently associated with durable slight to moderate improvements in function and pain for specific chronic pain conditions. Our findings provided some support for clinical strategies that focused on use of nonpharmacological therapies for specific chronic pain conditions. Additional comparative research on sustainability of effects beyond the immediate post-treatment period is needed, particularly for conditions other than low back pain.

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Introduction

Chronic pain substantially impacts physical and mental functioning, productivity, quality of life, and family relationships; it is the leading cause of disability and is often refractory to treatment.[1,2] Chronic pain is often defined as pain lasting 3 months or longer or persisting past the normal time for tissue healing, though definitions vary.[1,3] Chronic pain affects millions of adults in the United States, with an annual cost in personal and health system expenditures conservatively estimated at $560 billion to $635 billion.[1] Chronic pain is multifaceted and is influenced by multiple factors (e.g., genetic, central nervous system, psychological, and environmental factors) and complex interactions, making pain assessment and management a challenge.

Many pharmacological and nonpharmacological treatments are available for management of chronic pain and include a variety of noninvasive as well as surgical and interventional procedures. The National Pain Strategy (NPS) report[2] and 2011 Institute of Medicine (IOM) report[1] describe the need for evidence-based strategies for the management of chronic pain that address the biopsychosocial nature of this problem, including nonpharmacological treatment. Recently, guidelines on opioid use for chronic pain by the Centers for Disease Control and Prevention (CDC)[4] included a recommendation on the preferred use of nonopioid treatment over opioid therapy. These initiatives, and others, speak to the importance of understanding current evidence on noninvasive nonpharmacological treatment of chronic pain.

Musculoskeletal pain, particularly related to joints and the back, is the most common type of chronic pain.[1,5] This systematic review thus focuses on five of the most common causes of musculoskeletal pain: chronic low back pain, chronic neck pain, osteoarthritis, fibromyalgia and chronic tension headache.

This review focuses on noninvasive nonpharmacological treatments for chronic pain including exercise, mind-body practices, psychological therapies, multidisciplinary rehabilitation, mindfulness practices, manual therapies, physical modalities, and acupuncture. Many trials have examined the impact of these interventions on outcomes during or immediately after the course of treatment reporting improved function and reduced pain. However, given the persistence of chronic pain, understanding whether the benefits are durable would be very helpful for informing selection of therapies. Therefore, this report focuses on durability of treatment effects, defined as at least 1 month following the end of a course of treatment.

Rationale for This Review

Our review is intended to address some of the needs described in the NPS[2] and IOM[1] reports and others for evidence to inform guidelines and health care policy (including reimbursement policy) related to use of noninvasive nonpharmacological treatments as possible alternatives to opioids and other pharmacological treatments. This review also aims to provide additional insights into research gaps related to use of noninvasive nonpharmacological alternatives for treating five of the most common chronic pain conditions.

Scope and Key Questions

This Comparative Effectiveness Review focused on noninvasive nonpharmacological therapy, with a Key Question (KQ) for each of five common chronic pain conditions:

KQ 1: Chronic low back pain
KQ 2: Chronic neck pain
KQ 3: Osteoarthritis (knee, hip, hand)
KQ 4: Fibromyalgia
KQ 5: Chronic tension headache
KQ 6: Effects of age, sex, or presence of comorbidities (e.g., emotional or mood disorders) on estimates of benefits and harms.

For each condition, we addressed the following subquestions:

a. What are the benefits and harms of noninvasive nonpharmacological therapies compared with sham treatment, no treatment, waitlist, attention control, or usual care?
b. What are the benefits and harms of noninvasive nonpharmacological therapies compared with pharmacological therapy (e.g., opioids, NSAIDS, acetaminophen, antiseizure medications, antidepressants)?
c. What are the benefits and harms of noninvasive nonpharmacological therapies compared with exercise or (for headache) biofeedback? Exercise was chosen as a common comparator for all conditions except headache as it is recommended in most guidelines for these conditions and a frequent comparator in the chronic pain literature.

Interventions considered in the review include exercise (including aspects of physical therapy), mind-body practices (yoga, tai chi, qigong), psychological therapies (cognitive-behavioral therapy, biofeedback, relaxation techniques, acceptance and commitment therapy), multidisciplinary rehabilitation (including functional restoration), mindfulness practices (meditation, mindfulness-based stress reduction practices), musculoskeletal manipulation (e.g., chiropractic or osteopathic manipulation), and physical modalities (traction, ultrasound, transcutaneous electrical nerve stimulation [TENS], low-level laser therapy, interferential therapy, superficial heat or cold, bracing for knee, back or neck, electro-muscular stimulation and magnets), and acupuncture with a .focus common single active interventions and comparators. We assessed the persistence of effects for therapies at least 1 month following completion of a course of treatment. Studies of combination or adjunctive interventions were excluded. We categorized interventions *a priori* to provide a framework for the report realizing that there is some overlap and that other methods for such categorization are possible. We performed stratified analyses to evaluate specific techniques within broader intervention categories (e.g. we looked at different types of psychological therapies or exercise).

Details on the PICOTS (population, interventions, comparators, outcomes, timing, settings) inclusion and exclusion criteria are provided in the full report and in the published protocol.

Methods

The methods for this systematic review follow the Agency for Healthcare Research & Quality (AHRQ) *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[6] See the review protocol (http://effectivehealthcare.ahrq.gov/index.cfm) and the full report of the review for additional details.

Topic Refinement and Review Protocol

The review team developed initial KQs and PICOTS with input from the AHRQ Task Order Officer (TOO), representatives from the CDC and the Office of the Assistant Secretary for Planning and Evaluation (ASPE), and a group of Key Informants. The Evidence-based Practice Center review team considered the public comments received on the provisional Key Questions, PICOTS, and analytic framework (posted on the AHRQ Effective Health Care Web site), along with input from the AHRQ TOO, CDC and ASPE representatives, and a Technical Expert Panel convened for this report. The final version of the protocol for this review was posted on the AHRQ Effective Health Care Program Web site (www.effectivehealthcare.ahrq.gov) and registered in the PROSPERO international database of prospectively registered systematic reviews (CRD42017067729).

Literature Search Strategy

A research librarian conducted searches in Ovid® MEDLINE®, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews through November 1, 2017. ClinicalTrials.gov was searched for unpublished trials. A *Federal Register* notice was posted in an effort to identify unpublished data. No responses were received. Reference lists of included articles and the bibliographies of systematic reviews published since 2010 were reviewed for includable literature.

Inclusion and Exclusion Criteria, Study Selection, and Data Abstraction

Inclusion and exclusion criteria were developed *a priori* based on the Key Questions and PICOTS and are detailed in Table 1 of the report and the published protocol. We focused on randomized controlled trials (RCTs) reporting outcomes at least 1 month following the completion of a course of treatment. Trials comparing interventions with placebo/sham and trials where no active intervention was received (including usual care, waitlist control, minimal intervention) served as one set of comparators. To evaluate comparative effectiveness, exercise was chosen as a common active comparator for all conditions except headache, for which biofeedback was considered the common comparator, and we sought trials of intervention compared with pharmacological treatment.

Details regarding process and inclusion/exclusion of studies are provided in the full report and Appendixes B and C. We abstracted data on study characteristics, funding source, populations, interventions, comparators, and results.

Quality Assessment of Individual Studies

Study quality was independently assessed by two investigators using predefined criteria[7,8] and based on methods recommended in the AHRQ *Methods Guide for Effectiveness and Comparative Effectiveness Research*.[6] Studies were rated as "good," "fair," or "poor." (See Appendix E).

Data Analysis and Synthesis

Data were synthesized qualitatively (ranges and descriptive analysis) and quantitatively using meta-analysis where appropriate.[9] Duration of followup post-intervention was reported and

categorized as short term (<6 months), intermediate term (≥6 to <12 months) and long term (≥12 months). Primary outcomes were function and pain.

Analyses were stratified by disease type, intervention, control group (usual care, exercise or pharmacological treatment) and length of followup (short, intermediate, and long term). We performed additional sensitivity and subgroup analyses based on specific interventions (e.g., type of acupuncture, type of exercise, intervention intensity etc.) and control types, and by excluding outlying studies and studies rated poor quality.

We categorized the magnitude of effects for function and pain using the system described in our previous reviews.[10-12] We classified effects for measures with a 0-100 scale for pain or function as slight/small (5-10 points), moderate (>10–20 points), or large/substantial (>20 points). The moderate range for functional outcomes roughly corresponds to reported minimum clinically important differences for the measure. Small (slight) effects may not meet standard thresholds for minimal clinically important difference (MCID) but such thresholds may vary between patients and small average effects may be associated with larger effects in some patients. In some situations, interventions with small benefits may be warranted (e.g., when harms and costs are small). Additional information is found in the full report and Appendix H.

Grading the Strength of Evidence for Major Comparisons and Outcomes

The overall strength of evidence (SOE) for each KQ and primary outcome (pain, function) was graded high, moderate, low, or insufficient based on study limitations; consistency of results across studies; the directness of the evidence linking the interventions with health outcomes; effect estimate precision; and reporting bias.[13,14] When all studies for a primary outcome were rated poor quality, we rated the SOE as insufficient (see Appendix G).

Peer Review and Public Commentary

Peer reviewers with expertise in primary care and management of the included chronic pain conditions were invited to provide written comments on the draft report. The AHRQ Task Order Officer and an Evidence-based Practice Center Associate Editor provided comments and editorial review. The draft report was posted on the AHRQ Web site for 4 weeks for public comment.

Results

Results of Literature Searches

Database searches resulted in 4,996 potentially relevant articles. After dual review of abstracts and titles, 1,193 articles were selected for full-text dual review and 218 publications (202 trials) met inclusion criteria. We included 68 trials (74 publication) on chronic low back pain, 25 trials on chronic neck pain, 53 trials (56 publications) on osteoarthritis, 47 trials (54 publications) on fibromyalgia, and nine trials on chronic tension headache. The majority of trials compared nonpharmacological interventions with usual care, waitlist, no treatment, attention control, or placebo/sham (93%); few trials employed pharmacological treatments (5%) or exercise (17%) (Note: some trials had more than one comparator group). Little evidence beyond 12 months was available.

The majority of trials (59%) were rated fair quality, and 36 percent were rated as poor, with only 5 percent considered good quality. Attrition was greater than 20 percent in 28 percent of trials. For a number of interventions, providers and patients could not be effectively blinded. Other methodological shortcomings were unclear reporting of randomization or allocation concealment methods. Adherence to interventions was poorly reported.

Key points are presented in the following sections for interventions and outcomes for which there was low or moderate strength of evidence. All outcomes were considered to be direct. Interventions and outcomes with no or insufficient evidence are discussed in the full report. If differences were not statistically significant but confidence intervals were close to 0 (continuous outcomes) or 1 (dichotomous outcomes) results were interpreted as showing no clear difference, but favoring one treatment.

Key Question 1: Chronic Low Back Pain

Exercise

- Exercise was associated with slightly greater effects on short-term function than usual care, an attention control or a placebo intervention (6 trials, pooled standardized mean difference [SMD] -0.31, 95% confidence interval [CI] -0.58 to -0.04, I^2=57%); there was no evidence of effects on intermediate-term function (3 trials, pooled SMD -0.15, 95% CI -0.48 to 0.18, I^2=51%) or long-term function (1 trial, difference 0.00 on the 0 to 100 Oswestry Disability Index [ODI], 95% CI -11.4 to 11.4) (SOE: Low).
- Exercise was associated with slightly to moderately greater effects on pain than usual care, an attention control or a placebo intervention at short-term (6 trials, pooled difference -0.81 on a 0 to 10 scale, 95% CI -1.26 to -0.,36, I^2=0%), intermediate-term (3 trials, pooled difference -1.37, 95% CI -2.10 to -0.65, I^2=34%), and long-term (1 trial, difference -1.55, 95% CI -2.378 to -0.32) followup (SOE: Moderate for short term, low for intermediate term and long term).

Psychological Therapies

- Psychological therapy was associated with slightly greater effects on function than usual care or an attention control at short-term (3 trials, pooled SMD -0.25, 95% CI -0.38 to -0.12, I^2=0%), intermediate-term (3 trials, pooled SMD -0.25, 95% CI -0.37 to -0.13, I^2=0%), and long-term followup (3 trials, pooled SMD -0.27, 95% CI -0.39 to -0.15, I^2=0%) (SOE: Moderate).
- Psychological therapy was associated with slightly greater effects on pain than usual care or an attention control at short-term (3 trials, pooled difference -0.76 on a 0 to 10 scale, 95% CI -0.99 to -0.53, I^2=0%), intermediate-term (3 trials, pooled difference -0.71, 95% CI -0.94 to -0.48, I^2=0%), or long-term followup (3 trials, pooled difference -0.53, 95% CI -0.78 to -0.27, I^2=0%) (SOE: Moderate).

Physical Modalities

Ultrasound

- No evidence of difference was found between ultrasound versus sham ultrasound in short-term pain (2 trials, SOE: low).

Low-Level Laser Therapy

- One trial found low-level laser therapy associated with slightly greater effects than sham laser on short-term function (difference -8.2 on the 0 to 100 ODI, 95% CI -13.6 to -2.8) and moderately greater effects on pain (difference -16.0 on a 0 to 100 scale, 95% CI -28.3 to -3.7) (SOE: low).

Traction

- Two trials found no evidence of difference between traction versus sham traction in short-term pain or function (SOE: low).

Manual Therapies

Spinal Manipulation

- Spinal manipulation was associated with slightly greater effects than sham manipulation, usual care, an attention control, or a placebo intervention in short-term function (3 trials, pooled SMD -0.34, 95% CI -0.63 to -0.05, I^2=61%) and intermediate-term function (3 trials, pooled SMD -0.40, 95% CI -0.69 to -0.11, I^2=76%) (SOE: low)
- There was no evidence of differences between spinal manipulation versus sham manipulation, usual care, an attention control or a placebo intervention in short-term pain (3 trials, pooled difference -0.20 on a 0 to 10 scale, 95% CI -0.66 to 0.26, I^2=58%), but manipulation was associated with slightly greater effects than controls on intermediate-term pain (3 trials, pooled difference -0.64, 95% CI -0.92 to -0.36, I^2=0%) (SOE: low for short term, moderate for intermediate term).

Massage

- Massage was associated with slightly greater effects on short-term function than sham massage or usual care (4 trials, SMD -0.30, 95% CI -0.46 to -0.14, I^2=0%). There was no evidence of differences between massage versus controls in intermediate-term function (3 trials, SMD -0.09, 95% CI -0.24 to 0.06, I^2=0%) (SOE: moderate for short term, low for intermediate term).
- Massage was associated with slightly greater effects on short-term pain than sham massage or usual care (4 trials, pooled difference -0.52 on a 0 to 10 scale, 95% CI -0.81 to -0.23, I^2=0%). There was no evidence of differences between massage versus controls in intermediate-term pain (3 trials, difference -0.01, 95% CI -0.40 to 0.38, I^2=0%) (SOE: moderate for short term, low for intermediate term).

Mindfulness-Based Stress Reduction

- There was no evidence of differences between mindfulness-based stress reduction (MBSR) versus usual care or an attention control in short-term function (4 trials, pooled SMD -0.25, 95% CI -0.53 to 0.04, I^2=53%), intermediate-term function (1 trial, SMD -0.20, 95% CI -0.47 to 0.06) or long-term function (1 trial, SMD -0.20, 95% CI -0.47 to 0.06) (SOE: low).
- MBSR was associated with slightly greater effects than usual care or an attention control on short-term pain (3 trials, pooled difference -0.73 on a 0 to 10 scale, 95% CI -1.18 to -0.28, I^2=93%), after excluding two poor-quality trials; MBSR was also associated with small effects on intermediate-term pain (1 trial, difference -0.75, 95% CI -1.17 to -0.33),

with no statistically significant effects on long-term pain (1 trial, SMD -0.22, 95% CI -0.64 to 0.20) (SOE: moderate for short term, low for intermediate and long term).

Mind-Body Practices—Yoga

- Yoga was associated with slightly greater effects on function than an attention or waitlist control at short-term (6 trials, pooled SMD -0.50, 95% CI -0.72 to -0.29, I^2=54%) and intermediate-term (3 trials, pooled SMD -0.33, 95% CI -0.49 to -0.16) followup (SOE: moderate for short term, low for intermediate term).
- Yoga was associated with moderately greater effects on pain than an attention or waitlist control at short-term (5 trials, pooled difference -1.10 on a 0 to 10 scale, 95% CI -1.77 to -0.42, I^2=74%) and intermediate-term (2 trials, pooled difference -1.17, 95% CI -1.91 to -0.44, I^2=26%) followup (SOE: low for short term, moderate for intermediate term).

Acupuncture

- Acupuncture was associated with slightly greater effects on short-term function than sham acupuncture or usual care (4 trials, pooled SMD -0.22, 95% CI -0.35 to -0.08, I^2=44%). There was no evidence of differences between acupuncture versus controls in intermediate-term function (3 trials, pooled SMD -0.08, 95% CI -0.36 to 0.20, I^2=75%) or long-term function (1 trial, adjusted difference -3.4 on the 0 to 100 ODI, 95% CI -7.8 to 1.0) (SOE: low).
- Acupuncture was associated with slightly greater effects on short-term pain than sham acupuncture, usual care, an attention control, or a placebo intervention (5 trials, pooled difference -0.55 on a 0 to 10 scale, 95% CI -0.86 to -0.24, I^2=30%). There was no evidence of a difference in intermediate-term pain (5 trials, pooled mean difference -0.25, 95% CI -0.67 to 0.16, I^2=33%); one trial found acupuncture associated with greater effects on long-term pain (mean difference -0.83, 95% CI -1.51 to -0.15) (SOE: moderate for short term, low for intermediate term and long term).

Multidisciplinary Rehabilitation

- Multidisciplinary rehabilitation was associated with slightly greater effects on function than usual care at short-term followup (4 trials, pooled SMD -0.31, 95% CI -0.57 to -0.05, I^2=70%) and intermediate-term followup (4 trials, pooled SMD -0.37, 95% CI -0.64 to -0.10, I^2=50%); there was no evidence of differences in long-term function (2 trials, pooled SMD -0.04, 95% CI -0.31 to 0.24, I^2=35%) (SOE: low).
- Multidisciplinary rehabilitation was associated with slightly greater effects on pain than usual care at short-term followup (4 trials, pooled difference -0.51 on a 0 to 10 scale, 95% CI -0.89 to -0.13, I^2=23%) and intermediate-term followup (4 trials, pooled difference -0.63, 95% CI -1.04 to -0.22, I^2=0%); the long-term difference was smaller and not statistically significant (2 trials, pooled difference -0.34, 95% CI -0.86 to 0.18, I^2=0%) (SOE: moderate for short term and intermediate term, low for long term).

Comparative Effectiveness of Interventions

- One trial found no differences between low-level laser therapy versus exercise therapy in intermediate-term function or pain (SOE: low).
- There was no evidence of difference between spinal manipulation versus exercise in short-term function (3 trials, pooled SMD 0.01, 95% CI -0.22 to 0.25; I^2=62%) or

intermediate-term function (4 trials, pooled SMD 0.02, 95% CI -0.13 to 0.18; I^2=48%) (SOE: low).

- There was no evidence of difference between spinal manipulation versus exercise in short-term pain (3 trials, pooled difference 0.31 on a 0 to 10 scale, 95% CI -0.30 to 0.92; I^2=60%) or intermediate-term pain (4 trials, pooled difference 0.22, 95% CI -0.09 to 0.52, I^2=9.4%) (SOE: low).
- One trial found no differences between massage versus exercise in intermediate-term or function or pain (SOE: low).
- There was no statistically significant difference between yoga versus exercise in short-term or intermediate-term function or pain (SOE: low).
- One trial found no evidence of differences between qigong versus exercise in short-term function (difference 0.9 on the RRoland-Morris Disability Questionnaire, 95% CI -0.1 to 2.0), although intermediate-term results slightly favored exercise (difference 1.2, 95% CI 0.1 to 2.3) (SOE: low).
- One trial found qigong associated with slightly lower effects on pain versus exercise at short-term followup (difference 7.7 on a 0 to 100 scale, 95% CI 0.7 to 14.7), but the difference at intermediate-term was not statistically significant (difference 7.1, 95% CI -1.0 to 15.2) (SOE: low).
- Multidisciplinary rehabilitation was associated with slightly greater effects than exercise on short-term function (6 trials, pooled SMD -0.28, 95% CI -0.54 to -0.01, I^2=39%) and intermediate-term function (5 trials [excluding outlier trial], pooled SMD -0.22, 95% CI -0.40 to -0.03, I^2=0%); there was no effect on long-term function (2 trials [excluding outlier trial], pooled SMD -0.06, 95% CI -0.36 to 0.25, I^2=0%) (SOE: moderate for short term and intermediate term, low for long term).
- Multidisciplinary rehabilitation was associated with slightly greater effects than exercise on short-term pain (6 trials, pooled difference -0.75 on a 0 to 10 scale, 95% CI -1.18 to -0.31, I^2=0%) and intermediate-term pain (5 trials [excluding outlier trial], pooled difference -0.55, 95% CI -0.95 to -0.15, I^2=0%); there was no effect on long-term pain (2 trials [excluding outlier trial], pooled difference 0.00, 95% CI -0.94 to 0.95) (SOE: moderate for short term and intermediate term, low for long term).

Key Question 2: Chronic Neck Pain

Exercise

- Across types of exercise, there was no clear improvement in function (3 trials [excluding outlier trial], pooled SMD -0.23, 95% CI -0.71 to 0.15) or pain (3 trials [excluding outlier trial], pooled SMD -0.72, 95% CI -1.49 to 0.06) versus no treatment or advice alone in the short-term (SOE: low).
- A subgroup of two trials of combination exercises (including 3 of the following 4 exercise categories: muscle performance, mobility, muscle re-education, aerobic) suggests a slight benefit in function and pain versus no treatment or advice alone over the short term and function in the long term (SOE: low).

Psychological

- No evidence of differences in function (Neck Disability Index, 0-80 scale) or pain (Visual Analog Scale for Pain [VAS], 0-10 scale) in the short term (adjusted difference 0.1, 95% CI -2.9 to 3.2 and 0.2, 95% CI -0.4 to 0.8, respectively) or intermediate term (adjusted difference 0.2, 95% CI -2.8 to 3.1 and 0.2, 95% CI -0.3 to 0.8, respectively) from one trial comparing relaxation training and no intervention or exercise (SOE: low for all).

Physical Modalities

- Low-level laser therapy was associated with a moderate improvement in short-term function (2 trials, pooled difference -14.98 , 95% CI -23.88 to -6.07, I^2=39%, 0-100 scale) and pain (3 trials, pooled difference -1.81 on a 0-10 scale, 95% CI -3.35 to -0.27, I^2=75%) compared with sham (SOE: moderate for function and pain).

Manual Therapies

- The effects of massage on function versus self-management attention control were slight and not statistically significant in one trial (N=64) in the short term (≥5 point improvement on the Neck Disability Index, 39% versus 14%, relative risk [RR] 2.7, 95% CI 0.99 to 7.5) and intermediate term (57% versus 31%, RR 1.8, 95% CI 0.97 to 3.5) (SOE: low for both time periods).

Mind-Body Practices

- Alexander Technique resulted in a slight improvement in function in the short term (difference -5.56 on a 0-100% scale, 95% CI -8.33 to -2.78) and intermediate term (difference -3.92, 95% CI -6.87 to -0.97) compared with usual care alone based on one trial (SOE: low).

Acupuncture

- Acupuncture was associated with slightly greater effects on short-term and intermediate-term function versus sham acupuncture, placebo (sham laser) or usual care (short term, 5 trials, pooled SMD -0.40, 95% CI -0.64 to -0.17, I^2=67.7%; intermediate term, 3 trials, pooled SMD -0.19, 95% CI -0.35 to -0.02). One trial reported no difference in function in the long term (SMD -0.23, 95% CI -0.61 to 0.16) (SOE: low for all time periods). A sham comparator was used in all but one trial.
- There was no evidence of differences in pain comparing acupuncture with sham acupuncture, or placebo interventions in the short term (4 trials [excluding outlier trial], pooled difference -0.2 on a 0-10 scale, 95% CI -0.59 to 0.05, I^2=2%), intermediate term (3 trials, pooled difference 0.45, 95% CI -0.34 to 1.25, I^2=59%) or long term (1 trial, difference -1.8, 95% CI -1.34 to 0.64). (SOE: low for all time periods).

Comparative Effectiveness of Interventions for Chronic Neck Pain

- There was no clear evidence that massage improved pain in the intermediate term versus exercise (P>0.05, data not reported) in one trial (SOE: low).
- No clear evidence that basic body awareness therapy improved function in the short term versus exercise in one trial (SOE: low).

Key Question 3: Osteoarthritis

Exercise (Knee)

- Exercise was associated with slightly greater improvement in function than usual care, no treatment or sham intervention short term (7 trials, pooled SMD -0.25, 95% CI -0.4 to -0.09, I^2=0%), at intermediate term (9 trials [excluding outlier trial] pooled SMD -0.78, 95%CI -1.37 to -0.19, I^2=91.4%), and long term (2 trials, pooled SMD -0.24, 95%CI -0.37 to -0.11 I^2=0%) (SOE: moderate for short term; low for intermediate and long term).
- Exercise was associated with a slight improvement in pain short term (7 trials, pooled difference -0.44 on a 0 to 10 scale, 95% CI -0.82 to -0.05, I^2=35%) versus usual care, no treatment or sham intervention (SOE: moderate), and with moderately greater effect on pain in the intermediate term (9 trials, pooled difference -1.61 on a 0 to 10 scale, 95% CI -2.51 to -0.72, I^2=91%) compared with usual care, an attention control, or no treatment (SOE: low). Long term, there was no clear difference between exercise and improvement in pain but data were limited (2 trials, difference -0.24, 95% CI -0.72 to 0.24) (SOE: low).

Psychological Therapy (Knee)

- Two trials of pain coping skills training and cognitive behavioral training versus usual care found no evidence of differences in function (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC] physical function, 0-100) or pain (WOMAC pain, 0-100); treatment effects were averaged over short term to intermediate term (difference -0.3, 95% CI -8.3 to 7.8 for function and -3.9, 95% CI -1.8 to 4.0 for pain) and intermediate term to long term (mean 35.2, 95% CI 31.8 to 38.6 vs. mean 37.5, 95% CI 33.9 to 41.2, and mean 34.5, 95% CI 30.8 to 38.2 vs. mean 38.0, 95% CI 34.1 to 41.8), respectively (SOE: low).

Physical Modalities (Knee)

Ultrasound

- One trial found continuous and pulsed ultrasound was associated with better short-term function (difference of -6.2, 95% CI -8.36 to -4.20, and -5.71, 95% CI -7.72 to -3.70 on a 0-24 scale) and short-term pain intensity (difference -3.3, 95% CI -4.64 to -1.96, and -3.37, 95% CI -4.73 to -2.01 on a 0-10 scale) (SOE: low).
- One trial found no evidence of differences between continuous and pulsed ultrasound versus sham in intermediate-term function (difference -2.9, 95% CI -9.19 to 3.39 and 1.6, 95% CI -3.01 to 6.22, on a 0-68 scale) or pain (difference -1.6, 95% CI -3.26 to 0.06 and 0.2, 95% CI -1.34 to 1.74, on a 0-20 scale). There was also no evidence of difference between groups for VAS pain during rest or on movement (SOE: low).

Transcutaneous Electrical Nerve Stimulation

- There was no evidence of difference from one trial between transcutaneous electrical nerve stimulation (TENS) and placebo TENS in intermediate-term function as measured by the WOMAC function subscale (proportion of patients who achieved MCID (≥9.1), 38% vs. 39%, RR 1.2 (95% CI 0.6 to 2.2); and difference -1.9 (95% CI -9.7 to 5.9) on a 0-100 scale) or intermediate-term pain (proportion of patients who achieved MCID (≥20)

in VAS pain, 56% vs 44%, RR 1.3 (95% CI 0.8 to 2.0); and mean difference -5.6 (95% CI -14.9 to 3.6) on the 0-100 WOMAC pain subscale) (SOE: low for function and pain).

Electromagnetic Field

- One trial found pulsed electromagnetic fields were associated with slight improvements in function (difference -3.48, 95% CI -4.44 to -2.51 on a 0-85 WOMAC Activities of Daily Living subscale) and pain (difference -0.84, 95% CI -1.10 to -0.58 on a 0-25 WOMAC pain subscale) versus sham short-term but differences may not be clinically significant (SOE: low).

Acupuncture (Knee)

- There was no evidence of differences between acupuncture versus control interventions (sham acupuncture, waitlist or usual care) on function in the short term (4 trials [excluding outlier trial], pooled SMD -0.05, 95% CI -0.32 to 0.38) or the intermediate term (4 trials, pooled SMD -0.15, 95% CI -0.31 to 0.02, I^2=0%) (SOE: low for short term; moderate for intermediate term). Stratified analysis showed no differences between acupuncture and sham treatments (4 trials) but moderate improvement in function compared with usual care (2 trials) short term.
- There was no evidence of differences between acupuncture versus control interventions (sham acupuncture, waitlist, or usual care) on pain in the short term (6 trials, pooled SMD -0.27, 95% CI -0.56 to 0.02, I^2=75%) or clinically meaningful differences in the intermediate term (4 trials, pooled SMD -0.16, 95% CI -0.31 to 0.02, I^2=0%); no individual trial was statistically significant. (SOE: low for short term; moderate for intermediate term). Short-term differences were significant for acupuncture versus usual care but not for acupuncture versus sham acupuncture.

Exercise for Osteoarthritis of the Hip

- Exercise was associated with a slight improvement in function versus usual care in the short term (3 trials, pooled SMD -0.33, 95% CI, -0.53 to -0.12, I^2=0.0%) and intermediate term (2 trials, pooled SMD -0.28, 95% CI -0.50 to -0.05, I^2=0.0%). (SOE: low for short and intermediate term).
- Exercise tended toward slightly greater improvement in short-term pain compared with usual care (3 trials, pooled SMD -0.34, 95% CI, -0.63 to -0.04, I^2=48.2%), but the results were no longer significant at intermediate term (2 trials, pooled SMD -0.14, 95% CI -0.37 to 0.08, I^2=0%) (SOE: low for short and intermediate term).

Physical Modalities for Osteoarthritis of the Hand

- One trial of low-level laser treatment versus sham demonstrated no improvement in terms of function (difference 0.2, 95% CI -0.2 to 0.6) or pain (difference 0.1, 95% CI -0.3 to 0.5) in the short term (SOE: low).

Multidisciplinary Rehabilitation for Osteoarthritis of the Hand

- One trial of multidisciplinary rehabilitation versus waitlist control demonstrated no short-term differences between groups in function (adjusted difference 0.49, 95% CI, -0.09 to 0.37 on 0-36 scale), pain (adjusted difference 0.40, 95% CI, -0.5 to 1.3 on a 0-20 scale), or with regard to the proportion of Osteoarthritis Research Society International Outcome

Measures in Rheumatology responders (odds ratio [OR] 0.82, 95% CI, 0.42 to 1.61) (SOE: low for all outcomes).

Comparative Effectiveness of Interventions for Osteoarthritis

- Knee Osteoarthritis: One trial of pain coping skills training versus strengthening exercises found no evidence of differences in WOMAC physical function scores (0-68 scale) at short term (mean difference 2.0, 95% CI -2.4 to 6.4) or intermediate term (mean difference 3.2, 95% CI -0.6 to 7.0) or in WOMAC pain scores (0-20 scale) at short term (mean difference -0.1, 95% CI -1.2 to 1.0) or intermediate term (mean difference 0.4, 95% CI -0.8 to 1.6) (SOE low).
- Hip Osteoarthritis: Manual therapy was associated with slight improvements in short-term (mean difference 11.1, 95% CI 4.0 to 18.6, 0-100 scale Harris Hip Score) and intermediate-term (mean difference 9.7, 95% CI, 1.5 to 17.9) function, and in short-term pain (mean differences of -0.72, 95% CI -1.38 to -0.05 for pain at rest; and -1.21, 95% CI -2.29 to -0.25 for pain walking) versus exercise (SOE: low for both function and pain).

Key Question 4: Fibromyalgia

Exercise

- Exercise was associated with slightly greater effects on function compared with an attention control, no treatment, or usual care in the short term (7 trials, pooled mean difference -7.61 on a 0 to 100 scale, 95% CI, -12.78 to -2.43, I^2=59.9%) (SOE: low) and intermediate-term (8 trials, pooled mean difference, -6.04, 95% CI –9.05 to -3.03, I^2=0%) (SOE: moderate). There were no clear effects long term (3 trials, pooled mean difference -4.33, 95% CI -10.18 to 1.52, I^2=0%) (SOE: low).
- Exercise had a slightly greater effect on VAS pain (0-10 scale) compared with usual care, an attention control or no treatment short term (6 trials [excluding outlier trial] pooled mean difference -0.89, 95% CI -1.32 to -0.46, I^2=0%) but there were no clear effects at intermediate term (7 trials, pooled mean difference -0.41, 95% CI -0.87 to 0.05, I^2=9.5%) or long term (4 trials, pooled mean difference -0.18, 95% CI -0.77 to 0.42, I^2=0%) (SOE: moderate for all time frames).

Psychological Therapies

- Cognitive behavioral therapy (CBT) was associated with a slightly greater effect on the Fibromyalgia Impact Questionnaire (FIQ) Total Score than usual care or waitlist in the short-term (2 trials, pooled mean difference -10.67, 95% CI -17 to -4.30, I^2=0%, 0-100 scale). The pooled estimate at intermediate term was not statistically significant due to heterogeneity, however individual trials showed a greater effect than usual care and a third trial using the 0 to 10 FIQ Physical Impairment Scale showed a greater effect of CBT than an attention control (mean difference -1.8, 95% CI -2.9 to -0.70) (SOE: low for short term and intermediate term).
- CBT was associated with a slight improvement in pain (on a 0-10 scale) compared with usual care or waitlist in the short term (3 trials, pooled mean difference -0.78, 95% CI -1.30 to -0.17) but not in the intermediate term (2 trials, pooled mean difference -0.44, 95% CI -1.30 to 0.01) (SOE: low for short term and intermediate term).

Physical Modalities

- One parallel trial showed no differences between magnetic mattress pads compared with sham or usual care in intermediate-term function (difference on the 0-80 scale FIQ -5.0, 95% CI -14.1 to 4.1 vs. sham and -5.5, 95% CI -14.4 to 3.4 vs. usual care) or pain (difference -0.6, 95% CI -1.9 to 0.7 and -1.0, 95% CI -2.2 to 0.2, respectively on a 0-10 scale) (SOE: low).

Manual Therapies

- Myofascial release therapy was associated with a slightly greater effect on intermediate-term function as measured by the FIQ (mean 58.6 ± 16.3 vs. 64.1 ± 18.1 on a 100 point scale, P=0.048 for group by repeated measures [analysis of variance] ANOVA), but not long-term function (mean 62.8 ± 20.1 vs. 65.0 ± 19.8 on the FIQ, 0-100 scale, P=0.329), compared with sham in one trial (SOE: low).
- Myofascial release therapy was associated with slightly greater effects on long-term pain based on the sensory (mean 18.2 ± 8.3 vs. 21.2 ± 7.9 on a 0-33 scale, P=0.038 for group by repeated measures ANOVA) and evaluative (mean 23.2 ± 7.6 vs. 26.7 ± 6.9 on a 0-42 scale, P=0.036) domains of the McGill Pain Questionnaire (MPQ) in one trial; there were no differences for the affective domain of the MPQ or for VAS pain (SOE: low).

Mindfulness-Based Stress Reduction Therapy

- No clear short-term effects of MBSR were seen on function compared with waitlist or an attention control (mean difference 0 to 0.06 on a 0-10 scale) in two trials (SOE: moderate).
- No clear short-term effects of MBSR on pain (mean difference 0.1 on a 0-100 VAS pain scale in one trial; mean difference -1.38 to -1.59 on the affective and -0.28 to -0.71 on the sensory dimension [scales not reported] of the Pain Perception Scale in one trial) compared with waitlist or an attention control in two trials (SOE: moderate). Intermediate and long-term outcomes were not reported.

Mind-Body Practices

- Over the short term, two trials of mind-body practices reported a slight improvement in function for qigong compared with waitlist (mean difference -7.5, 95% CI -13.3 to -1.68) and a large improvement for tai chi compared with attention control (mean difference -23.5, 95% CI -30 to -17) based on 0-100 scale total FIQ score; heterogeneity may be explained by duration and intensity of intervention and control condition. Significantly more participants in the tai chi group also showed clinically meaningful improvement on total FIQ (RR 1.6, 95% CI 1.1 to 2.3) consistent with a slight effect (SOE: low).
- Qigong and tai chi were associated with moderately greater improvement in pain (0-10 scale) compared with waitlist and an attention control in the short term (2 trials, pooled mean difference -1.54, 95% CI -2.67, -0.41, I^2=75%). Significantly more participants in the tai chi group also showed clinically meaningful improvement on VAS pain (RR 2.0, 95% CI 1.1 to 3.8) consistent with a slight effect (SOE: low).

Acupuncture

- Acupuncture was associated with slightly greater effects on function based on 0-100 FIQ Total Score in patients with fibromyalgia than sham acupuncture in the short-term (2

trials, pooled difference -8.63, 95% CI =12.12 to -5.13, I^2=0%) and intermediate-term (2 trials, pooled mean difference -9.41, 95% CI -13.96 to -4.85, I^2=27.4%) (SOE: moderate).
- There was no clear effect of acupuncture on pain (0-10 scale) versus sham acupuncture in the short term (3 trials, pooled mean difference -0.13, 95% CI -1.06 to 0.79, I^2=72%) or intermediate term (3 trials, pooled mean difference – 0.53, 95% CI -1.15 to 0.09, I^2=45.5%) (SOE: low)

Multidisciplinary Rehabilitation

- Multidisciplinary treatment was associated with a slight improvement in function (based on a 0-100 FIQ total score) versus usual care or waitlist in the short term (3 trials, pooled mean difference -6.52, 95% CI -12.84 to -0.21, I^2=67.3%) and versus usual care at intermediate term (3 trials, pooled mean difference -7.84, 95% CI -11.43 to -4.25, I^2=18.2%) and long term (2 trials, pooled mean difference -8.42, 95% CI -13.76 to -3.08, I^2 =24.9%). More multidisciplinary treatment participants experienced a clinically meaningful improvement in FIQ total score compared with usual care at short (odds ratio [OR] 3.1, 95% CI 1.6 to 6.2), intermediate (OR 3.1, 95% CI 1.5 to 6.4) and long term (OR 8.8, 95% CI 2.5 to 30.9) in one trial (SOE: low for short, intermediate and long term).
- Multidisciplinary treatment was associated with a slight improvement in pain compared with usual care or waitlist at intermediate term (3 trials, pooled mean difference -0.68, 95% CI -1.07 to -0.30, I^2=0%); there were no clear differences compared with usual care or waitlist in the short term (2 trials [excluding an outlier trial], pooled mean difference on a 0-10 scale -0.24, 95% CI -0.63 to 0.15, I^2=0%) or with usual care in the long-term (2 trials, pooled mean difference -0.25, 95% CI -0.68 to 0.17, I^2=0%) (SOE: low for short, intermediate and long term).

Comparative Effectiveness of Interventions for Fibromyalgia

- CBT was associated with a slight benefit compared with pharmacological treatment (pregabalin; duloxetine) for function (mean difference -4.0 on the 0-100 FIQ, 95% CI -7.7 to -0.27), but not for pain (mean difference 0.2 on a 0-100 VAS, 95% CI -4.0 to 4.4) at intermediate term in one trial (SOE: low).
- There was no evidence of an effect for multidisciplinary treatment versus aerobic exercise at long term for function (mean difference -1.10, 95% CI -8.40 to 6.20, 0-100 FIQ total score) or pain (mean difference 0.10, 95% CI -0.67 to 0.87, 0-10 FIQ pain scale) in one trial (SOE: low).

Key Question 5: Chronic Tension Headache

Manual Therapies

- Spinal manipulation therapy was associated with slight to moderate improvements, respectively, compared with usual care in function (difference -5.0, 95% CI -9.02 to -1.16 on the Headache Impact Test, scale 36-78 and difference -10.1, 95% CI -19.5 to -0.64 on the Headache Disability Inventory, scale 0-100) and pain intensity (difference -1.4 on a 0-10 Numerical Rating Scale scale, 95% CI -2.69 to -0.16) over the short term in one trial (SOE: low). Approximately a quarter of the patients had comorbid migraine.

Acupuncture

- Laser acupuncture was associated with slight improvement in pain intensity (median difference -2, IQR 6.3, on a 0-10 VAS scale) and in the number of headache days per month (median difference -8, IQR 21.5) over the short term versus sham in one trial (SOE: low).

Comparative Effectiveness of Interventions for Chronic Tension Headache

- No studies compared the interventions of interest to biofeedback and evidence from comparisons with pharmacological interventions was insufficient.

Key Question 6: Differential Efficacy

Evidence was insufficient to determine whether factors such as age, sex or comorbidities modify the effects of treatment.

Harms

Although data on harms were limited, no evidence suggested serious harms for the interventions included in the review. Many trials did not report harms, withdrawals due to adverse events, or differences between compared interventions in risk of harms or withdrawals. Trials that did report such data found infrequent or rare occurrences of nonserious treatment-related adverse events (e.g., discomfort, soreness, bruising, increased pain, worsening of symptoms), few withdrawals from nonpharmacological treatments due to adverse events, and no differences between comparison groups in frequency of intervention-related adverse events or withdrawals.

Discussion

Key Findings and Strength of Evidence

The key findings of this review, including SOE ratings, are summarized for each chronic pain condition in the Results and evidence summary Tables A–M. Interventions and comparators with insufficient evidence or no evidence (no RCTs meeting inclusion criteria) for either function or pain outcomes are not shown. Domains used to determine the overall SOE are shown in Appendix G of the full report. All outcomes were considered direct.

The strength of evidence was low (limited confidence in the estimates) or insufficient (no confidence in the estimated effects) for many interventions and was limited by small numbers of trials for specific comparisons at our specified time frames, particularly for long-term followup. We focused on evaluating the persistence of effects for therapies at least 1 month beyond the course of treatment, using the following definitions for post-intervention followup: short term (1 to <6 months), intermediate term (≥6 to <12 months) and long term (≥12 months). Evidence was particularly limited on long-term outcomes.

The majority of trials compared interventions with usual care, and very few trials employed pharmacological treatments or exercise as comparators. In general, effect sizes for most interventions were small, based on mean differences. There tended to be more evidence for the effects of interventions on pain than for function and effects on function were generally smaller or not clearly present.

No trials directly compared interventions with opioids and few trials reported effects of interventions on opioid use. Our previous reviews found opioids associated with small to moderate effects on pain during treatment (effects would not be expected to persist) with evidence almost exclusively from short-term (≤3 month) trials.[10,11,15]

Harms were poorly reported across interventions. No serious intervention-related adverse events requiring medical attention were identified; reported adverse events were generally minor (e.g., muscle soreness or increased pain with exercise, bruising with acupuncture) and time-limited (e.g., temporary worsening of pain).

Table A. Chronic low back pain: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Exercise	slight +	none +	none +	slight ++	moderate +	moderate +
Psychological Therapies: CBT primarily	slight ++	slight ++	slight ++	slight ++	slight ++	slight ++
Physical Modalities: Ultrasound	insufficient evidence	no evidence	no evidence	none +	no evidence	no evidence
Physical Modalities: Low-Level Laser Therapy	slight +	none +	no evidence	moderate +	none +	no evidence
Manual Therapies: Spinal Manipulation	slight +	slight +	no evidence	none +	slight ++	no evidence
Manual Therapies: Massage	slight ++	none +	no evidence	slight ++	none +	no evidence
Manual Therapies: Traction	none +	no evidence	no evidence	none +	no evidence	no evidence
Mindfulness Practices: MBSR	none +	none +	none +	slight ++	slight +	none +
Mind-Body Practices: Yoga	slight ++	slight +	no evidence	moderate +	moderate ++	no evidence
Acupuncture	slight +	none +	none +	slight ++	none +	slight +
Multidisciplinary Rehabilitation	slight +	slight +	none +	slight ++	slight ++	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive behavioral therapy; MBSR = mindfulness-based stress reduction; none = no effect/no statistically significant effect; SOE = strength of evidence.

Table B. Chronic low back pain: effects of nonpharmacological interventions compared with exercise

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Physical Modalities: Low-Level Laser Therapy	no evidence	none +	no evidence	no evidence	slight +	no evidence
Manual Therapies: Spinal Manipulation	none +	none +	no evidence	none +	slight +	no evidence
Manual Therapies: Massage	no evidence	none +	no evidence	no evidence	none +	no evidence
Mind-Body Practices: Yoga	none +	none +	no evidence	slight +	none +	no evidence
Mind-Body Practices: Qigong	none +	slight favoring exercise +	no evidence	slight favoring exercise +	none +	no evidence
Multidisciplinary Rehabilitation	slight ++	slight ++	none +	slight ++	slight ++	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; SOE = strength of evidence.

Table C. Chronic neck pain: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Exercise	none +	no evidence	no evidence	none +	no evidence	no evidence
Psychological Therapies: PT-lead relaxation training	none +	none +	no evidence	none +	none +	no evidence
Physical Modalities: Low-Level Laser Therapy	moderate ++	no evidence	no evidence	moderate ++	no evidence	no evidence
Manual Therapies: Massage	none +	none +	no evidence	no evidence	no evidence	no evidence
Mind-Body Practices: Alexander Technique	slight +	slight +	no evidence	no evidence	no evidence	no evidence
Acupuncture	slight +	slight +	none +	none +	none +	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement

Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; PT = physical therapist; SOE = strength of evidence.

Table D. Chronic neck pain: effects of nonpharmacological interventions compared with exercise

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Psychological Therapies: PT-lead relaxation training	none +	none +	no evidence	none +	none +	no evidence
Manual Therapies: Massage	no evidence	no evidence	no evidence	no evidence	none +	no evidence
Mind-Body Practices: Body Awareness Therapy	none +	no evidence	no evidence	no evidence	no evidence	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; PT = physical therapist; SOE = strength of evidence.

Table E. Osteoarthritis of the knee: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Exercise	slight ++	slight +	slight +	slight ++	moderate +	none +
Psychological Therapies: Pain coping, CBT	none +	none +	none +	none +	none +	none +
Physical Modalities: Ultrasound	slight +	none +	no evidence	slight +	none +	no evidence
Physical Modalities: TENS	no evidence	none +	no evidence	no evidence	none +	no evidence
Physical Modalities: Electromagnetic Field	none +	no evidence	no evidence	none +	no evidence	no evidence
Acupuncture	none +	none ++	no evidence	none +	none ++	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; none = no effect/no statistically significant effect; TENS = transcutaneous electrical nerve stimulation; SOE = strength of evidence

Table F. Osteoarthritis of the knee: effects of nonpharmacological interventions compared with exercise

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Psychological Therapies: Pain coping	none +	none +	no evidence	none +	none +	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; SOE = strength of evidence

Table G. Osteoarthritis of the hip: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Exercise	slight +	slight +	insufficient evidence	slight +	none +	insufficient evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; SOE = strength of evidence

Table H. Osteoarthritis of the hip: effects of nonpharmacological interventions compared with exercise

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Manual Therapies	slight +	slight +	no evidence	slight +	insufficient evidence	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
SOE = strength of evidence

Table I. Osteoarthritis of the hand: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Physical Modalities: Low-Level Laser Therapy	none +	no evidence	no evidence	none +	no evidence	no evidence
Multidisciplinary Rehabilitation	none +	no evidence	no evidence	none +	no evidence	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; SOE = strength of evidence

Table J. Fibromyalgia: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Exercise	slight +	slight ++	none +	slight ++	none ++	none ++
Psychological Therapies: CBT	slight +	slight +	insufficient evidence	slight +	none +	insufficient evidence
Physical Modalities: Magnetic Pads	insufficient evidence	none +	no evidence	insufficient evidence	none +	no evidence
Manual Therapies: Massage (Myofascial Release)	no evidence	slight +	none +	insufficient evidence	insufficient evidence	slight +
Mindfulness Practices: MBSR	none ++	no evidence	no evidence	none ++	no evidence	no evidence
Mind-Body Practices: Qigong, Tai Chi	slight +	no evidence	no evidence	moderate +	no evidence	no evidence
Acupuncture	slight ++	slight ++	no evidence	none +	none +	no evidence
Multidisciplinary Rehabilitation	slight +	slight +	slight +	none +	slight +	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; MBSR = mindfulness-based stress reduction; none = no effect/no statistically significant effect; SOE = strength of evidence

Table K. Fibromyalgia: effects of nonpharmacological interventions compared with pharmacological treatments

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
CBT vs. pregabalin; duloxetine	no evidence	slight +	no evidence	no evidence	none +	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; none = no effect/no statistically significant effect; SOE = strength of evidence

Table L. Fibromyalgia: effects of nonpharmacological interventions compared with exercise

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Multidisciplinary Rehabilitation	no evidence	no evidence	none +	no evidence	no evidence	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; SOE = strength of evidence

Table M. Chronic tension headache: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Manual Therapies: Spinal manipulation	slight +	no evidence	no evidence	moderate +	no evidence	no evidence
Acupuncture	no evidence	no evidence	no evidence	slight + (laser) insufficient evidence (needle)	insufficient evidence (needle)	insufficient evidence (needle)

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
SOE = strength of evidence

Findings in Relationship to What Is Already Known

Many reviews have addressed the effects of interventions for chronic pain management during or immediately following treatments. We focused on evaluating the sustainability of effects for at least 1 month post-intervention.

This review updates our previous review on low back pain[10] by incorporating new evidence on nonpharmacological treatments for chronic low back pain. Consistent with the prior review, we found exercise, yoga, various psychological therapies, acupuncture, spinal manipulation and low-level laser therapy associated with small to moderate effects on function and/or pain. This report differs from the prior review in and focusing on durability of treatment effects 1 month or longer after completion of a course of treatment, basing estimates on meta-analyses when poolable data were available, and conducting stratified and sensitivity analyses to evaluate sources of heterogeneity and robustness of findings. For example, subanalyses of specific interventions within a given category of intervention (e.g., aerobic exercise within the general category of exercise suggested that despite the inherent heterogeneity within some of the categories, effect estimates for specific interventions may be similar). Although we found some evidence that beneficial effects of some nonpharmacological therapies persist for up to 12 months following the end of a course of a treatment, data on longer-term (>12 months) outcomes were very sparse.

Our findings indicate that a number of nonpharmacological treatments improve pain and/or function for specific chronic pain conditions included in this review. This is consistent with other reviews including a recent Institute for Clinical and Economic Review (ICER) review on chronic low back pain and neck pain,[16] an AHRQ report on knee osteoarthritis treatment[17] and with recent reviews that included a variety of chronic pain conditions which examined exercise,[18] acupuncture,[19] and complementary health approaches[20] for chronic pain management, as well as a review of chronic pain treatment guidelines on the use of manual and physical therapies.[21]

Applicability

The applicability of our findings may be impacted by a number of factors. Included trials provided limited information on, symptom duration, clinical characteristics, comorbid conditions and concomitant treatments, thus it is not clear to what extent this reflects the populations seen in clinical practice or may how these factors impact our results. In addition, with the exception of fibromyalgia, information regarding diagnostic criteria for the pain condition of interest was limited. Information on presence of overlapping chronic pain conditions or psychosocial factors was generally not provided in included trials. The extent to which these characteristics were present in trial populations and their impact on our results is not clear. Across conditions, a majority of trial participants were female. The age of included populations generally reflected the ages impacted by the conditions. Evidence to evaluate how effectiveness varies by ages was limited. There was also heterogeneity in populations enrolled in the trials with regard to duration of chronic pain, severity of pain (most trials enrolled patients with at least moderate pain at baseline), as well as other factors (e.g., use of medications, medical and psychological comorbidities). Our findings are generally most applicable to persons without such comorbidities who have moderate or severe intensity pain that has persisted for >1 year. The heterogeneity in populations across included trials likely is consistent with the heterogeneity seen in clinical practice, so our findings may be applicable to most primary care clinical settings.

Variability in interventions, comparators and co-interventions may impact applicability. For interventions, there was variability in the numbers of sessions, length of sessions, duration of treatment, methods of delivering the intervention and the experience and training of those providing the intervention. To address heterogeneity within intervention categories we abstracted details of techniques or methods used (e.g., specific type of psychological intervention or yoga) and attempted to stratify by them, however in most cases, data were insufficient to do so. We stratified by comparator where possible. In general, there were no clear differences in effects based on intervention factors or comparators; however analyses were limited by small numbers of trials. In clinical practice, most chronic pain patients likely use a combination of therapies and patients may continue to receive therapies if benefit is perceived It is unclear to what extent our findings represents conditions under which the various interventions are currently delivered. Evidence to identify optimal techniques and delivery of interventions is needed.

Implications for Clinical and Policy Decisionmaking

Our review provides some evidence that an array of nonpharmacological treatments provide small to moderate benefits in function and pain that are durable for more than 1 month for five chronic pain conditions addressed in this review. Musculoskeletal pain, particularly of back and joint pain, is the most common single type of chronic pain. Age-adjusted rates of adults reporting pain in the last three months were highest for low back pain (28%), neck pain (15%), knee pain (19.5%), and severe headache or migraine (16%).[1,5] The evidence synthesized in this review may help inform guidelines and health care policy (including reimbursement policy) related to use of noninvasive nonpharmacological treatments, and inform policy decisions regarding funding priorities for future research.

Recent guidelines from the CDC[4] in the United States and the Canadian Guidelines for Opioid Use in Chronic Non-Cancer Pain[21] recommend nonopioid treatment as preferred treatment for chronic pain. Further, American College of Physicians guidelines recommend nonpharmacological therapies over medications for chronic back pain.[12] Our findings support the feasibility of these guidelines by showing that there are nonpharmacological treatments for chronic pain that have evidence of sustained effectiveness after the completion of therapy. Importantly, some interventions, such as exercise, multidisciplinary rehabilitation, mind-body interventions, cognitive behavioral therapy and some complementary and integrative medicine therapies such as acupuncture and spinal manipulation also were associated with some sustained effects on function, although evidence beyond 12 months is sparse. At the same time, there was no evidence suggesting serious harms, although data on harms were limited.

Evidence reviewed in our report may also help inform decisions regarding prioritization of nonpharmacological therapies by clinicians selecting therapy. Consistent with a biopsychosocial understanding of chronic pain,[1,2] evidence was somewhat more robust for “active” interventions that engage patients in movement and address psychological contributors to pain, particularly at longer-term followup, versus more “passive” treatments focused on symptom relief such as massage. Active interventions include exercise, multidisciplinary rehabilitation, psychological therapies (particularly cognitive-behavioral therapy), and mind-body interventions. This provides some support for clinical strategies that focus on “active” interventions as primary therapies, with “passive” interventions used in a more adjunctive or supplementary role. Research is needed to compare “active” versus “passive” strategies.

Our review also has policy implications related to treatment access and reimbursement. Given heterogeneity in chronic pain, variability in patient preferences for treatments, and

differential responses to specific therapies in patients with a given chronic pain condition, policies that broaden access to a broader array of effective nonpharmacological treatments may have greater impact than those that focus on one or a few therapies. Several considerations could inform policy decisions regarding access to and coverage of nonpharmacological therapies. Efforts could prioritize access to interventions with evidence of persistent effectiveness across different pain conditions, such as exercise, multidisciplinary rehabilitation, psychological interventions, mind-body interventions, and acupuncture. Because the level of supporting evidence varies from condition to condition, policymakers may need to consider the degree to which evidence may be reasonably extrapolated across conditions (e.g., effectiveness of psychological therapies for chronic back pain may not necessarily be extrapolated to osteoarthritis). Although the Affordable Care Act has improved access to complementary and integrative medicine therapies, variability in reimbursement and authorization procedures remain a potential barrier. Although evidence supports the use of multidisciplinary rehabilitation over exercise therapy or usual care, primarily for low back pain, cost and availability remain important barriers, particularly in rural areas. Our report suggests that less-intensive multidisciplinary rehabilitation may be similarly effective to high-intensity multidisciplinary rehabilitation, which could inform decisions about more efficient methods for delivering this intervention. Not all patients may require multidisciplinary rehabilitation.[22] Policy efforts that focus on use of multidisciplinary rehabilitation in persons more likely to benefit (e.g., severe functional deficits, failure to improve on standard nonmultidisciplinary therapies, significant psychosocial contributors to pain) could also inform efforts to deliver this modality efficiently.

Limitations of the Evidence Base and the Systematic Review Process

Evidence was sparse for most interventions. Data on long-term outcomes was particularly limited. There were also limited data on outcomes other than pain and function and on harms. Few trials directly compared an included intervention versus pharmacological therapy or the specified active comparator (exercise or biofeedback). Only 5 percent of included trials across conditions were considered to be of good quality; the majority were considered fair (59%).

There were limitations in the systematic review process. We did not include trials of patients with chronic pain conditions other than those specified in the methods and excluded trials of patients with diffuse or mixed pain conditions. Some noninvasive nonpharmacological interventions (e.g., self-management education) were excluded, and we did not address invasive therapies. Trials that evaluated active comparators other than biofeedback (for headache) or exercise (all other conditions) or interventions as adjunctive treatment were excluded. Some meta-analyses were based on two or three trials; findings based on such meta-analyses must be interpreted with caution.

Research Recommendations

The gaps in the available evidence are many across the common conditions we included (Table N). Four primary issues relate to the need (1) to understand the longer-term sustainability of intervention effects; (2) for standardization of interventions for future trials; (3) for standardization of research protocols for collection and reporting of outcomes including harms; and (4) for comparisons of interventions with pharmacological interventions. For many of these areas, future research would benefit from considering recommendations from organizations such as the Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials (IMMPACT)[23] and the Analgesic, Anesthetic, and Addiction Clinical Trials Translations,

Innovations, Opportunities, and Networks (ACTTION)[24] and the research priorities outlined in the recent Federal Pain Research Strategy.[25]

Table N. Summary of evidence gaps and research recommendations

Research Component	Evidence Gap	Future Research Recommendation
Study Design Methods and Reporting	Sparse evidence on the sustainability of effects; Limited information on adherence and need to maximize retention.	Traditional (explanatory) and pragmatic trials with long-term followup and use of methods to enhance recruitment, retention and adherence. Documentation of adherence. Consider recommendations from IMMPACT, ACTTION and Federal Pain Research Strategy
Patient populations	Information on overlapping chronic pain conditions or psychosocial factors was generally not provided in included trials	Documentation of coexisting conditions and factors in trials with sufficient sample-size to evaluate the differential impact of conditions and factors.
Interventions and comparators	Lack of information on optimal techniques, duration and frequency of treatment; Lack of evidence comparing interventions to pharmacological agents	Research leading to standardization of techniques and their delivery to be used in future trials and understanding best combinations of interventions. Pragmatic trials may provide valuable information. Trails comparing interventions with pharmacological treatments.
Outcomes measures	Lack of consistency in types outcomes measures used for function and pain across trials makes it challenging to compare results across trials. Commonly used VAS or NRS for pain do not capture the impact of pain or allow for accurate classification or evaluation of changes in chronic pain. Common or know harms are not routinely collected	Standardized protocols for types of outcomes to be assessed (including harms). Use measures that incorporate understanding of pathophysiological mechanisms and address multiple domains of pain. Report the proportions of patients achieving a clinically meaningful improvement for measures of pain and function as well as outcomes related to change in use of opioids, health care utilization and quality of life. Consider recommendations from IMMPACT, ACTTION and Federal Pain Research Strategy

ACTTION = Analgesic, Anesthetic, and Addiction Clinical Trials Translations, Innovations, Opportunities, and Networks; IMMPACT = Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials; NRS = Numerical Rating Scale; VAS = Visual Analog Scale

Conclusions

Exercise, multidisciplinary rehabilitation, acupuncture, cognitive behavioral therapy, and mind-body practices were most consistently associated with durable slight to moderate improvements in function and pain for specific chronic pain conditions. Our findings provide some support for clinical strategies that focus on use of nonpharmacological therapies for specific chronic pain conditions. Additional comparative research on sustainability of effects beyond the immediate post-treatment period is needed, particularly for conditions other than low back pain.

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Introduction

Background

Nature and Burden of Chronic Pain

Chronic pain substantially impacts physical and mental functioning, productivity, quality of life, and family relationships; it is the leading cause of disability; and is often refractory to treatment.[1,2] A monumental public health challenge, chronic pain affects millions of adults in the United States, with a conservative annual cost in personal and health system expenditures estimated at $560 billion to $635 billion.[3]

Pain is usually regarded as chronic when it lasts or recurs for more than 3 to 6 months, however definitions vary.[4,5] For purposes of this report, chronic pain is defined as pain lasting 3 months or longer, or persisting past the normal time for tissue healing.[3,6] Nervous system changes that occur with chronic pain, combined with its psychological and cognitive impacts, have led to conceptualization of some types of chronic pain as a distinct disease entity.[3] Chronic pain is multifaceted and influenced by multiple factors (e.g., genetic, central nervous system, psychological, and environmental factors) and complex interactions of factors, making pain assessment and management a challenge. A number of characteristics influence the development of and response to chronic pain, including sex, age, presence of comorbidities, and psychosocial factors. For example, women report chronic pain more frequently than do men, are at higher risk for some conditions such as fibromyalgia,[3] and may respond to treatment differently than men. Older adults are more likely to have comorbidities and are more susceptible to polypharmacy, impacting choices and consequences of therapies. Pain is greatly influenced by psychosocial factors, which may predict who will develop chronic disabling pain, as well as who will respond to various treatments.

Management of Chronic Pain

Many pharmacological and nonpharmacological treatments are available for management of chronic pain and include a variety of noninvasive as well as surgical and interventional procedures. The National Pain Strategy Task Force report recommends that pain management be integrated, multimodal, interdisciplinary, evidence-based, and tailored to individual patient needs.[7] In addition to addressing biological factors when known, optimal management of chronic pain must also address psychosocial contributors to pain, while taking into account individual susceptibility and treatment responses. Self-care is also an important part of chronic pain management.

Opioids have been used in the treatment of chronic pain. In the past 20 years, evidence shows only modest short-term benefits of these drugs.[8-10] Lack of evidence on long-term effectiveness[11] and safety concerns[12] have been noted in the literature. The recent evidence-based Centers for Disease Control guidelines on opioid use for chronic pain,[13] which include a recommendation on the preferred use of nonopioid treatment over opioid therapy, has prompted additional primary research on alternative methods of managing chronic pain.

Other pharmacological treatments for chronic pain include nonsteroidal anti-inflammatory drugs, acetaminophen, muscle relaxants, antiseizure medications, antidepressants, and corticosteroids, used alone or in combination with each other or with opioids. Each has potential side effects and contraindications.

Nonpharmacological treatments for chronic pain examined in this review include exercise, mind-body practices, psychological therapies, multidisciplinary rehabilitation, mindfulness practices, manual therapies, physical modalities, and acupuncture.

Rationale for This Review

The review is intended to address some of the needs described in the National Pain Strategy Task Force[7] and Institute of Medicine[3] reports and others for evidence to inform guidelines and health care policy (including reimbursement policy) related to use of noninvasive nonpharmacological treatments. Both the Institute of Medicine report and the National Pain Strategy Task Force report describe the need for evidence-based strategies for the treatment of chronic pain that address the biopsychosocial nature of this disease, including nonpharmacological treatment. These initiatives, and others, speak to the importance of understanding current evidence on noninvasive nonpharmacological treatment of chronic pain.

Many trials have examined the impact of interventions on outcomes during or immediately after the course of treatment. A number of them are associated with improved function and reduced pain. However, given the persistence of chronic pain, understanding whether the benefits are durable would be very helpful for informing selection of therapies. This review also aims to provide additional insights into research gaps related to use of noninvasive nonpharmacological alternatives for treating chronic pain. Musculoskeletal pain, particularly related to joints and the back, is the most common single type of chronic pain.[3,14] This systematic review thus focuses on five of the most common causes of musculoskeletal pain: chronic low back pain, chronic neck pain, osteoarthritis (OA), fibromyalgia, and chronic tension headache.

Scope and Key Questions

This Comparative Effectiveness Review focused on noninvasive nonpharmacological therapy for five common chronic pain conditions: low back pain, neck pain, OA, fibromyalgia, and headache. Individual pain management strategies considered in the review include exercise (including aspects of physical therapy), mind-body practices (yoga, tai chi, qigong), psychological therapies (cognitive-behavioral therapy, biofeedback, relaxation techniques, acceptance, and commitment therapy), multidisciplinary rehabilitation (including functional restoration training), mindfulness practices (meditation, mindfulness-based stress reduction practices), manual therapies (e.g., musculoskeletal manipulation), physical modalities (traction, ultrasound, transcutaneous electrical nerve stimulation, low-level laser therapy, interferential therapy, superficial heat or cold, bracing for knee, back or neck, electro-muscular stimulation, and magnets), and acupuncture.

We focused on single active interventions and comparators over the long term. The Key Questions, PICOTS (populations, interventions, comparators, outcomes, timing, settings, and study designs), and analytic framework that guided this review are provided below.

Key Questions

Key Question 1: Adults with chronic low back pain

Key Question 2: Adults with chronic neck pain

Key Question 3: Adults with osteoarthritis-related pain

Key Question 4: Adults with fibromyalgia

Key Question 5: Adults with chronic tension headache

Key Questions 1–5 incorporate the following subquestions:

a. What are the benefits and harms of noninvasive nonpharmacological therapies compared with sham treatment, no treatment, waitlist, attention control, or usual care?
b. What are the benefits and harms of noninvasive nonpharmacological therapies compared with pharmacological therapy (e.g., opioids, nonsteroidal anti-inflammatory drugs, acetaminophen, antiseizure medications, antidepressants)?
c. What are the benefits and harms of noninvasive nonpharmacological therapies compared with exercise or, for headache, biofeedback?

The three-part format for Key Questions 1–5 reflects the following research concepts:

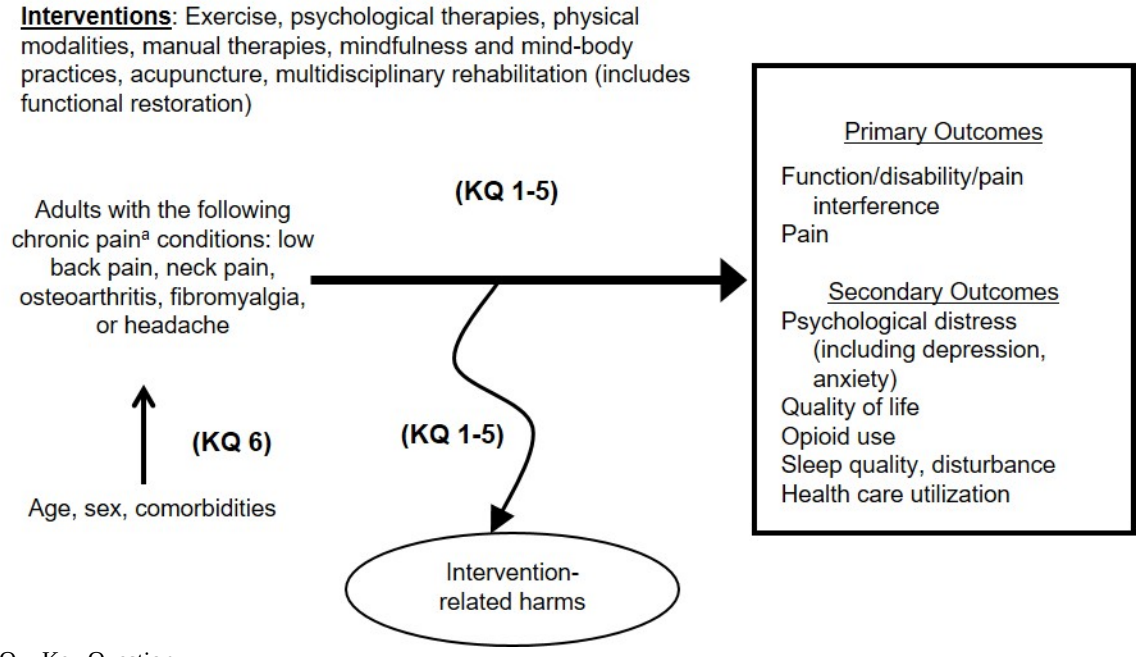
- Part "a" answers the question of whether the various interventions work overall compared with sham, waitlist control, attention control, no treatment, or usual care. For this review, usual care was defined as care that might be provided or recommended by a primary care provider.
- Part "b" answers the question of whether the various interventions work compared with pharmacological alternatives.
- Part "c" answers the question of how outcomes for individual interventions (e.g., acupuncture) compare with a common comparator. Exercise is the most frequent comparison in the literature for many chronic pain conditions, so it provides a common comparator for analysis. It is also recommended in most guidelines for conditions including low back pain, neck pain, fibromyalgia, and osteoarthritis and is widely available. Exercise served as common comparator for these conditions. For chronic headache, biofeedback provided a common comparator for analysis.

Key Question 6: Do estimates of benefits and harms differ by age, sex, or presence of comorbidities (e.g., emotional or mood disorders)?

Analytic Framework

The analytic framework (Figure 1) illustrates the population, interventions, outcomes, and adverse effects that guided the literature search and synthesis.

Figure 1. Analytic framework



KQ = Key Question

[a] Chronic pain is defined as pain lasting ≥12 weeks or pain persisting past the normal time for tissue healing

Methods

The methods for this systematic review follow the Agency for Healthcare Research and Quality (AHRQ) *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*[15] and the Preferred Reporting Items for Systamtic Reviews and Meta-Analyses (PRISMA) checklist. See the review protocol (http://effectivehealthcare.ahrq.gov/index.cfm) for details.

Topic Refinement and Review Protocol

The Evidence-based Practice Center (EPC) review team developed initial Key Questions and PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, Studies, Settings) with input from the AHRQ Task Order Officer (TOO), representatives from the Centers for Disease Control and Prevention (CDC) and the Office of the Assistant Secretary for Planning and Evaluation (ASPE), and a group of Key Informants. The provisional Key Questions, PICOTS, and analytic framework were posted on the AHRQ Web site for public comment from December 27, 2016 to January 23, 2017.

After reviewing public comments, the EPC research team developed the final protocol with input from the AHRQ TOO, CDC and ASPE representatives, and a Technical Expert Panel (TEP) convened for this report. The TEP consisted of nine members with expertise in primary care, rheumatology, pain medicine, behavioral sciences, physical medicine and rehabilitation, and physical therapy. TEP members had expertise in treating patients with one or more of the five conditions included in this report. Suggestions for including additional chronic pain conditions and additional interventions were made; however, all were considered beyond the scope and resources for this review.

The final version of the protocol for this review was posted on the AHRQ Effective Health Care Program Web site (www.effectivehealthcare.ahrq.gov) on April 27, 2017. The protocol was also registered in the PROSPERO database of prospectively registered systematic reviews (CRD42017067729).

Literature Search Strategy

A research librarian conducted searches in Ovid® MEDLINE®, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews through November 1, 2017. Searches were conducted without publication date restrictions with the exception of studies of chronic low back pain, as we relied on a recent AHRQ review[16] to identify primary studies for inclusion through 2016 (see Appendix A for full search strategies). As there are multiple manufacturers/sources for many of the devices examined in this review, a Federal Register notice was posted in an effort to identify unpublished data. We also searched for unpublished studies in ClinicalTrials.gov. Reference lists of included articles and the bibliographies of systematic reviews published since 2010 were reviewed for includable literature. Literature searches were updated during the public comment and peer review period to capture any new publications. Resulting citations and any suggested during peer review and public comment were evaluated against the inclusion/exclusion criteria following the same process of dual review as all other studies considered for inclusion in the report. Pertinent new literature was incorporated in the final report.

Inclusion and Exclusion Criteria and Study Selection

Inclusion and exclusion criteria were developed *a priori* based on the Key Questions and PICOTS, in accordance with the AHRQ *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[15] Criteria are detailed below in Table 1. Abstracts were reviewed by at least two investigators, and full-text articles were retrieved for all citations deemed potentially appropriate for inclusion by at least one of the reviewers. Two investigators then independently reviewed all full-text articles for final inclusion. Discrepancies were resolved by discussion and consensus. A list of the included studies appears in Appendix B; excluded studies and primary reason for exclusion are listed in Appendix C.

The focus of this review is on randomized controlled trials (RCTs) reporting on longer-term outcomes (at least 1 month post intervention) that otherwise meet our PICOTS criteria.

Table 1. Inclusion and exclusion criteria

PICOTS	Inclusion	Exclusion
Population	**General Inclusion Criteria** • Adults with the following chronic pain (defined as pain lasting 12 weeks or longer or pain persisting past the time for normal tissue healing) conditions: low back pain, neck pain, osteoarthritis pain, fibromyalgia, or tension headache. **KQ1: Low back pain** • Adults with chronic, nonradicular low back pain **KQ2: Neck pain** • Adults with chronic neck pain **KQ3: Osteoarthritis** • Adults with osteoarthritis-related pain (primary or secondary osteoarthritis) of the hip, knee or hand **KQ4: Fibromyalgia** • Adults with fibromyalgia **KQ5: Headache** • Adults with primary chronic tension headache (International Classification of Headache Disorders, 3rd edition definition). o Primary headaches are attributed to the headache condition itself, not headache caused by another disease or medical condition. Tension headaches are the most common. o Chronic headache is defined as 15 or more days each month for at least 12 weeks or history of headache more than 180 days a year.	**General Exclusion Criteria** • Acute pain • Children (<18 years), pregnant or breastfeeding women • Patients with chronic pain related to "active" cancer, infection, inflammatory arthropathy, • <90% of study sample has the defined condition of interest or <90% received the treatment(s) of interest • Treatment for addiction • Pain at the end of life • Neuropathic pain **KQ1: Low back pain** • Patients with radiculopathy • Low back pain associated with severe or progressive neurological deficits • Failed back surgery syndrome **KQ2: Neck pain** • Patients with radiculopathy or myelopathy • Traumatic spinal cord injury • Neck pain associated with progressive neurological deficit, loss of strength **KQ3: Osteoarthritis** • Other types of arthritis (e.g., rheumatoid) • Patients with joint replacement **KQ4: Fibromyalgia** • Conditions with generalized pain not consistent with fibromyalgia • Systemic exertion intolerance disease, (myalgic encephalomyelitis/chronic fatigue syndrome) • Somatization disorder (Briquet's syndrome) **KQ5: Headache** • Migraine headache • Mixed headache (also known as coexistent tension and migraine headache, chronic daily headache, transformed migraine) • Trigeminal neuralgia • Cluster headache • Secondary headache types as defined in *The International Classification of Headache Disorders*, 3rd edition[17] (i.e., headaches due to an underlying pathology such as cancer, prior medical procedures, temporomandibular joint disorders, neck pathology, cervicogenic headache, and medication over-use headache) • Traumatic brain injury

PICOTS	Inclusion	Exclusion
Interventions	**All KQs:** • Exercise (exercise as part of physical therapy, supervised exercise, home exercise, group exercise, formal exercise program) • Psychological therapies (cognitive and/or behavioral therapy, biofeedback, relaxation training) • Physical modalities (traction, ultrasound, transcutaneous electrical nerve stimulation, low-level laser therapy, interferential therapy, electro-muscular stimulation diathermy, superficial heat or cold, bracing for knee, back, neck, hand and magnets) • Manual therapies (musculoskeletal manipulation, massage) • Mindfulness practices (meditation, mindfulness-based stress reduction practices) • Mind-body practices (yoga, tai chi, qigong) • Acupuncture • Multidisciplinary/interdisciplinary rehabilitation[a]	**All KQs:** • Invasive nonsurgical treatments (e.g., injections, nerve block, spinal cord stimulators, parenterally-administered medications) • Surgical interventions (including minimally invasive surgical interventions) • Diet interventions or dietary supplementation • Studies evaluating incremental value of adding a noninvasive nonpharmacological intervention to another noninvasive nonpharmacological intervention • Self-management interventions or programs, self-management education programs • Others not listed for inclusion
Comparators	**All KQs, subquestion a** • Sham treatment • Waitlist • Usual care • No treatment • Attention control intended to control for nonspecific effects (e.g., time, attention, expectations); **All KQs subquestion b** • Nonopioid pharmacological therapy (NSAIDS, acetaminophen, anti-seizure medications, antidepressants) • Opioid analgesics **KQs 1-4, 6 subquestion c** • Exercise[b] **KQ 5, 6 subquestion c** • Biofeedback[c]	**All KQs:** • Supplements (e.g., glucosamine, chondroitin, d-ribose, herbal or homeopathic treatments) • Over-the-counter topical agents (e.g., aloe, capsaicin) • Invasive nonsurgical treatments (e.g., injections, nerve block, spinal cord stimulators, parenterally-administered medications) • Surgical interventions (including minimally invasive surgical interventions) • Studies evaluating incremental value of adding a noninvasive nonpharmacological intervention to another noninvasive nonpharmacological intervention • Comparisons within nonpharmacological intervention types (e.g., comparisons of different types of exercise with each other, different types of massage with each other) • Others not listed for inclusion

PICOTS	Inclusion	Exclusion
Outcomes	**All KQs:** Primary efficacy outcomes; we will focus on outcomes from validated measures for • Function/disability/pain interference[d] • Pain[d] Harms and Adverse effects Secondary outcomes • Psychological distress (including measures of depression and anxiety) • Quality of life • Opioid use • Sleep quality, sleep disturbance • Health care utilization	**All KQs:** • Intermediate outcomes (e.g., biomarkers for inflammation) • Other nonclinical outcomes
Timing	Duration of followup: short term (1 to <6 months), intermediate term (≥6 to <12 months) and long term (≥12 months); focus on longer term (>12 month) effects. Trials lasting ≥6 months that include a supervised intervention followed by continued home treatment as part of the intervention will be included even though the only followup occurs directly after the intervention.	• Studies with <1 month followup after treatment
Studies	Randomized controlled trials or high quality systematic reviews of randomized controlled trials published in English; cross-over trials with random assignment of initial treatment will be considered.	**All KQs:** • Studies reporting on intermediate outcomes only • Nonrandomized studies • Abstracts, editorials, letters, conference proceedings • Duplicate publications of the same study that do not report on different outcomes • Single site reports from multicenter trials • White papers • Narrative reviews • Articles identified as preliminary reports when results are published in later versions • Indirect comparisons • Studies with fewer than 15 patients per treatment arm • Systematic reviews on treatment of chronic neck pain, fibromyalgia, chronic headache, or osteoarthritis that are of low methodological quality. Those that do not report outcomes or time frames of interest may be excluded. Systematic reviews may be excluded based on currency or relevance (e.g., if there is a substantial new body of evidence reflected in a later review).
Settings	Any nonhospital setting or in self-directed care	• Hospital care, hospice care, emergency department care

KQ = Key Question; NSAID = nonsteroidal anti-inflammatory drug; PICOTS = population, interventions, comparators, outcomes, timing, studies, settings

[a] Multidisciplinary rehabilitation (MDR) (also known as interdisciplinary rehabilitation), is defined as a coordinated program with biopsychosocial treatment components (e.g., exercise therapy and cognitive-behavioral therapy) provided by professionals from at least two different specialties. Functional restoration training is included as part of MDR

[b] Different forms of exercise will not be compared to each other. Exercise will be compared with nonexercise interventions for low back pain, neck pain, fibromyalgia and osteoarthritis

[c] Different forms of biofeedback will not be compared to each other. Biofeedback will be compared with the noninvasive interventions for chronic headache

[d] The magnitude of effects for pain and function will be classified using the same system as in the AHRQ-funded noninvasive treatment for low back pain review recognizing that small effects using this system may not meet standard thresholds for clinically meaningful effects. A small/slight effect was defined for pain as a mean between-group difference following treatment of 5 to 10 points on a 0- to 100-point visual analog scale (VAS), 0.5 to 1.0 points on a 0- to 10-point numeric rating scale, or equivalent; for function as a mean difference of 5- to 10-point difference on the 0- to 100-point Oswestry Disability Index (ODI) or 1 to 2 points on the 0- to 24-point Roland-Morris Disability Questionnaire (RDQ), or equivalent; and for any outcome as a standardized mean difference (SMD) of 0.2 to 0.5. A moderate effect was defined for pain as a mean difference of 10 to 20 points on a 0- to 100-point VAS, for function as a mean difference of 10 to 20 points on the ODI or 2 to 5 points on the RDQ, and for any outcome as an SMD of 0.5 to 0.8. Large/substantial effects were defined as greater than moderate. We will apply similar methodology to outcomes measures for the other condition. The clinical relevance of effects classified as small/slight might vary for individual patients depending on preferences, baseline symptom severity, harms, cost, and other factors

Data Abstraction and Data Management

Using templates, data from included trials were abstracted into categories that included but were not limited to: study design, year, setting, country, sample size, eligibility criteria, attrition, population and clinical characteristics (including age, sex, comorbidities, diagnostic classifications/information), intervention characteristics (including the type, number, intensity, duration of, and adherence to treatments), comparator characteristics, and results (including harms). We also recorded the funding source and role of the sponsor. All abstracted study data were verified for accuracy and completeness by a second team member (Appendix D). Details are further outlined in the protocol.

Quality (Risk of Bias) Assessment of Individual Studies

Predefined criteria were used to assess the quality of included trials. We focused on trials with the least potential for bias and the fewest limitations. RCTs were assessed based on criteria and methods established in the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 8.5 Risk of Bias Tool),[18] and precepts for appraisal developed by the Cochrane Back and Neck Group.[19] These criteria and methods were used in conjunction with the approach recommended in the AHRQ *Methods Guide for Effectiveness and Comparative Effectiveness Research*.[15] Two team members independently appraised each included study, with disagreements resolved by consensus. Studies were rated as "good," "fair," or "poor" as described in Table 2. Assessments of included studies are in Appendix E.

Table 2. Criteria for grading the quality of individual studies

Rating	Description and criteria
Good	• Least risk of bias, results generally considered valid • Employ valid methods for selection, inclusion, and allocation of patients to treatment; report similar baseline characteristics in different treatment groups; clearly describe attrition and have low attrition; use appropriate means for preventing bias (e.g., blinding of patients, care providers, and outcomes assessors); and use appropriate analytic methods (e.g., intention-to-treat analysis)
Fair	• Susceptible to some bias but not enough to necessarily invalidate results • May not meet all criteria for good quality, but no flaw is likely to cause major bias; the study may be missing information making it difficult to assess limitations and potential problems • Category is broad; studies with this rating will vary in strengths and weaknesses; some fair-quality studies are likely to be valid, while others may be only possibly valid
Poor	• Significant flaws that imply biases of various kinds that may invalidate results; "fatal flaws" in design, analysis or reporting; large amounts of missing information; discrepancies in reporting; or serious problems with intervention delivery • Studies are at least as likely to reflect flaws in the study design or execution as the true difference between the compared interventions • Considered to be less reliable than higher quality studies when synthesizing the evidence, particularly if discrepancies between studies are present

Data Analysis and Synthesis

Data were synthesized qualitatively (e.g., ranges and descriptive analysis) and quantitatively using meta-analysis where appropriate. Results are organized by Key Question (i.e., by condition) and intervention and then by comparators for each subquestion (e.g., intervention vs. waitlist or sham for subquestion a). To the extent that the interventions were distinct, we explored separating them out for analysis and reporting. For example, we categorized various forms of exercise based on their primary mechanisms of action (Appendix F). Interventions with similar characteristics were combined (e.g., cognitive-behavioral therapy [CBT] and acceptance and commitment therapy [ACT], which is a type of CBT).[20] Duration of followup postintervention was reported and categorized as short term (1 to <6 months), intermediate term (≥6 to <12 months), and long term (≥12 months).

Prioritized outcomes of function and pain, based on validated measures, are presented first. Based on input from stakeholders, improvement in function was prioritized as the most important outcome. There is overlap between functional outcome measures and quality of life measures. Short-Form 36 (SF-36) and EuroQoL-5 Dimensions (EQ-5D) are two such outcome measures and they were categorized as quality of life measures for this report. For some conditions, such as OA, results were organized by affected region (e.g., knee, hip, hand). Based on input from stakeholders, improvement in function was prioritized as the most important outcome.

Results for continuous outcomes as well as dichotomous outcomes were synthesized. Binary outcomes based on the proportion of patients achieving specific thresholds of success for improved function, or other measure of success as defined in the trials (e.g., ≥30% improvement in pain score), were reported and a risk ratio and 95% confidence interval were calculated to evaluate the presence of an association and estimate relative effect size using the Rothman Episheet.[21] For continuous outcomes, mean differences between treatments and 95% confidence intervals were calculated using GraphPad or Stata®/IC 12.1 (StataCorp, College Station, TX) to provide effect sizes and determine presence of a statistical association.

We conducted meta-analysis to quantitatively synthesize evidence. To determine the appropriateness of meta-analysis, we considered clinical and methodological diversity and assessed statistical heterogeneity. Two continuous primary outcomes (pain and function) and one

secondary outcome (quality of life) provided adequate data for meta-analysis. Mean difference (MD) was used as the effect measure if the studies reported outcomes using the same scale, or if the outcomes could be converted to the same scale (e.g., 0-100 pain ratings were converted to 0-10 scale); otherwise, standardized mean difference (SMD) was used when the reported outcomes used different scales but measured the same underlying construct (e.g., function). In the primary analysis, MD and SMD were calculated using the followup score, and sensitivity analyses were conducted using the change score from the baseline. When standard deviation (SD) was not reported, or could not be calculated from the reported data, it was imputed using the average SD from the studies of the same meta-analysis, or using the SD value from the baseline if the baseline SD was reported and the followup SD was not.

We assumed random effects across studies and used both the Dersimonian-Laird method[22] and the profile-likelihood model[23] to combine studies. Statistical heterogeneity among the studies was assessed using the standard Cochran's chi-square test and the I^2 statistic.[24] Primary analyses were stratified by disease type, intervention, control group (usual care, exercise, or pharmacological treatment) and length of followup (short, intermediate, and long term). Controls included usual care, waitlist, no treatment, placebo, sham treatment, attention control, or other groups that involved at most minimal active treatment. We performed additional sensitivity and subgroup analyses based on specific interventions (e.g., type of acupuncture, type of exercise, intervention intensity etc.) and control types (as described above) and by excluding outlying studies and studies rated as poor.

To facilitate interpretation of results across trials and interventions, we categorized the magnitude of effects for function and pain outcomes as in our previous reviews.[16,25] In general we classified effects for measures with a 0 to 100 scale for pain or function as small/slight (5 to 10 points), moderate (>10 to 20 points), or large/substantial (>20 points) (see additional information in Assessing Applicability).

Grading the Strength of Evidence for Major Comparisons and Outcomes

The strength of evidence for each Key Question and primary outcome (function, pain, harms) was initially assessed by one researcher with experience in determining strength of evidence for each primary clinical outcome in accordance with AHRQ guidance[26,27] and as described in the protocol. The initial assessment was independently reviewed by at least one other experienced senior investigator. The overall strength of evidence was determined based on assessment of study limitations (graded low, moderate, high); consistency of results across trials (graded consistent, inconsistent, or for single studies, unknown); the directness of the evidence linking the interventions with health outcomes (graded direct or indirect); effect estimate precision (graded precise or imprecise); and reporting bias (suspected or undetected). Bodies of evidence consisting of RCTs were initially considered high strength. All outcomes were considered direct.

The final strength of evidence grade was assigned by evaluating and weighing the combined results of the above domains and considering the highest quality evidence available. While studies rated as poor quality were not excluded, such studies were considered to be less reliable than higher quality studies when synthesizing the evidence, particularly when discrepancies across studies were noted. The strength of evidence was assigned an overall grade of high, moderate, low, or insufficient according to a four-level scale (Table 3). When all of the studies for a primary outcome were rated poor quality, we rated the strength of evidence as insufficient. Strength of evidence tables for primary outcomes are presented in Appendix G.

Table 3. Description of the strength of evidence grades

Strength of Evidence	Description
High	We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable, i.e., another study would not change the conclusions.
Moderate	We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.
Low	We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.
Insufficient	We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.

Assessing Applicability

Applicability was assessed using the PICOTS framework by examining the abstracted characteristics of the patient populations for each condition (e.g., demographic characteristics, condition-specific diagnostic criteria, symptoms, presence of medical and psychiatric comorbidities, and other psychosocial factors); the interventions (e.g., availability in the United States; dose, frequency, or intensity of treatment, and methods for administration); and clinical settings (e.g., primary care, specialty setting, or developing country vs. developed country) in which the included studies are performed.

The magnitude of effects for pain and function (Appendix H) were classified with the system used in our previous AHRQ review on noninvasive treatment for low back pain,[25] recognizing that small effects using this system may not meet standard thresholds for clinically meaningful effects. We applied the following definitions:

- Small/slight effect
  - For pain: as a mean between-group difference following treatment of 5 to 10 points on a 0-to 100-point visual analog scale (VAS), 0.5 to 1.0 point on a 0- to 10-point numeric rating scale (NRS), or equivalent
  - For function: as a mean difference of 5 to 10 points on the 0- to 100-point Oswestry Disability Index (ODI) or Western Ontario and McMaters Universities Osteoarthritis Index (WOMAC) or 1 to 2 points on the 0- to 24-point Roland-Morris Disability Questionnaire (RDQ) or Lequesne Index (LI), or equivalent
  - For any outcome: as a SMD of 0.2 to 0.5

- Moderate effect
  - For pain: as a mean difference of 10 to 20 points on a 0- to 100-point VAS
  - For function: as a mean difference of 10-20 points (on a 0-100 scale) on the ODI or WOMAC or 2-5 points on RDQ or LI, or equivalent
  - For any outcome: as a SMD of >0.5 to 0.8

- Large effect
  - For pain: as a mean difference of ≥20 points on a 0- to 100-point VAS
  - For function: as a mean difference of ≥20 (on a 0-100 scale) on the ODI or WOMAC or 5 points on RDQ or LI, or equivalent
  - For any outcome: as a SMD of >0.8

Information regarding effect size definitions for other outcome measures is available in Appendix H. There is variability across individual patients regarding what may constitute a clinically import effect, which is influenced by a number of factors such as preferences, duration and type of chronic pain, baseline symptom severity, harms, and costs.

Peer Review and Public Commentary

Peer reviewers with expertise in primary care and management of the included chronic pain conditions were invited to provide written comments on the draft report. The AHRQ TOO and an EPC Associate Editor provided comments and editorial review. The draft report was posted on the AHRQ Web site for 4 weeks for public comment. A disposition of comments report with authors' responses to the peer and public review comments will be posted after publication of the final Comparative Effectiveness Review on the AHRQ Web site.

Results

Introduction

Results are organized by Key Question (i.e., by condition) and intervention and then organized by comparators for each subquestion. We categorized post-intervention followup as short term (1 to <6 months), intermediate term (≥6 to <12 months) and long term (≥12 months). We prioritized function and pain outcomes based on validated measures. For some conditions (e.g., osteoarthritis [OA]), results are organized by affected region.

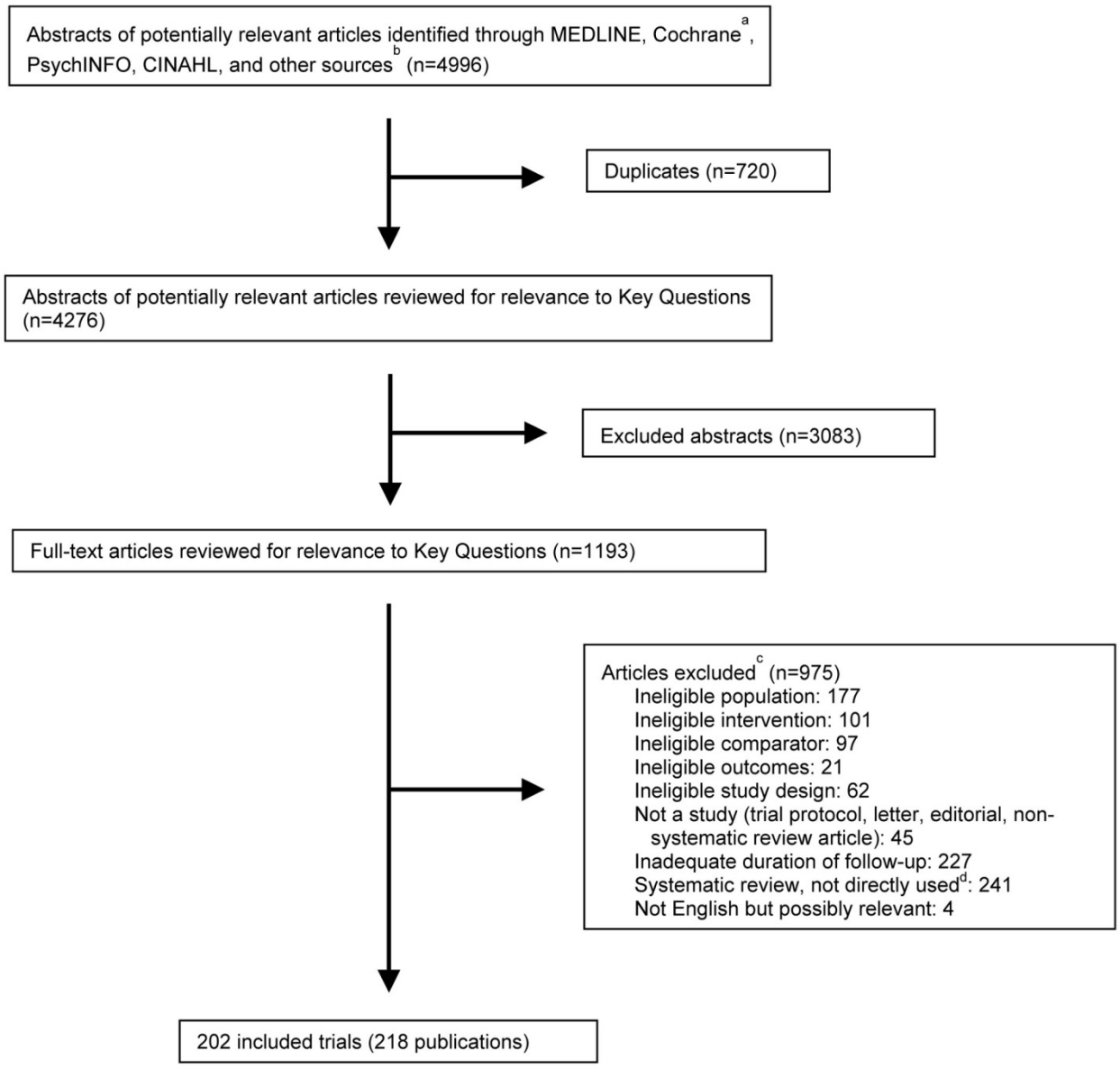
We synthesized data qualitatively and quantitatively, using meta-analysis where appropriate. Two continuous primary outcomes (pain, function) provided adequate data for meta-analysis. For meta-analyses providing pooled estimates, we report results from heterogeneity testing. I-squared and corresponding P-values describe the degree and statistical significance of heterogeneity across studies; pooled (subtotal) estimates are statistically significant if the confidence interval does not include the value of 0 for mean differences (MDs) or the value of 1 for risk ratios (RR). (See the Methods section of this report and the protocol for additional details on data analysis and synthesis.) In general, if effect estimates tended to favor one treatment but failed to reach statistical significance with confidence interval crossing the null value of zero or one (perhaps due to sample size), the results are interpreted as showing no clear difference between treatments. If effect estimates are close to zero and not statistically significant, results are interpreted as no difference between groups.

A list of acronyms and abbreviations appears at the end of the report.

Results of Literature Searches

The search and selection of articles are summarized in the literature flow diagram (Figure 2). Database searches resulted in 4,996 potentially relevant articles. After dual review of abstracts and titles, 1,193 articles were selected for full-text dual review, and 218 publications were determined to meet inclusion criteria and were included in this review. One-fourth of the trials excluded at full text did not meet our criteria for followup duration (i.e., a minimum of 1 month of followup after termination of the intervention, or post-intervention if the intervention duration was at least 6 months). Other common reasons for exclusion of primary trials included ineligible population and ineligible intervention or comparator (i.e., combination of treatments or if treatments were additive in nature). Data abstraction and quality assessment tables for all included studies are available in Appendixes D and E.

Figure 2. Literature flow diagram



[a] Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews
[b] Other sources include prior reports, reference lists of relevant articles, systematic reviews, etc.
[c] Publications may be included or excluded for multiple interventions
[d] Studies checked for inclusion

Description of Included Studies

A total of 202 trials (in 218 publications) were included. For each intervention category, the comparisons evaluated and their respective studies are listed in Table 4.

Table 4. Overview of included studies

Intervention	Comparator	Chronic Low Back Pain: n=68 (74 Publications)	Chronic Neck Pain: n=25	Osteoarthritis: n=53 (56 Publications)	Fibromyalgia: n=47 (54 Publications)	Chronic Tension Headache : n=9
Exercise	Sham, usual care, waitlist, no treatment, attention	6[28-33]	6[34-39]	Knee OA: 18 (21)[40-60] Hip OA: 4[40,61-63] Hand OA: 1[64]	21 (23)[65-87]	0
	Pharmacological therapy	0	1[88]	0	1[82]	0
Psychological Therapies	Sham, usual care, waitlist, no treatment, attention	5[89-93]	1[38]	Knee OA: 2[94,95] Hip, Hand OA: 0	10 (11)[67,86,87,96-103]	2[104,105]
	Pharmacological therapy	0	0	0	3[96,106,107]	2[105,108]
	Exercise (or biofeedback for CTTH)	1[109]	1[38]	Knee OA: 1[110] Hip, Hand OA: 0	5[67,86,87,111,112]	0
Physical Modalities	Sham, usual care, waitlist, no treatment, attention	7[113-119]	5[120-124]	Knee OA: 13[125-137] Hip OA: 0 Hand OA: 2[138,139]	2[140,141]	1[142]
	Pharmacological therapy	0	0	0	0	0
	Exercise (or biofeedback for CTTH)	1[143]	0	0	0	0
Manual Therapies	Sham, usual care, waitlist, no treatment, attention	10[93,119,144-151]	2[152,153]	Knee OA: 2[40,154] Hip OA: 1[40] Hand OA: 0	2[155,156]	1[157]
	Pharmacological therapy	0	0	0	0	1[158]
	Exercise (or biofeedback for CTTH)	5[147,159-162]	1[152]	Knee OA: 1[40] Hip OA: 2[40,163] Hand OA: 0	0	0
Mindfulness Practices	Sham, usual care, waitlist, no treatment, attention	5 (7)[89,164-169]	0	0	2 (3)[170-172]	0
	Pharmacological therapy	0	0	0	0	0
	Exercise (or biofeedback for CTTH)	0	0	0	0	0
Mind-body Practices	Sham, usual care, waitlist, no treatment, attention	7[173-179]	1[180]	Knee OA: 2[181,182] Hip, Hand OA: 0	2[183,184]	0
	Pharmacological therapy	0	0	0	0	0
	Exercise (or biofeedback for CTTH)	5[174-176,185,186]	2[187,188]	0	0	0
Acupuncture	Sham, usual care, waitlist, no treatment, attention	**8[149,189-195]**	**8[180,196-202]**	Knee OA: **9[60,203-210]** Hip, Hand OA: 0	**3[211-213]**	**3[214-216]**
	Pharmacological therapy	0	**2[196,217]**	0	0	0
	Exercise (or biofeedback for CTTH)	0	0	Knee OA: **1[60]** Hip, Hand OA: 0	0	0

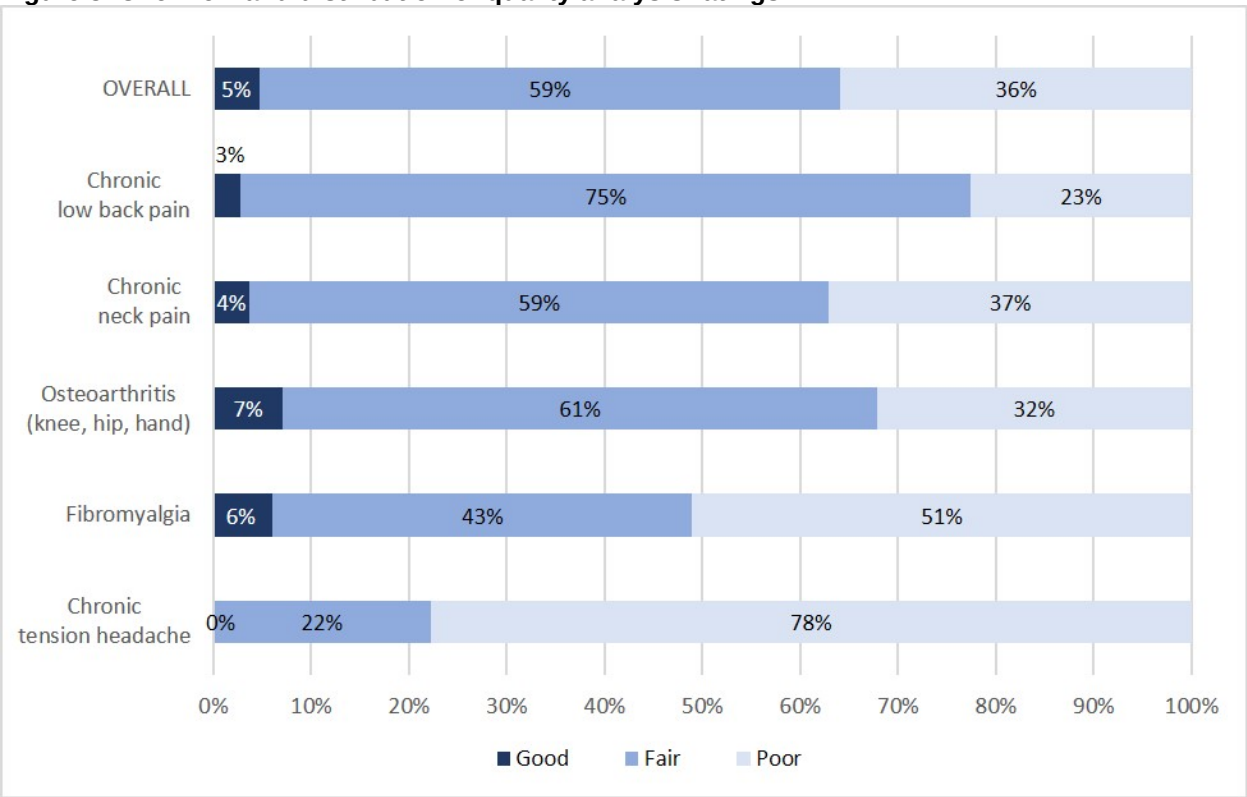
Intervention	Comparator	Chronic Low Back Pain: n=68 (74 Publications)	Chronic Neck Pain: n=25	Osteoarthritis: n=53 (56 Publications)	Fibromyalgia: n=47 (54 Publications)	Chronic Tension Headache: n=9
Function Restoration Training	Sham, usual care, waitlist, no treatment, attention	0	0	0	0	0
	Pharmacological therapy	0	0	0	0	0
	Exercise (or biofeedback for CTTH)	0	0	0	0	0
Multi-disciplinary Rehabilitation	Sham, usual care, waitlist, no treatment, attention	**7**[218-223]	0	Knee, Hip OA: 0 Hand OA: **1**[224]	**6 (8)**[85,225-231]	0
	Pharmacological therapy	**1**[232]	0	0	0	0
	Exercise (or biofeedback for CTTH)	**9 (13)**[109,233-244]	0	0	**1**[85]	0

CTTH = chronic tension-type headache; OA = osteoarthritis

Thirty-five percent of the included trials were small (<70 participants). Across trials, most patients were female (>57%), with a mean ages ranging from 31 to 76 years; patients with OA tended to be older in general than those in the other conditions (range, 52 to 76 years). Mean pain duration for patients with chronic low back pain, chronic neck pain, and OA were similar and varied widely from 6 months to 15 years. Mean symptom duration in trials of fibromyalgia and chronic tension headache tended to be at least 4 years (up to 22 years). Exercise interventions were the most commonly studied for OA and fibromyalgia. Psychological therapies were most commonly studied for fibromyalgia, and manual therapies were most commonly studied for chronic low back pain. We identified trials of acupuncture for all included conditions. Multidisciplinary rehabilitation was studied primarily for chronic low back pain and fibromyalgia. Most trials of multidisciplinary rehabilitation used a functional restoration approach either explicitly or implicitly. There were no trials of functional restoration training for any condition. Limited evidence was available for hip or hand OA or chronic tension headache. The majority of trials compared nonpharmacological interventions with usual care, waitlist, no treatment, attention control, or placebo/sham, with very few trials employing pharmacological treatments or exercise as comparators. Little long-term evidence was available across conditions and interventions.

The majority of trials (59%) were rated fair quality with only 5 percent considered good quality (Figure 3). For chronic tension headache, no study was considered good quality. In the majority of trials (72%), attrition was under 20 percent and therefore rated as acceptable. Across trials where attrition was not acceptable, the range was 20 to 63 percent. A primary methodological limitation in many trials was the inability to effectively blind participants and in many cases providers. Poor reporting of randomization and allocation concealment methods were common shortcomings. Acceptable adherence, defined as completion of a minimum of 80 percent of planned treatment, was reported in 44 percent of trials. It was either unclear (40%) or unacceptable (16%) in the majority of trials.

Figure 3. Overview and distribution of quality analysis ratings



Key Question 1: Chronic Low Back Pain

Exercise for Chronic Low Back Pain

Key Points

- Exercise was associated with slightly greater effects on short-term function than usual care, an attention control, or a placebo intervention (6 trials, pooled standardized mean difference [SMD] −0.31, 95% confidence interval [CI] −0.58 to −0.04, I^2=57%); there were no effects on intermediate-term function (3 trials, pooled SMD −0.15, 95% CI −0.48 to 0.18, I^2=51%) or long-term function (1 trial, MD 0.00 on the 0 to 100 Oswestry Disability Index [ODI], 95% CI −11.4 to 11.4) (strength of evidence [SOE]: low).
- Exercise was associated with slightly to moderately greater effects on pain than usual care, an attention control, or a placebo intervention at short-term (6 trials, pooled MD −0.81 on a 0 to 10 scale, 95% CI −1.26 to −0.36, I^2=0%), intermediate-term (3 trials, pooled MD −1.37, 95% CI −2.10 to −0.65, I^2=34%), and long-term (1 trial, MD –1.55, 95% CI −2.38 to −0.32) followup (SOE: moderate for short-term, low for intermediate-term and long-term).
- No trial evaluated exercise versus pharmacological therapy.
- Comparisons involving exercise versus other nonpharmacological therapies are addressed in the sections for the other therapies.

- Harms were not reported in most trials; one trial did not find an association between exercise and increased pain versus placebo and one trial reported no adverse events (SOE: low).

Detailed Synthesis

Six trials of exercise therapy for low back pain met inclusion criteria (Table 5 and Appendix D).[28-33] Two trials evaluated neuromuscular re-education exercise (motor control exercises),[28,29] two trials muscle performance exercises (Pilates),[32,33] and two trials combined exercise techniques.[30,31] Sample sizes ranged from 60 to 154 (total sample=553). Three trials compared exercise versus an attention control;[29,30,32] two trials compared exercise versus usual care;[31,33] and one trial compared exercise versus a placebo intervention (detuned diathermy and ultrasound).[28] Four trials were conducted in the United States, Europe, or Australia, and two trials[32,33] were conducted in Brazil. The duration of exercise therapy ranged from 6 to 12 weeks and the number of exercise sessions ranged from 10 to 24. One trial reported outcomes through long-term followup,[29] three trials reported outcomes through intermediate-term followup,[28,30] and the remainder only evaluated short-term outcomes.

Five trials were rated fair quality and one trial[31] poor quality (Appendix E). In two fair-quality trials,[28,33] the main methodological limitation was the inability to blind interventions. Limitations in the other trials included unclear randomization and allocation concealment methods, high loss to followup, and baseline differences between intervention groups.

Table 5. Chronic low back pain: exercise

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Costa, 2009[28] 4 and 10 months Duration of pain: Mean 328 to 335 weeks *Fair*	A: Neuromuscular re-education (motor control exercise) (n=77), 12 sessions over 8 weeks B: Placebo (detuned shortwave diathermy and detuned ultrasound) (n=77) 12 sessions, two sessions/week for 4 weeks, then 1 session/week for 4 weeks	A vs. B Age: 55 vs. 53 years Female: 58% vs. 62% Baseline RDQ (0-24): 13.1 vs. 13.4 Baseline pain (0-10 VAS): 6.8 vs. 6.6	4 months RDQ: 5.3 vs. 4.3, adjusted difference 1.0 (95% CI 0.3 to 1.8) Pain (0-10 VAS): 5.0 vs. 5.6, adjusted difference 1.4 (95% CI 0.3 to 2.4) 10 months RDQ: 11.4 vs. 12.3, adjusted difference −1.0 (95% CI −2.8 to 0.8) Pain: 5.0 vs. 6.3, adjusted difference −1.0 (95% CI −1.9 to −0.1)	4 months Global impression of recovery (−5 to +5): 1.5 vs. 0.3, adjusted difference 1.4 (95% CI 0.3 to 1.8) 10 months Global impression of recovery: 1.2 vs. −0.3, adjusted difference 1.6 (95% CI 0.6 to 2.6)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Goldby, 2006[29] 3, 6, 12 and 24 months Duration of pain: Mean 11 to 12 years *Fair*	A: Neuromuscular re-education (motor control exercise) (n=84), 10 sessions over 10 weeks B: Attention control (education) (n=40)	A vs. B Age: 43 vs. 41 years Female: 68% vs. 68% Race: 80% vs. 62% Baseline ODI (0-100): 40.5 vs. 33.5 Baseline LBO (0-75): 43.9 vs. 44.0 vs. 47.6 Baseline back pain (0-100 NRS): 45.8 vs. 37.6	<u>3 months</u> ODI (0-100): 31.00 vs. 28.1, difference 2.9 (95% CI −3.89 to 9.69) LBO (0-75): 50.92 vs. 54.4, difference −3.48 (95% CI −9.67 to 2.71) Back pain (0-100 NRS): 28.81 vs. 34.4, difference −5.59 (95% CI −17.86 to 6.68) <u>6 months</u> ODI: 25.81 vs. 23.9, difference 1.91 (95% CI −6.28 to 10.10) LBO: 55.42 vs. 57.85, difference −2.43 (95% CI −9.14 to 4.28) Back pain: 23.16 vs. 30.25, difference −7.09 (95% CI −20.22 to 6.04) <u>12 months</u> ODI: 24.76 vs. 26.9 difference −2.14 (95% CI −10.14 to 5.86) LBO: 53.86 vs. 50.95, difference 2.91 (95% CI −4.29 to 10.11) Back pain: 29.23 vs. 30, difference −0.77 (95% CI −14.13 to 12.59) <u>24 months</u> ODI: 27 vs. 27; difference 0.00 (95% CI −11.44 to 11.44) LBO: 54.7 vs. 55.2, difference −0.5 (95% CI −9.20 to 8.20) Back pain: 35.4 vs. 50.9, difference −15.50 (95% CI −33.06 to 2.06)	<u>3 months</u> Nottingham Health Profile: 94.97 vs. 94.32, difference 0.65 (95% CI −36.97 to 38.27) <u>6 months</u> Nottingham Health Profile: 76.3 vs. 77.50, difference −1.20 (95% CI −37.76 to 35.36) <u>12 months</u> Nottingham Health Profile: 70.06 vs. 87.47 difference −17.41 (95% CI −56.12 to 21.30) <u>24 months</u> Nottingham Health Profile: 82 vs. 83, difference −1.00 (95% CI −60.85 to 58.85)
Kankaaanpaa, 1999[30] 3 and 9 months Duration of pain: Mean 7 to 9 years *Fair*	A. Combined exercise (exercises, stretching, relaxation, muscle function and ergonomic advice) (n=30), 24 sessions over 12 weeks B. Attention Control (n=24) (thermal therapy and minimal massage)	A vs. B Age: 40 vs. 39 years Female: 36.6% vs. 33.3% Baseline Pain and Disability Index (0-70 PDI): 13.2 vs. 9.5 Baseline back pain (0-100 mm VAS): 55.2 vs. 47.0	<u>3 months</u> Pain and Disability Index (0-70): 5.7 vs. 12.6, difference −6.9 (95% CI −11.69 to - 2.11) Back pain (0-100 VAS): 26.6 vs. 43.4; difference −16.80 (95% CI −31.12 to −2.47) <u>9 months</u> Pain and Disability Index: 5.7 vs. 11.4, difference −5.7 (95% CI −11.31 to −0.09) Back pain intensity: 23.9 vs. 45.1, difference −21.20 (95% CI −32.69 to −9.71)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Miyamoto, 2013[32] 4.5 months Duration of pain: Mean 5 to 6 years *Fair*	A. Muscle performance (Pilates) (n=43),12 sessions over 6 weeks B. Attention control (n=43) (education)	A vs. B Age: 41 vs. 38 years Female: 84% vs. 79% Baseline RDQ: 9.7 vs. 10.5 Baseline pain (0-10 VAS): 6.6 vs. 6.5	<u>4.5 months</u> RDQ (0-24): 4.5 vs. 6.7, adjusted difference −1.4 (95% CI −3.1 to 0.03) Patient-Specific Functional Scale (0-10): 6.9 vs. 6.1, adjusted difference 0.2 (95% CI −0.6 to 1.1) Pain (0-10 VAS): 4.5 vs. 5.3, adjusted difference −0.9 (95% CI −1.9 to 0.1)	<u>4.5 months</u> Global impression of recovery (−5 to +5): 2.4 vs. 1.7, adjusted difference 0.7 (95% CI −0.4 to 1.8)
Nassif, 2011[31] 4 months Duration of pain: NR *Poor*	A. Combined exercise (n=37) (stretching, stability, coordination, and muscle strengthening exercises), 24 sessions over 8 weeks B. Usual care (n=38)	A vs. B Age: 45 vs. 45 Female: 11% vs. 21% Baseline RDQ: 13.9 vs. 12.3 Baseline pain (0-10 VAS): 4.5 vs. 4.9	<u>4 months</u> RDQ (0-24): 10.0 vs. 10.6, difference −0.6 (95% CI −3.5 to 2.3) Quebec Back Pain Disability Questionnaire: 27.2 vs. 30.2, difference −3.0 (95% CI −11.7 to 5.7) Pain (0-10 NRS): 3.2 (2.3) vs. 3.5 (2.5), difference −0.3 (95% CI −1.6 to 1.0)	<u>4 months</u> Dallas Pain Questionnaire anxiety and depression: 31.2 vs. 28.9, difference 2.3 (95% CI −8.2 to 12.8)
Natour, 2014[33] 3 months Duration of pain: >1 year *Fair*	A. Exercise (Pilates) (n=30), 24 sessions over 12 weeks B. Usual care (n=30) (no treatment)	A vs. B Age: 48 vs. 48 Female: 80% vs. 77% Baseline RDQ: 1.1 vs. 10.6 Baseline pain (0-10 VAS): 5.5 vs. 5.8	<u>3 months</u> RDQ (0-24): 7.0 vs. 10.7, difference −3.6, P<0.001 Pain (0-10 VAS): 4.2 vs. 5.8, difference −1.6, P<0.001	<u>3 months</u> SF-36 physical function (0-100): 65.4 vs. 59.6, difference 5.8, P=0.026 SF-36 role physical: 56.4 vs. 40.0, difference 16.4, P=0.086 SF-36 bodily pain: 52.2 vs. 43.9, difference 8.3, P=0.030 SF-36 general health: 65.2 vs. 62.1, difference 3.1, P=0.772 SF-36 mental health: 67.9 vs. 65.3, difference 2.6, P=0.243 SF-36 social functioning: 86.0 vs. 80.4, difference 5.6, P=0.09 No differences on other SF-36 subscales

CI = confidence interval; LBO = Low Back Outcome Score; NHP = Nottingham Health Profile; NR = not reported; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; SF-36 = Short-Form 36 questionnaire; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Exercise Compared With Usual Care, an Attention Control, or a Placebo Intervention

Exercise was associated with slightly greater effects on short-term function than controls (6 trials, pooled SMD −0.31, 95% CI −0.58 to −0.04, I^2=57%) (Figure 4).[28-33] Four trials that evaluated function using the Roland-Morris Disability Questionnaire (RDQ) (0 to 24 scale) reported a pooled MD of −1.96 points (95% CI −3.14 to −0.78),[28,31-33] and one trial that used the

ODI (0 to 100 scale) reported a difference of 2.9 points (95% CI −3.89 to 9.69).[29] There were no clear differences in estimates when analyses were stratified according to the type of exercise (estimates ranged from −0.08 to −0.51 points) or the type of control and when the poor-quality trial was excluded. There were no differences between exercise versus controls in intermediate-term function (3 trials, pooled SMD −0.15, 95% CI −0.48 to 0.18, I^2=51%)[28-30] or long-term function (1 trial, difference 0.00, 95% CI −11.4 to 11.4 on the ODI).[29]

Exercise was associated with greater effects on short-term pain than usual care, an attention control, or a placebo intervention (6 trials, pooled difference −0.81 on a 0 to 10 scale, 95% CI −1.26 to −0.36, I^2=0%) (Figure 5).[28-33] There were no clear differences in estimates when analyses were stratified according to the type of exercise (difference −0.52, 95% CI −1.41 to 0.36 in 2 trials of neuromuscular re-education exercises, −1.12, 95% CI −2.28 to −0.14 in 2 trials of muscle performance exercises, and −0.90, 95% CI −2.63 to 0.68 in 2 trials of combined exercises), the type of control (usual care, attention control, or placebo intervention), and when the poor-quality trial was excluded. For intermediate-term pain (3 trials, pooled difference −1.37, 95% CI −2.10 to −0.65, I^2=34%)[28-30] and long-term pain (1 trial, difference −1.55, 95% CI −2.78 to −0.32),[29] effects of exercise on pain were moderate, but findings were based on small numbers of trials.

Data on effects of exercise on quality of life were limited. One trial[29] found no differences between exercise versus an attention control on the Nottingham Health Profile at short-term, intermediate-term, or long-term followup, and one trial[33] found exercise associated with higher scores on the Short-Form 36 (SF-36) physical functioning (difference 5.8 points on 0 to 100 scale, P=0.026), bodily pain (difference 8.3 points, P=0.03), and vitality subscales (difference 5.3 points, P=0.029) at short-term followup; there were no differences on other SF-36 subscales (Table 5).

No trial evaluated effects of exercise on use of opioid therapies or health care utilization. There was insufficient evidence to determine effects of duration of exercise therapy or number of sessions on outcomes.

Exercise Compared With Pharmacological Therapy

No trial of exercise versus pharmacological therapy met inclusion criteria.

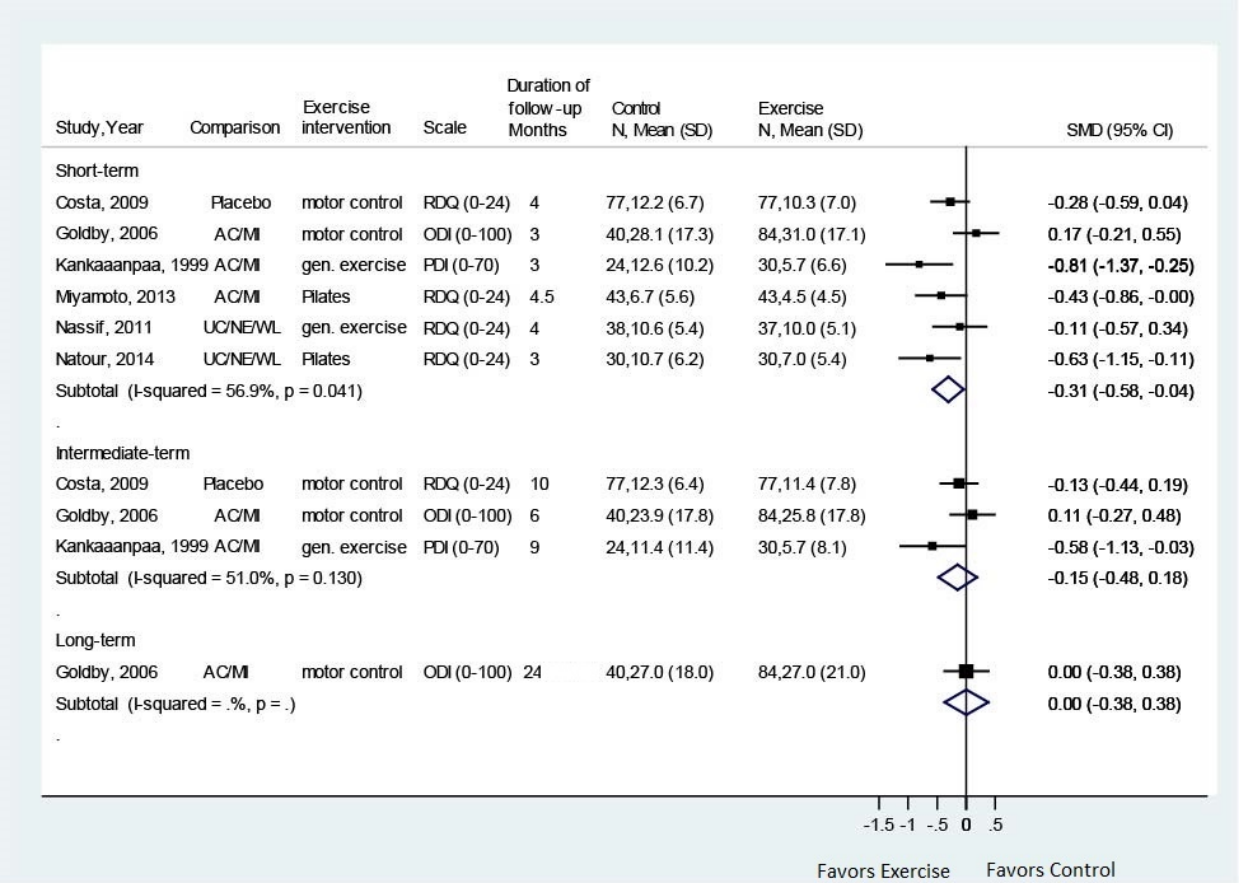
Exercise Compared With Other Nonpharmacological Therapies

Findings for exercise versus other nonpharmacological therapies are addressed in the sections for other nonpharmacological therapies.

Harms

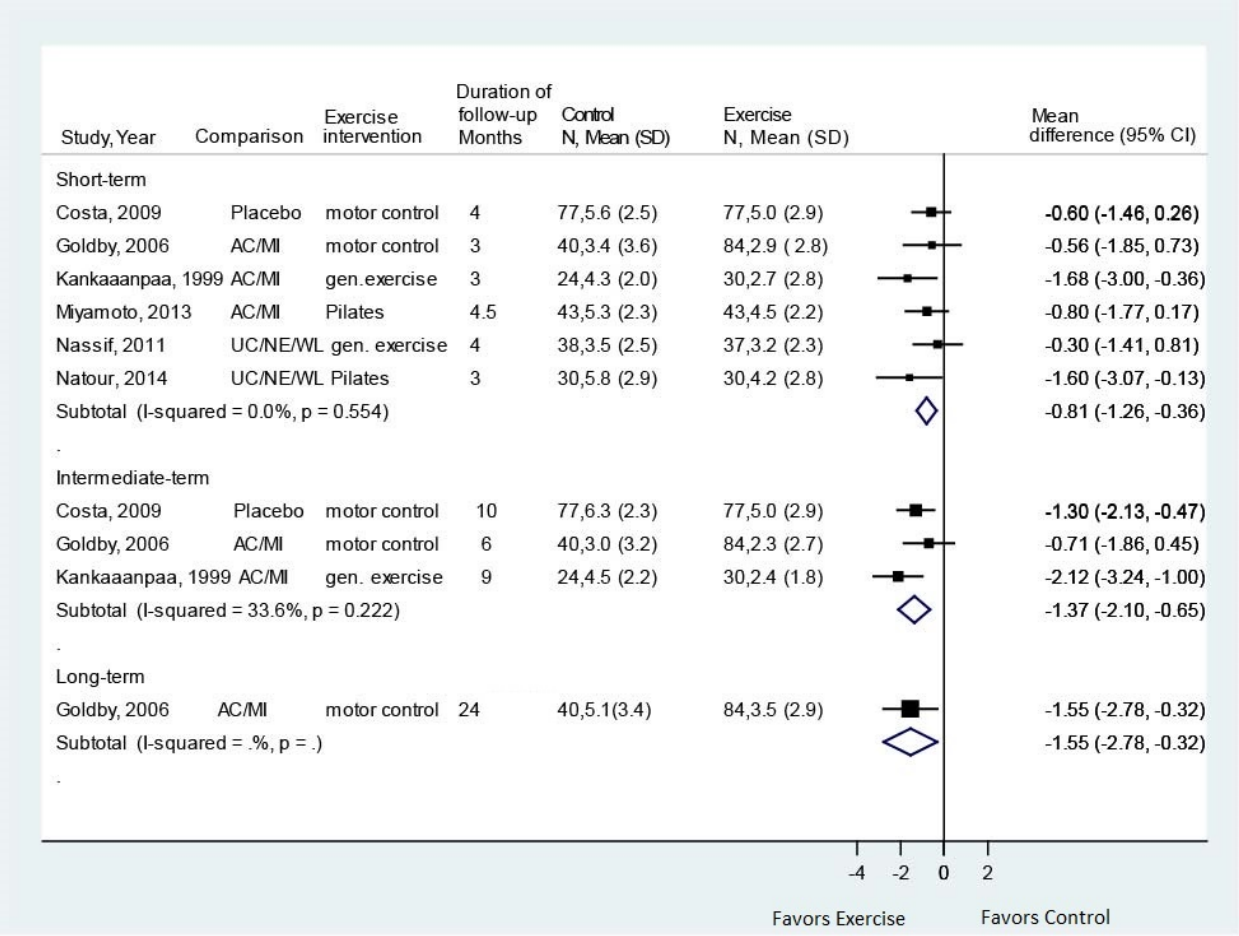
Harms were not reported in most trials. One trial[28] found no difference between exercise and a placebo intervention (detuned diathermy) in likelihood of increased pain, and another trial[32] reported no adverse events (Appendix D).

Figure 4. Exercise versus usual care, an attention control, or a placebo intervention for chronic low back pain: effects on function



AC = attention control; CI = confidence interval; MI = minimal intervention; N = number; NE = no exercise; ODI = Oswestry Disability Index; PDI = Pain Disability Index; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SMD = standardized mean difference; UC = usual care; WL = waitlist

Figure 5. Exercise versus usual care, an attention control, or a placebo intervention for chronic low back pain: effects on pain



AC = attention control; CI = confidence interval; MI = minimal intervention; N = number; NE = no exercise; SD = standard deviation; UC = usual care; WL = waitlist

Psychological Therapies for Chronic Low Back Pain

Key Points

- Psychological therapy was associated with slightly greater effects on function than usual care or an attention control at short-term (3 trials, pooled SMD −0.25, 95% CI −0.38 to −0.12, I^2=0%), intermediate-term (3 trials, pooled SMD −0.25, 95% CI −0.37 to −0.13, I^2=0%), and long-term followup (3 trials, pooled SMD −0.27, 95% CI −0.39 to −0.15, I^2=0%) (SOE: moderate).
- Psychological therapy was associated with slightly greater effects on pain than usual care or an attention control at short-term (3 trials, pooled MD −0.76 on a 0 to 10 scale, 95% CI −0.99 to −0.53, I^2=0%), intermediate-term (3 trials, pooled MD −0.71, 95% CI −0.94 to −0.48, I^2=0%), or long-term followup (3 trials, pooled MD −0.53, 95% CI −0.78 to −0.27, I^2=0%) (SOE: moderate).
- Evidence from one poor-quality trial was too unreliable to determine effects of psychological therapy versus exercise (SOE: insufficient).

- One trial reported no serious adverse events and one withdrawal due to adverse events in 468 patients (SOE: low).

Detailed Synthesis

Five trials (reported in 6 publications) of psychological therapies for low back pain met inclusion criteria (Table 6 and Appendix D).[89-93,109,165] Three trials evaluated group cognitive-behavioral therapy (CBT),[89-92] one trial evaluated respondent therapy (progressive muscle relaxation),[93] and one trial evaluated operant therapy.[109] Sample sizes ranged from 49 to 701 (total sample=1,311). The number of psychological therapy sessions ranged from six to eight, and the duration of therapy ranged from 6 to 8 weeks. In one trial[91,92] the duration of therapy was unclear. Three trials compared psychological therapies versus usual care,[89,90,93] one trial compared psychological therapy versus an attention control (advice),[91,92] and one trial compared psychological therapy versus exercise therapy.[109] All trials were conducted in the United States or the United Kingdom. Four trials reported outcomes through long-term (12 to 34 months) followup,[90-92,109,165] one trial evaluated outcomes through intermediate-term followup,[89] and one trial only evaluated short-term outcomes.[93]

Three trials[89-92] were rated fair quality and two trials poor quality (Appendix E).[93,109] The major methodological limitation in the fair-quality trials was the inability to effectively blind patients and caregivers to the psychological intervention. Other methodological shortcomings in the poor-quality trials included unclear randomization and allocation concealment methods and high attrition.

Table 6. Chronic low back pain: psychological therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Cherkin, 2016[89] Herman, 2017[166] Cherkin, 2017[165] (2 year data from Cherkin, 2016) 22 months Duration of pain: >3 months (>1 year in 80% of patients) *Fair*	A. CBT (n=116), 8 sessions over 8 weeks B. Usual care (n=112)	A vs. B 49 vs. 49 years Female: 59% vs. 66% Baseline modified RDQ (0-23): 11.5 vs. 10.9 Baseline pain bothersome-ness (0-10): 6.0 vs. 6.0	A vs. B <u>4.5 months</u> Modified RDQ (0-23): −4.38 (95% CI −5.3 to −3.47) vs. −2.96 (95% CI −3.79 to −2.14) Pain (0-10): −1.56 (95% CI −2.02 to −1.11) vs. −0.84 (95% CI −1.21 to −0.46) <u>10 months</u> Modified RDQ (0-23): −4.78 (95% CI −5.67 to −3.89) vs. −3.43 (95% CI −4.33 to −2.52) Pain (0-10): −1.76 (95% CI −2.14, −1.39) vs. −1.10 (95% CI −1.48, −0.71) ≥30% improvement in pain: 39.6% (95% CI 31.7 to 49.5) vs. 31.0% (95% CI 23.8 to 40.3) ≥30% improvement in modified RDQ: 58.8% (95% CI 50.6 to 68.4) vs. 48.6% (95% CI 40.3 to 58.6) <u>22 months</u> Modified RDQ (0-23): −4.59 (95% CI−5.60 to −3.57) vs. −2.74 (95% CI−3.81 to −1.68) ≥30% improvement in modified RDQ: 62.0% (95% CI 53.5 to 71.7) vs. 42.0% (95% CI 33.8 to 52.2) Pain: −1.79 (95% CI −2.21 to −1.37) vs. −1.25 (95% CI −1.69 to −0.81) ≥30% improvement in pain: 39.6% (95% CI 31.4 to 49.8) vs. 31.1% (95% CI 23.9 to 40.5)	A vs. B <u>4.5 months</u> PHQ-8 (0–24): −1.80 (95% CI −2.35 to −1.26) vs. −0.64 (95% CI −1.23 to −0.06) SF-12 Physical component (0-100): 3.78 (95% CI 2.56to 5.00) vs. 3.27 (95% CI 2.09 to 4.44) SF-12 Mental component (0-100): 2.13 (95% CI 0.86 to 3.40) vs. −1.11 (95% CI −2.39 to 0.17) <u>10 months</u> PHQ-8 (0–24): 1.72 (95% CI −2.28 to −1.16) vs. −0.88 (95% CI −1.50 to −0.27) SF-12 Physical component: 3.79 (95% CI 2.55 to 5.03) vs. 2.93 (95% CI 1.70 to 4.16) SF-12 Mental component: 1.81 (95% CI 0.59 to 3.03) vs. 0.75 (95% CI −0.58 to 2.08) Total costs: $6,428 (95% CI $4676 to $10,262) vs. $6,304 (95% CI $4,193, $9,805)
Johnson, 2007[90] 12 months Duration of pain: 6 months *Fair*	A. CBT (n=116), 8 sessions over 6 weeks B. Usual care (n=118)	A vs. B Age: 47 vs. 49 Female: 61% vs. 58% Baseline RDQ (0-24): 10.6 vs. 10.9 Baseline pain (0-100 VAS): 44.9 vs. 51.6	A vs. B <u>6 months</u> RDQ (0-24): 6.5 vs. 8.0, adjusted difference −1.09 (95% CI −2.28 to 0.09) Pain (0-100 VAS): 26.1 vs. 35.0, adjusted difference −4.60 (95% CI −11.07 to 1.88) <u>12 months</u> RDQ (0-24): 6.7 vs. 8.0, adjusted difference −0.93 (95% CI −2.30 to 0.45) Pain (0-100 VAS): 27.9 vs. 36.4, adjusted difference −5.49 (95% CI −12.43 to 1.44)	A vs. B <u>6 months</u> Quality of life (0-1 EQ-5D): 0.75 vs. 0.71, adjusted difference 0.03 (95% CI −0.05 to 0.10) <u>12 months</u> Quality of life (0-1 EQ-5D): 0.75 vs. 0.71, adjusted difference 0.03 (95% CI −0.04 to 0.09)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Lamb 2010[91] and 2012[92] 34 months Duration of pain: 13 years *Fair*	A. CBT (n=468), 8 sessions over unclear number of weeks B. Attention control (n=233)	A vs. B Age: 53 vs. 54 years Female: 59% vs. 61% Korff disability (0-100): 49 vs. 46 Baseline RDQ (0-24): 9 vs. 9 Baseline pain (0-100 Modified Von Korff): 59 vs. 59 Modified Von	A vs. B <u>3 months</u> Modified Von Korff disability (0-100): −13.2 (−15.74 to −10.59) vs. −8.9 (−12.27 to −5.56), adjusted difference −4.2 (−8.10 to −0.40) RDQ (0-24): −2.0 (−2.43 to −1.58) vs. −1.1 (−1.54 to −0.35) adjusted difference −1.1 (−1.71 to −0.38) Modified Von Korff pain (0-100): −12.2 (−14.56 to −9.83) vs. −5.4 (−8.40 to −2.49), adjusted difference −6.8 (−10.20 to −3.31) <u>4.5 months</u> Modified Von Korff disability: −13.9 (CI −16.25 to −11.55) vs. −5.7 (−9.22 to −2.28), adjusted difference −8.2 (−12.01 to −4.31) RDQ: −2.5 (−3.03 to −1.96) vs. −1.0 (CI −1.67 to −0.40), adjusted difference −1.5 (−2.22 to −0.70) Modified Von Korff pain: −13.7 (−16.20 to −11.29) vs. −5.7 (−8.99 to −2.41), adjusted difference −8.0 (−11.80 to −4.28) <u>10.5 months</u> Modified Von Korff disability: −13.8 (−16.28 to −11.39) vs. −5.4 (−8.90 to −1.99), adjusted difference −8.4 (−12.32 to −4.47) RDQ: −2.4 (−2.84 to −1.89) vs. −1.1 (−1.72 to −0.39), adjusted difference −1.3 (−2.06 to −0.56) Modified Von Korff pain: −13.4 (−15.96 to −10.77) vs. −6.4 (−9.66 to −3.14), adjusted difference −7.0 (−10.81 to −3.12) <u>34 months</u> Modified Von Korff disability: −16.7 (−19.43 to −13.93) vs. −11.2 (−15.59 vs. −6.86), adjusted difference −5.5 (−10.64 to −0.27) RDQ: −2.9 (−3.42 to −2.38) vs. −1.6 (−2.48 to −0.80), adjusted difference −1.3 (−2.26 to −0.27 Modified Von Korff pain: −17.4 (−20.35 to −14.44) vs. −12.8 (−17.52 to −7.99), adjusted difference −4.6 (−10.28 to 1.00)	A vs. B <u>3 months</u> SF-12 PCS (0-100): 3.7 (2.82 to 4.59) vs. 1.5 (0.26 to 2.83), adjusted difference 2.2 (0.74 to 3.57) SF-12 MCS (0-100): 1.3 (0.19 to 2.42) vs. 0 (−1.45 to 1.46), adjusted difference 1.3 (−0.36 to 2.96) <u>4.5 months</u> SF-12 PCS: 3.6 (2.72 to 4.52) vs. 1.8 (0.54 to 3.08), adjusted difference 1.8 (0.37 to 3.25) SF-12 MCS: 2.5 (1.44 to 3.48) vs. −0.09 (−1.61 to 1.43), adjusted difference 2.6 (0.85 to 4.25) <u>10.5 months</u> SF-12 PCS: 4.9 (4.00 to 5.84) vs. 0.8 (−0.52 to 2.11), adjusted difference 4.1 (2.63 to 5.62) SF-12 MSC: 0.9 (−0.10 to 1.90) vs. 0.7 (−0.75 to 2.20), adjusted difference 0.2 (−1.48 to 1.84) <u>34 months</u> EuroQol-5 Dimensions (EQ-5D): 0.07 (0.04 to 0.10) vs. 0.04 (−0.01 to 0.09), adjusted difference 0.03 (−0.03 to 0.08)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Poole, 2007[93] 4.5 months Duration of pain: 10.6 vs. 9.5 years *Poor*	A. Respondent therapy (progressive muscle relaxation) (n=54), 6 sessions over 6-8 weeks B. Usual care (n=45)	A vs. B Age: 46 vs. 47 Female: 65% vs. 51% Baseline Oswestry Disability Index (0-100% ODI): 33.2 vs. 36.6 Baseline pain (0-100 VAS): 40.7 vs. 40.6	A vs. B <u>4.5 month</u> ODI (0-100): 31.3 vs. 32.9 Pain (0-100 VAS): 41.3 vs. 42.7	A vs. B <u>4.5 month</u> Beck Depression Inventory (0-63): 12.6 vs. 12.8 SF-36 physical functioning (0-100): 57.3 vs. 52.2 SF-36 social functioning (0-100): 66.7 vs. 61.5 SF-36 emotional role limitations (0-100): 63.0 vs. 62.0 SF-36 pain (0-100): 48.8 vs. 44.4 SF-36 mental health (0-100): 64.4 vs. 67.7 SF-36 general health perception (0-100): 52.4 vs. 55.0
Turner, 1990[109] 12 months Duration of pain: 12.9 years *Poor*	A. Operant therapy (n=25), 8 sessions over 8 weeks B. Exercise (n=24)	Overall Age: 44 Female: 48% A vs. B Baseline function (0-100 SIP): 7.9 vs. 8.4 Baseline pain (0-78 McGill Pain Rating): 21.0 vs. 19.4	A vs. B <u>6 months</u> Sickness Impact Profile (0-100 SIP): 7.6 vs. 6.3 McGill Pain Questionnaire Pain Rating Index (0-78): 19.5 vs. 15.7 <u>12 months</u> Sickness Impact Profile (0-100 SIP): 5.3 vs. 4.7 McGill Pain Questionnaire Pain Rating Index: 16.4 vs. 14.9	A vs. B <u>6 months</u> CES-D Scale (0-60): 11.4 vs. 9.3 <u>12 months</u> CES-D Scale: 8.3 vs. 9.3

BDI = Beck Depression Inventory; CBT = cognitive-behavioral therapy; CES-D = Center for Epidemiologic Studies-Depression; CI = confidence interval; MCS = Mental Component Score; NHP = Nottingham Health Profile; NR = not reported; ODI = Oswestry Disability Index; PCS = Physical Component Score; RDQ = Roland-Morris Disability Questionnaire; SF-36, Short-Form 36 Questionnaire; SIP = Sickness Impact Profile; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Psychological Therapy Compared With Usual Care or an Attention Control

Psychological therapy was associated with slightly greater effects on function than usual care or an attention control at short-term (3 trials, pooled SMD −0.25, 95% CI −0.38 to −0.12, I^2=0%),[89,91,93] intermediate-term (3 trials, pooled SMD −0.25, 95% CI −0.37 to −0.13, I^2=0%),[89-91] and long-term followup (3 trials, pooled SMD −0.27, 95% CI −0.39 to −0.15, I^2=0%) (Figure 6).[90,91,165] Pooled differences on the RDQ or modified RDQ were −1.2 to −1.4 points at all time points. For short-term function, two fair-quality trials[89,91,92] evaluated CBT and one poor-quality trial[93] evaluated respondent therapy (progressive relaxation). Excluding the poor-quality trial of progressive relaxation,[93] which found no effect on short-term function (SMD −0.08, 95% CI −0.48 to 0.31), had no effect on the pooled estimate (2 trials, pooled SMD −0.27, 95% CI −0.43 to −0.06).

Psychological therapy was associated with slightly greater effects on pain than usual care or an attention control at short-term (3 trials, pooled difference −0.76 on a 0 to 10 scale, 95% CI −0.99 to −0.53, I^2=0%),[89,91,93] intermediate-term (3 trials, pooled difference −0.71, 95% CI −0.94 to −0.48, I^2=0%),[89-91] or long-term followup (3 trials, pooled difference −0.53, 95% CI −0.78 to −0.27, I^2=0%) (Figure 7).[90,92,165] Excluding a poor-quality trial of progressive relaxation, which found no effect on short-term function (MD −0.14, 95% CI −1.28 to 1.00), did not change the pooled estimate (2 trials, pooled difference −0.78, 95% CI −1.06 to −0.49). For intermediate-term and long-term pain, all trials were fair quality and evaluated CBT.

Effects of psychological therapy on short-term or intermediate-term SF-36 Physical Component (PCS) or Mental Component (MCS) scores were small (differences 0 to 2 points on a 0 to 100 scale) and not statistically significant, except for short-term MCS (2 trials, pooled difference 2.12, 95% CI 0.79 to 3.45).[89,91] One trial found no effect of psychological therapy on work status or health care visits[92] and one trial found no effect of psychological therapy on markers of health care utilization. [166]

Psychological Therapy Compared With Pharmacological Therapy

No trial of psychological versus pharmacological therapy met inclusion criteria.

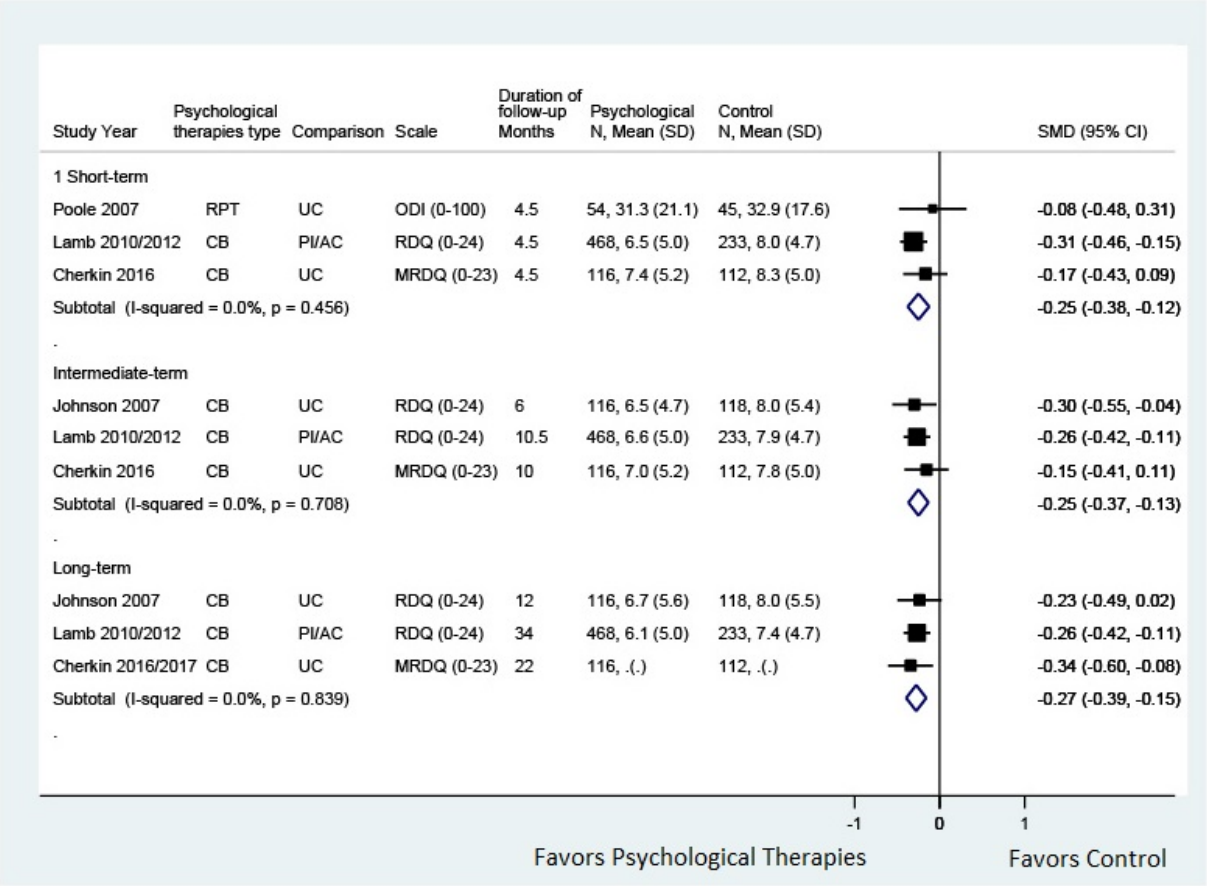
Psychological Therapy Compared With Exercise

One poor-quality trial found no differences between psychological versus exercise therapy in intermediate-term or long-term function.[109] Differences on the McGill Pain Questionnaire were less than 0.5 points on a 0 to 78 scale, and differences on the Sickness Impact Profile were 0.60 to 1.30 points on a 0 to 100 scale.

Harms

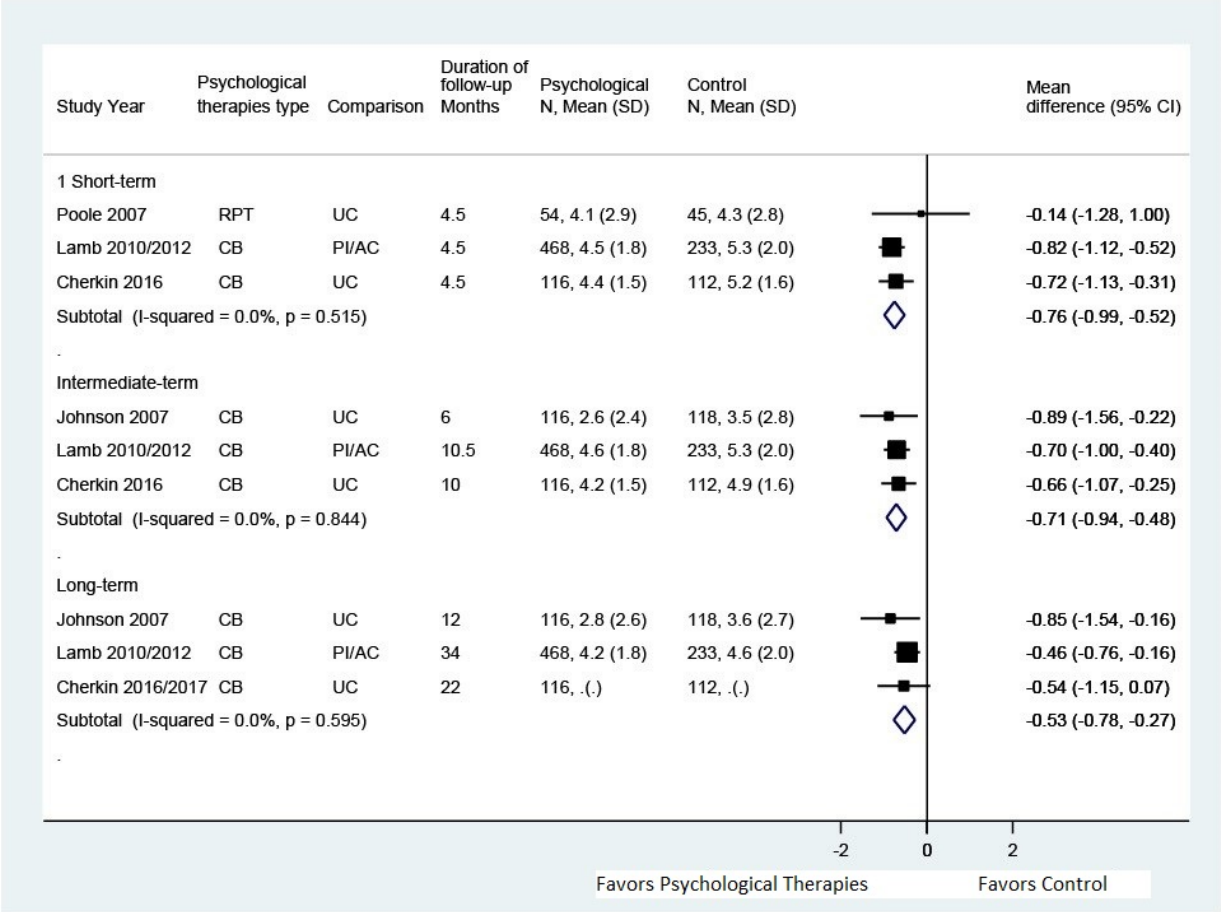
Data on harms were sparse. One trial reported no serious adverse events and one withdrawal due to adverse events among 468 patients randomized to CBT.[91,92]

Figure 6. Psychological therapy versus usual care or an attention control for chronic low back pain: effects on function



AC = attention control; CB = cognitive-behavioral therapy; CI = confidence interval; MRDQ = Modified Roland-Morris Disability Questionnaire; N = number; ODI = Oswestry Disability Index; PI = placebo intervention; RDQ = Roland-Morris Disability Questionnaire; RPT = respondent therapy (progressive relaxation); SD = standard deviation; SMD = standardized mean difference; UC = usual care

Figure 7. Psychological therapy versus usual care or an attention control for chronic low back pain: effects on pain



AC = attention control; CB = cognitive-behavioral therapy; CI = confidence interval; N = number; PI = placebo intervention; RPT = respondent therapy (progressive relaxation); SD = standard deviation; UC = usual care

Physical Modalities for Chronic Low Back Pain

Key Points

Ultrasound

- Two trials found inconsistent effects of ultrasound versus sham ultrasound on short-term function (SOE: insufficient).Two trials found no differences between ultrasound versus sham ultrasound in short-term pain (SOE: low).
- One trial found no differences between ultrasound versus sham ultrasound in risk of any adverse events or risk of serious adverse events (SOE: low).

Low-Level Laser Therapy

- One trial found low-level laser therapy associated with moderately greater effects than sham laser on short-term pain (MD −16.0 on a 0 to 100 scale, 95% CI −28.3 to −3.7) and slightly greater effects on function (MD −8.2 on the 0 to 100 ODI, 95% CI −13.6 to −2.8) (SOE: low).

- One trial found no differences between low-level laser therapy versus exercise therapy in intermediate-term function or pain (SOE: low).
- One trial of low-level laser therapy reported no adverse events (SOE: low).

Traction

- Two trials found no differences between traction versus sham traction in short-term pain or function (SOE: low).
- Harms were not reported in either trial.

Short-Wave Diathermy

- Data from a small, poor-quality trial were insufficient to determine effects of short-wave diathermy versus sham (detuned) diathermy (SOE: insufficient).

Detailed Synthesis

Ultrasound

Two trials (n=50 and n=455) of ultrasound versus sham ultrasound for low back pain met inclusion criteria (Table 7 and Appendix D).[115,116] The duration of ultrasound therapy was 4 and 8 weeks and the number of sessions was 6 and 10. Both trials evaluated outcomes at short-term (1 month) followup. One good-quality trial[116] was conducted in the United States and one fair-quality trial[115] in Iran (Appendix E). Methodological limitations in the fair-quality trial included failure to blind care providers and unclear blinding of outcome assessors.

Table 7. Chronic low back pain: physical modalities (ultrasound)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Ebadi, 2012[115] 1 month Duration of pain: Mean 6 to 8 years *Fair*	A. Ultrasound (n=25), 1.5 W/cm^2 at 1 MHz, 10 sessions over 4 weeks B. Sham ultrasound (n=25)	A vs. B Age: 31 vs. 37 years Female: 25% vs. 50% Functional Rating Index (mean, 0-100): 41 vs. 44 Pain intensity (mean, 0-100 VAS): 47 vs. 49	A vs. B <u>1 month</u> Functional Rating Index (0-40): 22.8 vs. 30.5; P=0.004 Pain (0-100 VAS): 27.7 vs. 25.5; P=0.48	

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Licciardone, 2013[116] 3 months Proportion with LBP duration >1 year: 50% *Good*	A. Ultrasound (n=233), 1.2 W/cm^2 at 1 MHz, 6 sessions over 8 weeks B. Sham ultrasound (n=222)	A vs. B Age: 38 vs. 43 years Female: 58% vs. 68% RDQ (0-24): 5 vs. 5 Pain intensity (0-100 VAS): 44 vs. 44	A vs. B <u>1 month, median (IQR)</u> RDQ (0-24): 3 (1-7) vs. 3 (1-7); P=0.93 Pain improved ≥30%: RR 1.03 (95% CI 0.87 to 1.23) Pain improved ≥50%: RR 1.09 (95% CI 0.88 to 1.35) Pain improved ≥20 mm on 0 to 100 VAS): RR 1.01 (95% CI 0.80 to 1.26) <u>2 months</u> RDQ (0-24): 3 vs. 4; P=0.76 ≥50% improvement in pain: RR 1.09 (95% CI 0.88 to 1.35) <u>3 months</u> RDQ (0-24): 3 vs. 3; P=0.93	A vs. B <u>1 month</u> SF-36 general health (0-100): 72 (52-87) vs. 74 (54-87); P=0.6 Lost 1 or more days work in past 4 weeks because of low back pain: 13% vs. 6%, P=0.11 Prescription drug use for LBP: 16% vs. 18%, P=0.54 SF-36 general health (0-100): 72 (52-87) vs. 74 (54-87), P=0.73 <u>2 months</u> SF-36 general health (0-100): 72 vs.72 (57-85); P=0.53 ≥50% improvement in pain: RR 1.09 (95% CI 0.88 to 1.35) <u>3 months</u> SF-36 general health (0-100): 72 vs. 74, P=0.66

CI = confidence interval; NR = not reported; RDQ = Roland-Morris Disability Questionnaire; RR = relative risk; SF-36 = Short-Form 36 Questionnaire; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Ultrasound Compared With Sham Ultrasound

Limited evidence indicated no clear differences between ultrasound versus sham ultrasound at short-term followup. One good-quality trial (n=455) found no difference between ultrasound versus sham ultrasound in the RDQ (median 3 vs. 3, P=0.93), likelihood for ≥50 percent improvement in pain (RR 1.09, 95% CI 0.88 to 1.35), SF-36 general health (median 72 vs. 74), likelihood of prescription drug use for low back pain (16% vs. 18%, P=0.54), or risk of serious adverse events (1.3% vs. 2.7%, RR 0.48, 95% CI 0.12 to 1.88) or any adverse event (6.0% vs. 5.9%, RR 1.03, 95% CI 0.49 to 2.13).[116] In the smaller (n=50) fair-quality trial, there was no difference between ultrasound versus sham ultrasound in pain (mean 27.7 vs. 25.5 on a 0 to 100 scale, P=0.48), although ultrasound was associated with better function (mean 22.8 vs. 30.5 on the 0 to 40 Functional Rating Index, P=0.004).[115] No trial evaluated longer-term outcomes.

Ultrasound Compared With Pharmacological Therapy or With Exercise

No trial of ultrasound versus pharmacological therapy or versus exercise met inclusion criteria.

Harms

One trial found no differences between ultrasound versus sham ultrasound in risk of any adverse event (RR 1.03, 95% CI 0.49 to 2.13) or serious adverse event (RR 0.48, 95% CI 0.12 to 1.88).[116]

Low-Level Laser Therapy

Three trials of low-level laser therapy (n=34, 56, and 71) met inclusion criteria (Table 8 and Appendix D).[117,118,143] One trial[118] evaluated neodymium:yttrium-aluminum-garnet (Nd:YAG) laser and two trials[117,143] evaluated gallium-arsenide (GaAs) laser. Two trials compared low-level laser therapy versus sham laser therapy[117,118] and one trial low-level laser therapy versus exercise plus sham laser.[143] One trial was conducted in the United States,[118] one in Iran,[143] and one in Argentina.[117] The duration of laser therapy ranged from 2 to 6 weeks and the number of sessions ranged from 10 to 12. One trial[117] reported intermediate-term outcomes and the other two trials reported short-term outcomes.

Two trials[118,143] were rated fair quality and one trial[117] poor quality (Appendix E). The major methodological limitation in the fair-quality trials was unclear allocation concealment methods.[118,143] The poor-quality trial also did not report randomization methods, did not conduct intention-to-treat analysis at intermediate-term followup, and reported high attrition; it was also unclear if timing of followup was the same in all patients.[117]

Table 8. Chronic low back pain: physical modalities (low-level laser therapy)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Basford, 1999[118] 2 months Duration of pain: 4.5 vs. 6.5 months *Fair*	A. Nd:YAG laser (542 mW/cm^2, 90 seconds, two sites, applied to eight points along L2 to S3 paraspinal tissues) (n=27) 12 sessions over 4 weeks B. Sham laser (n=29)	A vs. B Age: 48 vs.48 years Female: 40% vs. 55% Baseline ODI: 21 vs. 25 Baseline maximal pain, last 24 hours (0-100 VAS): 35.2 vs. 37.4	A vs. B <u>2 months</u> ODI (0-100): 14.7 vs. 22.9, difference -8.2 (95% CI −13.6 to −2.8); P=0.004 Maximal pain in last 24 hours (0-100 VAS): 19.1 vs. 35.1, difference −16.0 (95% CI −28.3 to −3.7); P=0.012	A vs. B <u>2 months</u> Patient perception of benefit (VAS, lower = less pain): 28.3 vs. 37.8 (95% CI −20.9 to 1.9); P=0.101

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Djavid, 2007[143] 1.5 months Duration of pain: 29 months vs. 29 months vs. 25 months *Fair*	A. GaAs laser (wavelength 810 nm, 50 mW wave, and 0.2211 cm^2 spot area laser applied to 8 points along L2 to S2-S3 paraspinal tissues, dose 27 J/cm^2) (n=16) 12 sessions over 6 weeks B. Low-level laser therapy plus exercise (n=19) C. Exercise plus sham laser (strengthening, stretching, mobilizing, coordination) (n=18)	A vs. B vs. C Age: 40 vs. 38 vs. 36 years Female: 5% vs. 7% vs. 2% Baseline ODI (0-100): 33.0 vs. 31.8 Baseline pain (0-10 VAS): 7.3 vs. 6.3	A vs. C <u>1.5 months</u> ODI (0-100): 20.8 vs. 24.1, difference in change from baseline −4.4 (95% CI −11.4 to 2.5) Pain (0-10 VAS): 4.4 vs. 4.3, difference in change from baseline −0.9 (95% CI −2.5 to 0.7) A vs. B <u>1.5 months</u> ODI (0-100): 20.8 vs. 16.8 difference in change from baseline −4.4 (95% CI −11.4 to 2.5) Pain (0-10 VAS): 4.4 vs. 2.4, difference in change from baseline −0.9 (95% CI −2.5 to 0.7)	NR
Soriano, 1998[117] 6 months Duration of pain: greater than 3 months *Poor*	A GaAs laser (wavelength 904 nm, pulse frequency 10,000 Hz, pulse width 200 nsec, peak power 20W, average power 40mW, administered at dose of 4 J/cm^2 per point to pain areas) (n=38) 10 sessions over 5 weeks B. Sham laser (n=33)	A vs. B Age: 63 vs. 64 years Female: 58% vs. 52% Baseline function: NR Baseline pain (1 to 10): 7.9 vs. 8.1	<u>6 months</u> No pain: 44.7% vs. 15%; P<0.01	Pain recurrence in subgroup of patients with a good or excellent response at end of treatment: 35 % vs. 70%; P=NR

CI =confidence interval; NR = not reported; ODI = Oswestry Disability Index; RDQ, Roland-Morris Disability Questionnaire; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Low-Level Laser Therapy Compared With Sham Laser

One fair-quality trial found Nd:YAG laser therapy associated with moderately lower pain (difference −16.0 on a 0 to 100 scale, 95% CI −28.3 to −3.7) and slightly better function (difference −8.2 points on the 0 to 100 ODI, 95% CI −13.6 to −2.8) at short-term followup.[118] A poor-quality trial found GaAs laser therapy associated with increased likelihood of having no pain at intermediate-term followup (44.7% vs. 15%, P<0.01), but the analysis was restricted to patients who reported that laser therapy was effective at the end of a 2-week course of treatment.[117]

Low-Level Laser Therapy Compared With Pharmacological Therapy

No trial of low-level laser therapy compared with pharmacological therapy met inclusion criteria.

Low-Level Laser Therapy Compared With Exercise Therapy

One fair-quality trial found no clear differences between GaAs laser therapy versus exercise plus sham laser in function (difference in change from baseline −4.4 on the 0 to 100 ODI, 95% CI −11.4 to 2.5) or pain (difference in change from baseline −0.9 on a 0 to 10 scale, 95% CI −2.5 to 0.7) at intermediate-term followup.[143] For pain, the difference at followup was similar to the baseline difference (mean 7.3 vs. 6.3), and final scores were very similar (4.4 vs. 4.3).

Harms

No adverse events were reported in any of the three trials of low-level laser therapy.[117,118,143]

Traction

Two trials of traction (n=151 and 60) met inclusion criteria (Table 9 and Appendix D).[113,114] One trial[113] evaluated continuous traction (12 sessions in 5 weeks) and the other[114] evaluated intermittent traction (20 sessions in 6 weeks). The comparator in both trials was sham traction (traction at <10% or 20% of body weight, compared with 35% to 50% for active traction). Both trials were conducted in the Netherlands and reported only short-term outcomes. The trials were rated fair quality due to failure to blind care providers (Appendix E).

Table 9. Chronic low back pain: physical modalities (traction)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Beurskens, 1997[113] 1.75 and 5 months Duration of pain: 1.5 months *Fair*	A. Continuous traction (n=77) B. Sham traction (20% body weight) (n=74) 12 sessions, 5 weeks	A vs. B Age: 39 vs. 42 years Female: 44% vs. 43% Baseline RDQ (0-24): 2 vs. 12 Baseline pain (0-100 VAS): 61 vs. 55	A vs. B <u>1.75 months</u> RDQ: 4.4 vs. 4.3, difference 0.1 (95% CI −1.8 to 1.9) Pain at the moment (0-100 VAS): 28.5 vs. 22.8, difference 5.7 (95% CI −4.6 to 15.9) <u>5 months</u> RDQ: 4.7 vs. 4.0, difference 0.7 (95% CI −1.1 to 2.6) Pain at the moment (0-100 VAS): 23.8 vs. 20.1, difference 3.7 (95% CI −8.4 to 15.8)	A vs. B <u>1.75 months</u> ADL disability (0 to 100 VAS): 27.1 vs. 29.4, difference −2.4 (95% CI −13.6 to 8.9) Work absence (days): 23.5 vs. 27.8, difference −4.3 (95% CI −14.7 to 6.1) Medical consumption: 34% vs. 25%, difference 9% (95% CI −6 to 24) <u>5 months</u> ADL disability: 25.7 vs. 25.8, difference 0.1 (95% CI −11.5.0 to 11.2) Work absence (days): 35.7 vs. 43.7, difference −8.0 (95% CI −27 to 11) Medical consumption: 45% vs. 42%, difference 3% (95% CI −13% to 19%)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Schimmel, 2009[114] 2 months Duration of pain: 1 year *Fair*	A. Intermittent traction (n=31) B. Sham traction (<10% body weight) (n=29) 20 sessions, 6 weeks	A vs. B Age (mean): 42 vs. 46 years Female: 39% vs. 52% Baseline ODI: 36 vs. 33 Baseline back pain (0-100 VAS): 61 vs. 53	A vs. B <u>2 months</u> ODI (0-100): 25 vs. 23 (SD, P not reported) Pain (0-100 VAS): 32 vs. 36; P=0.70	A vs. B <u>2 months</u> SF-36, total (0-100): 66 vs. 65 (SD, P-value not reported)

ADL = activities of daily living; CI = confidence interval; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SF-36 =Short-Form 36 Questionnaire; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Traction Compared With Sham Traction

There were no differences between traction versus sham traction at short-term followup in function (25 vs. 23 on the 0 to 100 ODI in one trial and 4.7 vs. 4.0 on the 0 to 24 RDQ, difference 0.7, 95% CI −1.1 to 2.6) or pain (32 vs. 36 on a 0 to 100 scale, P=0.70 and 24 vs. 20, difference 3.7, 95% CI −8.4 to 15.8).[113,114] One trial[114] also found no difference between intermittent traction versus sham on the total SF-36 (66 vs. 65 on a 0 to 100 scale) and one trial[113] found no difference between continuous traction versus sham in global perceived effect, work absence, or medical consumption.

Traction Compared With Pharmacological Therapy or With Exercise

No trial of low-level laser therapy compared with pharmacological therapy or with exercise met inclusion criteria.

Harms

Neither trial reported harms.

Short-Wave Diathermy

Data were insufficient from one poor-quality trial (n=68) to evaluate effects of short-wave diathermy (3 times weekly for 4 weeks) versus sham (detuned) diathermy for low back pain (Table 10 and Appendix D).[119] Methodological limitations included unclear randomization and allocation concealment methods, differential attrition, and baseline differences between groups (Appendix E). Although diathermy was associated with worse pain than sham treatment at short-term (8 weeks after completion of therapy) followup (25 vs. 13); statistical significance was not reported. There were no statistically significant differences in likelihood of using analgesics (7% vs. 22%, RR 0.34, 95% CI 0.08 to 1.50) or being unable to work or having limited activities (7% vs. 19%, RR 0.40, 95% CI 0.09 to 1.80), but estimates were imprecise.

Harms

Adverse events were not evaluated in the trial.

Table 10. Chronic low back pain: physical modalities (short-wave diathermy)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Gibson, 1985[119] 2 months Duration of pain: 2 to 12 months *Poor*	A. Short wave diathermy (active SWD) (n=34), 12 sessions, 3 session/per week for 4 weeks B. Placebo (detuned SWD) (n=34)	A vs. B Age: 35 vs. 40 years Female: 47% vs. 32% Pain (0-100 VAS): 45 vs. 48	A vs. B <u>2 months</u> Pain (0-100 VAS, median): 25 vs. 13 (IQR not reported) Unable to work or with limited activities: 7% vs. 19% RR 0.40, 95% CI 0.09 to 1.80	A vs. B <u>2 months</u> Using analgesics: 7% vs. 22%, RR 0.34, 95% CI 0.08 to 1.50

CI = confidence interval; IQR = interquartile range; RR = relative risk; SWD = short wave diathermy; VAS = visual analog scale
[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Manual Therapies for Chronic Low Back Pain

Key Points

Spinal Manipulation

- Spinal manipulation was associated with slightly greater effects than sham manipulation, usual care, an attention control, or a placebo intervention in short-term function (3 trials, pooled SMD −0.34, 95% CI −0.63 to −0.05, I^2=61%) and intermediate-term function (3 trials, pooled SMD −0.40, 95% CI −0.69 to −0.11, I^2=76%) (SOE: low).
- There was no evidence of differences between spinal manipulation versus sham manipulation, usual care, an attention control, or a placebo intervention in short-term pain (3 trials, pooled MD −0.20 on a 0 to 10 scale, 95% CI −0.66 to 0.26, I^2=58%), but manipulation was associated with slightly greater effects than controls on intermediate-term pain (3 trials, pooled MD −0.64, 95% CI −0.92 to −0.36, I^2=0%) (SOE: low for short term, moderate for intermediate term).
- There was no evidence of differences between spinal manipulation versus exercise in short-term function (3 trials, pooled SMD 0.01, 95% CI −0.22 to 0.25; I^2=62%) or intermediate-term function (4 trials, pooled SMD 0.02, 95% CI −0.13 to 0.18; I^2=48%) (SOE: low).
- There was no evidence of differences between spinal manipulation versus exercise in short-term pain (3 trials, pooled MD 0.31 on a 0 to 10 scale, 95% CI −0.30 to 0.92; I^2=60%) or intermediate-term pain (4 trials, pooled MD 0.22, 95% CI −0.09 to 0.52, I^2=9.4%) (SOE: low).
- No serious adverse events or withdrawals due to adverse events were reported in seven trials; nonserious adverse events with manipulation (primarily increased pain) were reported in 3 trials (SOE: low).

Massage

- Massage was associated with slightly greater effects on short-term function than sham massage or usual care (4 trials, SMD −0.30, 95% CI −0.46 to −0.14, I^2=0%). There was

no evidence of differences between massage versus controls in intermediate-term function (3 trials, SMD −0.09, 95% CI −0.24 to 0.06, I^2=0%) (SOE: moderate for short term, low for intermediate term).

- Massage was associated with slightly greater effects on short-term pain than sham massage or usual care (4 trials, pooled MD −0.52 on a 0 to 10 scale, 95% CI −0.81 to −0.23, I^2=0%). There was evidence of differences between massage versus controls in intermediate-term pain (3 trials, pooled MD −0.01, 95% CI −0.40 to 0.38, I^2=0%) (SOE: moderate for short term, low for intermediate term).
- One trial found no differences between massage versus exercise in intermediate-term function or pain (SOE: low).
- Two trials of massage reported no serious adverse events; in four trials, the proportion of massage patients who reported increased pain ranged from <1 to 26 percent (SOE: low).

Detailed Synthesis

Spinal Manipulation

Eight trials of spinal manipulation for low back pain met inclusion criteria (Table 11 and Appendix D).[119,144-147,160-162] All of the trials evaluated standard (high-velocity low-amplitude) manipulation techniques; one trial[162] evaluated flexion-distraction manipulation and one trial[145] evaluated both high-velocity low-amplitude and flexion-distraction manipulation. Sample sizes ranged from 75 to 1,001 (total sample=2,586). The number of manipulation therapy sessions ranged from 4 to 24 and the duration of therapy ranged from 4 to 12 weeks. In one trial, patients were randomized to 12 manipulation sessions over 1 month or to 12 sessions over 1 month plus biweekly maintenance sessions for an additional 10 months.[146] Two trials compared spinal manipulation versus usual care,[145,147] one trial spinal manipulation versus an attention control (minimal massage),[144] one trial spinal manipulation versus sham manipulation,[146] one trial spinal manipulation versus a placebo treatment (sham short-wave diathermy),[119] and four trials spinal manipulation versus exercise.[147,160-162] One trial was conducted in Egypt[146] and the rest in the United States, United Kingdom, or Australia. Six trials reported outcomes through intermediate-term followup,[144,146,147,160-162] and two trials only evaluated short-term outcomes.[119,145]

Two trials[119,146] were rated poor quality and the remainder fair quality (Appendix E). The major methodological limitation in the fair-quality trials was use of an unblinded design. Methodological shortcomings in the poor-quality trials included unclear randomization and allocation concealment methods, failure to report intention-to-treat analysis, and high attrition.

Table 11. Chronic low back pain: manual therapies (spinal manipulation)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Bronfort, 2011[160] 9 months Duration of pain: 5 years *Fair*	A. Standard manipulation (n=100), 12-24 sessions over 12 weeks B. Exercise (supervised) (n=100) C. Exercise (home) (n=101)	A vs. B Age: 45.2 vs. 44.5 vs. 45.6 years Female sex: 67% vs. 57% vs. 58% Baseline Modified RDQ (0-23): 8.7 vs. 8.4 vs. 8.7 Baseline pain (0-10 NRS): 5.4 vs. 5.1 vs. 5.2	A vs. B <u>4 months</u> Modified RDQ (0-23): 4.9 vs. 4.0 vs. 4.2, adjusted difference 0.5 (95% CI −1.0 to 2.1) for A vs. B and 0.7 (95% CI −0.9 to 2.3) for A vs. C Pain (0-10 NRS): 3.3 vs. 2.9 vs. 3.1, adjusted difference 0.3 (95% CI −0.5 to 1.0) for A vs. B and 0.1 (95% CI −0.6 to 0.9) for A vs. C <u>9 months</u> Modified RDQ (0-23): 5.1 vs. 3.8 vs. 4.1, adjusted difference 0.4 (95% CI −1.2 to 2.0) for A vs. B and −0.1 (95% CI −0.7 to 0.5) for A vs. C Pain (0-10 NRS): 3.3 vs. 2.8 vs. 2.8, adjusted difference 0.3 (95% CI −0.5 to 1.1) for A vs. B and 0.3 (95% CI −0.6 to 1.1) for A vs. C	A vs. B <u>4 months</u> SF-36 PCS (norm-based mean=50): 48.6 vs. 50.6 vs. 49.1, adjusted difference −1.8 (95% CI −4.4 to 0.9) for A vs. B and −0.3 (95% CI −3.0 to 2.4) for A vs. C SF-36 MCS (norm-based mean=50): 55.9 vs. 54.8 vs. 55.1, adjusted difference 0.4 (95% CI −2.0 to 2.9) for A vs. B and −0.5 (95% CI −3.0 to 2.1) for A vs. C OTC pain medication use, past week (days): 1.6 vs. 1.4 vs. 1.5, adjusted difference 0.4 (95% CI −0.4 to 1.1) for A vs. B and 0.4 (95% CI −0.3 to 1.2) for A vs. C <u>9 months</u> SF-36 PCS (norm-based mean=50): 48.4 vs. 50.4 vs. 49.6, adjusted difference −1.7 (95% CI −4.2 to 0.8) for A vs. B and −1.0 (95% CI −3.5 to 1.5) for A vs. C SF-36 MCS (norm-based mean=50): 55.2 vs. 53.9 (8.6) vs. 56.0, adjusted difference 2.4 (95% CI −0.2 to 5.0) for A vs. B and −2.2 (95% CI −4.9 to 0.5) for A vs. C OTC pain medication use, past week (days): 1.8 vs. 1.8 vs. 1.6, adjusted difference 0.1 (95% CI −0.8 to 0.9) for A vs. B and 0.4 (95% CI −0.4 to 1.3) for A vs. C

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Ferreira, 2007[161] 10 months Duration of pain: Not reported *Fair*	A. Standard manipulation and mobilization (n=80), 12 sessions over 8 weeks B. Exercise (motor control) (n=80) C: Exercise (general exercise) (n=80)	A vs. B vs. C Age: 54 vs. 52 vs. 55 years Female: 70 % vs. 66% vs. 70% Baseline RDQ (0-24): 12.4 vs. 14.0 vs. 14.1 Baseline pain (0-10 VAS): 6.2 vs. 6.3 vs. 6.5	A vs. B vs. C <u>4 months</u> RDQ (0-24): 7.7 vs. 8.4 vs. 10.1, difference 0.2 (95% CI −1.5 to 1.9) for A vs. B and −0.9 (95% CI −2.7 to 0.9) for A vs. C Pain (0-10 VAS): 4.3 vs. 4.3 vs. 4.8, difference 0.0 (95% CI −0.9 to 0.8) for A vs. B and −0.5 (95% CI −1.4 to 0.3) for A vs. C <u>10 months</u> RDQ (0-24): 9.2 vs. 8.8 vs. 9.6, difference 1.8 (95% CI 0.0 to 3.6) for A vs. B and 1.2 (95% CI −0.6 to 3.0) for A vs. C Pain (0-10 VAS): 4.9 vs. 4.9 vs. 5.2, difference 0.1 (95% CI −0.8 to 1.0) for A vs. B and −0.2 (95% CI −1.1 to 0.6) for A vs. C	A vs. B vs. C <u>4 months</u> Patient Specific Functional Scale (3-30): 17.3 vs. 16.4 vs. 15.0, difference 0.7 (95% CI −1.3 to 2.7) for A vs. B and 1.7 (95% CI −0.4 to 3.,8) for A vs. C <u>10 months</u> Patient Specific Functional Scale (3-30): 15.2 vs. 15.7 (6.8) vs. 13.9, difference −0.8 (95% CI −2.9 to 1.2) for A vs. B and 0.3 (95% CI −1.7 to 2.3) for A vs. C
Gibson, 1985[119] 2 months Duration of pain: 2 to 12 months *Poor*	A. Manipulation (technique unclear) and mobilization (n=41), 4 sessions over 4 weeks B. Placebo (detuned short-wave diathermy) (n=34)	A vs. B 34 vs. 40 years Female: 61% vs. 32% Baseline pain (0-100 VAS): 35 vs. 48	A vs. B <u>1 month</u> Pain (median [range], 0-100 VAS): 28 (0−96) vs. 27(0-80) <u>3 months</u> Pain (median [range], 0-100 VAS): 25 (4-90) vs. 6 (10-96) P<0.01	A vs. B <u>1 month</u> Using analgesics: 25% vs. 50% <u>3 months</u> Using analgesics: 18% vs. 22%
Gudavalli, 2006[162] 11 months Duration of pain: >3 months *Fair*	A. Flexion–distraction manipulation (n=123), 8-16 sessions over 4 weeks B. Exercise (n=112)	A vs. B Age: 42 vs. 41 years Female: 34% vs. 41% Baseline RDQ (0-24): 6.64 vs. 6.84 Baseline pain VAS (0-100: 38.00 vs. 35.70	A vs. B <u>2 months</u> RDQ (0-24): 3.50 (SD 0.50) vs. 3.75 (SD 0.51) Pain (0-100 VAS): 16.52 (SD 2.95) vs.12.04 (SD 2.53) <u>5 months</u> RDQ (0-24): 3.89 (SD 0.46) vs. 3.42 (SD 0.50) Pain (0-100 VAS): 18.26 (SD 2.64) vs. 8.92 (SD 2.89) <u>11 months</u> RDQ (0-24): 3.90 (SD 0.53) vs. 3.77 (SD 0.44) Pain (0-100 VAS): 17.10 (SD 2.55) vs. 12.36 (SD 2.43)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Haas, 2014[144] 10.5 months Duration of pain: 11 to 12 years *Fair*	A. Standard spinal manipulation (n=100), 6 sessions over 6 weeks B. Standard manipulation (n=100), 12 sessions over 6 weeks C. Standard manipulation (n=100), 18 sessions over 6 weeks D: Attention control (minimal massage) (n=100)	A vs. B vs. C vs. D Age: 41 vs. 42 vs. 41 vs. 41 Female: 49% vs. 49% vs. 52% vs. 49% Baseline Modified Von Korff functional disability (0–100): 44.8 vs.46.1 vs.45.2 vs. 45.2 Baseline Pain (0–100 VAS): 51.0 vs. 51.6 vs. 51. vs. 52.2 Baseline Von Korff pain intensity (0–100): 51.0 vs. 51.6 vs. 51.5 vs. 52.2	A vs. B <u>4 months</u> Von Korff functional disability (0-100): 25.6 vs. 24.0 vs. 24.1 vs. 27.1, adjusted difference −1.4 (95% CI −7.2 to 4.5) for A vs. D, −3.4 (95% CI −9.3 to 2.4) for B vs. D, and −2.9 (95% CI −8.8 to 2.9) for C vs. D Von Korff functional disability improved ≥50%: 51.5% vs. 59.8% vs. 54.0% vs. 49.5%, adjusted difference 2.5% (95% CI −11.5 to 16.5%) for A vs. D, 10.4% (95% CI −3.4 to 24.3%) for B vs. D, and 4.8% (95% CI −9.1 to 18.6%) for C vs. D Von Korff pain intensity (0-100): 32.5 vs. 33.7 vs. 32.1 vs. 34.9, adjusted difference −1.7 (95% CI −6.9 to 3.4) for A vs. D, −0.8 (95% CI −6.0 to 4.4) for B vs. D, and −2.4 (95% CI −7.6 to 2.9) for C vs. D <u>10.5 months</u> Von Korff functional disability (0-100): 22.6 vs. 22.4 vs. 19.1 vs. 28.0, adjusted difference −5.2 (95% CI −10.9 to 0.5) for A vs. D, −5.9 (95% CI −11.8 to −0.1) for B vs. D, and −8.8 (95% CI −14.4 to −3.3) for C vs. D Von Korff functional disability improved ≥50%: 57.6% vs. 57.7% vs. 62.0% vs. 58.9%, adjusted difference −1.1% (95% CI −14.8 to 12.6%) for A vs. D, −1.4% (95% CI −15.4 to 12.6%) for B vs. D, and 2.7% (95% CI −11.0 to 16.5%) for C vs. D Von Korff pain intensity (0-100): 30.7 vs. 31.9 (vs. 28.7 vs. 36.5, adjusted difference −5.4 (95% CI −11.1 to 0.4) for A vs. D, −4.6 (95% CI −10.3 to 1.2) for B vs. D, and −7.6 (95% CI −13.2 to −2.0) for C vs. D	A vs. B <u>4 months</u> SF-12 PCS (norm-based mean=50): 50.5 vs. 51.4 vs. 50.9 vs. 50.0, adjusted difference 0.0 (95% CI −2.4 to 2.3) for A vs. D, −0.8 (95% CI −3.2 to 1.6) for B vs. C, and −1.3 (95% CI −3.6 to 1.1) for C vs. D SF-12 MCS (norm-based mean=50): 52.8 vs. 50.8 vs. 51.3 vs. 51.8, adjusted difference −2.1 (95% CI −4.2 to 0.0) for A vs. D, −0.7 (95% CI −2.8 to 1.3) for B vs. D, and −0.1 (95% CI −2.2 to 2.1) for C vs. D EuroQoL (0-100): 77.8 vs. 77.0 vs. 74.5 vs. 73.9, difference −2.9 (95% CI −6.9 to 1.0) for A vs. D, −1.4 (95% CI −5.5 to 2.6) for B vs. D, and −1.5 (95% CI −5.8 to 2.7) for C vs. D <u>10.5 months</u> SF-12 PCS (norm-based mean=50): 50.8 vs. 52.6 vs. 52.5 vs. 50.7, adjusted difference −0.3 (95% CI −2.1 to 2.7) for A vs. D, −1.4 (95% CI −4.0 to 1.2) for B vs. D, and −2.2 (95% CI −4.5 to 0.2) for C vs. D SF-12 MCS (norm-based mean=50): 50.4 vs. 50.6 vs. 50.4 vs. 51.3, adjusted difference −0.2 (95% CI −2.7 to 2.3) for A vs. D, −1.1 (95% CI −3.7 to 1.6) for B vs. D, and 0.3 (95% CI −2.3 to 2.9) for C vs. D EuroQoL (0-100): 77.1 vs. 77.3 vs. 77.2 vs. 74.8, adjusted difference −1.3 (95% CI −5.4 to 2.7) for A vs. D, −0.9 (95% CI −4.9 to 3.1) for B vs. D, and −3.3 (95% CI −7.2 to 0.5) for C vs. D

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Hondras, 2009[145] 4.5 months Duration of pain: Mean 9 to 13 years *Fair*	A. Standard manipulation (n=96), 12 sessions over 6 weeks B. Flexion distraction manipulation (n=95), 12 sessions over 6 weeks C: Usual care (n=49)	A vs. B vs. C Age: 64 vs. 62 vs. 63 years Female: 45% vs. 44% vs. 41% Baseline RDQ (0-24), mean (SD): 6.5 vs. 6.6 vs. 5.7 Baseline pain (0-100 VAS): 42.1 (23.6) vs. 42.5 (25.2) vs. 42.4 (24.5)	<u>1.5 months</u> RDQ (0-24): adjusted difference −1.5 (95% CI −3.1 to 0.1) for A vs. C and −2.2 (95% CI −3.7 to −0.6) for B vs. C Global improvement from baseline (1-10): adjusted difference 1.3 (95% CI 0.2 to 2.3) for A vs. C and 1.6 (95% CI 0.5 to 2.7) for B vs. C <u>4.5 months</u> RDQ (0-24): adjusted difference −1.3 (95% CI −2.9 to 0.6) for A vs. C and −1.9 (95% CI −3.6 to −0.2) for B vs. C Global improvement from baseline (1-10): adjusted difference 1.7 (95% CI 0.5 to 2.8) for A vs. C and 1.8 (95% CI 0.6 to 3.0) for B vs. C	NR
Senna, 2011[146] 9 months Duration of pain: 18-19 months *Poor*	A. Standard manipulation (n=27), 12 sessions over 4 weeks B. Standard manipulation maintained (n=27) , 12 sessions over 4 weeks, plus every 2 weeks for 9 months C. Sham manipulation (n=40)	A vs. B Age: 40 vs. 42 vs. 42 years Female: 27% vs. 24% vs. 24% Baseline function (0-100 ODI): 39 vs. 40 vs. 38 Baseline pain (0-100 VAS): 42 vs. 43 vs. 41	A vs. B <u>3 months</u> ODI (0-100): 29.8 vs. 23.1 vs. 33.5; p>0.05 Pain (0-100 VAS): 35.2 vs. 25.9 vs. 35.2; p>0.05 <u>6 months</u> ODI (0-100): 32.2 vs. 22.4 vs. 35.3; p>0.05 Pain (0-100 VAS): 35.5 vs. 25.4 vs. 36.8; p>0.05 <u>9 months</u> ODI (0-100): 34.9 vs. 20.6 vs. 37.4 Pain (0-100 VAS): 38.5 vs. 23.5 vs. 38.3	A vs. B <u>3 months</u> SF-36, total (0-100): 29.2 vs. 32.8 vs. 26.4; p>0.05 <u>6 months</u> SF-36, total (0-100): 27.8 vs. 33.1 vs. 26.1; p>0.05 <u>9 months</u> SF-36, total (0-100): 27.6 vs. 33.70 vs. 25.9; p>0.05

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
UK BEAM Trial Team, 2004[147] 9 months Duration of pain: >3 months in 59% *Fair*	A: Standard manipulation (n=353), 8 sessions over 12 weeks B: Usual care (n=338) C: Exercise (n=310)	A vs. B vs. C Age: 42 vs. 42 vs. 44 Female: 63% vs. 53% vs. 55% Baseline RDQ (0-24): 8.9 and 8.9 vs. 9.0 vs. 9.2 Baseline Von Korff Pain (0-100): 61.4 and 61.6 vs. 60.5 vs. 60.8	A vs. B 9 months RDQ (0-24): 5.15 vs. 6.16, adjusted difference −1.01 (95% CI −1.81 to −0.22) Von Korff Disability (0-100): 29.85 vs. 35.50, adjusted difference −5.65 (95% CI −9.72 to −1.57) Von Korff Pain (0-100): 41.68 vs. 47.56, adjusted difference −5.87 (95% CI −10.17 to −1.58) A vs. C 9 months RDQ (0-24): 5.15 (0.29) vs. 5.74 (0.31) Von Korff Disability (0-100): 29.85 (1.50) vs. 29.73 (1.68) Von Korff Pain (0-100): 41.68 (1.58) vs. 41.54 (1.84)	A vs. B 9 months SF-36 PCS (0-100): 44.18 vs. 42.50, adjusted difference 1.68 (95% CI 0.18 to 3.19) SF-36 MCS (0-100): 48.09 vs. 46.41, adjusted difference 1.68 (95% CI −0.21 to 3.57) A vs. C 9 months SF-36 PCS (0-100): 44.18 (0.55) vs. 44.39 (0.63) SF-36 MCS (0-100): 48.09 (0.69) vs. 46.77 (0.81)

CI = confidence interval; MCS = Mental Component Summary; NR = not reported; ODI = Oswestry Disability Index; OTC = over-the-counter; PCS = Physical Component Score; RDQ = Roland-Morris Disability Questionnaire; SF-36 = Short-Form 36 Questionnaire; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Spinal Manipulation Compared With Sham Manipulation, Usual Care, an Attention Control, or a Placebo Intervention

Spinal manipulation was associated with slightly greater effects on function than controls at short-term followup (3 trials, SMD −0.34, 95% CI −0.63 to −0.05, I^2=61%)[144-146] and intermediate-term followup (3 trials, SMD −0.40, 95% CI −0.69 to −0.11, I^2=76%)[144,146,147] (Figure 8). Based on the original 0 to 100 scales (ODI and Von Korff functional disability [VF]) used in the trials, the difference was −4.94 (95% CI −9.36 to −0.53) for short-term function and −9.19 (95% CI −12.77 to −5.61) for intermediate-term function. Estimates were similar when a poor-quality trial[146] was excluded. For short-term function, one trial reported similar effects for standard manipulation (difference −1.3 on the RDQ, 95% CI −2.9 to 0.6) and flexion-distraction manipulation (differenced −1.9, 95% CI −3.6 to −0.2); therefore, results for both arms were combined for the pooled analysis.[145]

There was no clear difference between spinal manipulation versus sham manipulation, an attention control, or a placebo intervention in short-term pain (3 trials, pooled difference −0.20 on a 0 to 10 scale, 95% CI −0.66 to 0.26, I^2=58%) (Figure 9).[119,144,146] Two of the trials were rated poor quality; the results of the fair-quality trial[144] were consistent with the overall estimate (difference −0.21, 95% CI −0.68 to 0.25). Manipulation was associated with slightly greater effects on intermediate-term pain than sham manipulation, usual care, or an attention control (3 trials, pooled difference −0.64 on a 0 to 10 scale, 95% CI −0.92 to −0.36, I^2=0%).[144,146,147] The estimate was similar when a poor-quality trial[146] was excluded (2 trials, difference −0.60, 95% CI −0.98 to −0.22).[144,147]

Two trials found no clear differences between spinal manipulation versus controls on the SF-36 MCS and PCS at short term.[144,147] One trial[144] found no differences at short-term or intermediate-term followup and the other[147] found manipulation associated with slightly better PCS scores at intermediate-term followup, but the difference was very small (1.68 on a 0 to 100 scale, 95% CI 0.08 to 3.28).

Spinal Manipulation Compared With Pharmacological Therapy

No trial of spinal manipulation versus pharmacological therapy met inclusion criteria.

Spinal Manipulation Compared With Exercise

There were no differences between spinal manipulation versus exercise in function at short-term (3 trials, SMD 0.01, 95% CI −0.22 to 0.25, I^2=62%)[160-162] or intermediate-term followup (4 trials, SMD 0.02, 95% CI −0.13 to 0.18, I^2=48%)[147,160-162] (Figure 10). Excluding one trial[162] of flexion-distraction manipulation resulted in similar findings.

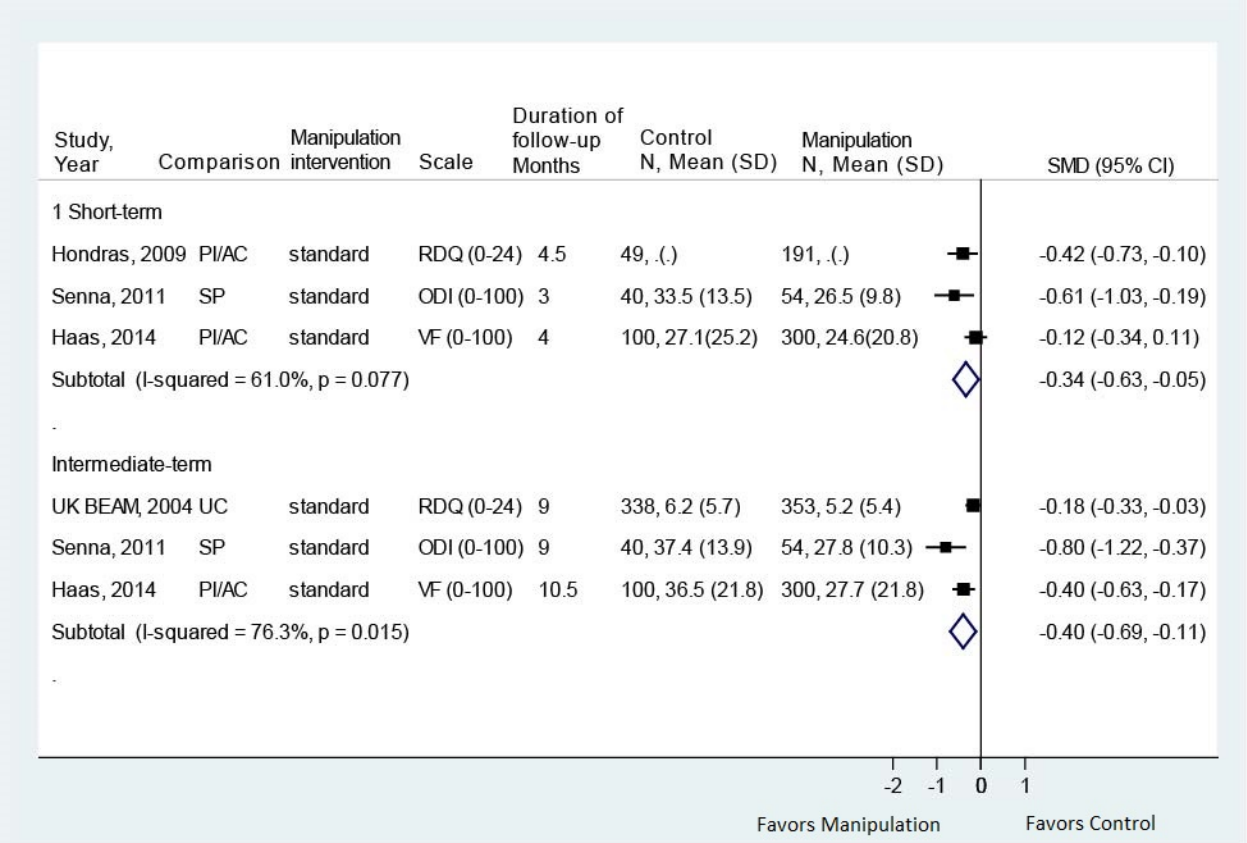
There were no differences between spinal manipulation versus exercise in short-term pain (3 trials, pooled difference 0.31, 95% CI −0.30 to 0.92, I^2=60%)[160-162] or intermediate-term pain (4 trials, pooled difference 0.22, 95% CI −0.09 to 0.52, I^2=9.4%) (Figure 11).[147,160-162] Excluding one trial[162] of flexion-distraction manipulation resulted in similar findings.

Two trials found no clear differences between spinal manipulation versus controls on the SF-36 MCS and PCS at short term.[147,160] One trial[144] found no differences at short-term or intermediate-term followup, and the other[147] found manipulation associated with slightly better PCS scores at intermediate-term followup, but the difference was very small (1.68 on a 0 to 100 scale, 95% CI 0.08 to 3.28).

Harms

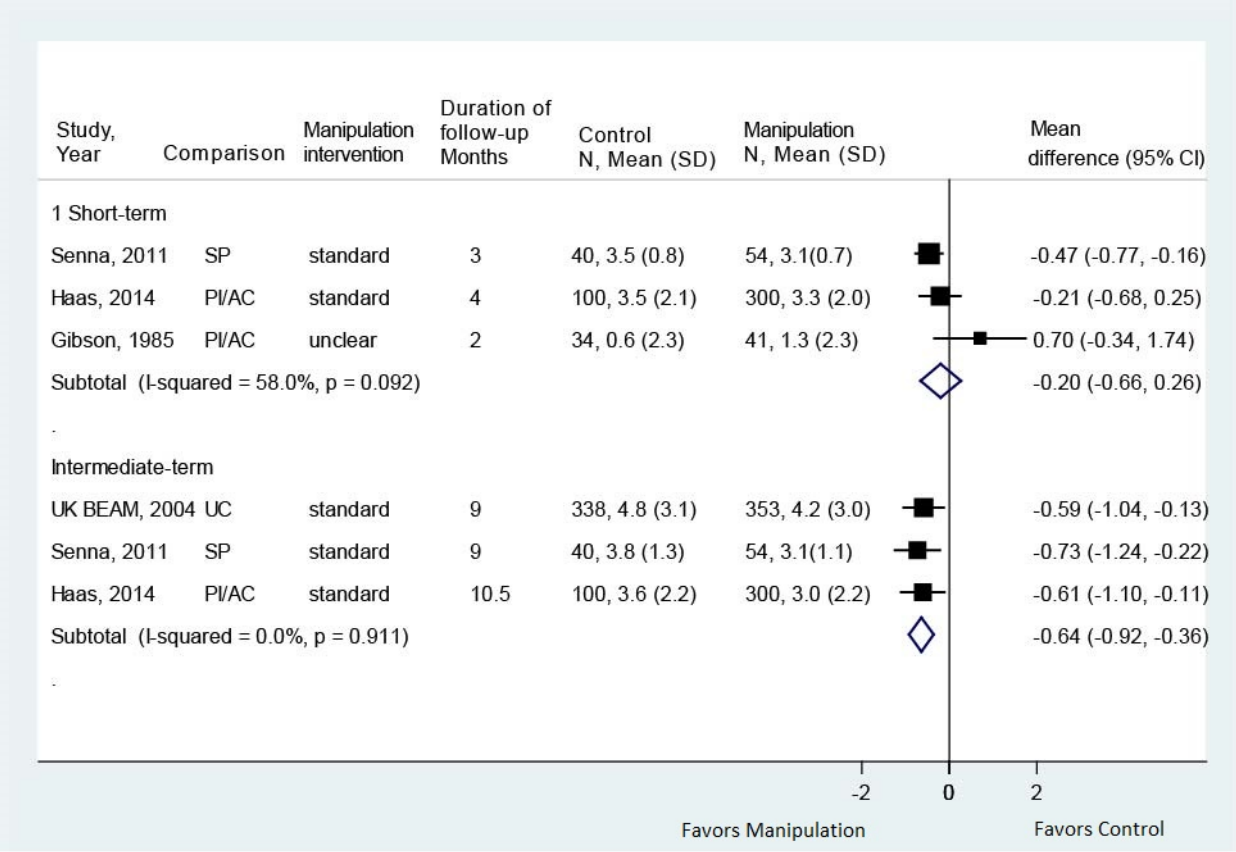
Seven trials reported no serious adverse events or withdrawals due to adverse events.[144-147,160-162] Nonserious adverse events (primarily increased pain) were reported in three trials.[144,146,160]

Figure 8. Spinal manipulation versus sham manipulation, usual care, an attention control, or a placebo intervention for chronic low back pain: effects on function



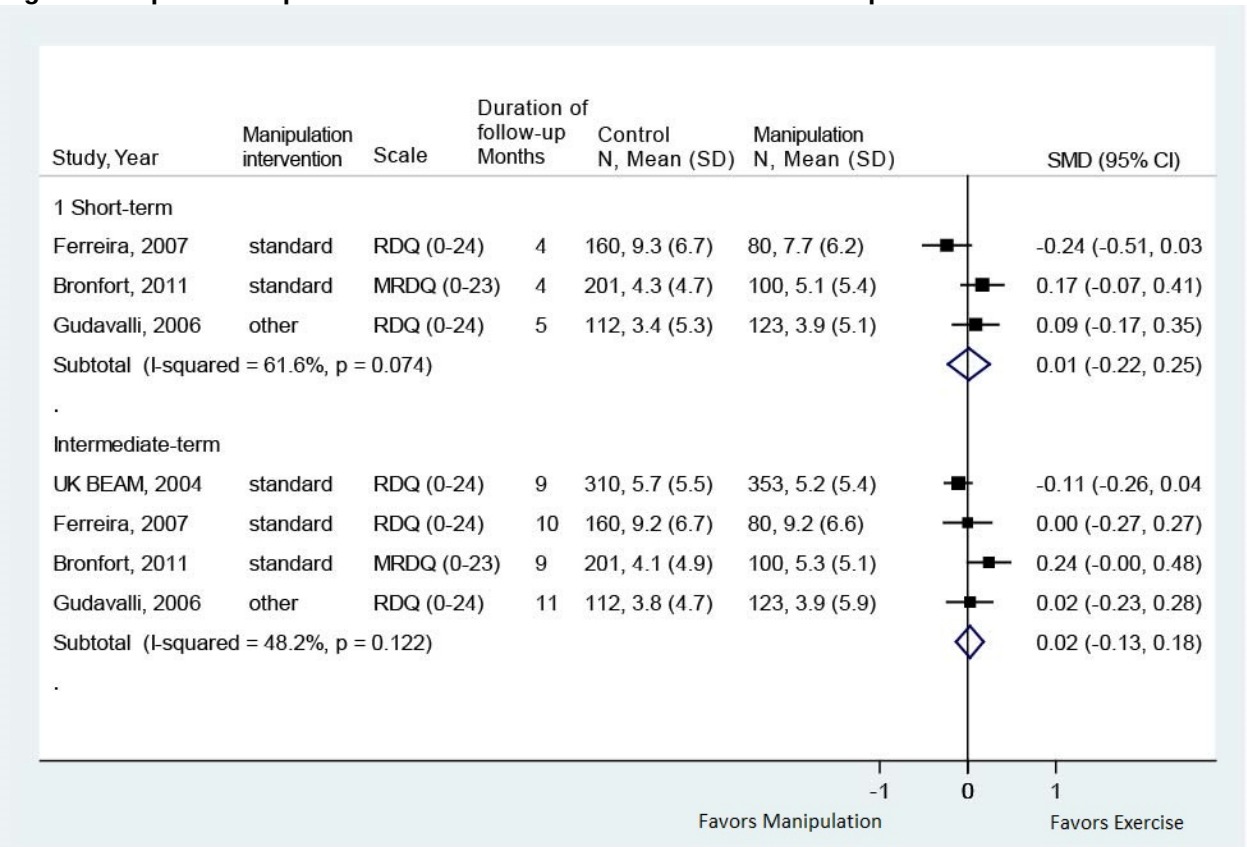
AC = attention control; CI = confidence interval; N = number; ODI = Oswestry Disability Index; PI = placebo intervention; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SMD = standardized mean difference; SP= sham manipulation; UC = usual care; UK BEAM = UK Back pain exercise and manipulation trial; VF = Von Korff functional disability

Figure 9. Spinal manipulation versus sham manipulation, usual care, an attention control, or a placebo intervention for chronic low back pain: effects on pain



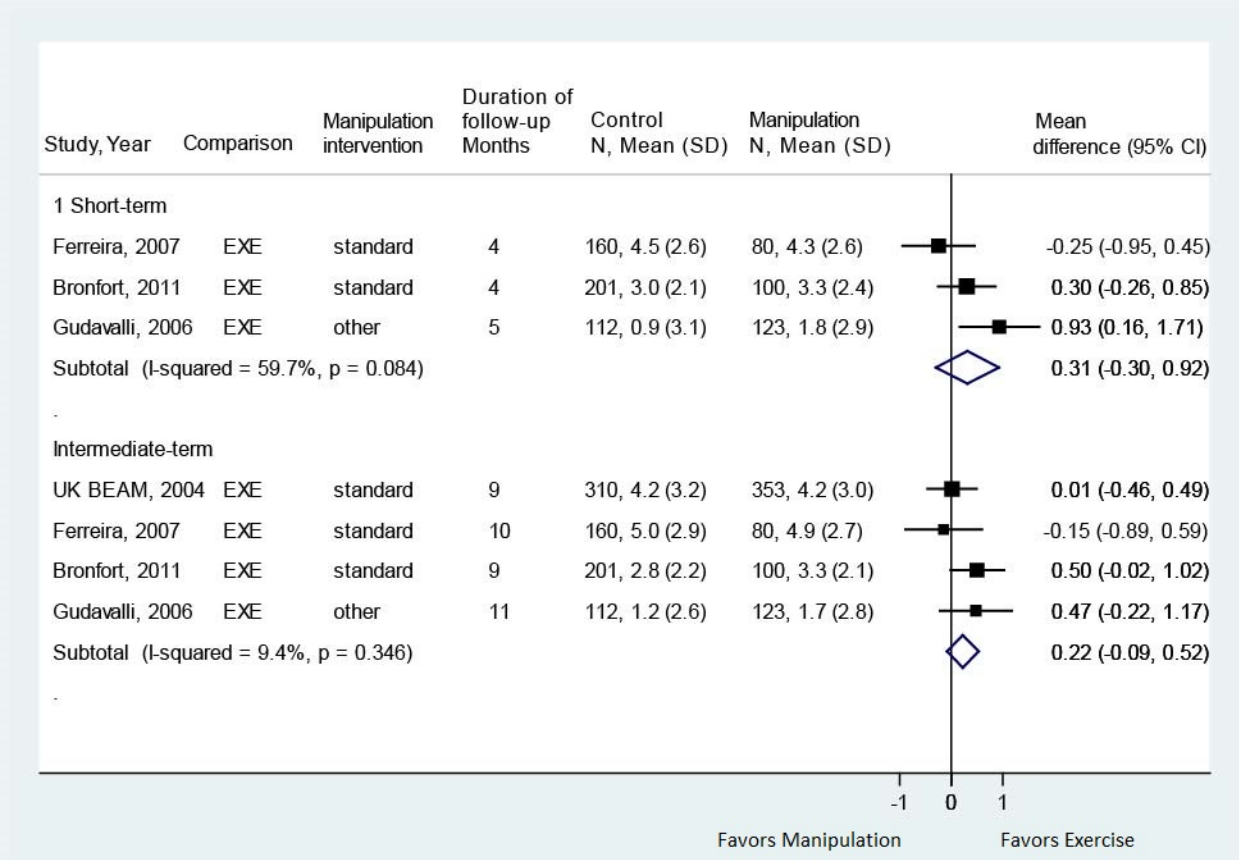
AC = attention control; CI = confidence interval; N = number; PI = placebo intervention; SD = standard deviation; SP = sham manipulation; UC = usual care; UK BEAM = UK Back pain exercise and manipulation trial

Figure 10. Spinal manipulation versus exercise for chronic low back pain: effects on function



CI = confidence interval; MRDQ = Modified Roland-Morris Disability Questionnaire; N = number; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SMD = standardized mean difference; UK BEAM = UK Back pain exercise and manipulation trial

Figure 11. Spinal manipulation versus exercise for chronic low back pain: effects on pain



CI = confidence interval; EXE = exercise; N = number; SD = standard deviation; UK BEAM = UK Back pain exercise and manipulation trial

Massage

Six trials of massage for low back pain met inclusion criteria (Table 12 and Appendix D).[93,148-151,159] Massage techniques varied across trials. Two trials evaluated reflexology,[93,151] one trial myofascial release,[148] one trial relaxation or structural massage,[150] and two trials mixed massage techniques that included Swedish massage.[149,159] Sample sizes ranged from 15 to 402 (total sample=1,027). Two trials compared massage versus sham massage,[148,151] three trials massage versus usual care,[93,150,159] and one trial compared massage versus an attention control (self-care education).[149] One trial was conducted in India[148] and the rest in the United States or Europe. The duration of massage therapy ranged from 6 to 10 weeks and the number of massage sessions ranged from 6 to 24. Three trials reported outcomes through intermediate-term followup,[149,150,159] and three only reported short-term outcomes.[93,148,151] No trial reported long-term outcomes.

All of the massage trials were rated fair-quality (Appendix E). Methodological limitations included unclear allocation concealment methods and unblinded design. One trial reported high loss to followup.[93]

Table 12. Chronic low back pain: manual therapies (massage)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Ajimsha, 2014[148] 1 month Duration of pain: 2.3 vs. 2.25 years *Fair*	A. Myofascial release (n=38) 24 sessions, 3 session/week for 8 weeks B. Sham myofascial release (n=36)	A vs. B Age: 36 vs. 34 years Female: 76% vs. 78% Baseline Quebec Back Disability Scale (0-100): 37.1 vs. 35.3 Baseline pain (0-78 McGill Pain): 23.2 vs. 23.0	A vs. B <u>1 month</u> Quebec Back Disability Scale (0-100): 28.7 vs. 32.5, MD −2.02, P<0.005 McGill Pain Questionnaire (0-78): 13.1 vs. 18.3, MD −3.25, P<0.005	NR
Cherkin, 2001[149] 10.5 months Duration of pain >1 year: 64% vs. 62% *Fair*	A. Mixed massage (including Swedish) (n=78) Up to 10 sessions over 10 weeks B. Attention control (self-care education) (n=90)	A vs. B Age: 46 vs. 44 years Female: 69% vs. 56% Baseline modified RDQ (0-23): 11.8 vs. 12.0 Baseline symptom bothersomeness (0-10): 6.2 vs. 6.1	A vs. B <u>10.5 months</u> Modified RDQ (0-23): 6.8 vs. 6.4, P=0.03 Symptom bothersomeness (0-10): 3.2 vs. 3.8, P=0.003	A vs. B <u>10.5 months</u> Low back pain medication: 2.5 vs. 4.0, P=0.69 SF-12 Mental Component Score: no differences, data not shown

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Cherkin, 2011[150] 9.5 months Duration of pain ≥1 year: 77% vs. 72% vs. 78% *Fair*	A. Structural massage (n=132): (myofascial, neuromuscular, and other soft-tissue techniques) 10 sessions for ten weeks B. Relaxation massage (n=136): 10 sessions for ten weeks C. Usual care (n=133)	A vs. B vs. C Age: 46 vs. 47 vs. 48 years Female: 66% vs. 65% vs. 62% Symptom bothersomeness (0-10): 5.6 vs. 5.6 vs. 5.8 Modified RDQ (0-23): 10.1 vs. 11.6 vs.10.5	A vs. B vs. C 9.5 months Symptom bothersomeness (0-10): 4.6 (95% CI 4.2 to 5.0) vs. 3.9 (95% CI 3.5 to 4.3) vs. 4.2 (95% CI 3.8 to 4.6) Modified RDQ (0-23): 7.2 (95% CI 6.4, 7.9) vs. 6.0 (95% CI 5.2 to 6.9) vs. 7.4 (95% CI 6.6 to 8.3), adjusted difference −0.3 (95% CI −1.4 to 0.9) for A vs. C and −1.4 (95% CI −2.6 to −0.2) for B vs. C	A vs. B vs. C 9.5 months SF-12 Mental (0-100): 52.4 (95% CI 50.9 to 53.8) vs. 53.5 (95% CI 52.2 to 54.8) vs. 51.9 (95% CI 50.2 to 53.6) SF-12 Physical (0-100): 37.7 (95% CI 36.8 to 38.7) vs. 37.9 (95% CI 37.0 to 38.7) vs. 37.7 (95% CI 36.8 to 38.6) Opioid use in last week for LBP: 4.8% (95% CI 3.1 to 7.3) vs. 4.9% (95% CI 3.1 to 7.9) vs. 4.9% (95% CI 2.7 to 8.7) Global rating of improvement "much better" or "gone": 26.1% (95% 19.8 to 34.6) vs. 36.2% (95% CI 29.1 to 45.0) vs. 20.5 (95% CI 14.5 to 29.0), RR 1.3 (95% CI 0.8, 2.0) for A vs. C and RR 1.8 (95% CI 1.2, 2.6) for B vs. C Health care costs (median): $38 (range $0 to $1443) vs. $78 (range $0 to $3,764) vs. $25 (range $0 to $8,082)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Little, 2008[159] 11.5 months Duration of pain: NR *Fair*	A. Mixed massage (including Swedish) (n=72), 6 sessions over 6 weeks/ B: Usual care (n=72) C: Exercise (regular exercise) (n=72) 5 times per week	Age: 45-46 years Female: 64-78% Baseline RDQ (0-24): 10.8-11.3 Baseline Deyo troublesome-ness (1-5): 3.3−3.4	A vs. B <u>10.5 months</u> RDQ (0-24): NR vs. 9.23 (5.3), difference −0.45 (95% CI −2.3 to 1.39) Von Korff disability (0-10): NR vs. 3.32 (2.25), difference 0.46 (95% CI −0.43 to 1.35) Von Korff pain (0-10): NR vs. 4.74 (2.20), difference 0.29 (95% CI −0.58 to 1.16) A vs. C <u>10.5 months</u> RDQ: −0.45 (−2.3 to 1.39) vs. −1.65 (−3.62 to 0.31) Von Korff disability: 0.46 (−0.43 to 1.35) vs. 0.05 (−0.92 to 1.02) Von Korff pain: 0.29 (−0.58 to 1.16) vs. −0.31 (−1.26 to 0.63)	A vs. B <u>10.5 months</u> Von Korff overall (0-10): NR vs. 4.19, difference 0.31 (95% CI −0.52 to 1.14) SF-36 PCS (0-100): NR vs. 56.1 (18.6), difference −1.45 (95% CI −9.04 to 6.15) SF-36 MCS (0-100): NR vs. 64.8 (17.5), difference −2.11 (95% CI −9.37 to 5.16) Deyo troublesomeness scale (1-5): NR vs. 3.05 (0.80), difference 0.04 (−0.25 to 0.33) A vs. C <u>10.5 months</u> Von Korff overall: 0.31 (−0.52 to 1.14) vs. −0.19 (−1.09 to 0.72) SF-36 Physical Component Score: −1.45 (−9.04 to 6.15) vs. −2.08 (−10.6 to 6.40) SF-36 Mental Component Score: −2.11 (−9.37 to 5.16) vs. 0.72 (−7.38 to 8.81) Deyo troublesomeness scale: 0.04 (−0.25 to 0.33) vs. −0.21 (−0.52 to 0.09)
Poole, 2007[93] 4.5 months Duration of pain: 10 vs. 11 vs. 9.5 years *Fair*	A. Reflexology (n=77) 6 sessions over 6−8 weeks B. Usual care (n=75)	A vs. B Age: 47 vs. 47 years Female: 62% vs. 51% Baseline ODI: 33.0 vs. 36.6 Baseline pain (0-100 VAS): 44.5 vs. 40.6	A vs. B <u>4.5 months</u> ODI (0-100): 29.0 (20.2) vs. 32.9 (17.6) Pain (0-100 VAS): 39.8 (29.2) vs. 42.7 (28.4)	A vs. B <u>4.5 months</u> Beck Depression Inventory (0-63): 11.6 (10.9) vs. 12.8 (9.2) SF-36 Physical Functioning: 57.1 (31.8) vs. 52.2 (29.5) SF-36 Social Functioning: 68.1 (31.8) vs. 61.5 (30.8) SF-36 Physical Limitations: 48.2 (46.4) vs. 37.8 (42.5) SF-36 Emotional Limitations: 55.0 (46.5) vs. 62.0 (44.0)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Quinn, 2008[151] 1.5 and 3 months Duration of pain: At least 3 months *Fair*	A. Reflexology (pressure massage stimulation) (n=7) 6 sessions over 6 weeks B. Sham reflexology (n=8)	A vs. B Age (median): 42 vs. 45 Female: 86% vs. 50% Baseline RDQ: 5 vs. 7.5 Baseline pain (0-10 VAS): 4.7 vs. 3.4	A vs. B <u>1.5 months, median (IQR)</u> RDQ: 4 (3 to 4.5) vs. 4.5 (1 to 7) Pain (0-10 VAS): 2.1 (1.5 to 4.9) vs. 4.1 (2.7 to 5.1) McGill Pain Questionnaire (0-77): 11 (6 to 17) vs. 6.5 (5 to 13) <u>3 months, median (IQR)</u> RDQ: 4 (2 to 5) vs. 3.5 (1.8 to 4.8) VAS: 2.2 (1.6 to 3.2) vs. 3.2 (2.6 to 4.6) McGill Pain Questionnaire (0-77): 6 (4 to 13) vs. 7.5 (3.8 to 9.8)	A vs. B <u>1.5 months, median (IQR)</u> SF-36 General health: 52.9 (49 to 54) vs. 42.2 (40 to 51) SF-36 Physical functioning: 48.6 (47 to 50) vs. 43.4 (40 to 50) SF-36 Mental health: 47.2 (43 to 56) vs. 47.2 (42 to 53) <u>3 months, median (IQR)</u> SF-36 General health: 48.2 (46 to 52) vs. 47.0 (38 to 53) SF-36 Physical functioning: 50.7 (44 to 51) vs. 45.5 (44 to 50) SF-36 Mental health: 52.8 (39 to 53) vs. 48.6 (44 to 51)

Abbreviations: CI = confidence interval; IQR = interquartile range; NR = not reported; MCS = Mental Component Summary; PCS = Physical Component Summary; ODI = Oswestry Disability Index; RDQ =Roland-Morris disability questionnaire; SF-36 = Short-Form 36 questionnaire; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Massage Compared With Sham Massage, Usual Care, or an Attention Control

Massage was associated with slightly greater effects on short-term function than sham massage or usual care (4 trials, SMD −0.30, 95% CI −0.46 to −0.14, I^2=0%) (Figure 12).[93,148,150,151] The massage technique was myofascial release in one trial (difference −3.80, 95% CI −8.20 to 0.60 on the 0 to 100 Quebec Back Disability Scale),[148] structural or relaxation massage in one trial (difference −1.72 on the 0 to 23 modified RDQ, 95% CI −2.78 to −0.66),[150] and foot reflexology in two trials (difference 0.50 on the 0 to 24 RDQ, 95% CI −1.85 to 2.85 in one trial[151] and −3.90 on the 0 to 100 ODI, 95% CI −9.97 to 2.17 in the other trial[93]). Estimates were similar when trials were stratified according to whether the comparator was sham massage or usual care. There was no effect on intermediate-term function (3 trials, SMD −0.09, 95% CI −0.24 to 0.06, I^2=0%) (Figure 12).[149,150,159]

Massage was associated with slightly greater effects on short-term pain than sham massage or usual care (4 trials, pooled difference −0.52 on a 0 to 10 scale, 95% CI −0.81 to −0.23, I^2=0%) (Figure 13).[93,148,150,151] On a 0 to 10 scale, effects were −0.29 (95% CI −1.21 to 0.63) and −1.00 (95% CI −2.41 to 0.41) points in two trials of foot reflexology,[93,151] −0.67 points (95% CI −1.08 to −0.25) in a trial of myofascial release,[148] and −0.35 points (95% CI −0.82 to 0.12) in a trial of relaxation or structural massage.[150] Estimates were similar when trials were stratified according to whether the comparator was sham massage or usual care. There was no difference between massage (structural or relaxation massage or mixed massage techniques, including Swedish massage) versus an attention control or usual care in intermediate-term pain (3 trials, difference −0.01, 95% CI −0.40 to 0.38, I^2=0%).[149,150,159]

One trial found no difference between massage versus usual care in use of opioids at intermediate-term followup or health care costs.[150] There was insufficient evidence to determine effects of duration of massage or number of massage sessions on findings. Two trials[150,159] found no differences between massage versus usual care on the SF-36 MCS or PCS Scores at intermediate-term followup, and one trial[93] found no effects on various SF-36 subscales or the Beck Depression Inventory at short-term followup.

Massage Compared With Pharmacological Therapies

No trial of massage versus pharmacological therapy met inclusion criteria.

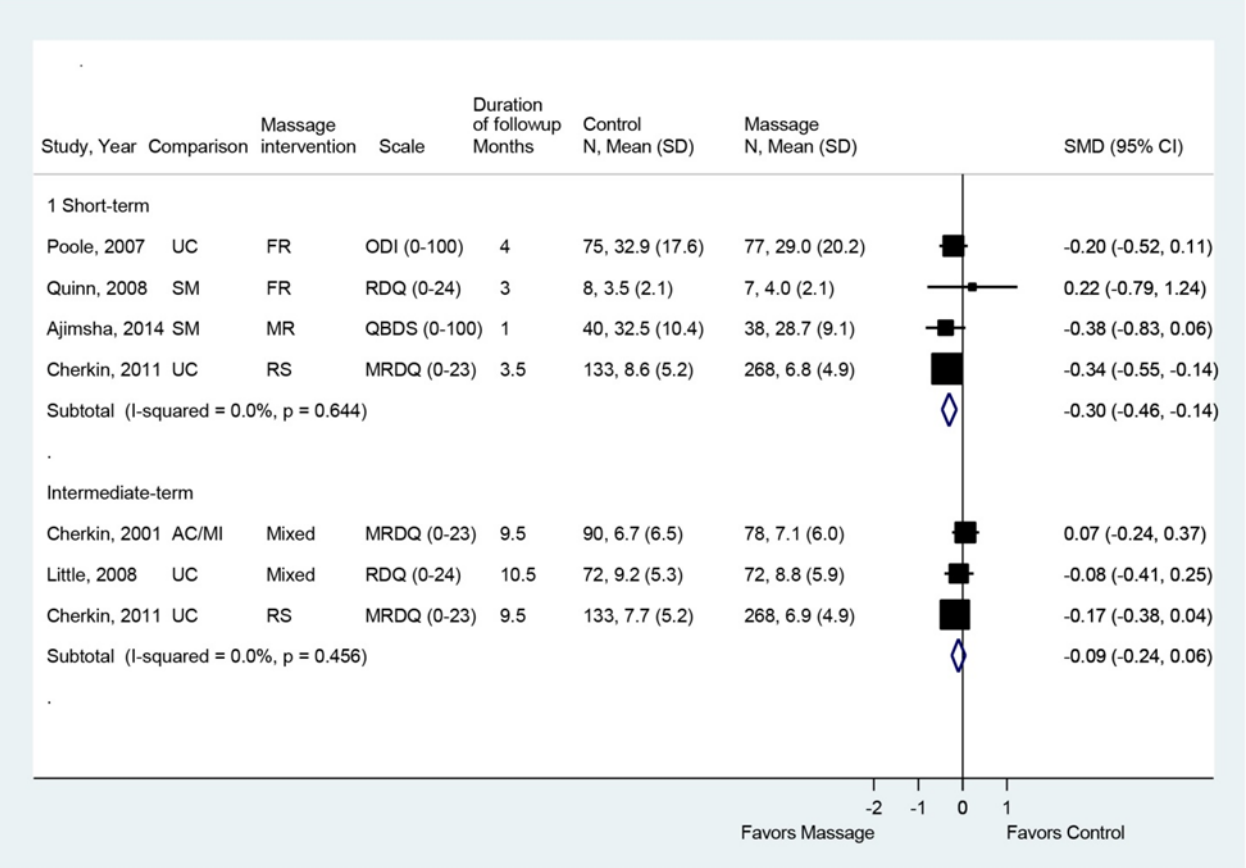
Massage Compared With Exercise

One trial found no differences between massage versus exercise in intermediate-term function (difference 1.2 on the 0 to 24 RDQ, 95% CI −1.47 to 3.87), pain (difference 0.60 on the 0 to 10 Von Korff pain scale, 95% CI −0.67 to 1.87), or the SF-36 MCS or PCS scores (differences 0 to 3 points on 0 to 100 scales, P>0.05).[159]

Harms

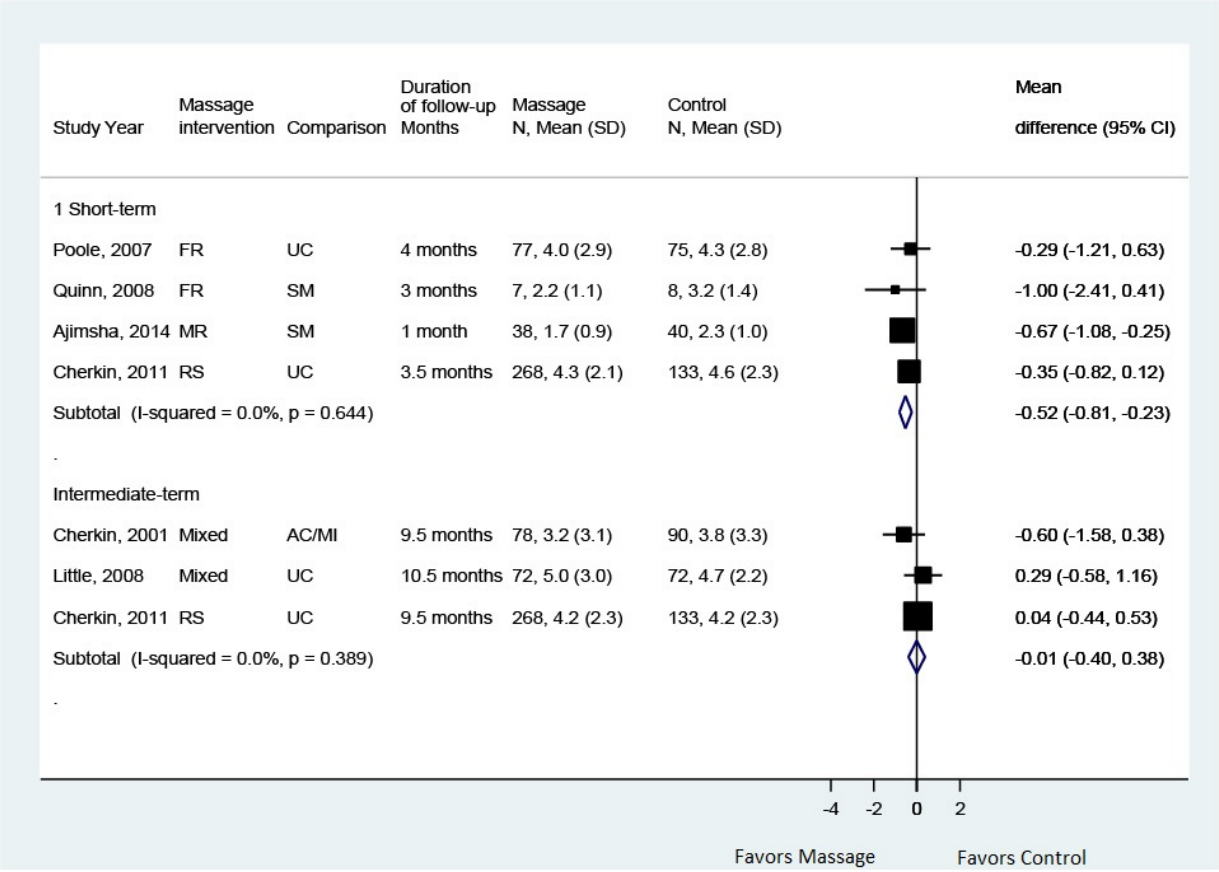
Two trials[148,149] reported no serious adverse events, and one trial[151] reported no adverse events. In four trials, the proportion of massage patients who reported increased pain ranged from <1 to 26 percent.[148-150,159]

Figure 12. Massage versus sham massage, usual care, or attention control intervention for chronic low back pain: effects on function



AC = attention control; CI = confidence interval; FR = foot reflexology; MD = mean difference; MI = minimal intervention; MRDQ = Modified Roland-Morris Disability Questionnaire; MR = myofascial release; N = number; QBDS = Quebec Back Pain Disability Scale; RDQ = Roland-Morris Disability Questionnaire; RS = relaxation/structural; SD = standard deviation; SM = sham massage, SMD = standardized mean difference; UC = usual care

Figure 13. Massage versus sham massage, usual care, or attention control for chronic low back pain: effects on pain



AC = attention control; CI = confidence interval; FR = foot reflexology; MI = minimal intervention; MR = myofascial release; N = number; RS = relaxation/structural; SD = standard deviation; SM = sham massage, UC = usual care

Mindfulness-Based Stress Reduction for Chronic Low Back Pain

Key Points

- There was no evidence of differences between mindfulness-based stress reduction (MBSR) versus usual care or attention control in short-term function (4 trials, pooled SMD −0.25, 95% CI −0.53 to 0.04, I^2=53%), intermediate-term function (1 trial, SMD −0.20, 95% CI −0.47 to 0.06), or long-term function (1 trial, SMD −0.20, 95% CI −0.47 to 0.06) (SOE: low).
- MBSR was associated with slightly greater effects than usual care or an attention control on short-term pain (3 trials, pooled MD −0.73 on a 0 to 10 scale, 95% CI −1.18 to −0.28, I^2=93%) after excluding two poor-quality trials; MBSR was also associated with small effects on intermediate-term pain (1 trial, MD −0.75, 95% CI −1.17 to −0.33), with no statistically significant effects on long-term pain (1 trial, MD −0.22, 95% CI −0.64 to 0.20) (SOE: moderate for short term, low for intermediate and long term).
- One trial reported temporarily increased pain in 29 percent of patients undergoing MBSR, and three trials reported no harms (SOE: low).

Detailed Synthesis

Five trials (7 publications) of MBSR for low back pain met inclusion criteria (Table 13 and Appendix D).[89,164-169] In three trials,[89,165-168] the MBSR intervention was closely modeled on the program developed by Kabat-Zinn;[245] in the other two trials, the MBSR intervention appeared to have undergone some adaptations from the original Kabat-Zinn program.[164,169] In all trials, the main intervention consisting of 1.5 to 2 hour weekly group sessions for 8 weeks. Sample sizes ranged from 35 to 282 (total sample=625). Three trials compared MBSR versus usual care[89,164-166,169] and two trials compared MBSR versus an attention control (education).[167,168] Four trials[89,165-169] were conducted in the United States and one trial[164] in Iran. One trial focused on patients on opioid therapy for low back pain.[169] One trial reported outcomes through long-term (22 months after 8-week MBSR course) followup,[89,165,166] and the others only evaluated short-term outcomes.

Three trials[89,165-168] were rated fair quality and two trials poor quality (Appendix E).[164,169] The major methodological limitation in the fair-quality trials was the inability to effectively blind patients and caregivers to the MBSR intervention. One poor-quality trial reported unclear randomization and allocation concealment methods and had high attrition,[164] and another poor-quality trial reported a large baseline difference in baseline pain scores (Brief Pain Inventory score 6.3 on a 0 to 10 scale with MBSR versus 4.9 with usual care).[169]

Table 13. Chronic low back pain: mindfulness-based stress reduction

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Banth, 2015[164] 1 month Duration of pain: ≥6 months *Poor*	A. Mindfulness-based stress reduction (n=NR) 8 1.5-hour sessions over 8 weeks B. Usual care (n=NR) 48 of 88 patients were analyzed, n for each group NR	A vs. B (NR) Age: 40 years Female: 100% Baseline function: NR McGill Pain questionnaire total score (0-45): 26.08 vs. 26.71	A vs. B <u>1 month</u> McGill Pain questionnaire total score (0-45): 13.58 vs. 23.60	A vs. B <u>1 month</u> SF-12 Mental component (0-100): 31.54 (4.3) vs. 24.29 (5.2) SF-12 Physical component (0-100): 28.08 (4.2) vs. 21.08 (3.3)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Cherkin, 2016[89] Herman, 2017[166] Cherkin, 2017[165] (2 year data from Cherkin, 2016) 22 months Duration of pain: >3 months (>1 year in 80% of patients) *Fair*	A. Mindfulness-based stress reduction (n=113), 8 2-hour sessions over 8 weeks (optional 6 hour retreat) B. Usual care (n=112)	A vs. B 50 vs. 49 years Female: 61% vs. 66% Baseline modified RDQ (0-23): 11.8 vs. 10.9 Baseline pain bothersomeness (0-10): 6.1 vs. 6.0	A vs. B <u>4.5 months</u> Modified RDQ (0-23), mean change from baseline: −4.33 (95% CI −5.16 to −3.51) vs. −2.96 (95% CI −3.79 to −2.14) Pain bothersomeness (0-10), mean change from baseline: −1.48 (95% CI −1.86 to −1.11) vs. −0.84 (95% CI −1.21 to −0.46) ≥30% improvement in RMDQ: 60.5% (95% CI 52.0 to 70.3) vs. 44.1% (95% CI 35.9to 54.2) ≥30% improvement in pain bothersomeness: 43.6% (95% CI 35.6 to 53.3) vs. 26.6% (95% CI 19.8 to 35.9) <u>10 months</u> Modified RDQ, mean change from baseline:−5.3 (95% CI −6.16to −4.43) vs. −4.78 (95% CI −5.67to −3.89) vs. −3.43 (95% CI −4.33 to −2.52) Pain bothersomeness, mean change from baseline: −1.95 (95% CI −2.32 to −1.59) vs. −1.10 (95% CI −1.48 to −0.71) ≥30% improvement in RMDQ: 68.6% (95% CI 60.3 to 78.1) vs. 48.6% (95% CI 40.3t o 58.6) ≥30% improvement in pain bothersomeness: 48.5% (95% CI 40.3 to 58.3) vs. 31.0% (95% CI 23.8 to 40.3) <u>22 months</u> Modified RDQ (0-23): −4.09 (95% CI−5.08 to −3.10) vs. −2.74 (95% CI−3.81to −1.68) ≥30% improvement in modified RDQ: 55.4% (95% CI 46.9 to 65.5) vs. 42.05% (95% CI 33.8 to 52.2) Pain bothersomeness: −1.57 (95% CI −1.97 to −1.17) vs. −1.25 (95% CI −1.69 to −0.81 ≥30% improvement in pain bothersomeness: 41.2% (95% CI 33.2 to 51.0) vs. 31.1% (95% CI 23.9 to 40.5)	A vs. B <u>4.5 months</u> SF-12 MCS, mean change from baseline (0-100): 0.45 (95% CI −0.85 to 1.76) vs. 2.13 (95% CI 0.86 to 3.40) vs. −1.11 (95% CI −2.39 to 0.17) SF-12 PCS, mean change from baseline (0-100): 3.58 (95% CI 2.15 to 5.01) vs. 3.27 (95% CI 2.09 to 4.44) Used medications for LBP: 43.4% (95% CI 35.9to 52.6) vs. 54.2 (95% CI 46.2 to 63.6) <u>10 months</u> SF-12 MCS, mean change from baseline: 2.01 (95% CI 0.74 to 3.28) vs. 0.75 (95% CI −0.58 to 2.08) SF-12 PCS, mean change from baseline: 3.87 (95% CI 2.55 to 5.19) vs. 2.93 (95% CI 1.70 to 4.16) Used medications for LBP: 46.8% (95% CI 39.2 to 55.9) vs. 52.9% (95% CI 45.1 to 62.0) Total costs: $5,580 (95% CI $3,465, $8,343) vs. $6,304 (95% CI $4,193, $9,805)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Morone, 2009[168] 4 months Duration of pain: Mean 9.4 to 11 years *Fair*	A. Mindfulness-based stress reduction (n=16), 8 1.5-hour sessions over 8 weeks B. Attention control (education) (n=19)	A vs. B Age 78 vs. 73 years Female: 69% vs. 58% Baseline RDQ: 8.8 vs. 11.3 Baseline McGill Pain Questionnaire Current Pain (0-10): 2.9 vs. 4.4	A vs. B <u>4 months</u> RDQ: 7.6 (95% CI 6.2 to 8.7) vs. 10.0 (95% CI 8.7 to 11.2) McGill Pain Questionnaire Total Score (0-45): 12.4 (95% CI 10.4 to 14.6) vs. 12.0 (95% CI 10.2 to 13.7) McGill Pain Questionnaire Current Pain (0-10): 2.3 (95% CI 1.6 to 2.8) vs. 3.7 (95% CI 3.1 to 4.3)	A vs. B <u>4 months</u> SF-36 Pain Score (10-62): 41.4 (95% CI 39.8 to 43.1) vs. 40.5 (95% CI 38.7 to 42.2)
Morone, 2016[167] 4.5 months Duration of pain: Mean 11 years *Fair*	A. Mindfulness-based stress reduction (n=140), 8 1.5-hour sessions over 8 weeks, with 6 monthly booster sessions B. Control, (health education) (n=142)	A vs. B Age: 75 vs. 74 years Female: 66% vs. 66% Baseline RDQ (0-24): 15.6 vs. 15.4 Baseline Pain (0-20 NRS): 11.0 vs. 10.5	A vs. B <u>4.5 months</u> RDQ: 12.2 vs. 12.6, adjusted difference −0.4 (95% CI −1.5 to 0.7) RDQ improved ≥2.5 points: 49.2% (58/117) vs. 48.9% (66/135), P=0.97 Pain (0-20 NRS): 9.5 vs. 10.6, adjusted difference −1.1 (95% CI −2.2 to −0.01) Pain improved ≥30%: 36.7% (43/117) vs. 26.7% (36/135), P=0.09	A vs. B <u>4.5 months</u> SF-36 Global Health Composite (9-67): 42.4 vs. 41.2, adjusted difference 0.2 (95% CI −1.9 to 2.4) SF-36 Physical Health Composite (20 to 65): 41.2 vs. 41.2, adjusted difference −0.1 (95% CI −1.9 to 1.8)
Zgierska, 2016[169] 4.5 months Duration of pain: Mean 14 years *Poor*	A. Mindfulness-based stress reduction (n=21): 8 weekly 2 hour group sessions plus 30 minutes/day, 6 days/week of at home practice B. Usual care (n=14)	Overall Age: 51.8 years Female: 80% Baseline ODI (0-100): 68.1 vs. 64.5 Baseline Brief Pain Inventory pain intensity (0-10): 6.3 vs. 4.9 Baseline Opioid dose 166.9 vs. 120.3	A vs. B <u>4.5 months</u> ODI (0-100): −5.0 (95% CI 9.7 to 0.2) vs. 1.6 (95% CI −4.3 to 7.4) Brief Pain Inventory pain intensity: −0.5 (95% CI −1.1 to 0.02) vs. 0.5 (95% CI 0.2 to 1.2)	A vs. B <u>4.5 months</u> Opioid dose (mg morphine equivalents): −10.1 (95% CI −35.5 to 15.2) vs. −0.2 (95% CI −31.4 to 30.9)

CI = confidence interval; MCS = Mental Component Summary; NR = not reported; NRS = numeric rating scale; ODI = Oswestry Disability Index; PCS = Physical Component Summary; RDQ = Roland-Morris Disability Questionnaire; SF-36 = Short-Form 36 Questionnaire; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

MBSR Compared With Usual Care or an Attention Control

MBSR was associated with no statistically significant differences in short-term function compared with usual care or an attention control (4 trials, pooled SMD −0.25, 95% CI −0.53 to 0.04, I^2=53%) (Figure 14).[89,167,168] Three trials[89,167,168] evaluated function using the RDQ (pooled difference −0.95 points on a 0 to 24 scale, 95% CI −2.07 to 0.17), and one trial[169] used the ODI (difference −3.00 points on a 0 to 100 scale, 95% CI −11.39 to 5.39). One trial found no difference between MBSR versus an attention control in intermediate-term (SMD −0.20, 95% CI −0.47 to 0.06) or long-term function (SMD −0.20, 95% CI −0.47 to 0.06).[89,165] There was no

clear difference between MBSR versus controls in likelihood of a clinically meaningful effect on function (≥30% improvement in RDQ or RDQ improved by ≥2.5 points) at short term (2 trials, 1.17, 95% CI 0.88 to 1.57).[89,167] Data were restricted to one trial for intermediate-term (RR 1.41, 95% CI 1.13 to 1.77)[89] and long-term followup (RR 1.32, 95% CI 1.00 to 1.74).[165]

MBSR was associated with no statistically significant effects on short-term pain compared with usual care or an attention control, when all trials were included in the analysis (5 trials, pooled difference −0.88 on a 0 to 10 scale, 95% CI −1.82 to 0.05, I^2=93%) (Figure 15).[89,164,167-169] However, statistical heterogeneity was substantial. Excluding two poor-quality trials,[164,169] which reported the largest effect in favor of MBSR (−1.40 points) as well as the only trial with results that favored usual care (0.40 points), resulted in a small effect on short-term pain (3 trials, pooled difference −0.73, 95% CI −1.18 to −0.28, I^2=45%) and reduced statistical heterogeneity.[89,167,168] Estimates were similar when analyses were stratified according to whether the trial evaluated usual care or an attention control comparator. One trial found MBSR associated with slightly greater effects than an attention control on intermediate-term pain (difference −0.75 on a 0 to 10 scale, 95% CI −1.17 to −0.33); there was no statistically significant effect on long-term pain (difference −0.22, 95% CI −0.64 to 0.20).[165] MBSR was associated with greater likelihood of a clinically meaningful effect on pain (defined as ≥30% improvement) at short-term (2 trials, RR 1.49, 95% CI 1.14 to 1.95, I^2=0%)[89,167] and intermediate-term followup (1 trial, RR 1.56, 95% CI 1.14 to 2.14),[89] but not at long-term followup (41% vs. 31%, RR 1.32, 95% CI 0.95 to 1.85).[165]

Three trials found no clear differences between MBSR versus usual care or an attention control on quality of life measured by the SF-12 or SF-36.[89,164,167] One trial found MBSR associated with less medication use for low back pain at short term (43% vs. 54%) but not at intermediate term (47% vs. 53%); MBSR was associated with slightly greater decrease in severity of depression (difference 0.63 points on the PHQ-8 at intermediate-term), with no clear differences in measures of health care utilization.[89,166]

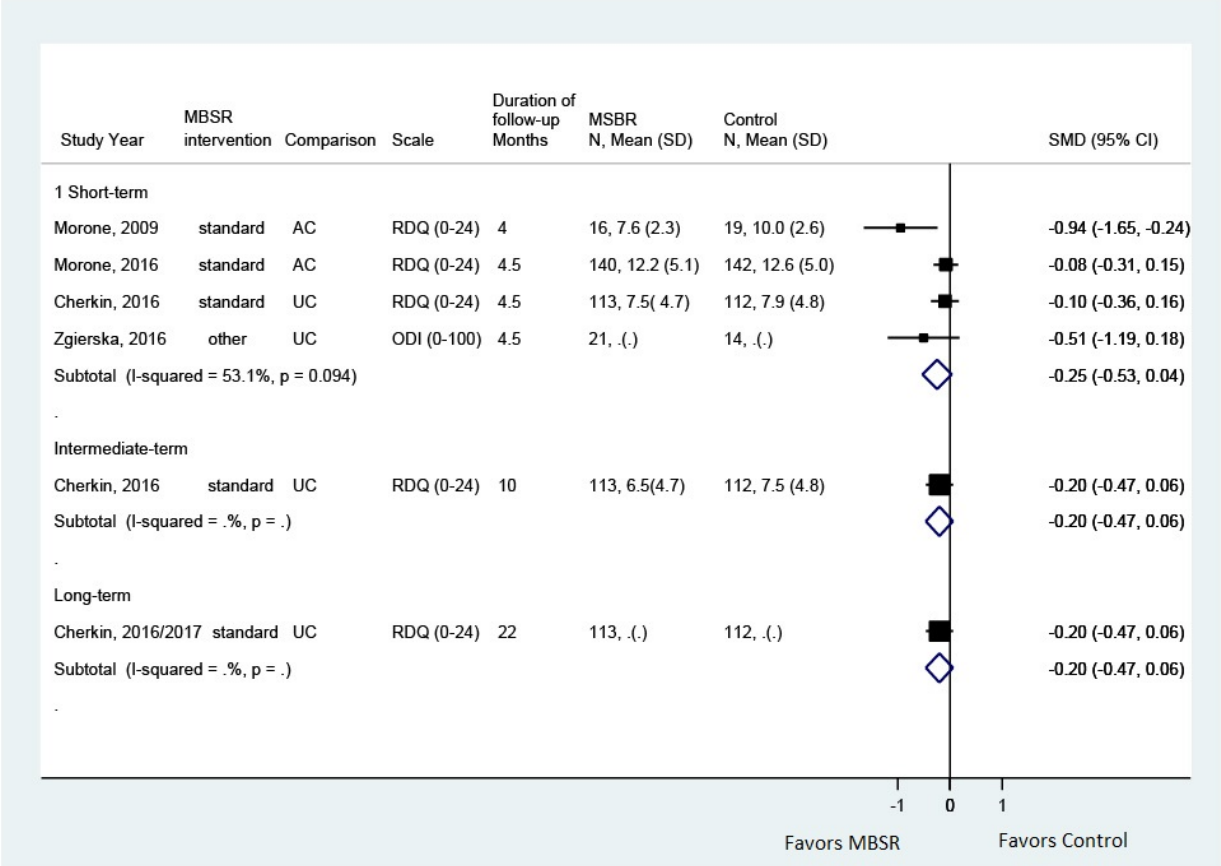
MBSR Compared With Pharmacological Therapy or With Exercise

No trial of MBSR versus pharmacological or versus exercise therapy met inclusion criteria.

Harms

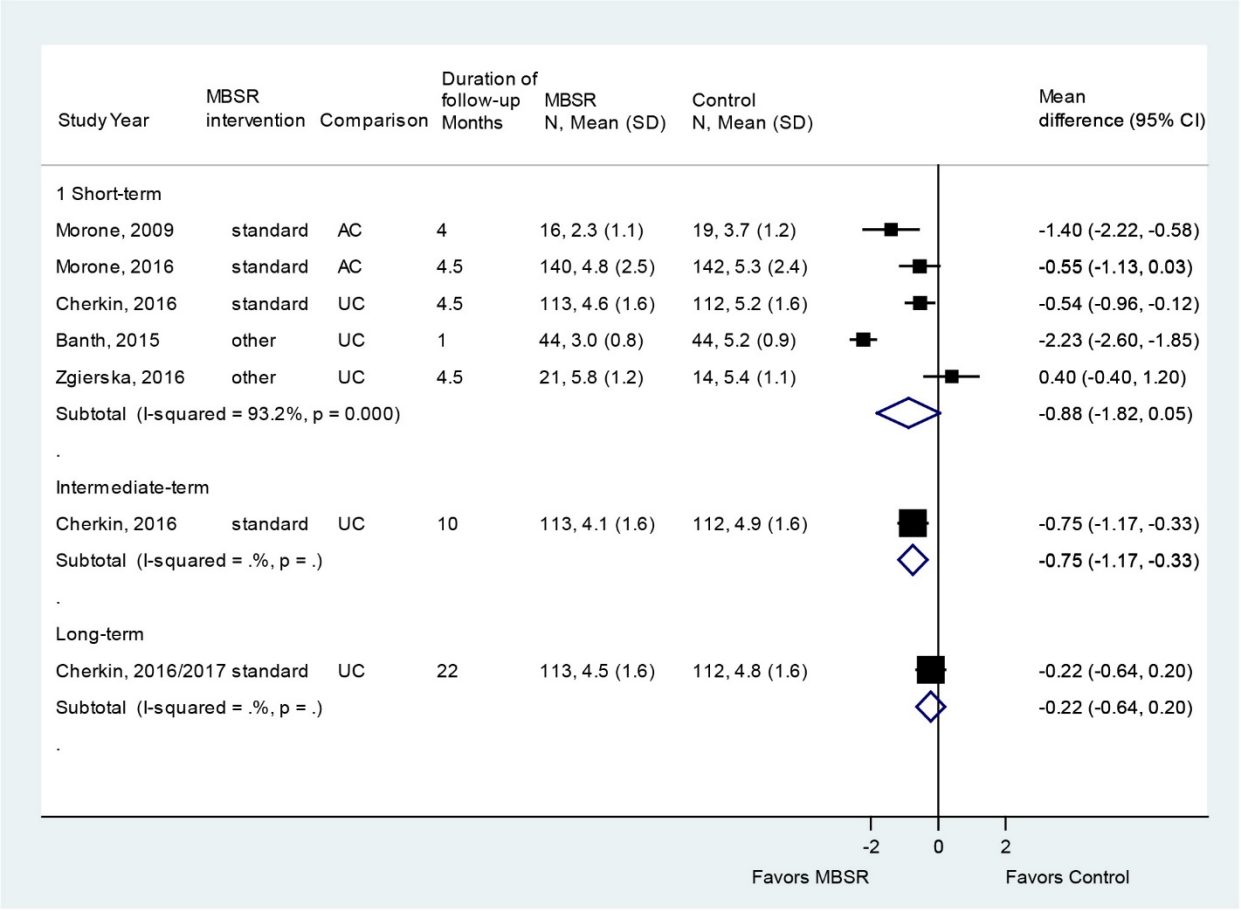
In one trial, 29 percent of MBSR patients reported temporarily increased pain.[89] Three trials[167-169] reported no adverse events and one trial[164] did not report adverse events.

Figure 14. Mindfulness-based stress reduction versus usual care or an attention control for chronic low back pain: effects on function



AC = attention control; CI = confidence interval; MBSR = mindfulness-based stress reduction; N = number; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SMD = standardized mean difference; UC = usual care

Figure 15. Mindfulness-based stress reduction versus usual care or an attention control for chronic low back pain: effects on pain



AC = attention control; CI = confidence interval; MBSR = mindfulness-based stress reduction; N=number; SD = standard deviation; UC = usual care

Mind-Body Practices for Chronic Low Back Pain

Key Points

Yoga

- Yoga was associated with slightly greater effects on function than an attention or waitlist control at short-term (6 trials, pooled SMD −0.50, 95% CI −0.72 to −0.29, I^2=54%) and intermediate-term (3 trials, pooled SMD −0.33, 95% CI −0.49 to −0.16) followup (SOE: moderate for short term, low for intermediate term).
- Yoga was associated with moderately greater effects on pain than an attention or waitlist control at short-term (5 trials, pooled MD −1.10 on a 0 to 10 scale, 95% CI −1.77 to −0.42, I^2=74%) and intermediate-term (2 trials, pooled MD −1.17, 95% CI −1.91 to −0.44, I^2=26%) followup (SOE: low for short term, moderate for intermediate term).
- Yoga was associated with no statistically significant differences versus exercise in short-term or intermediate-term pain or function (SOE: low).

- Yoga was not associated with increased risk of harms versus controls (SOE: low).

Qigong

- One trial found no evidence of differences between qigong versus exercise in short-term function (MD 0.9 on the RDQ, 95% CI −0.1 to 2.0), although intermediate-term results slightly favored exercise (MD 1.2, 95% CI 0.1 to 2.3) (SOE: low).
- One trial found qigong associated with slightly lower effects on pain versus exercise at short-term followup (MD 7.7 on a 0 to 100 scale, 95% CI 0.7 to 14.7), but the difference at intermediate-term was not statistically significant (MD 7.1, 95% CI −1.0 to 15.2) (SOE: low).
- One trial found no difference between qigong versus exercise in risk of adverse events (SOE: low).

Detailed Synthesis

Yoga

Eight trials of yoga for low back pain met inclusion criteria (Table 14, Appendix D).[173-179,186] Four trials evaluated Iyengar yoga,[177-179,186] two trials Viniyoga,[175,176] and two trials Hatha yoga.[173,174] Sample sizes ranged from 60 to 313 (total sample=1,466). Five trials compared yoga versus an attention control (education),[174-177,179] two trials yoga versus wait list control,[173,178] and four trials yoga versus exercise.[174-176,186] One trial was conducted in India[186] and the rest in the United States or Europe. The duration of yoga therapy ranged from 4 to 24 weeks and the number of sessions ranged from 4 to 48. In one trial, patients who received 12 weeks of yoga therapy were randomized to ongoing once-weekly maintenance sessions or to no maintenance.[174] Three trials reported outcomes through intermediate-term followup,[174,177,178] and five only reported short-term outcomes.[173,175,176,179,186]

All of the trials were rated fair quality (Appendix E). Trials could not effectively blind patients; other methodological limitations included unclear allocation or randomization methods and high attrition.

Table 14. Chronic low back pain: mind-body practices (yoga)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Groessl, 2017[173] 3.5 months Duration of pain: >6 months *Fair*	A. Hatha yoga (n=75): Two sessions per week for 12 weeks, 15–20 minutes of home practice on days without sessions B. Wait list (n=75): Usual care, with yoga started after 6 months	A vs. B Age: 53 vs. 54 years Female: 27% vs. 25% Baseline RDQ (0-24): 9.40 vs. 10.3 Baseline pain (0-10 Brief Pain Inventory): 4.64 vs. 4.68	A vs. B <u>3.5 months</u> RDQ (0-24): −3.37 (95% CI −4.51 to −2.23) vs. −0.89 (95% CI−2.02 to 0.23); between group difference −2.48 (95% CI - 4.08 to −0.87) Pain intensity, Brief Pain Inventory (0-10): −0.44 (95% CI- 0.78 to - 0.11) vs. 0.15 (95% CI −0.18 to 0.47); between-group difference −0.59 (95% CI −1.05 to −0.13)	A vs. B <u>3.5 months</u> Opioid medication use: 9% vs. 7%, P=0.40 Other medical treatments for pain: 39% vs. 37, P=0.42

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Nambi, 2014[186] 5.5 months Duration of pain: >3 months *Fair*	A. Iyengar yoga (29 poses) (n=30) 5 sessions a week for 4 weeks B. Exercise (stretching exercises for soft tissue flexibility and range of motion) (n=30)	A vs. B Age: 44 vs. 43 years Female: 63% vs. 43% Baseline function, Physically unhealthy days: 18.0 vs. 17.8 Baseline pain (0-10 VAS): 6.7 vs. 6.7	A vs. B <u>5 months</u> Physically unhealthy days: 2.6 vs. 6.9, P=0.001 Pain (0-10 VAS): 1.8 vs. 3.8, P=0.001	A vs. B <u>5 months</u> Mentally unhealthy days: 2.1 vs. 5.0, P=0.001 Activity limitation (days): 2.0 vs. 5.0, P=0.001
Saper, 2017[174] 10 months Duration of pain: >3 months *Fair*	A. Hatha yoga (n=127) 12 sessions over 12 weeks, with or without ongoing weekly maintenance sessions B. Exercise (n=129) C. Attention control (education) (n=64)	A vs. B vs. C Age: 46 vs. 46 vs. 44 Female: 57% vs. 70% vs. 66% Baseline modified RDQ: 13.9 vs. 15.6 vs. 15.0 Baseline pain (0-10 NRS): 7.1 vs. 7.2 vs. 7.0	A1 (no maintenance) vs. A2 (maintenance) vs. C, mean (SE) <u>3.5 months</u> Modified RDQ (0-23): 10.1 (0.77) vs. 9.5 (0.77) vs. 11.6 (0.75) Pain (0-10 NRS): 4.3 (0.32) vs. 4.6 (0.32) vs. 5.5 (0.31) <u>9 months</u> Modified RDQ (0-23): 9.2 vs. 8.9 vs. 11.1 Pain (0-10 NRS): 4.3 vs. 4.4 vs. 5.2 A1 vs. A2 vs. B1 vs. B2 <u>3.5 months</u> Modified RDQ (0-23): 10.1 (0.77) vs. 9.5 (0.77) vs. 10.4 (0.84) vs. 10.1 (0.83) Pain (0-10 NRS): 4.3 (0.32) vs. 4.6 (0.32) vs. 4.7 (0.35) vs. 4.8 (0.34) <u>9 months</u> Modified RDQ (0-23): 9.2 (0.88) vs. 8.9 (0.88) vs. 8.9 (0.96) vs. 9.4 (0.94) Pain (0-10 NRS): 4.3 (0.36) vs. 4.4 (0.35) vs. 4.0 (0.39) vs. 4.1 (0.37)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Sherman, 2005[175] 3.5 months Duration of pain: 3 to 15 months *Fair*	A. Viniyoga (n=36) 12 sessions 1 session/week for 12 weeks B. Exercise (n=35) C. Attention control (self-care advice) (n=30)	A vs. B vs. C Age: 44 vs. 42 vs. 45 Female: 69% vs. 63% vs. 67% Baseline RDQ: 8.1 vs. 9.0 vs. 8.0 Baseline symptom bothersomeness (0-10): 5.4 vs. 5.7 vs. 5.4	A vs. B <u>3.5 months</u> Modified RDQ (0-23): 3 vs. 5 (estimated from graph), adjusted difference −1.5 (−3.2 to 0.2)[b] Reduction in RDQ score ≥50%:69% vs. 50%, RR 1.4 (95% CI 0.91 to 2.1) Bothersomeness: 1.8 vs. 3.3 (estimated from graph), adjusted difference −1.4 (95% CI −2.5 to −0.2)[b] Medication use: 21% vs. 50%, RR 0.41 (95% CI 0.20 to 0.87) A vs. C <u>3.5 months</u> Symptom bothersomeness (0-10): 1.8 vs. 4.1, adjusted difference −2.2 (95% CI −3.2 to −1.2) Modified RDQ (0-23): 3 vs. 7, adjusted difference −3.6 (95% CI −5.4 to −1.8) Reduction in RDQ ≥50%: 69% vs. 30%, RR 2.3 (95% CI 1.3 to 4.2)	A vs. B <u>3.5 months</u> Medication use: 21% vs. 59%, RR 0.35 (95% CI 0.15 to 0.73) SF-36: No significant differences (data not provided)
Sherman, 2011[176] 3.5 months Duration of pain: 3 to 6 months *Fair*	A. Viniyoga (n=92) 12 sessions 1 session/week for 12 weeks B. Exercise (n=91) C. Attention control (self-care advice) (n=30)	A vs. B Age: 47 vs. 49 vs. 50 Female: 67% vs. 63% vs. 60% Baseline RDQ: 9.8 vs. 8.6 vs. 9.0 Baseline symptom bothersomeness (0-10): 4.9 vs. 4.5 vs. 4.7	A vs. B <u>3.5 months</u> Modified RDQ (0-23): 4.49 (95% CI 3.51 to 5.48) vs. 4.26 (95% CI 3.30 to 5.22), adjusted difference −0.35 (95% CI −1.52 to 0.83) Reduction in RDQ score ≥50%: 60% vs. 51%, RR 1.17 (95% CI 0.88 to 1.54) Symptom bothersomeness (0-10): 3.59 (95 % CI 3.12 to 4.06) vs. 3.34 (95% CI 2.86 to 3.81) A vs. C <u>3.5 months</u> Modified RDQ (0-23): 4.49 vs. 5.73, adjusted difference −1.81 (95% CI −3.12 to −0.50) Reduction in RDQ score ≥50%: 60% vs. 31%, RR 1.90 (95% CI 1.21 to 2.99) Symptom bothersomeness (0-10): 3.59 (95% CI 3.12 to 4.06) vs. 3.80 (95% CI 3.14 to 4.46)	A vs. B <u>3.5 months</u> LBP better, much better, or completely gone: 51% vs. 51%, RR 1.00 (95% CI 0.75 to 1.34) A vs. C LBP better, much better, or completely gone: 51% vs. 20%, RR 2.57, 95% CI 1.39 to 4.78)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Tilbrook, 2011[177] 3 and 6 months Duration of pain: 96 vs. 72 months *Fair*	A. Iyengar yoga (n=156) 12 sessions 1 session/week for 12 weeks B. Attention control (self-care advice) (n=157)	A vs. B Age: 46 vs. 46 Female: 68% vs. 73% Baseline RDQ (0-24): 7.84 vs. 7.75 Baseline Aberdeen Back Pain Scale (0-100): 25.36 vs. 26.69	A vs. B MD in change from baseline (95% CI) <u>3 months</u> RDQ (0-24): −1.48 (−2.62 to −0.33) Aberdeen Back Pain Scale (0 to 100): −1.74 (−4.32 to 0.84) <u>6 months</u> RDQ(0-24): −1.57 (−2.71 to −0.42) Aberdeen Back Pain Scale: −0.73 (−3.30 to 1.84)	A vs. B MD in change from baseline (95% CI) <u>3 months</u> SF-12 PCS (0-100): 1.24 (−0.83 to 3.33) SF-12 MCS (0-100): 2.02 (−0.34 to 4.37) <u>6 months</u> SF-12 PCS: 0.80 (−1.28 to 2.87) SF-12 MCS: 0.42 (−1.92 to 2.77)
Williams, 2005[179] 3 months Duration of pain: 11.3 vs. 11.0 years *Fair*	A. Iyengar yoga (n=30), 16 sessions 1 session/week for 16 weeks B. Attention control (education) (n=30)	A vs. B Age: 49 vs. 48 Female: 65% vs. 70% Pain Disability Index (7-70): 14.3 vs. 21.2 Pain intensity, McGill Pain Questionnaire (0-10 VAS): 2.3 vs. 3.2	A vs. B <u>3 months</u> Pain Disability Index (7-70): 3.9 vs. 12.7, P=0.009 Pain, McGill Pain Questionnaire (0-10 VAS): 0.6 vs. 2.0, P=0.039 Present Pain Index (0-5): 0.5 vs. 1.1, P=0.013	A vs. B <u>3 months</u> Stopped or decreased medication use: 50% vs. 33%, P=0.007
Williams, 2009[178] 6 months Duration of pain: 47 vs. 78 months *Fair*	A. Iyengar yoga (n=43) 48 sessions for 24 weeks B. Waitlist (standard medical care) (n=47)	A vs. B Age: 48 vs. 48 years Female: 74% vs. 79% Oswestry Disability Index (0-100): 25.2 vs. 23.1 Pain (0-100 VAS): 41.9 vs. 41.2	A vs. B <u>6 months</u> Oswestry Disability Index (0-100): 19.3 vs. 23.5, P=0.001 Pain (0-100 VAS): 22.2 vs. 38.3, P=0.0009	A vs. B <u>6 months</u> Beck Depression Inventory (0-63): 4.6 vs. 7.8, P=0.0004

CI = confidence interval; EQ = EuroQol; LBP = low back pain; NR = not reported; NRS = numeric rating scale; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; RR = risk ratio; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Adjusted for baseline scores

Yoga Compared With an Attention Control or Waitlist

Yoga was associated with slightly greater effects on short-term function than controls (6 trials, pooled SMD −0.50, 95% CI −0.72 to −0.29, I^2=54%) (Figure 16).[173-177,179] Results were similar when trials were stratified according to whether they evaluated Viniyoga (2 trials, pooled SMD −0.56, 95% CI −1.38 to 0.19),[175,176] Hatha yoga (2 trials, SMD −0.44, 95% CI −0.82 to −0.08),[173,174] or Iyengar yoga (2 trials, SMD −0.54, 95% CI −1.41 to 0.14).[177,179] All trials evaluated function using the RDQ or modified RDQ, with a MD on a 0 to 24 or 0 to 23 scale of −2.24 (95% CI −3.30 to −1.18, I^2=52%).[173-177] Yoga was also associated with greater effects on

intermediate-term function than controls (3 trials, pooled SMD −0.33, 95% CI −0.49 to −0.16, I^2=0%).[174,177,178] In two trials that evaluated function with the RDQ or modified RDQ, the MD was −1.58 points (95% CI −2.47 to −0.70, I^2=0%).[174,177]

Yoga was associated with moderately greater effects on short-term pain than an attention or wait list control (5 trials, pooled difference −1.10, 95% CI −1.77 to −0.42 on a 0 to 10 scale, I^2=74%) (Figure 17).[173-176,179] Estimates were similar from two trials of Viniyoga (pooled difference −1.25, 95% CI −3.78 to 1.27),[175,176] two trials of Hatha yoga (difference −0.80, 95% CI −1.46 to −0.20),[173,174] and one trial of Iyengar yoga (MD −1.40, 95% CI −2.27 to −0.53).[179] No trials were rated poor quality. Yoga was also associated with greater effects on intermediate-term pain than controls, based on two trials (pooled MD −1.17, 95% CI −1.91 to −0.44, I^2=26%).[174,178]

Data on effects of yoga on quality of life were limited. One trial found no difference between yoga versus an attention control on the SF-36 Physical and Mental Component Summaries at short-term or intermediate-term followup (differences 0.42 to 2.02 points on a 0 to 100 scale).[177] One other trial found no differences between yoga versus an attention control on the SF-36, but data were not provided.[175]

One trial found yoga associated with lower (better) scores on the Beck Depression Inventory than waitlist at intermediate-term followup (mean 4.6 vs. 7.8 on a 0 to 63 scale, P=0.004)[178] and one trial found no difference between yoga versus waitlist in opioid use (9% vs. 7%, P=0.40) or other medical treatments for pain (39% vs. 37%, P=0.42) at short-term followup.[173]

Yoga Compared With Pharmacological Therapy

No trial of yoga versus pharmacological therapy met inclusion criteria.

Yoga Compared With Exercise

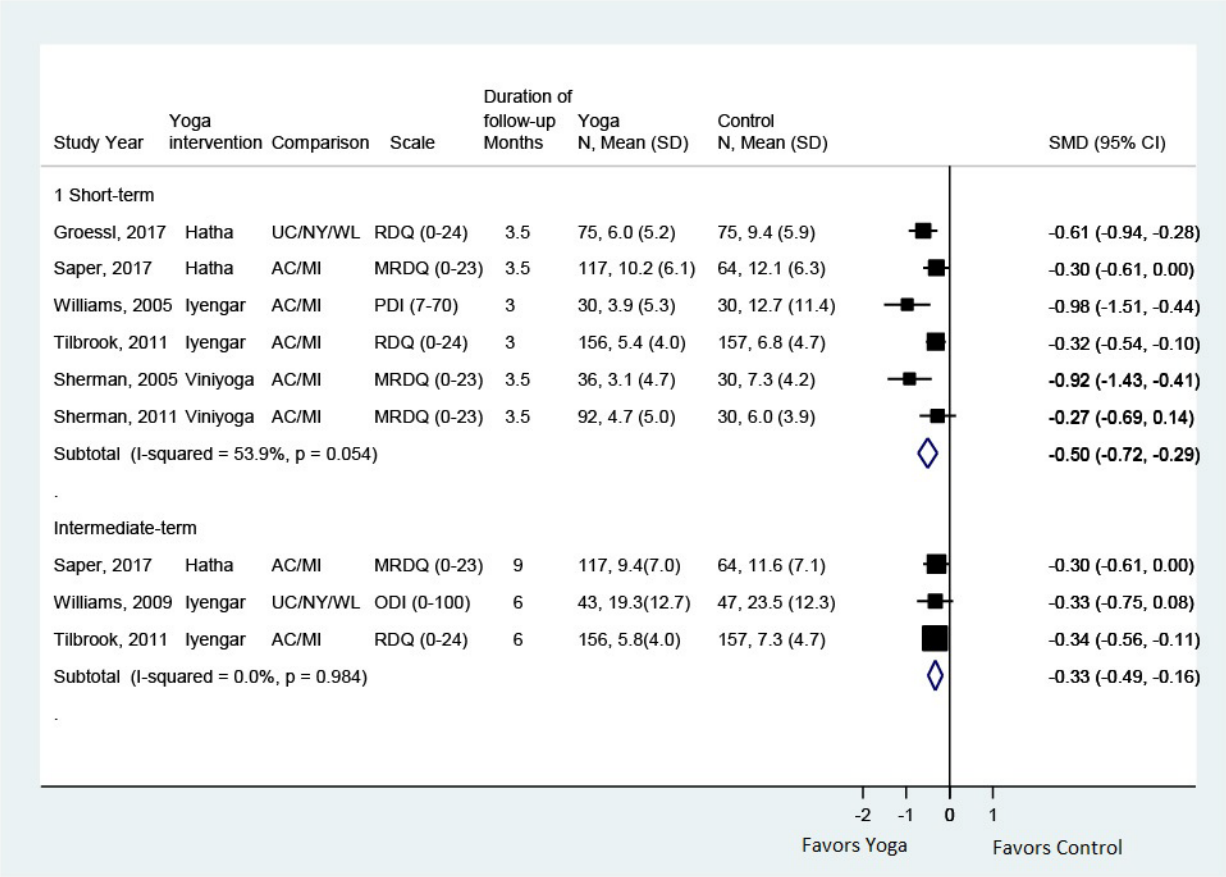
There were no differences between yoga versus exercise in short-term function (3 trials, pooled SMD −0.10, 95% CI −0.34 to 0.13, I^2=38%)[174-176] or intermediate-term function (1 trial, SMD −0.01, 95% CI −0.26 to 0.24)[174] (Figure 18). One trial found no difference between yoga versus exercise on the SF-36 at short-term followup (data not provided).[175]

Effects of yoga versus exercise on short-term pain were not statistically significant and there was marked heterogeneity (4 trials, pooled difference −0.89 on a 0 to 10 scale, 95% CI −1.99 to 0.21, I^2=92%) (Figure 19).[174-176,186] In one trial of Viniyoga,[176] results favored exercise (difference 0.25, 95% CI −0.41 to 0.91), and in three trials (one each of Viniyoga, Iyengar yoga, and Hatha yoga)[174,175,186] effects favored yoga (MDs of −0.30 to −2.00). No trials were rated poor quality. One trial found no difference between yoga versus exercise in intermediate-term pain (difference 0.30, 95% CI −0.39 to 0.99).[174]

Harms

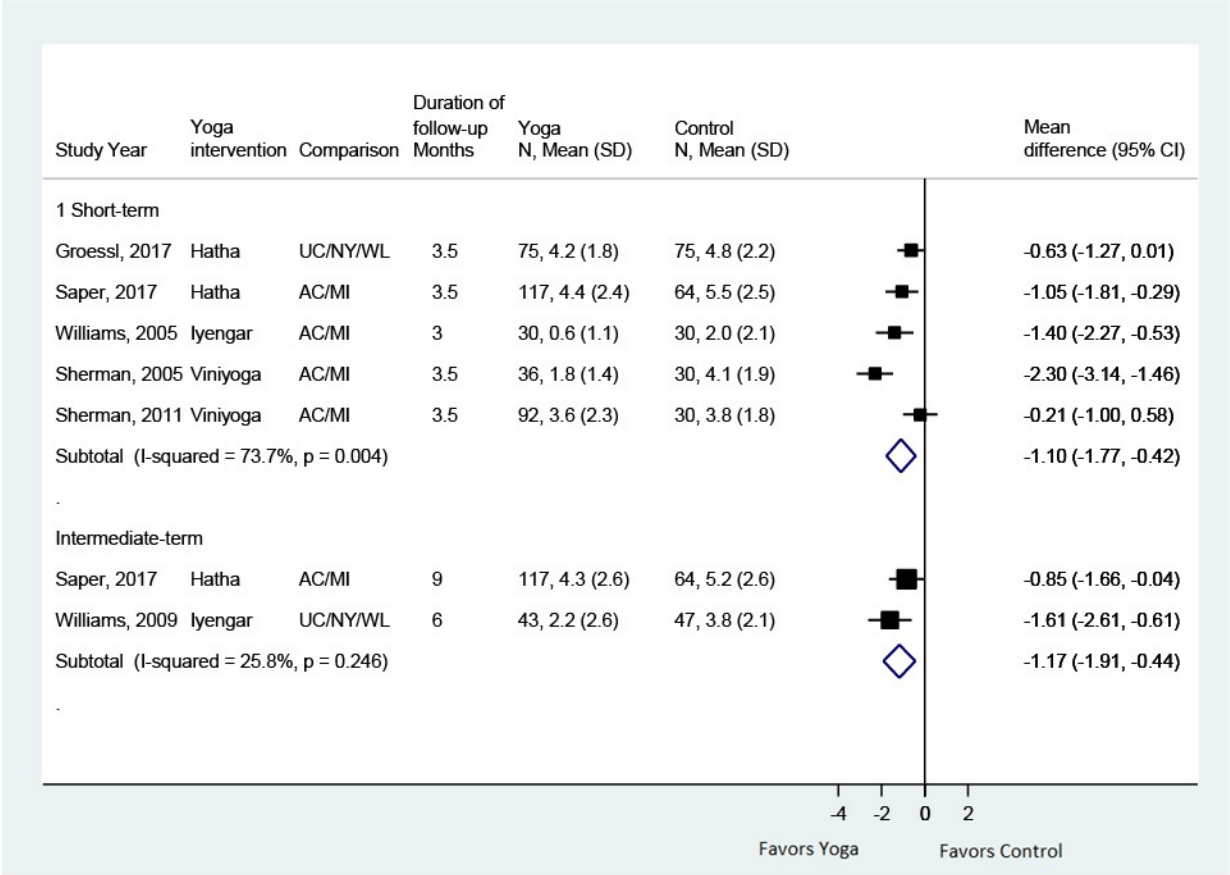
Data on harms were limited, but trials reported no clear difference between yoga versus control interventions in risk of any adverse event.[174,176,177] For serious adverse events, one trial reported a case of cellulitis in a patient randomized to yoga.[174]

Figure 16. Yoga versus attention control or waitlist for chronic low back pain: effects on function



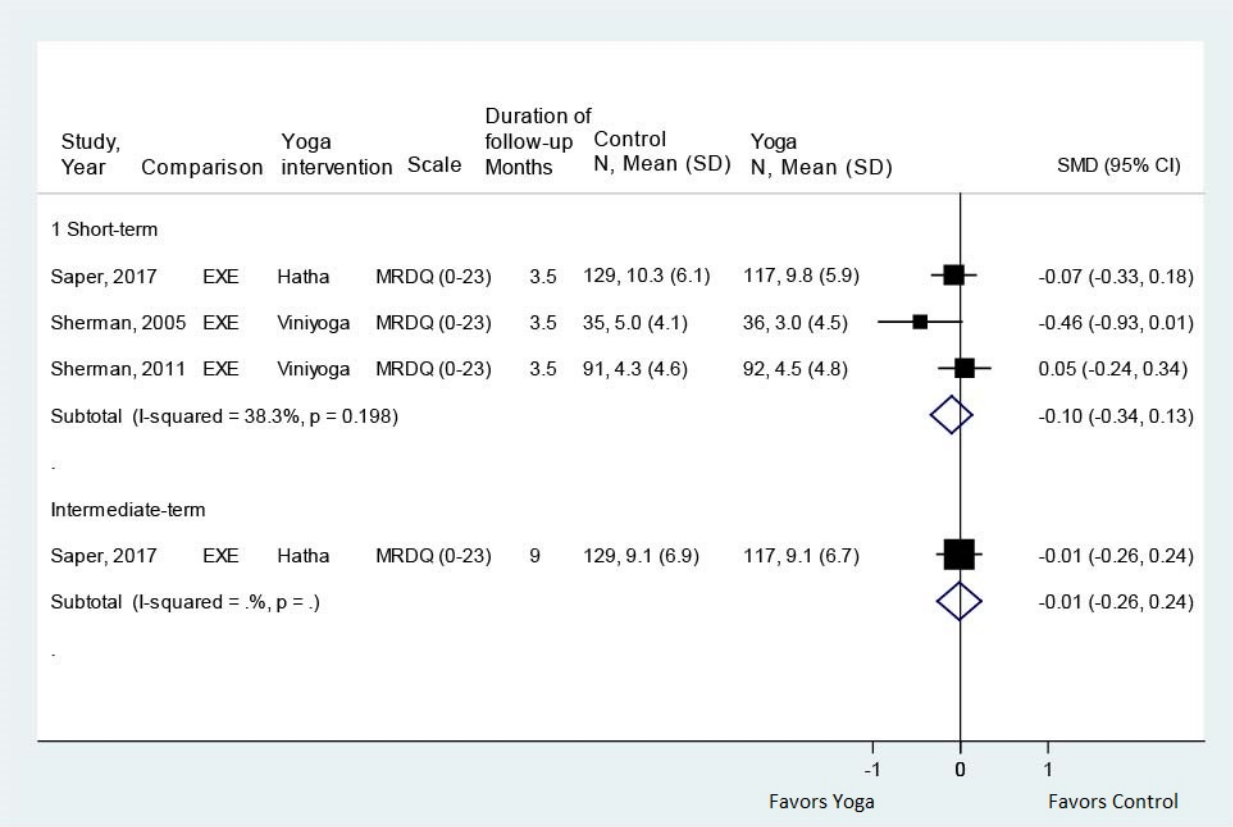
AC = attention control; CI = confidence interval; MI = minimal intervention; MRDQ = Modified Roland-Morris Disability Questionnaire; N = number; NY = no yoga; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SMD = standardized mean difference; UC = usual care; WL = waitlist

Figure 17. Yoga versus attention control or waitlist for chronic low back pain: effects on pain



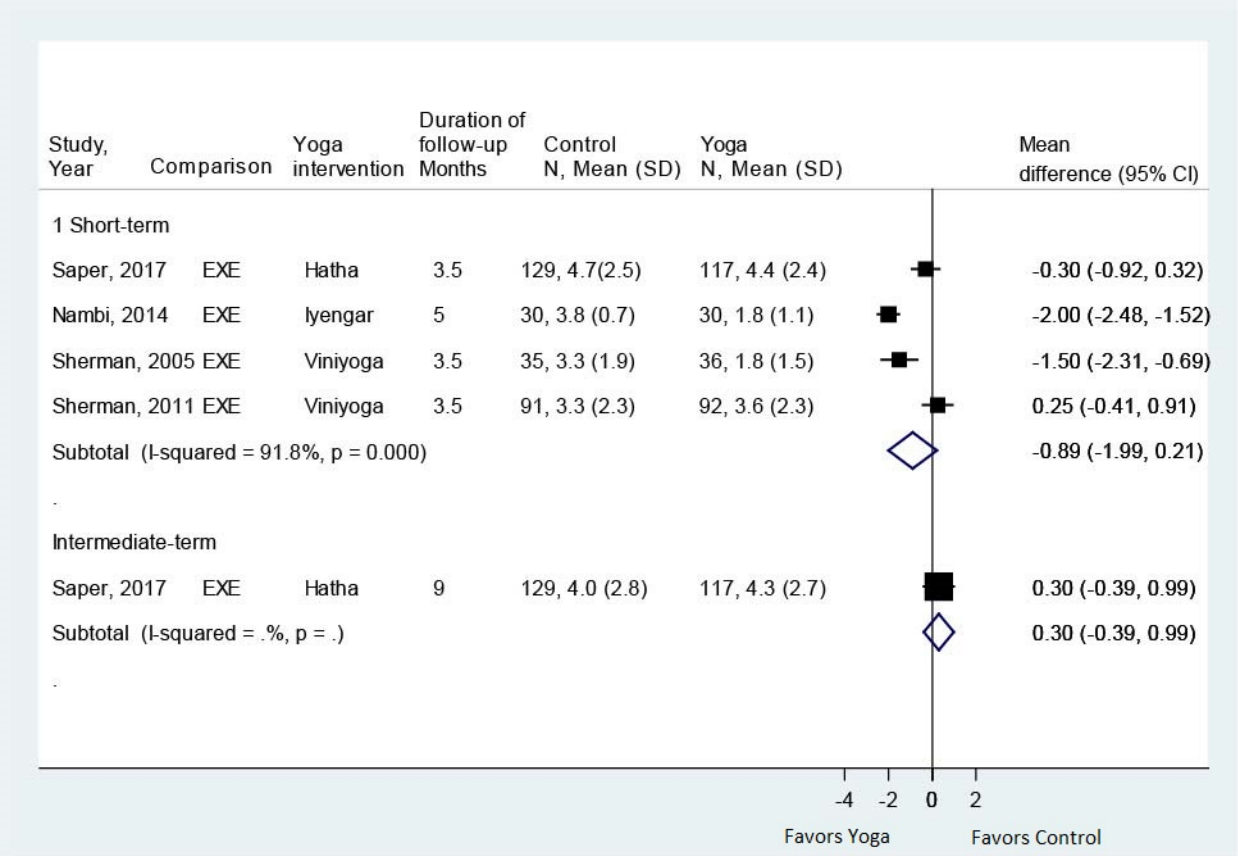
AC = attention control; CI = confidence interval; MI = minimal intervention; N=number; NY = no yoga; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; UC = usual care; WL = waitlist

Figure 18. Yoga versus exercise for chronic low back pain: effects on function



CI = confidence interval; EXE = exercise; MRDQ = Modified Roland-Morris Disability Questionnaire; N = number; SD = standard deviation; SMD = standardized mean difference

Figure 19. Yoga versus exercise for chronic low back pain: effects on pain



CI = confidence interval; EXE = exercise; N = number; SD = standard deviation

Qigong

There was no difference between qigong versus exercise in short-term function (difference 0.9 on the 0 to 24 RDQ, 95% CI −0.1 to 2.0), although intermediate-term results slightly favored exercise (difference 1.2, 95% CI 0.1 to 2.3). One German trial (n=125) compared qigong (weekly sessions for 3 months) versus exercise therapy (including stretching and strengthening) (Table 15 and Appendix D).[185] It was rated fair quality due to baseline differences between groups, unblinded design, and suboptimal compliance (Appendix E). Qigong was associated with slightly worse pain versus exercise at short-term followup (MD 7.7 on a 0 to 100 scale, 95% CI 0.7 to 14.7), but the difference at intermediate-term was not statistically significant (MD 7.1, 95% CI −1.0 to 15.2). There were no differences in sleep, measures of the SF-36 PCS or MCS scores, or in risk of adverse events.

Table 15. Chronic low back pain: mind-body practices (qigong)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Blodt, 2015[185] 3 and 9 months Duration of pain: Mean 3 years *Fair*	A. Qigong (movement exercises and exercise to change "qi") (n=64) 12 sessions over 12 weeks B. Exercise (strengthening, stretching and relaxation exercises) (n=63)	A vs. B Age (mean): 46 vs. 48 years Female: 91% vs. 70% Baseline RDQ: 6.2 vs. 5.7 Baseline pain (0-100 VAS): 55.6 vs. 52.1	A vs. B <u>3 months</u> RDQ (0-24): 4.1 vs. 3.1, difference 0.9 (95% CI –0.1 to 2.0) Average low back pain (0-100 VAS): 35.1 vs. 27.4, difference 7.7 (95% CI 0.7 to 14.7) <u>9 months</u> RDQ: 4.3 vs. 3.1, difference 1.2 (95% CI 0.1 to 2.3) Average low back pain (0-100 VAS): 35.9 vs. 28.8, difference 7.1 (95% CI –1.0 to 15.2)	A vs. B <u>3 months</u> SF-36 Bodily pain (0-100): 43.0 vs. 44.6, difference 1.5 (95% CI −1.2 to 4.2) SF-36 Physical component score: 45.8 vs. 46.6, difference −0.8 (95% CI –3.4 to 1.9) SF-36 Mental component score: 45.4 vs. 46.6, difference 11.2 (95% CI –4.9 to 2.4) Quality of sleep (0-10): 4.6 vs. 4.5, difference 0.0 (95% CI–0.9 to 1.0) Sleep satisfaction (0-10): 5.0 vs. 4.8, difference 0.3 (95% CI –0.6 to 1.1) <u>9 months</u> SF-36 Bodily pain: 41.4 vs. 43.4, difference −2.0 (95% CI −5.4 to 1.4) SF-36 Physical component score: 44.8 vs. 46.5, difference −1.8 (95% CI −4.9 to 1.3) SF-36 Mental component score: 45.0 vs. 45.5, difference −0.5 (95% CI −4.6 to 3.6) Quality of sleep: 4.5 vs. 4.7, difference −0.2 (95% CI −1.0 to 0.7) Sleep satisfaction: 5.1 vs. 5.1, difference −0.1 (95% CI –0.9 to 0.8)

CI = confidence interval; RDQ = Roland-Morris Disability Questionnaire; SF-36 = Short-Form 36 Questionnaire; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Acupuncture for Chronic Low Back Pain

Key Points

- Acupuncture was associated with slightly greater effects on short-term function than sham acupuncture or usual care (4 trials, pooled SMD −0.22, 95% CI −0.35 to −0.08, I^2=44%). There was no evidence of differences between acupuncture versus controls in intermediate-term function (3 trials, pooled SMD −0.08, 95% CI −0.36 to 0.20, I^2=75%) or long-term function (1 trial, adjusted MD −3.4 on the 0 to 100 ODI, 95% CI −7.8 to 1.0) (SOE: low).
- Acupuncture was associated with slightly greater effects on short-term pain than sham acupuncture, usual care, an attention control, or a placebo intervention (5 trials, pooled MD −0.55 on a 0 to 10 scale, 95% CI −0.86 to −0.24, I^2=30%). There was no evidence of differences in intermediate-term pain (5 trials, pooled MD −0.25, 95% CI −0.67 to 0.16, I^2=33%); one trial found acupuncture associated with greater effects on long-term pain (MD −0.83, 95% CI −1.51 to −0.15) (SOE: moderate for short term, low for intermediate term and long term).
- There was no clear difference between acupuncture versus control interventions in risk of withdrawal due to adverse events. Serious adverse events were rare with acupuncture and control interventions (SOE: low).

Detailed Synthesis

Eight trials of acupuncture for low back pain met inclusion criteria (Table 16 and Appendix D).[149,189-195] All trials evaluated needle acupuncture to body acupoints; one trial also evaluated electroacupuncture.[190] Sample sizes ranged from 40 to 1,162 (total sample=2,621). Four trials compared acupuncture versus sham acupuncture,[189,191-193] three trials acupuncture versus usual care,[191,193,195] two trials acupuncture versus a placebo intervention (sham transcutaneous electrical nerve stimulation [TENS]),[190,194] and one trial acupuncture versus an attention control (self-care education).[149] One trial was conducted in Asia[192] and the rest in the United States or Europe. The duration of acupuncture therapy ranged from 6 to 12 weeks and the number of acupuncture sessions ranged from 6 to 15. One trial reported outcomes through long-term followup,[195] four trials through intermediate-term followup,[149,189-191] and the remainder only evaluated short-term outcomes.

One trial was rated good quality,[189] five trials fair quality,[149,191-193,195] and two trials[190,194] poor quality (Appendix E). Limitations in the fair-quality and poor-quality trials included unblinded design, unclear randomization or allocation concealment methods, and high attrition.

Table 16. Chronic low back pain: acupuncture

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Brinkhaus, 2006a[189] 4 and 10 months Duration of pain: 14.7 vs. 13.6 years *Good*	A: Needle acupuncture to body acupoints (n=140) 12 sessions over 8 weeks B: Sham acupuncture (n=70)	A vs. B Age: 59 vs. 58 years Female: 64% vs. 75% Baseline Functional (FFbH-R) score: 57.1 vs. 57.2 Baseline pain (0-100 VAS): 63 vs. 66 Baseline Pain Disability Index (0-70): 28.9 vs. 31.5	A vs. B <u>4 months</u> Functional (0-10, FFbH-R 0, higher scores indicate better function): 66.0 vs. 64.1, difference 1.9 (95% CI −4.2 to 8.0) Number of days with limited function in past 6 months: 40.9 vs. 59.5, difference −18.6 (95% CI −33.3 to −3.9) Pain (0-100 VAS): 38.4 vs. 42.1, difference −3.8 (95% CI −12.4 to 4.9) Pain Disability Index (0-70): 19.3 vs. 21.4, difference −2.1 (95% CI −6.3 to 2.1) <u>10 months</u> Functional (0-100 FFbH-R): 66.0 vs. 63.1, difference 2.9 (95% CI −3.2 to 9.0) Number of days with limited function in past 6 months: 42.4 vs. 52.9, difference −10.5 (95% CI −27.0 to 6.1) Pain (0-100 VAS): 39.2 vs. 44.9, difference −5.7 (95% CI −14.4 to 3.0) Pain Disability Index: 19.0 vs. 23.0, difference −4.0 (95% CI −8.1 to 0.1)	A vs. B <u>4 months</u> SF-36 bodily pain subscale (0-100): 53.6 vs. 49.6, difference 3.9 (95% CI −2.7 to 10.7) SF-36 PCS (0-100): 39.3 vs. 37.6, difference 1.7 (95% CI −1.3 to 4.7) SF-36 MCS (0-100): 49.9 vs. 46.8, difference 3.1 (95% CI −0.5 to 6.6) Allgemaine Depressionssskala (ADS, t standard): 49.7 vs. 50.3, difference −0.6 (95% CI −2.5 to 3.7) <u>10 months</u> SF-36 bodily pain subscale: 52.4 vs. 44.0, difference 8.5 (95% CI 1.7 to 15.2) SF-36 PCS: 38.9 vs. 36.1, difference 2.8 (95% CI −0.2 to 5.7) SF-36 MCS: 50.5 vs. 47.2, difference 3.3 (95% CI 0.1 to 6.5) ADS: 48.2 vs. 50.7, difference −2.5 (95% CI −5.3 to 0.4)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Carlsson, 2001[190] 1, 3, 6 months Duration of pain: 6 months or longer *Poor*	A. Needle acupuncture or electroacupuncture (n=34), 8 sessions over 8 weeks, with followup session at 3 and 6 months B. Placebo (sham transcutaneous electrical nerve stimulation) (n=16)	A vs. B (NR) Age: 50 years Female: 66% Baseline function: NR Baseline Pain (0-100 VAS): 57 vs. 46	A vs. B <u>1 month</u> Pain (0-100 VAS): 50 vs. 60, P not reported Global assessment "pain improved": 47% vs. 13%, RR 3.76 (95% CI 0.98 to 14.4) <u>3 months</u> Pain (0-100 VAS): 42 vs. 56, P not reported Global assessment "pain improved": 44% vs. 13%, RR 6.87 (95% CI 1.87 to 25.1) <u>≥6 months outcomes</u> Pain (0-100 VAS): 41 vs. 50, P not reported Global assessment "pain improved": 41% vs. 13%, RR 3.29 (95% CI 0.85 to 12.8)	A vs. B <u>≥6 months</u> Analgesic intake (tablets per week): 21.4 vs. 21.5 Work full time: 32% vs. 31%
Cherkin, 2001[149] 9.5 months Duration of pain: 3 to 12 months, mean not reported *Fair*	A. Needle acupuncture (n=94),10 sessions over 10 weeks B. Attention control (education) (n=90)	A vs. B Age: 54 vs. 44 years Female: 52% vs. 44% Baseline symptom bothersomeness (0-10): 6.2 vs. 6.1 Baseline modified RDQ (0-23): 12. vs. 12.0	A vs. B <u>9.5 months</u> Symptom bothersomeness (0-10): 4.5 vs. 3.8, adjusted P=0.002 Modified RDQ (0-23): 8.0 vs. 6.4, adjusted P=0.05	A vs. B <u>9.5 months</u> ≥1 work-loss day due to LBP in past month: No difference (data not reported) Medication use: 51% vs. 62%, P<0.05 Provider visits:1.9 (SD 3.7) vs. 1.5 (SD 4.0) LBP medication fills: 4.4 (SD 8.9) vs. 4.0 (SD 8.6) Imaging studies: 0.2 (SD 0.4) vs. 0.1 (SD 0.4) Cost of services (1998 $): 252 (SD 46) vs. 200 (SD 45)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Cherkin, 2009[191] 4.5 and 10.5 months Duration of pain: 3 to12 months, mean not reported *Fair*	A. Needle acupuncture (individualized) (n=157), 10 sessions over 7 weeks B. Needle acupuncture (standardized) (n=158), 10 sessions over 7 weeks C. Sham acupuncture (n=162) D. Usual care (n=161)	A vs. B vs. C vs. D Age: 47 vs. 49 vs. 47 vs. 46 years Female: 68% vs. 56% vs. 60% vs. 64% Symptom bothersomeness (0-10): 5.0 vs. 5.0 vs. 4.9 vs. 5.4 Baseline pain (0-10 VAS): 5.0 vs. 5.0 vs. 4.9 vs. 5.3 Baseline modified RDQ (0-23): 10.8 vs. 10.8 vs. 9.8 vs. 11.0	A vs. B <u>4.5 months</u> Symptom bothersomeness (0-10): 3.8 (2.5) vs. 3.7 (2.6) vs. 3.5 (2.7) vs. 4.4 (2.6) ≥2 point decrease in symptom bothersomeness: 49% vs. 44% vs. 48% vs. 41% Modified RDQ (0-23): 6.8 (5.5) vs. 6.7 (5.8) vs. 6.4 (6.0) vs. 8.4 (6.0) <u>10.5 months</u> Symptom bothersomeness (0-10): 3.7 (2.6) vs. 3.5 (2.7) vs. 3.4 (2.7) vs. 4.1 (2.6) ≥2 point decrease in symptom bothersomeness: 52% vs. 49% vs. 50% vs. 47% Modified RDQ (0-23): 6.0 (5.4) vs. 6.0 (5.8) vs. 6.2 (5.8) vs. 7.9 (6.5) ≥3 point decrease on RMDQ: 65% vs. 65% vs. 59% vs. 50% >7 days with cutting down on activities due to LBP in the past month: A, B and C 5-7% vs. D 18%, P=0.0005	A vs. B <u>10.5 months</u> SF-36 PCS: No differences, data not provided SF-36 MCS: No differences, data not provided Missed work/school for >1 day in past month: A, B and C 5-10% vs. D 16%, P=0.01 Mean total costs of back-related health services: $160-221 across groups, P=0.65
Cho, 2013[192] 1.5 and 4 months Duration of pain: 3 months *Fair*	A. Needle acupuncture (n=57), 12 sessions over 6 weeks B. Sham acupuncture (n=59)	A vs. B Age: 42 vs. 42 years Female: 83% vs. 86% Baseline ODI (0-100): 28.2 vs. 24.2 Baseline pain (0-10 VAS): 6.5 vs. 6.4	A vs. B <u>1.5 months</u> ODI (0-100): 15.5 vs. 15.5, SD not reported Symptom bothersomeness (0-10 VAS): 2.83 (2.34) vs. 3.99 (2.06) Pain (0-10 VAS): 2.78 (2.32) vs. 4.06 (2.19) <u>4 months</u> ODI: 15.3 vs. 15.3, SD not reported Symptom bothersomeness: 2.85 (2.44) vs. 3.63 (2.37) Pain (0-10 VAS): 2.79 (2.44) vs. 3.52 (2.53)	A vs. B <u>1.5 months</u> Beck Depression Inventory (0-63): 6 vs. 7.5, SD not reported <u>4 months</u> Beck Depression Inventory: 6 vs. 7, SD not reported

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Haake, 2007[193] 1.5 and 4.5 months Duration of pain: Mean 8 years *Fair*	A. Needle acupuncture (n=387), 10-15 sessions over 5 weeks B. Sham acupuncture (n=387) C. Usual care (n=388)	A vs. B vs. C Age: 50 vs. 49 vs. 51 years Female: 57% vs. 64% vs. 58% Baseline Hannover Functional Ability Questionnaire (0-100): 46.3 vs. 46.3 vs. 46.7 Baseline Von Korff Chronic Pain Grade Scale (0-100): 67.7 vs. 67.8 vs. 67.8	A vs. B <u>1.5 months</u> Hannover Functional Ability (0-100): 65.4 (22.9) vs. 61.3 (22.7) vs. 56.0 (22.0) Von Korff Chronic Pain Grade Scale (0-100): 45.4 (19.4) vs. 48.5 (19.5) vs. 54.8 (18.4) <u>4.5 months</u> Hannover Functional Ability (0-100): 66.8 (23.1) vs. 62.2 (23.0) vs. 55.7 (22.7) Von Korff Chronic Pain Grade Scale: 40.2 (22.5) vs. 43.3 (23.0) vs. 52.3 (21.2)	A vs. B <u>1.5 months</u> SF-12 PCS (0-100): 40.3 vs. 39.2 vs. 36.1 SF-12 MCS (0-100): 50.5 vs. 50.2 vs. 48.6 Treatment response (≥33% improvement in pain or ≥12% improvement in function): 55.0% (213/387) vs. 51.9% (201/387) vs. 41.9% (162/387), RR 1.05 (95% CI 0.93 to 1.21) for A vs. B and RR 1.31 (95% CI 1.13 to 1.52) for A vs. C <u>4.5 months</u> SF-12 PCS (0-100): 41.6 vs. 39. vs. 35.8 SF-12 MCS (0-100): 50.7 vs. 50.9 vs. 49.2 Treatment response: 47.6% (184/387) vs. 44.2% (171/387) vs. 27.4% (106/387), RR 1.08 (95% CI 0.92 to 1.25) for A vs. B and RR 1.74 (95% CI 1.43 to 2.11) for A vs. C
Kerr, 2003[194] 4.5 months Duration of pain: Mean 86 vs. 73 months *Poor*	A. Needle acupuncture (n=26), 6 sessions over 6 weeks B. Placebo (sham TENS) (n=20)	A vs. B Age: 43 vs. 43 years Female: 50% vs. 35% Baseline function: NR Baseline pain (0-100 VAS): 79.7 vs. 76	A vs. B <u>4.5 months</u> Pain relief "yes": 91% vs. 75%, RR 1.19 (95% CI 0.89 to 1.60)	

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Thomas, 2006[195] 9 and 21 months Duration of pain: Mean 17 weeks *Fair*	A. Needle acupuncture (n=147), 10 sessions over 12 weeks B. Usual care (n=68)	A vs. B Age: 42 vs. 44 Female: 62% vs. 58% Baseline ODI (0-100): 33.7 vs. 31.4 Baseline McGill Present Pain Index (0-5): 2.64 vs. 2.70	A vs. B <u>9 months</u> ODI (0-100): 20.6 vs. 19.6, adjusted difference −0.5 (−5.1 to 4.2) McGill Present Pain Index (0-5): 1.43 vs. 1.53, adjusted difference −0.1 (−0.4 to 0.3) <u>21 months</u> ODI: 18.3 vs. 21.0, adjusted difference −3.4 (−7.8 to 1.0) McGill Present Pain Index: 1.42 (1.1) vs. 1.71, adjusted difference −0.2 (−0.6 to 0.1)	A vs. B <u>9 months</u> SF-36 bodily pain (0-100): 64.0 vs. 58.3, adjusted difference 5.6 (95% CI −0.2 to 11.4) <u>21 months</u> Used medication for LBP in the past 4 weeks: 40% vs. 59%, difference −19% (−35 to −3), P=0.03 <u>21 months</u> SF-36 bodily pain: 67.8 vs. 59.5, adjusted difference 8.0 (2.8 to 13.2)

CI = confidence interval; FFbH-R = Funktionsfragebogen Hannover-Rücken (Hannover Functional Ability Questionnaire-back); MCS = Mental Component Summary; NR = not reported; ODI = Oswestry Disability Index; PCS = Physical Component Summary; RDQ = Roland-Morris Disability Questionnaire; RR = Relative risk; SF-36 = Short-Form 36 Questionnaire; TENS = transcutaneous electrical nerve stimulation; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Acupuncture Compared With Sham Acupuncture, Usual Care, an Attention Control, or a Placebo Intervention

Acupuncture was associated with slightly greater effects on short-term function than sham acupuncture or usual care (4 trials, pooled SMD −0.22, 95% CI −0.35 to −0.08, I^2=44%) (Figure 20).[189,191-193] Each trial measured function using a different scale; across trials the SMD ranged from −0.34 to 0.00. Differences were slightly greater in trials that compared acupuncture against usual care (2 trials, SMD −0.42, 95% CI −0.60 to −0.21)[191,193] than against sham acupuncture (4 trials, SMD −0.13, 95% CI −0.24 to 0.01).[189,191-193] None of the trials were rated poor quality. There were no differences between acupuncture versus controls in intermediate-term function (3 trials, pooled SMD −0.08, 95% CI −0.36 to 0.20, I^2=75%)[149,189,191] or long-term function (1 trial, adjusted difference −3.4 on the 0 to 100 ODI, 95% CI −7.8 to 1.0).[195]

Acupuncture was associated with slightly greater effects on short-term pain than sham acupuncture, usual care, an attention control, or a placebo intervention (5 trials, pooled difference −0.55 on a 0 to 10 scale, 95% CI −0.86 to −0.24, I^2=30%) (Figure 21).[189-193] The pooled estimate was similar when poor-quality trials were excluded. When stratified according to the type of control intervention, acupuncture was associated with greater effects when compared with usual care (2 trials, pooled MD −1.00, 95% CI −1.60 to −0.28)[191,193] than when compared with sham acupuncture (4 trials, pooled MD −0.20, 95% CI −0.66 to 0.19).[189,191-193] There was no difference between acupuncture versus controls in intermediate-term pain (5 trials, pooled MD −0.25, 95% CI −0.67 to 0.16, I^2=33%).[149,189-191,195] One trial found acupuncture associated with greater effects on long-term pain than usual care (MD −0.83, 95% CI −1.51 to −0.15).[195]

Data on effects of acupuncture on quality of life were limited. In two trials, differences between acupuncture versus sham acupuncture or usual care on short-term or intermediate-term

SF-36 PCS and MCS scores were small (range 0.65 to 3.95 points on a 0 to 100 scale), and most differences were not statistically significant.[189,193] Two trials found no clear effects of acupuncture and controls on measures of depression.[189,192]

Two trials found no clear differences between acupuncture versus an attention control in measures of health care utilization (provider visits, medication fills, imaging studies, costs of services),[149,191] and one trial found no clear differences at intermediate-term followup between acupuncture versus placebo TENS in likelihood of working full time.[190]

One trial found acupuncture associated with a higher likelihood of short-term (4.5 months) treatment response (defined as ≥33% pain improvement and ≥12% functional improvement) versus usual care (48% vs. 27%, RR 1.74, 95% CI 1.43 to 2.11), but there was no difference versus sham acupuncture (RR 1.08, 95% CI 0.92 to 1.25).[193]

No trial evaluated effects of acupuncture on use of opioid therapies or health care utilization. There was insufficient evidence to determine effects of duration of acupuncture or number of acupuncture sessions on findings.

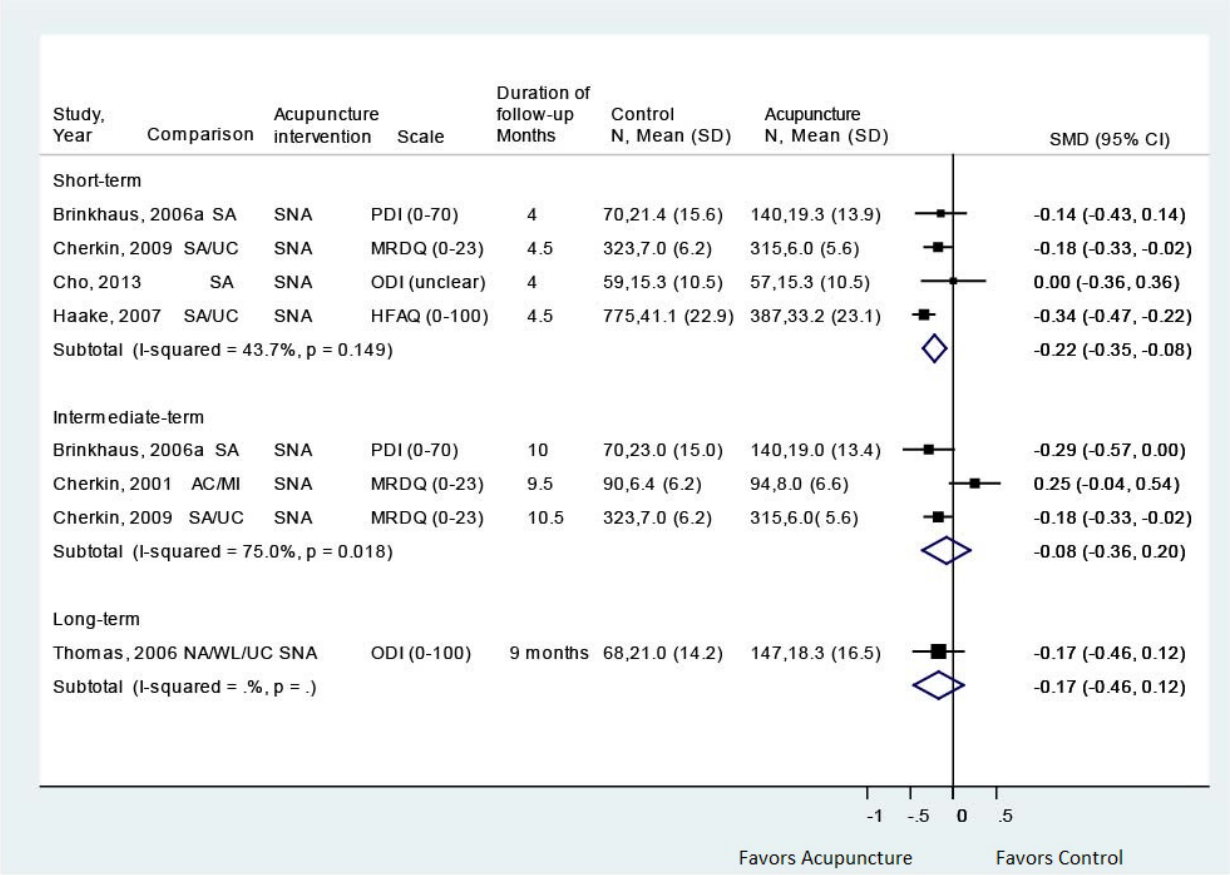
Acupuncture Compared With Pharmacological Therapy or With Exercise

No trial of acupuncture versus pharmacological therapy or versus exercise met inclusion criteria.

Harms

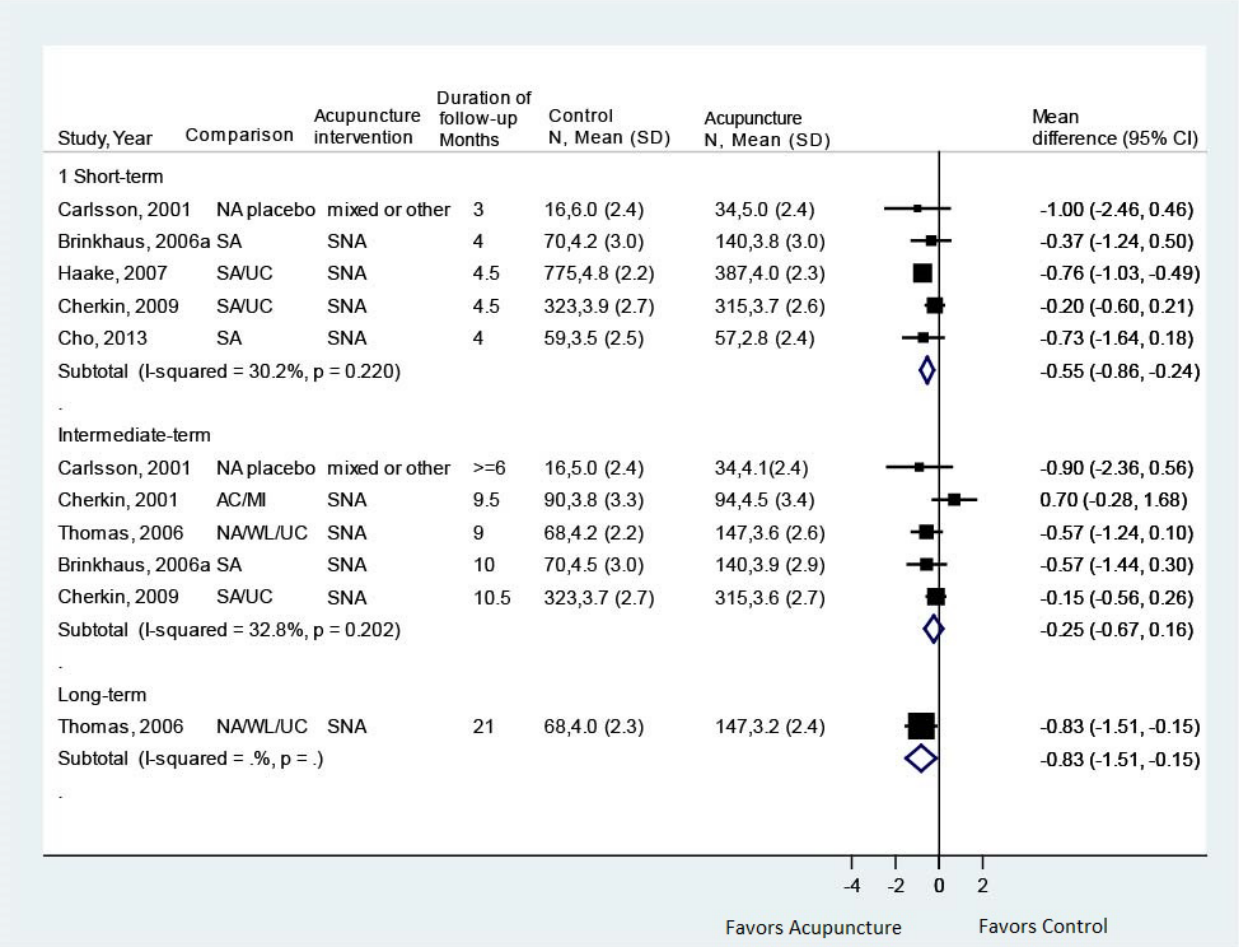
Data on harms were limited but indicated no clear difference between acupuncture versus control interventions in risk of withdrawal due to adverse events.[191,195] Serious adverse events were rare with acupuncture and control interventions.[149,189,191-193]

Figure 20. Acupuncture versus sham acupuncture, usual care, attention control, or a placebo intervention for chronic low back pain: effects on function



AC = attention control; CI = confidence interval; HFAQ = Hannover Functional Ability Questionnaire; MI = minimal intervention; MRDQ = Modified Roland-Morris Disability Questionnaire; N = number; NE = no exercise; ODI = Oswestry Disability Index; PDI = Pain Disability Index; SA=sham acupuncture; SD = standard deviation; SMD = standardized mean difference; SNA =standard needle acupuncture; UC = usual care; WL = waitlist

Figure 21. Acupuncture versus sham acupuncture, usual care, an attention control, or a placebo intervention for chronic low back pain: effects on pain



AC = attention control; CI = confidence interval; MI = minimal intervention; N = number; NA = needle acupuncture; SA=sham acupuncture; SD = standard deviation; SNA = standard needle acupuncture; UC = usual care; WL = waitlist

Multidisciplinary Rehabilitation for Chronic Low Back Pain

Key Points

- Multidisciplinary rehabilitation was associated with slightly greater effects on function than usual care at short-term (4 trials, pooled SMD −0.31, 95% CI −0.57 to −0.05, I^2=70%) and intermediate-term followup (4 trials, pooled SMD −0.37, 95% CI −0.64 to −0.10, I^2=50%); there was no evidence of differences in long-term function (2 trials, pooled SMD −0.04, 95% CI −0.31 to 0.24, I^2=35%) (SOE: low).
- Multidisciplinary rehabilitation was associated with slightly greater effects on pain than usual care at short-term followup (4 trials, pooled MD −0.51 on a 0 to 10 scale, 95% CI −0.89 to −0.13, I^2=23%) and intermediate-term followup (4 trials, pooled MD −0.63, 95% CI −1.04 to −0.22, I^2=0%); the long-term difference was smaller and not statistically significant (2 trials, pooled MD −0.34, 95% CI −0.86 to 0.18, I^2=0%) (SOE: moderate for short term and intermediate term, low for long term).

- Multidisciplinary rehabilitation was associated with slightly greater effects than exercise on short-term function (6 trials, pooled SMD −0.28, 95% CI −0.54 to −0.01, I^2=39%) and intermediate-term function (5 trials [excluding outlier trial], pooled SMD −0.22, 95% CI −0.40 to −0.03, I^2=0%); there was no effect on long-term function (2 trials [excluding outlier trial], pooled SMD −0.06, 95% CI −0.36 to 0.25, I^2=0%) (SOE: moderate for short term and intermediate term, low for long term).
- Multidisciplinary rehabilitation was associated with slightly greater effects than exercise on short-term pain (6 trials, pooled MD −0.75 on a 0 to 10 scale, 95% CI −1.18 to −0.31, I^2=0%) and intermediate-term pain (5 trials [excluding outlier trial], pooled MD −0.55, 95% CI −0.95 to −0.15, I^2=0%); there was no effect on long-term pain (2 trials [excluding outlier trial], pooled MD 0.00, 95% CI −0.94 to 0.95) (SOE: moderate for short term and intermediate term, low for long term).
- Data on harms were sparse; no serious harms were reported (SOE: insufficient).

Detailed Synthesis

Sixteen trials (reported in 21 publications) of multidisciplinary rehabilitation for low back pain met inclusion criteria (Table 17 and Appendix D).[32,109,116,159,218-223,232-244] In accordance with our definition for multidisciplinary rehabilitation, the intervention in all trials included a psychological therapy and an exercise therapy component, with therapy developed by clinicians from at least two disciplines. Most multidisciplinary rehabilitation interventions incorporated techniques and approaches consistent with principles of functional restoration.[246] The intensity of multidisciplinary rehabilitation varied substantially, with treatment ranging from 4 to 150 hours. Five trials evaluated a multidisciplinary rehabilitation intervention that met our criteria for high intensity (≥20 hours/week or >80 hours total).[218,223,233,234,241] The duration of therapy ranged from 4 days to up to 13 weeks. Sample sizes ranged from 20 to 459 (total sample=1,904). Six trials compared multidisciplinary rehabilitation versus usual care,[218-223] nine trials compared multidisciplinary rehabilitation versus exercise therapy,[109,220,233,234,236-241] and one trial compared multidisciplinary rehabilitation versus oral medications.[232] One trial[232] was conducted in Iran and the remainder were conducted in the United States, the United Kingdom, or Australia. Five trials reported outcomes through long-term (12 to 60 months) followup,[109,218,232,233,239] eight trials evaluated outcomes through intermediate-term followup,[109,221-223,234,236,238,241,242] and three trials only evaluated short-term outcomes.[219,237,240]

Ten trials[218,220,221,233,234,237-241] were rated fair quality and six trials poor quality (Appendix E).[109,219,222,223,232,236] The major methodological limitation in the fair-quality trials was the inability to effectively blind patients and caregivers to the multidisciplinary rehabilitation. Other methodological shortcomings included unclear randomization and allocation concealment methods and high attrition.

Table 17. Chronic low back pain: multidisciplinary rehabilitation

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Abbassi, 2012[222] 10.25 months Duration of pain: ~6 years *Poor*	A. Multidisciplinary rehabilitation (n=12), 7 sessions over 7 weeks B. Multidisciplinary pain management (spouse-assisted) (n=10). 7 sessions over 7 weeks C: Usual care (n=11)	A + B + C Overall Age (mean): 45 years Female: 88% A vs. B vs. C Baseline RDQ (0–24): 12.1 vs. 11.2 vs. 8.4 Baseline pain (0-10 VAS): 4.6 vs. 5 vs. 3.6	A vs. B vs. C <u>10.25 months</u> RDQ (0–24): 8.8 vs. 8.2 vs. 10.4, P=0.44 Pain (0–10 VAS): 3.7 vs. 2.8 vs. 4.3, P=0.44	NR
Bendix, 1995,[233] 1997,[243] 1998[244] 60 months Duration of pain: >6 months *Fair*	A. Multidisciplinary rehabilitation (n=46), 18 sessions over 6 weeks (total ~135 hours) B. Multidisciplinary rehabilitation (n=43), 12 sessions over 6 weeks (total 24 hours) C. Exercise (n=43)	A vs. B vs. C Age: 40 vs. 44 vs. 42 Female: 75% vs. 77% vs. 74% Baseline pain (0-10 NRS): 5.3 vs. 5.9 vs. 5.4 Baseline Low Back Pain Rating Scale (0-30): 15.5 vs. 15.3 vs. 14.4	A vs. B vs. C <u>3.25 months</u> Back pain (0-10 NRS): 2.7 vs. 5.6 vs. 4.4, P<0.001 Low Back Pain Rating Scale (0-30): 8.5 vs. 16.1 vs. 13.5, P=0.002 <u>12 months</u> Back pain (0-10 NRS): 3.3 vs. 6.5 vs. 5.3, P=0.005 Low Back Pain Rating Scale (0-30): 8.9 vs. 16.4 vs. 13.7, P<0.001 <u>24 months</u> Back pain (0-10 NRS): 3 vs. 6 vs. 5, P=0.08 Low Back Pain Rating Scale (0-30): 10 vs. 17 vs. 14, P=0.003 <u>60 months</u> Back pain (0-10 NRS): 4 vs. 6 vs. 5, P=0.3 Low Back Pain Rating Scale (0-30): 8 vs. 16 vs. 14, P=0.02	A vs. B vs. C <u>3.25 months</u> Days of sick leave: 25 vs.122 vs. 13, P=0.005 Health care system contacts: 0.5 vs. 2.8 vs. 1.3, P=0.05 <u>12 months</u> Days of sick leave: 52 vs. 295 vs. 100, P=0.002 Health care system contacts: 4.5 vs. 12.0 vs. 11.8, P=0.002 Days of sick leave: 2.5 vs. 37 vs. 11, P=0.06 <u>24 months</u> Health care system contacts: 5 vs. 21 vs. 14, P=0.03 Overall assessment (1-5): 2 vs. 3 vs. 3, P=0.005 <u>60 months</u> Overall assessment (1-5): 2 vs. 3 vs. 3, P=0.004 Increase in proportion able to work: 30% vs. 23% vs. 0%, P=0.001 Days of sick leave: 13 vs. 11 vs. 88, P=0.2 Health care system contacts: 15 vs. 10 vs. 24, P=0.2 Back surgery: 5% vs. 10% vs. 10%, P=0.7

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Bendix,1996,[218] 1998[244] 60 months Duration of pain: >6 months *Fair*	A. Multidisciplinary rehabilitation (n=55), 18 sessions over 6 weeks (total ~135 hours) B. Usual care (n=51)	A vs. B Age 41 vs.40 years Female: 71% vs. 69% Baseline pain (0-10 NRS): 6.1 vs. 6.1 Baseline Low Back Pain Rating Scale (0-30): 16.9 vs. 15.9	A vs. B <u>3.25 months</u> Back pain (0-10 NRS): 5.7 vs. 6.9, P=0.05 Low Back Pain Rating Scale (0-30): 12.1 vs. 16.8, P<0.001 <u>24 months</u> Back pain (0-10 NRS): 6 vs. 6.5, P=0.5 Low Back Pain Rating Scale (0-30): 16 vs. 15, P=0.9 <u>60 months</u> Back pain (0-10 NRS): 5 vs. 5, P=1.0 Low Back Pain Rating Scale (0-30): 12 vs. 16, P=0.2	A vs. B <u>3.25 months</u> Days of sick leave: 10 vs. 122, P=0.02 Contacts to health-care system: 1.6 vs. 5.3, P<0.001 <u>24 months</u> Days of sick leave: 15 vs. 123, P<0.001 Health care system contacts: 12 vs. 26, P<0.001 <u>60 months</u> Days of sick leave: 10 vs. 50, P=0.4 Health care system contacts: 16 vs. 48, P=0.1 Back surgery: 7% vs. 12%, P=0.4
Bendix, 2000[234] 10 months Duration of pain: Not reported *Fair*	A. Multidisciplinary rehabilitation (n=59), 18 sessions over 8 weeks (total ~139 hours) B. Exercise (n=68)	A vs. B Age: 40 vs. 43 years Female: 66% vs. 65% Baseline function: NR Baseline pain: NR	A vs. B <u>10 months</u> Back pain (0–10): 5.1 vs. 5.7, P=0.33 Low Back Pain Rating Scale (0–30 ADL): 12 vs. 13, P=0.41	A vs. B <u>10 months</u> Overall assessment (1–5): 1.7 vs. 2.7, P=0.03 Work capable: 75% vs. 69%, P=0.64 Health care contacts (number): 2.5 vs. 4, P=0.28
Harkapaa, 1989[219] 1 month Duration of pain: >2 years *Poor*	A. Multidisciplinary rehabilitation (inpatient) (n=156), 3 weeks (number of sessions and total hours unclear) B. Multidisciplinary rehabilitation (outpatient) (n=150), 15 sessions over 8 weeks (total hours unclear) C. Usual care (n=153)	A vs. B vs. C Age: 45 vs. 45 vs. 45 years Female: 37% vs. 39% vs. 35% Baseline function, LBP Disability Index (0-45): 16.7 vs. 17.6 vs. 16.7 Baseline Pain Index (0-400): 184.9 vs. 178.6 vs. 175.8	A vs. B vs. C <u>1 month</u> LBP Disability Index (0-45): 13.8 vs. 14.7 vs. 17.3, P<0.004 for A vs. C and P<0.01 for B vs. C Pain Index (0-400): 127 vs. 145 vs. 160, P<0.001 for A vs. C and P<0.04 for B vs. C	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Jousset, 2004[235] 5 months Duration of pain: >4 months *Poor*	A. Multidisciplinary rehabilitation (n=44), 25 sessions over 5 weeks (total 150 hours) B. Exercise (n=42)	A vs. B Age: 41 vs. 40 years Female: 30% vs. 37% Baseline function Quebec Disability Scale (0-100): 34.6 vs. 31.6 Baseline pain (0-10 NRS): 5.0 vs. 4.6	A vs. B <u>5 months</u> Quebec Disability Scale (0-100): 22.0 vs. 22.9, P=0.80 Pain (0-10 NRS): 3.1 vs. 4.0, P=0.01 Dallas Pain Questionnaire ADL (0-100): 36.7 vs. 41.5, P=0.36	A vs. B <u>5 months</u> Hospital Anxiety Depression Scale (0-21): 12.7 vs. 13.4 (6.4), P=0.62 Dallas Pain Questionnaire Social interest (0-100): 19.6 vs. 24.3, P=0.37
Lambeek 2010[221] 9 months Duration of pain: >4 months *Fair*	A. Multidisciplinary rehabilitation (n=66), 26+ sessions over up to 13 weeks (total hours unclear) B. Usual care (n=68)	A vs. B Age: 46 vs. 47 years Female: 44% vs. 40% Baseline modified RDQ (0-23): 14.7 vs. 15.0 Baseline pain (0-10 VAS): 5.7 vs. 6.3	A vs. B <u>3 months</u> Modified RDQ (0-23): 4.8 vs. 5.0 (0.9), adjusted difference 0.06, 95% CI −2.3 to 2.5 Pain (0-10 VAS): 1.3 vs. 2.3, adjusted difference 0.5, 95% CI −0.6 to 1.6 <u>9 months</u> Modified RDQ (0-23): 7.2 vs. 4.4, adjusted difference −2.9, 95% CI −4.9 to −0.9 Pain (0-10 VAS): 1.6 vs. 1.9, adjusted difference 0.21, 95% CI −0.8 to 1.2	A vs. B <u>9 months</u> General practitioner visits (# of patients): 13 vs. 29 Medical specialist visits (# of patients): 13 vs. 29 Total costs (pounds): 13,165 (SD 13,600) vs. 18,475 (SD 13,616), MD −5,310 (95% CI −10,042 to −391)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Monticone 2013[239] 23 months Duration of pain: 25 vs. 26 months *Fair*	A. Multidisciplinary rehabilitation (n=45), 26 sessions over 5 weeks (total 26 hours) B. Exercise (n=45)	A vs. B Age: 49 vs. 50 years Female: 60% vs. 56% Baseline RDQ (0-24): 15.3 vs. 15.0 Baseline pain (0-10 VAS): 7.0 vs. 7.0	A vs. B <u>11 months</u> RDQ (0-24): 1.3 (1.6) vs. 11.0 (2.0) Pain (0-10 VAS): 1.4 (1.1) vs. 5.3 (1.2) <u>23 months</u> RDQ (0-24): 1.4 vs. 11.1, difference −9.7, 95% CI −10.4 to −9.0 Pain (0-10 VAS): 1.5 vs. 6.2, difference −4.7, 95% CI −5.1 to −4.3	A vs. B <u>11 months</u> SF-36 physical pain (0-100): 79.0 (14.6) vs. 52.0 (16.2) SF-36 physical functioning (0-100): 85.7 (19.6) vs. 62.1 (19.4) SF-36 general health (0-100): 85.0 (13.8) vs. 56.4 (15.9) SF-36 mental health (0-100): 89.8 (13.0) vs. 54.1 (11.9) <u>23 months</u> SF-36 physical pain: 80.4 vs. 61.8, difference 18.6, 95% CI 12.8 to 24.3 SF-36 physical functioning (0-100): 87.6 vs. 65.0, difference 22.6, 95% CI 15.0 to 30.1 SF-36 general health: 86.3 vs. 63.1, difference 23.2, 95% CI 17.3 to 29.1 SF-36 mental health: 91.0 vs. 58.8, difference 32.2, 95% CI 27.4 to 37.0)
Monticone 2014[240] 3 months Duration of pain: 15 vs. 14 months *Fair*	A. Multidisciplinary rehabilitation (n=10), 16 sessions over 8 weeks (total 16 hours) B. Exercise (n=10)	A vs. B Age: 59 vs. 57 years Female: 7% vs. 4% Baseline function (0-100 ODI): 26 vs. 24 Baseline pain (0-10 NRS): 5 vs. 4	A vs. B <u>3 months</u> ODI (0-100): 8 vs. 15, P=0.027 Pain (0-10 NRS): 2 vs. 3, P=1.0	A vs. B <u>3 months</u> SF-36 bodily pain (0-100): 65 vs. 55, P=0.261 SF-36 general health (0-100): 71 vs. 55, P=0.018 SF-36 social function (0-100): 81 vs. 61, P=0.001 SF-36 emotional role (0-100): 77 vs. 57, P=0.007 SF-36 mental health (0-100): 88 vs. 67, P=0.001

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Nicholas, 1991[236] 11 months Duration of pain: 7 years *Poor*	A. Multidisciplinary rehabilitation (cognitive treatment) (n=10) B. Multidisciplinary rehabilitation (behavioral treatment) (n=10) C. Multidisciplinary rehabilitation (cognitive treatment and relaxation treatment) (n=8) D. Multidisciplinary rehabilitation (behavioral treatment and relaxation training) (n=9) E. Exercise + attention control (psychologist-led group discussions) (n=10) F. Exercise (n=11) For all multidisciplinary rehabilitation interventions, 19 sessions over 5 weeks (total 21.5 hours)	Overall Age: 41 years Female: 51% A vs. B vs. C vs. D vs. E vs. F Baseline function, (0-100 Sickness Impact Profile): 37.13 vs. 34.24 vs. 33.41 vs. 20.53 vs. 27.12 vs. 28.06 Baseline pain (0-5 categorical scale): 2.78 vs. 2.96 vs. 3.80 vs. 2.27 vs. 2.84 vs. 2.77	A vs. B vs. C vs. D vs. E vs. F <u>5 months</u> Sickness Impact Profile (0-100): 24.42 (11.78) vs. 15.44 (14.12) vs. 25.69 (8.50) vs. 14.86 (9.08) vs. 19.40 (6.89) vs. 29.78 (8.76) Pain (0-5 categorical scale): 2.18 (0.55) vs. 1.87 (0.73) vs. 3.20 (0.93) vs. 2.22 (0.48) vs. 2.64 (0.90) vs. 3.18 (0.72) <u>11 months</u> Sickness Impact Profile (0-100): 23.85 (12.50) vs. 12.80 (8.62) vs. 20.77 (8.29) vs. 12.87 (6.68) vs. 18.94 (12.79) vs. 25.18 (8.08) Pain (0-5 categorical scale): 2.56 (0.97) vs. 2.66 (1.06) vs. 3.30 (0.83) vs. 1.88 (0.65) vs. 2.70 (0.84) vs. 3.22 (0.69)	A vs. B vs. C vs. D vs. E vs. F <u>5 months</u> Spielberger State Anxiety Inventory (20-80): 57.17 (10.30) vs. 37.57 (12.92) vs. 55.71 (10.47) vs. 36.40 (6.28) vs. 41.13 (11.70) vs. 54.00 (12.03) Beck Depression Inventory (0-63): 18.67 (9.01) vs. 8.14 (5.77) vs. 16.14 (3.80) vs. 9.00 (6.07) vs. 9.88 (5.46) vs. 19.17 (8.78) Medication use (0-5): 1.50 (1.26) vs. 0.57 (0.73) vs. 1.86 (0.64) vs. 1.60 (1.02) vs. 1.50 (0.71) vs. 1.83 (1.07) <u>11 months</u> Spielberger State Anxiety Inventory (20-80): 42.83 (9.42) vs. 37.43 (12.26) vs. 47.17 (17.01) vs. 40.67 (11.81) vs. 46.56 (11.51) vs. 53.40 (18.78) Beck Depression Inventory (0-63): 18.67 (10.04) vs. 8.00 (5.93) vs. 12.83 (6.69) vs. 13.17 (8.51) vs. 10.56 (5.21) vs. 17.60 (6.09) Medication use (0-5): 1.17 (1.37) vs. 0.71 (0.88) vs. 1.67 (1.37) vs. 1.33 (0.75) vs. 1.44 (0.96) vs. 1.60 (1.49)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Nicholas, 1992[237] 5 months Duration of pain: 5.5 years *Fair*	A. Multidisciplinary rehabilitation (n=10), 18 sessions over 5 weeks, (total 31.5 hours) B. Exercise + attention control (psychologist-led group discussions) (n=10)	Overall Age: 44 years Female: 45% A vs. B Baseline function (0-100 Sickness Impact Profile): 30.87 vs. 32.10 Baseline pain (0-5 categorical scale): 3.13 vs. 2.84	A vs. B <u>5 months</u> Pain intensity (0-5 categorical scale): 2.89 (0.64) vs. 2.75 (1.11)	A vs. B <u>5 months</u> Beck Depression Inventory (0-63): 14.44 (5.98) vs. 18.50 (9.26) Using medication: 44% vs. 88%
Roche, 2007,[241] 2011[242] 10.75 months Duration of pain: >4 months *Fair*	A. Multidisciplinary rehabilitation (n=68), 25 sessions over 5 weeks (total 150 hours) B. Exercise therapy (n=64)	A vs. B Age: 41 vs. 39 years Female: 32% vs. 38% Baseline function (0-100 Dallas Pain Questionnaire daily activities (0-100): 51.8 vs. 51 Baseline Pain (0-10 VAS): 4.7 vs. 4.5	A vs. B <u>10.75 months</u> Dallas Pain Questionnaire daily activities (0-100): 31.4 vs. 39.1, difference −7.7 (95% CI −16.15 to 0.75) Pain (0-10 VAS): 2.9 vs. 3.5, difference −0.6 (95% CI −1.49 to 0.29)	A vs. B <u>10.75 months</u> Dallas Pain Questionnaire anxiety/depression (0-100): 21.9 vs. 25.5, difference −3.6 (95% CI −12.56 to 5.36)
Strand, 2001[223] 11 months Duration of pain: 10 vs. 9 years *Fair*	A. Multidisciplinary rehabilitation (n=81), 20 sessions over 4 weeks (total 120 hours) B. Usual Care (n=36)	A vs. B Age: 45 vs. 42 years Female: 59% vs. 64% Baseline function (0-100 Disability Rating Index): 55.6 vs. 58.3 Baseline pain (0-100 VAS): 48.3 vs. 53.0	A vs. B <u>11 months</u> Disability Rating Index (0-100): −27.3 (95% CI −34 to −21) vs. −3.3 (95 % CI −10 to 14) vs. −16.4 (95% CI −26 to −7.3) vs. 0.2 (95% CI −14 to 14), difference −3.8 (95% CI −13.9 to 6.3) Pain (0-100 VAS): −21.1 (95% CI −31 to −11) vs. −2.3 (95% CI −9.4 to 4.8) vs. −23.1 (95% CI −37 to 9.2) vs. 7.1 (95% CI −7.7 to 22), difference −1.0 (95% CI −11.7 to 9.6)	A vs. B <u>11 months</u> Working: 47% vs. 58% difference −11% (95% CI −8 to 30)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Tavafian, 2008[232] 12 months Duration of pain: 9 months *Poor*	A. Multidisciplinary program (n=37), 5 sessions over 0.5 weeks (total hours unclear) B. Medications (acetaminophen, NSAID and chlordiazepoxide) (n=37)	A vs. B Age: 43 vs. 45 years Female, %: 100 vs. 100 Baseline SF-36 Physical (0-100): 41.2 vs. 42.3 Baseline SF-36 Mental (0-100): 47.5 vs. 47.7	NR	A vs. B <u>3 months</u> SF-36 Physical (0-100): 76.7 vs. 51.2, difference 25.5 (95% CI 14.69 to 36.31) SF-36 MCS (0-100): 80.4 vs. 57.4, difference 23.0 (95% CI 10.78 to 35.22) <u>6 months</u> SF-36 PCS (0-100): 66.6 vs. 51.2, difference 15.4 (95% CI 2.35 to 28.45) SF-36 MCS (0-100): 66.9 vs. 57.9, difference 9.0 (95% CI −3.88 to 21.88) <u>6 months</u> SF-36 PCS (0-100): 64.7 v s. 51.1, difference 13.6 (95% CI −1.48 to 28.68) SF-36 MCS (0-100): 65.1 vs. 60.2, difference 4.9 (95% CI −7.57 to 17.37)
Turner, 1990[109] 12 months Duration of pain: 12.9 years *Poor*	A. Multidisciplinary rehabilitation (n=24), 16 sessions over 2 weeks (total 32 hours) B. Exercise (n=24)	Overall Age: 44 years Female: 48% A vs. B Baseline function (Sickness Impact Profile): 8.5 vs. 8.4 Baseline pain (0-78 MPQ): 25.5 vs. 19.4	A vs. B <u>6 months</u> Sickness Impact Profile (0-100): 4.5 vs. 6.3 McGill Pain Questionnaire Pain Rating Index (0-78): 13.3 vs. 15.7 <u>12 months</u> Sickness Impact Profile (0-100): 4.8 vs. 4.7 McGill Pain Questionnaire Pain Rating Index (0-78): 18.2 vs. 14.9	A vs. B <u>6 months</u> Center for Epidemiologic Studies-Depression Scale (0-60): 8.3 vs. 9.3 <u>12 months</u> Center for Epidemiologic Studies-Depression Scale (0-60): 10.0 vs. 9.3

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
van der Roer, 2008[238] 10 months Duration of pain: ~50 weeks *Fair*	A. Multidisciplinary rehabilitation (n=60), 30 sessions over 10 weeks (total hours unclear) B. Exercise (n=54)	A vs. B Age: 42 vs. 42 years Female: 55% vs. 48% Baseline function RDQ (0-24): 11.6 vs. 12.1 Baseline pain (0-10 NRS): 6.2 vs. 5.9	A vs. B <u>4 months</u> RDQ (0-24): 7.4 vs. 7.7, adjusted difference 0.13 (95% CI −2.24 to 2.50) Pain (0-10 NRS): 4.1 vs. 4.8 , adjusted difference −0.97 (95% CI −1.88 to −0.06) <u>10 months</u> RDQ (0-24): 6.7 vs. 7.1, adjusted difference 0.06 (−2.22 to 2.34) Pain (0-10 VAS): 3.9 vs. 4.6, adjusted difference −1.02 (−2.14 to 0.09)	A vs. B <u>4 months</u> Global Perceived Effect positive (%): 38.2% vs. 39.8%, OR 0.93 (95% CI 0.36 to 2.43) <u>10 months</u> Global Perceived Effect positive (%): 45.0% vs. 32.3%, OR 1.71 (95% CI 0.67 to 4.38)
Von Korff, 2005[220] 22.5 months Duration of pain: >3 months *Fair*	A. Multidisciplinary rehabilitation (n=119), 4 sessions over 5 weeks (total 4 hours) B. Usual care (n=121)	A vs. B Age: 50 vs. 50 years Female: 65% vs. 60% Modified RDQ (0-23): 12.3 vs. 11.4 Baseline pain (0-10 NRS): 5.7 vs. 5.8	A vs. B <u>4.5 months</u> Function Modified RDQ (0-23): 9.2 (6.6) vs. 10.1 (6.4), P=0.0003 >1/3 reduction in RDQ: 42.2% vs. 23.7%, adjusted OR 3.5, P=0.0007 Pain (0-10 NRS): 4.2 (2.0) vs. 4.7 (2.2), P=0.007 <u>10.5 months</u> Modified RDQ (0-23): 8.4 vs. 9.1, P=0.0063 >1/3 reduction in RDQ: 44.6% vs. 22.7%, adjusted OR 2.1, P=0.03 Pain (0-10 NRS): 4.0 vs. 4.7, P=0.004 <u>22.5 months</u> Modified RDQ (0-23): 8.1 vs. 9.1, P=0.0078 >1/3 reduction in RDQ: 49.4% vs. 37.0%, adjusted OR 1.8, P=0.08 Pain (0-10 NRS): 4.3 vs. 4.6, P=0.115	A vs. B <u>4.5 months</u> SF-36 Social Functioning (0-100): 74.4 vs. 73.6, P=0.26 SF-36 Mental Health (0-100): 70.3 vs. 69.5, P=0.23 <u>10.5 months</u> SF-36 Social Functioning (0-100): 74.4 vs. 73.6, P=0.26 SF-36 Mental Health (0-100): 70.3 vs. 69.5, P=0.23 <u>22.5 months</u> SF-36 Social Functioning (0-100): 76.7 vs. 76.3, P=0.28 SF-36 Mental Health (0-100): 71.0 vs. 72.4, P=0.98

ADL = activity of daily living; CI = confidence interval; LBO = Low Back Outcome Score; MCS = Mental Component Summary; MPQ = McGill Pain Questionnaire; NHP = Nottingham Health Profile; NR = not reported; NSAID = nonsteroidal anti-inflammatory drug; ODI = Oswestry Disability Index; PCS = Physical Component Summary; RDQ = Roland-Morris Disability Questionnaire; SF-36 = Short-Form 36Q; STAI-S = Spielberger State Anxiety Inventory; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Multidisciplinary Rehabilitation Compared With Usual Care

Multidisciplinary rehabilitation was associated with slightly greater effects on function than controls at short-term (4 trials, pooled SMD −0.31, 95% CI −0.57 to −0.05, I^2=70%),[218-221] and intermediate-term followup (4 trials, pooled SMD −0.37, 95% CI −0.64 to −0.10, I^2=50%) (Figure 22).[220-223] There was no difference in long-term function (2 trials, pooled SMD −0.04, 95% CI −0.31 to 0.24, I^2=35%).[218,220] In trials that measured function using the RDQ, the

difference was 0.70 points at short term and 1.9 points at intermediate term. Evaluation of a high-intensity multidisciplinary rehabilitation intervention or exclusion of poor-quality trials had little effect on estimates. At short-term followup, effects on function were somewhat larger with high intensity multidisciplinary rehabilitation interventions (2 trials, pooled SMD −0.51, 95% CI −0.93 to −0.22)[218,219] than with nonhigh intensity interventions (3 trials, pooled difference −0.20, 95% CI −0.38 to 0.03),[219-221] but the interaction was not statistically significant (P=0.18). At intermediate term, there were no clear differences between high intensity (1 trial, SMD −0.59, 95% CI −0.99 to −0.19)[223] and nonhigh intensity (3 trials, pooled difference −0.29, 95% CI −0.68 to 0.06)[220-222] interventions (P=0.47 for interaction).

Multidisciplinary rehabilitation was associated with slightly greater effects than usual care on pain at short-term (4 trials, pooled difference −0.51 on a 0 to 10 scale, 95% CI −0.89 to −0.13, I^2=23%)[218-221] and intermediate-term followup (4 trials, pooled difference −0.63, 95% CI −1.04 to −0.22, I^2=0%)[220-223] (Figure 23). The long-term difference was smaller and not statistically significant (2 trials, pooled difference −0.34, 95% CI −0.86 to 0.18, I^2=0%).[218,220] Excluding poor-quality trials[219,222,223] had little effect on estimates. At short-term followup, effects on pain were somewhat larger with high intensity multidisciplinary rehabilitation interventions (2 trials, pooled difference −0.87, 95% CI −1.56 to −0.33)[218,219] than with nonhigh intensity interventions (3 trials, pooled difference −0.35, 95% CI −0.70 to 0.14),[219-221] but the interaction between intensity and effects of multidisciplinary rehabilitation was not statistically significant (P=0.45). At intermediate term, estimates were similar for high intensity (1 trial, difference −0.53, 95% CI −1.36 to 0.30)[223] and nonhigh intensity (3 trials, pooled difference −0.66, 95% CI −1.19 to −0.12) interventions (P=0.81 for interaction). [220-222]

Data on other outcomes was limited. One trial found no differences between multidisciplinary rehabilitation versus usual care on the SF-36 Social Functioning or Mental Functioning subscales.[220] Three trials reported inconsistent effects on work or disability/sick leave status.[218,220,223] Two trials found multidisciplinary rehabilitation associated with fewer health system contacts versus usual care.[218,221]

Multidisciplinary Rehabilitation Compared With Pharmacological Therapy

One poor-quality trial (n=74) found multidisciplinary rehabilitation (intensity unclear) associated with greater effects on short-term quality of life than oral medications (acetaminophen, NSAIDs, and chlordiazepoxide).[232] The difference on the SF-36 PCS was 25.5 points (95% CI 14.7 to 36.3) and on the SF-36 MCS was 23.0 points (95% CI 10.8 to 35.2). Effects were smaller at intermediate term and statistically significant for the SF-36 PCS (difference 15.4, 95% CI 2.35 to 28.45) but not for the SF-36 MCS (difference 9.0, 95% CI −3.88 to 21.9). Effects were not statistically significant at long-term (12 month) followup (differences 13.6 and 4.9 points, respectively).

Multidisciplinary Rehabilitation Compared With Exercise

Multidisciplinary rehabilitation was associated with slightly greater effects on short-term function than exercise (6 trials, pooled SMD −0.28, 95% CI −0.54 to −0.01, I^2=39%) (Figure 24).[233,235-238,240] Estimates were similar when a poor-quality trial[236] was excluded and when analyses were restricted to trials of high-intensity multidisciplinary rehabilitation (2 trials, pooled difference −0.14, 95% CI −0.47 to 0.20).[233,235] Multidisciplinary rehabilitation was associated with substantially greater effects than exercise on intermediate-term function (6 trials, pooled SMD −1.01, 95% CI −1.93 to −0.09, I^2=96%), but statistical heterogeneity was very large.[109,234,236,238,239,241,242] Excluding an outlier trial (SMD −5.31, 95% CI −6.20 to −4.42)[239]

eliminated statistical heterogeneity and resulted in a markedly attenuated (small) effect (5 trials, pooled SMD −0.22, 95% CI −0.40 to −0.03, I^2=0%). There was no difference between multidisciplinary rehabilitation versus exercise in long-term function (3 trials, pooled SMD −1.80, 95% CI −4.36 to 0.76, I^2=98%).[109,233,239] Excluding an outlier trial[239] resulted in a pooled SMD close to 0 (−0.06, 95% CI −0.36 to 0.25, I^2=0%).

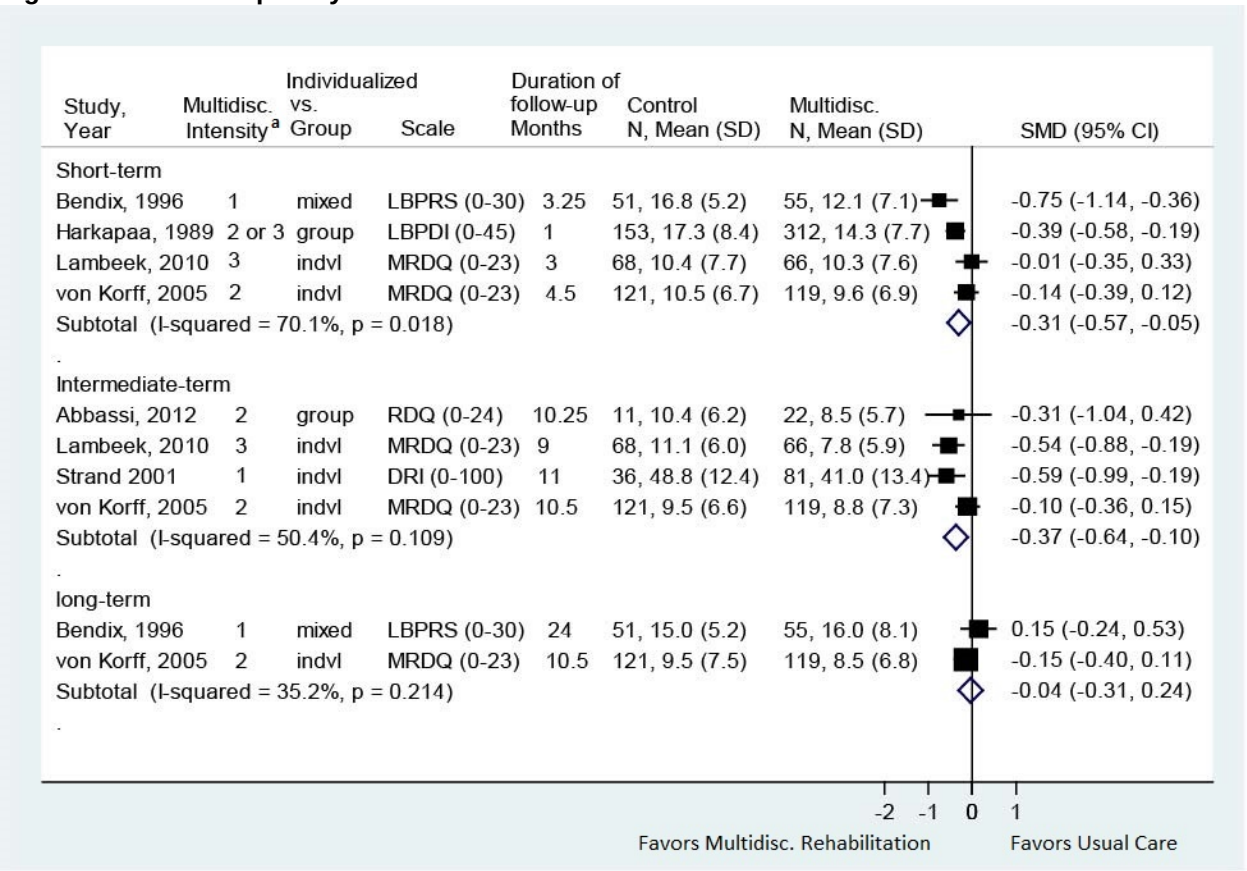
Multidisciplinary rehabilitation was associated with slightly greater effects on short-term pain versus exercise (6 trials, pooled difference −0.75 on a 0 to 10 scale, 95% CI −1.18 to −0.31, I^2=0%) (Figure 25). Estimates were similar when one poor-quality trial[236] was excluded (5 trials, pooled difference −0.50, 95% CI −1.07 to 0.11), and there were no clear differences when analyses were stratified according to intensity of multidisciplinary rehabilitation. In two trials that evaluated high intensity multidisciplinary rehabilitation, the pooled difference was −0.56 (95% CI −1.53 to 0.36).[233,235] Estimates at intermediate term (6 trials, pooled difference −1.17 points, 95% CI −2.70 to 0.36, I^2=96%)[234,236,238,240-242] and long term (3 trials, pooled difference −1.63, 95% CI −5.30 to 2.05, I^2=99%)[109,233,239] favored multidisciplinary rehabilitation, but effects were not statistically significant. Substantial statistical heterogeneity was present in analyses of intermediate-term and long-term pain, with an outlier trial[239] that reported substantially larger effects than the other trials. For intermediate term, the outlier trial reported a MD of −3.90 points, versus −0.31 to −0.78 points in the other trials. Excluding the outlier trial eliminated statistical heterogeneity and resulted in a small, statistically significant difference in intermediate-term pain that favored multidisciplinary rehabilitation (5 trials, pooled difference −0.55, 95% CI −0.95 to −0.15, I^2=0%); there was no difference in long-term pain (2 trials, pooled difference 0.00, 95% CI −0.94 to 0.95, I^2=50%). For intermediate-term pain, exclusion of a poor-quality trial[236] (5 trials, pooled difference −1.52, 95% CI −3.34 to 0.39) or restriction of analyses to high intensity multidisciplinary rehabilitation interventions (2 trials, pooled difference −0.60, 95% CI −1.41 to 0.21)[234,241,242] did not reduce heterogeneity and differences remained not statistically significant.

Data on other outcomes was limited. One trial found multidisciplinary rehabilitation associated with better scores versus exercise on SF-36 subscales at short-term followup (differences 10 to 21 points).[240] Four trials found no clear differences between multidisciplinary rehabilitation versus exercise on severity of depression.[109,235-237] Two trials found no clear effects on work status[233,241,242] and one trial found high intensity multidisciplinary rehabilitation associated with fewer days or sick leave than exercise, but nonhigh intensity rehabilitation associated with more days of sick leave.[233] Two trials found inconsistent effects on number of health system contacts.[233,234]

Harms

Data on harms were sparse and reported in only two trials. One study reported no clear difference between multidisciplinary rehabilitation versus exercise in risk of transient worsening of pain,[240] and one trial reported no harms with either multidisciplinary rehabilitation or medications alone.[232]

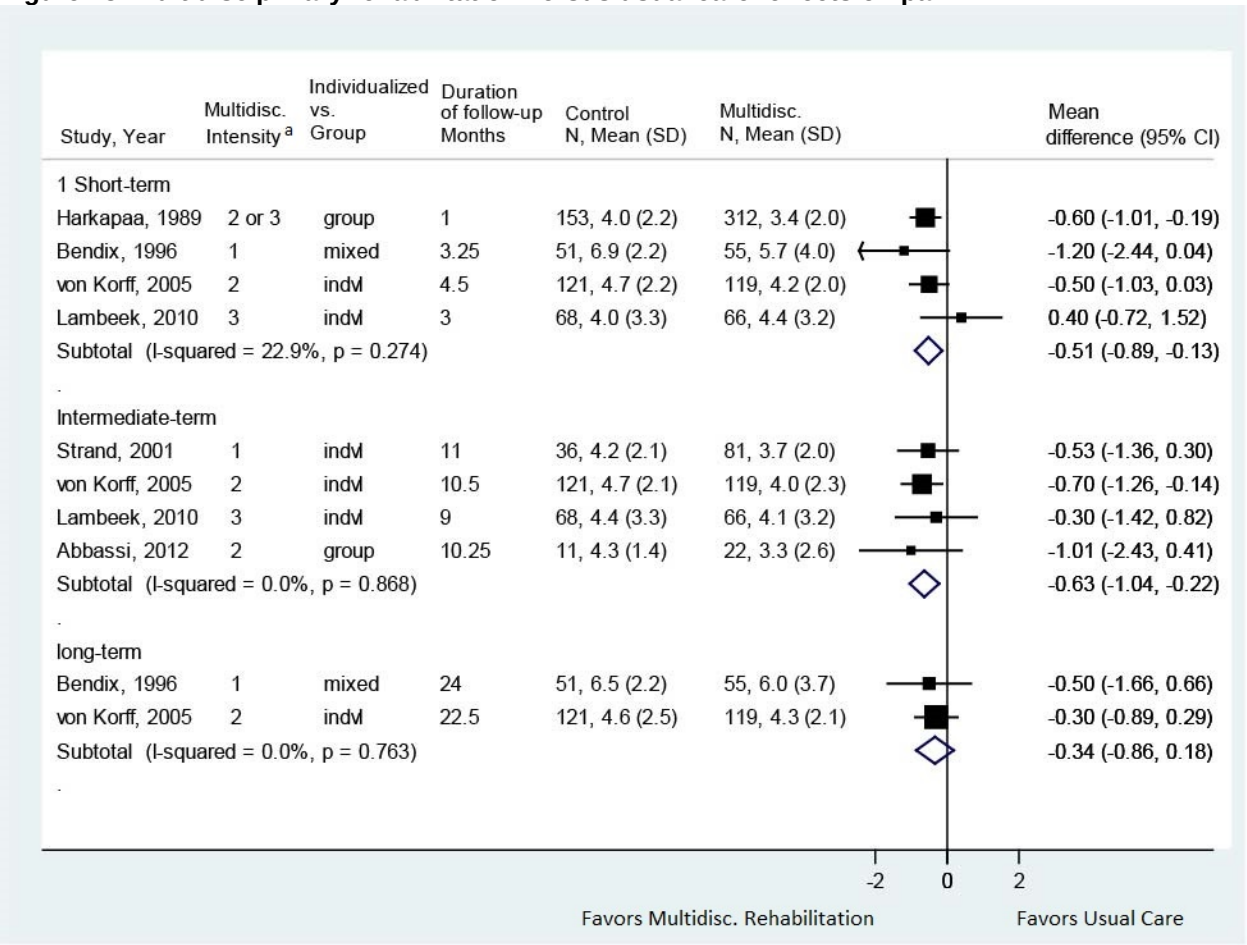
Figure 22. Multidisciplinary rehabilitation versus usual care: effects on function



CI = confidence interval; DRI= Disability Rating Index; indvl = individual; LBPDI = low back pain disability index; LBPRS = low back pain rating scale; MRDQ = Modified Roland-Morris Disability Questionnaire; N = number; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SMD = standardized mean difference

[a] Multidisciplinary rehabilitation intensity: 1= high, 2= not high, 3= unclear or not reported

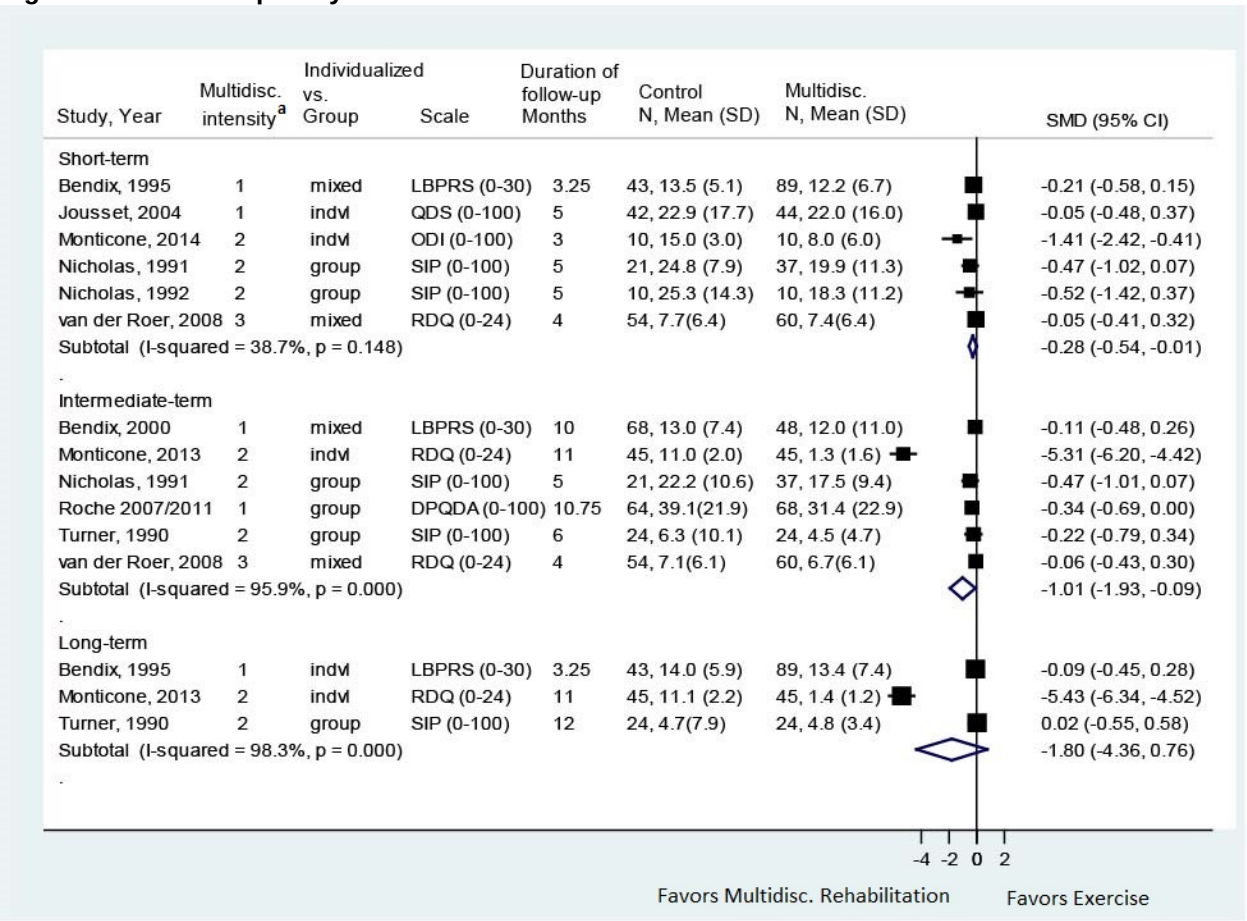
Figure 23. Multidisciplinary rehabilitation versus usual care: effects on pain



CI = confidence interval; indvl = individual; N = number; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation

[a] Multidisciplinary rehabilitation intensity: 1 = high, 2 = not high, 3 = unclear or not reported

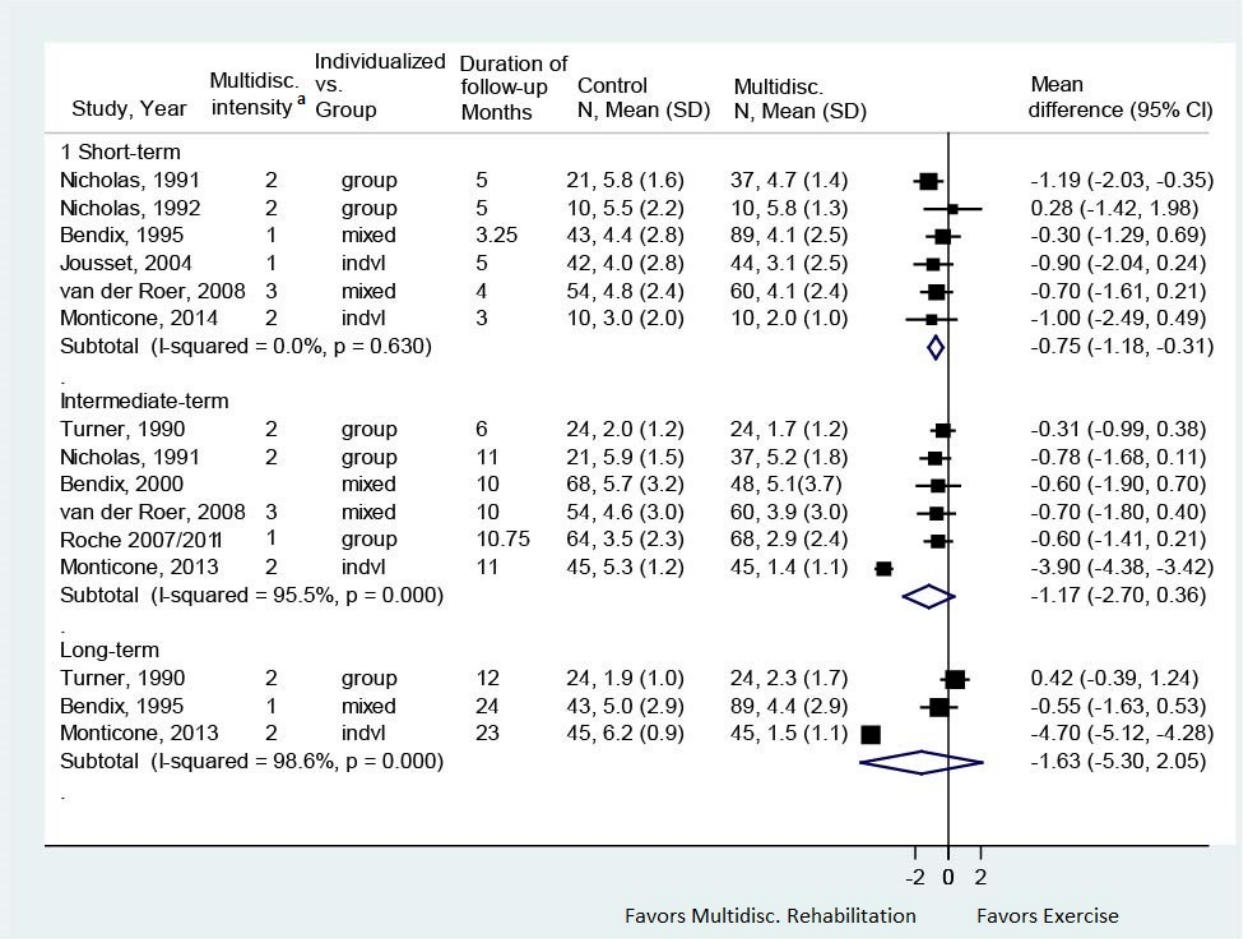
Figure 24. Multidisciplinary rehabilitation versus exercise: effects on function



CI = confidence interval; DPQDA = Dallas Pain Questionnaire daily activities; indvl = individual; LBPRS = low back pain rating scale; N = number; ODI = Oswestry Disability Index; QDS = Quebec Disability Scale; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SIP = Sickness Impact Profile; SMD = standardized mean difference

[a] Multidisciplinary rehabilitation intensity: 1= high, 2= not high, 3= unclear or not reported

Figure 25. Multidisciplinary rehabilitation versus exercise care: effects on pain



CI = confidence interval; indvl = individual; N = number; SD = standard deviation
[a] Multidisciplinary rehabilitation intensity: 1 = high, 2 = not high, 3 = unclear or not reported

Key Question 2: Chronic Neck Pain

Exercise for Chronic Neck Pain

Key Points

- Across types of exercise, there was no clear improvement in function (3 trials [excluding outlier trial], pooled SMD −0.23, 95% CI −0.71 to 0.15) or pain (3 trials [excluding outlier trial], pooled SMD −0.72, 95% CI −1.49 to 0.06) versus no treatment or advice alone in the short term (SOE: low).
- A subgroup of two trials of combination exercises (including 3 of the following 4 exercise categories: muscle performance, mobility, muscle re-education, aerobic) suggests a slight benefit in function and pain versus no treatment or advice alone over the short term and function in the long term (SOE: low).

- The effect of exercise versus NSAIDs and muscle relaxants on function and pain was indeterminate at short or intermediate term due to insufficient evidence from a single poor-quality trial (SOE: insufficient).
- Harms were poorly reported in trials of exercise with only two trials describing adverse events. No serious harms were reported in either trial. Minor complaints included muscle pain with exercise, knee pain, and lumbar spine pain (SOE: low).

Detailed Synthesis

Seven trials of exercise therapy for neck pain met inclusion criteria (Table 18 and Appendix D).[34-39,88] Four trials evaluated participants with chronic neck pain associated with office work,[34,36,38,39] one included patients with chronic neck pain following whiplash,[37] one assessed participants with nonspecific neck pain,[35] and one included patients with cervical arthritis.[88] Across trials, participants were predominately female (>80%) with mean ages ranging from 38 to 52 years.

Four trials evaluated muscle performance exercises (resistive training),[34,36,38,39] and three combined exercise techniques.[35,37,88] Sample sizes ranged from 40 to 230 (total sample=771). Four trials compared exercise versus an attention control,[34,36,37,39] one versus no treatment,[38] one versus waitlist,[35] and one versus pharmacologic care.[88] Four trials were conducted in Europe,[34,35,38,39] one in Australia,[37] one in China,[36] and one in Turkey.[88] The duration of exercise therapy ranged from 6 weeks to 12 months, and the number of supervised exercise sessions ranged from 3 to 52. Three trials reported outcomes through long-term followup,[34,37,39] two through intermediate-term followup,[38,88] and two evaluated only short-term outcomes.[35,36]

Three trials were rated fair quality[36-38] and four poor quality[34,35,39,88] (Appendix E). In the three fair-quality trials, the main methodological limitation was the inability to blind interventions. Limitations in the other trials included inability to blind interventions, unclear randomization and allocation concealment methods, unclear or high loss to followup, and baseline differences between intervention groups.

Table 18. Chronic neck pain: exercise therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Andersen, 2008[b34] 6 and 12 months Duration of pain, NR *Poor*	A. Dynamic strengthening exercise (muscle performance exercise) (n=61): for the neck/shoulder muscles, performed in in the workplace; 20 minute sessions, 3 times a week (2 of the 3 weekly sessions were supervised by experienced instructors) B. Lifestyle physical exercise and activity increase (combination exercise) (n=59): workplace activities such as steppers placed near the copying machines, punch bags in the hall, group sessions of Nordic walking, and strength and aerobic fitness exercise programs C. Control group (n=62): ergonomics, stress management, organization of work, cafeteria food quality Treatment lasted 1 year. All groups were allowed 1 hour per week during working time for activities	A + B + C Age: 45 years Female: 78% Office workers: 100% A vs. B vs. C Pain VAS (0-10): 5.0 vs. 5.0 vs. 4.7	A vs. C <u>6 months</u> Pain VAS: 3.4 vs. 4.2, difference −0.80 (−0.87 to −0.73) <u>12 months</u>[c] Pain VAS: 3.8 vs. 4.6, difference −0.80 (−0.87 to −0.73) Days of pain in last 3 months (0-90): 25 vs. 30, p>0.05 B vs. C <u>6 months</u> Pain VAS: 3.6 vs. 4.2, difference −0.60 (−0.67 to −0.53) <u>12 months</u>[c] Pain VAS: 3.6 vs. 4.6, difference −1.0 (−1.07 to −0.93) Days of pain in last 3 months: 26 vs. 30, p>0.05	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Aslan Telci, 2012[88] 6 months Pain duration: 12 months *Poor*	A. Combination exercises (n=20): consisting of posture, active range of motion, stretching, isometric and dynamic strengthening and endurance exercises, relaxation and proprioception exercises. Clinic followup once a week to maintain motivation and check whether exercises performed correctly for a total of 3 weeks and home exercise for at least another month. B. NSAIDs and muscle relaxants for 15 days (n=20): all patients received verbal advice regarding pain control, posture, and ergonomics.	A vs. B Age: 48 vs. 52 years Female: 85% vs. 75% BMI: 25 vs. 27 Employed: 50% vs. 40% Education year: 12 vs. 11 NDI (0-50): 14.0 vs. 10.7 Pain VAS (0-10): 6.7 vs. 6.4	A vs. B <u>3 month</u> NDI: 9.4 vs. 11.5, difference −2.2 (95% CI −5.8 to 1.5) Pain VAS: 4.1 vs. 5.1, difference −1.0 (95% CI −2.3 to 0.3) <u>6 month</u> NDI: 11.9 vs. 13.7, difference −1.8 (95% CI −5.7 to 2.1) Pain VAS: 4.5 vs. 5.3, difference −0.8 (95% CI −2.3 to 0.7)	A vs. B <u>3 month</u> NHP (0-100): 89.2 vs. 230.0, difference −140.8 (95% CI −214.0 to −67.5) BDI (0-63): 6.8 vs. 10.7, difference −4.0 (95% CI −8.4 to 0.5) <u>6 month</u> NHP: 122.3 vs. 257.6, difference −135.3 (95% CI −209.1 to −61.5) BDI: 8.3 vs. 11.8, difference −3.8 (95% CI −8.5 to 1.0)
Lauche, 2016[35] 3 months Pain duration: NR *Poor*	A. Combination exercises (n=37): weekly 60-75 minute session for 12 weeks; ergonomic principles, proprioceptive exercises, and isometric and dynamic mobilization, stretching, strengthening neck and core exercises, and relaxation exercises; illustrated written exercises for home use ≥15 minutes/day. B. Wait list (n=39): continuing usual activities/therapies	A vs. B Age: 47 vs. 49 years Female: 86% vs. 82% years Pain recently (0-100): 46.2 vs. 51.5 Pain considered tolerable (0-100): 20.5 vs. 20.7	A vs. B <u>3 month</u> NDI: 25.1 vs. 29.4, difference −4.3 (95% CI −10.2 to 1.6) Recent pain VAS: 33.1 vs. 44.6, difference −11.5 (95% CI −20.8 to −2.2) Pain with motion VAS: 34.9 vs. 45.5, difference −10.6 (95% CI −18.5 to −2.7)	A vs. B <u>3 month</u> SF-36 PCS (0-100): difference 2.0 (95% CI −1.6 to 5.6) SF-36 MCS (0-100): difference 0.5 (95% CI −3.9 to 4.9)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Li 2017[36] 1.5 months Duration of pain, 4 years *Fair*	A. Progressive resistance training (muscle performance exercise) (38 randomized/36 analyzed) ≥3 sessions per week for six weeks. Sessions consisted of four cervical isometric exercises, each repeated 8-12 times. Resistance progressively increased every 2 weeks, starting at 30% of maximal strength and increased to 70%. B. Fixed resistance training (muscle performance exercise) (35 randomized/32 analyzed) ≥3 sessions per week for six weeks. Sessions consisted of four cervical isometric exercises, each repeated 8-12 times. Resistance was fixed at 70% of the participant's maximal strength. C. Attention control (36 randomized/34 analyzed). Subjected received information and had weekly discussions about workplace ergonomics, stress management, relaxation, meditation, and diet.	A vs. B vs. C Age: 36 vs. 34 vs. 34 BMI: 21 vs. 22 vs. 22 Years working: 9 vs. 9 vs. 10 Pain duration (years): 3 vs. 4 vs. 4 Work (days/week): 5 vs. 6 vs. 5 Computer use (hours/day): 7 vs. 8 vs. 7 NDI (mean, 0-50): 28.3 vs. 28.9 vs. 27.8 Pain VAS (mean 0-10): 5.3 vs. 5.4 vs. 5.2	A vs. C <u>1.5 month</u> NDI (mean, 0-50): 14.9 (4.9) vs. 26.6 (5.4), P<0.05 Pain VAS (mean, 0-10): 1.9 (0.9) vs. 5.1 (1.0), P<0.05 B vs. C <u>1.5 month</u> NDI: 15.8 (4.8) vs. 26.6 (5.4), P<0.05 Pain VAS: 2.5 (0.9) vs. 5.1 (1.0), P=NR	None

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Stewart, 2007[37] 1.5 and 12 months Pain duration: 9 months *Fair*	A. Combination exercise, plus advice (n=66); aerobic, stretching, functional, speed and endurance, trunk and limb strengthening; 1 hour per session for 12 session over 6 weeks B. Advice alone (n=68): included reassurance of a favorable outcome and encouragement to resume light activity	A vs. B Age: 44 vs. 43 years Female: 73% vs. 62% PSFS (0-10): 3.9 vs. 4.1 NDI (mean, 0-50): 18.2 vs. 19.7 Pain VAS (mean, 0-10): 5.2 vs. 5.3	A vs. B <u>1.5 months</u> PSFS: 6.4 vs. 5.6, difference 0.9 (95% CI 0.3 to 1.6) NDI: 12.0 vs. 15.7, difference −2.7 (95% CI −4.5 to −0.9) Pain VAS: 3.2 vs. 4.3, difference −1.1 (95% CI −1.8 to −0.3) <u>12 months</u> PSFS: 6.6 vs. 6.0, difference 0.6 (95% CI −0.1 to 1.4) NDI: 12.1 vs. 15.5, difference −2.3 (95% CI −4.9 to 0.3) Pain VAS: 3.5 vs. 3.8, difference −0.2 (95% CI 0.6 to −1.0)	A vs. B <u>1.5 months</u> Bothersomeness (0-10) 3.6 vs. 4.8, P=0.019 SF 36 physical (0-100): 42.1 vs. 38.9, P=0.003 SF 36 mental (0-100): 51.4 vs. 46.4, P=0.005 Global Perceived Effect (−5 to 5) 2.5 vs. 1.5, P=0.006 <u>12 months</u> Bothersomeness 4.1 vs. 4.0, P=0.480 SF 36 physical: 42.3 vs. 38.9, P=0.003 SF 36 mental: 48.4 vs. 46.1, P=0.33 Global Perceived Effect: 2.3 vs. 1.9, P=0.48
Viljanen, 2003[38] 3 and 9 months Pain duration: 11 years *Fair*	A. Dynamic strengthening exercises (muscle performance exercises) (n=135): physical-therapist guided; 3 times per week for 12 weeks, 30 minute sessions B. No intervention (n=130)	A vs. B Age: 45 vs. 44 years Female: 100% vs. 100% Office workers: 100% Computer work >6 hours per day: 33% vs. 35% Depression index (10-40): 16 vs. 16 Neck disability scale[e] (0-80): 29 vs. 26 Pain VAS (0-10): 4.8 vs. 4.1	A vs. B <u>3 months</u> Neck disability scale[e]: 15 vs. 14, adjusted difference −0.1 (95% CI −3.1, 2.9) Pain VAS: 2.9 vs. 2.9, adjusted difference 0.4 (95% CI −0.3, 1.0) <u>9 months</u> Neck disability scale[e]: 19 vs. 17, adjusted difference −0.1 (95% CI −3.0 to 2.9) Pain VAS: 3.1 vs. 3.2, adjusted difference 0.5 (95% CI −0.1 to 1.0)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Waling 2002[d39] 6 and 36 months Pain duration: 6.8 years *Poor*	A. Strength training (muscle performance exercise) (n=29): for neck and shoulder muscles, 3 times per week for 10 weeks, 1 hour/session B. Endurance training (muscle performance exercise) (n=28): using arm-cycling and arm exercises, 30 repetition maximum, 3 times per week for 10 weeks, 1 hour/session C. Coordination training (neuromuscular reeducation exercises) (n=25): focus on balance and postural stability 3 times per week for 10 weeks, 1 hour/session D. Reference group (n=21): stress management 1 time per week for 10 weeks, 2 hour/session	A vs. B vs. C vs. D Age: 38 vs. 39 vs. 38 vs. 39 years Female: 100% all groups Office workers: 100% Pain VAS at present (0-10): 2.6 vs. 2.8 vs. 3.3 vs. 3.7	A vs. B vs. C vs. D <u>6 months</u> Frequent pain (% with pain several times per week or more): 76% vs. 91% vs. 78 % vs. 73%, P=0.50 <u>36 months</u> Pain VAS at present: 3.1 vs. 2.2 vs. 2.7 vs. 1.6, P=0.073 Pain VAS in general (0-10): 3.2 vs. 2.9 vs. 2.9 vs. 2.0, P=0.249 Pain VAS at worst (0-10): 6.1 vs. 5.8 vs. 5.7 vs. 5.8, P=0.902 Frequent pain: 47% vs. 50% vs. 58% vs. 39%, P=0.66	NR

BDI = Beck Depression Inventory; BMI = body mass index; CI = confidence interval; HADS = Hospital Anxiety and Depression Scale; MCS = Mental Component Summary; MD = mean difference; NDI = Neck Disability Index; NHP = Nottingham Health Profile; NR = not reported; NSAID = nonsteroidal anti-inflammatory drug; PCS = Physical Component Summary; PSFS = Patient Specific Functional Scale; SF-36 = Short-Form 36 questionnaire; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Cluster RCT where clusters were formed from participants working on the same floor

[c] Intervention lasted 12 months and followup is at the end of the intervention

[d] Cluster RCT where clusters were formed from participants selecting a time that best fit their schedule

[e] Neck disability scale was created by investigators from responses to eight questions related to functional limitations due to pain; this scale is not the same as the more common NDI

Exercise Compared With No Treatment or an Attention Control

Across types of exercise, there was no clear improvement in function versus no treatment, attention control, or advice alone in the short term (4 trials, pooled SMD −0.73, 95% CI −1.57 to 0.12, I^2=95.1%), but statistical heterogeneity was very large[35-38] (Figure 26). Excluding an outlier trial (SMD −2.22, 95% CI −2.74 to −1.70)[36] reduced the statistical heterogeneity and resulted in an attenuated effect (SMD −0.23, 95% CI −0.61 to 0.15, I^2=72.6%). However, two studies that included combination exercises (3 of the following 4 exercise categories: muscle performance, mobility, muscle re-education, aerobic) found small improvement in function compared with controls (2 trials, pooled SMD −0.44, 95% CI −0.76 to −0.09, data not shown in figure).[35,37] A fair-quality study reported a continued small benefit with combination exercise in the long term (SMD −0.38, 95% CI −0.74 to −0.03).[37]

Exercise tended toward moderately greater effects on short-term pain compared with no treatment or an attention control (4 trials, pooled MD −1.31, 95% CI −2.76 to 0.14, I^2=94.2%), but statistical heterogeneity was very large,[35-38] (Figure 27). Excluding an outlier trial (MD −2.92, 95% CI −3.38 to −2.46)[36] reduced the statistical heterogeneity and resulted in an attenuated effect (MD −0.72, 95% CI −1.49 to 0.06, I^2=63.7%). The effect of exercise on reducing pain was substantially greater in trials assessing combination exercises (2 trials, pooled MD −1.12, 95% CI −1.82 to −0.43; data not shown in figure).[35,37] There were no differences in pain comparing exercise versus controls in intermediate term (2 trials, pooled MD −0.25, 95% CI −0.71 to 0.20, I^2=0%)[34,38]or long term (3 trials, pooled MD 0.12, 95% CI −0.52 to 0.76, I^2=37.8%).[34,37,39]

Data on effects of exercise on quality of life were limited. One fair-quality trial[37] found significant improvement in SF-36 PCS and MCS in the short term (difference in change score 3.60 on a 0-100 scale, 95% CI 1.23 to 5.97 and 4.00, 95% CI 1.24 to 6.77, respectively) and PCS in the long term (difference in change score 3.80, 95% CI 1.30 to 6.30). A poor-quality trial found no difference in SF-36 PCS or MCS in the short term.[35] No trial evaluated effects of exercise therapies on use of opioid therapies or health care utilization.

There was insufficient evidence to determine effects of duration of exercise therapy or number of sessions on outcomes.

Exercise Compared With Pharmacological Therapy

One poor-quality trial (N=40)[88] comparing 1.5 months of home combination exercises (posture, stretching, strengthening and endurance exercises) versus ibuprofen plus thiocolchicoside for 15 days found no between-group difference in function (Neck Disability Index [NDI]) at 3-month (MD −2.2 on 0-50 scale, 95% CI −5.8 to 1.5) or 6-month followup (MD of −1.8, 95% CI −5.7 to 2.1). The study reported similar results for pain intensity (MD −1.0 on a 0-10 scale, 95% CI −2.3 to 0.3 at 3-month and MD −0.8, 95% CI −2.3 to 0.7 at 6-month followup). The exercise group reported a better quality of life compared with the medication group at 3-month and 6-month followup using the Turkish version of the Nottingham Health Profile (MD −141, scale not stated though usual scale 0-100, 95% CI −214 to −68; MD −135, 95% CI −209 to −62, respectively).[88] The groups scored comparably on the Beck Depression Inventory at both followup periods (Table 18).

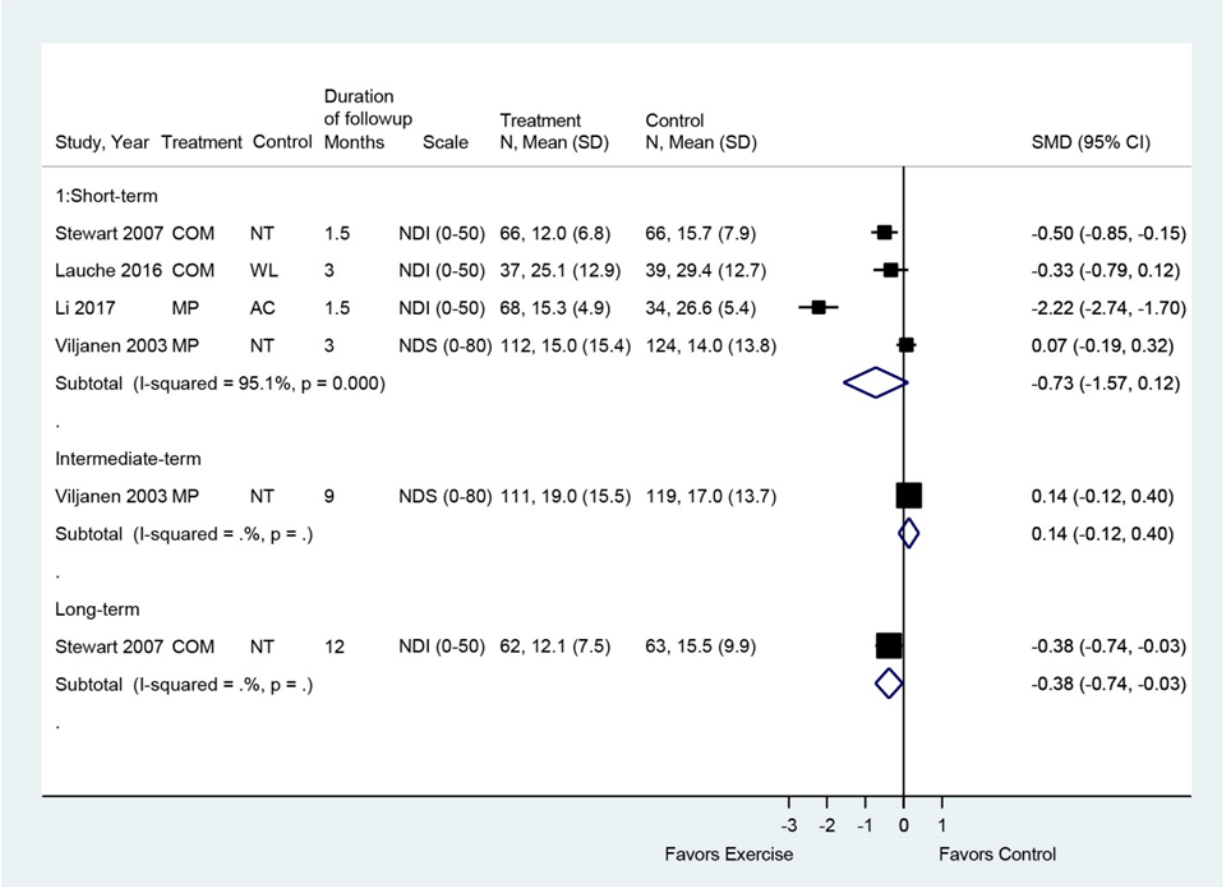
Exercise Compared With Other Nonpharmacological Therapies

Findings for exercise versus other nonpharmacological therapies are addressed in the sections for other nonpharmacological therapies.

Harms

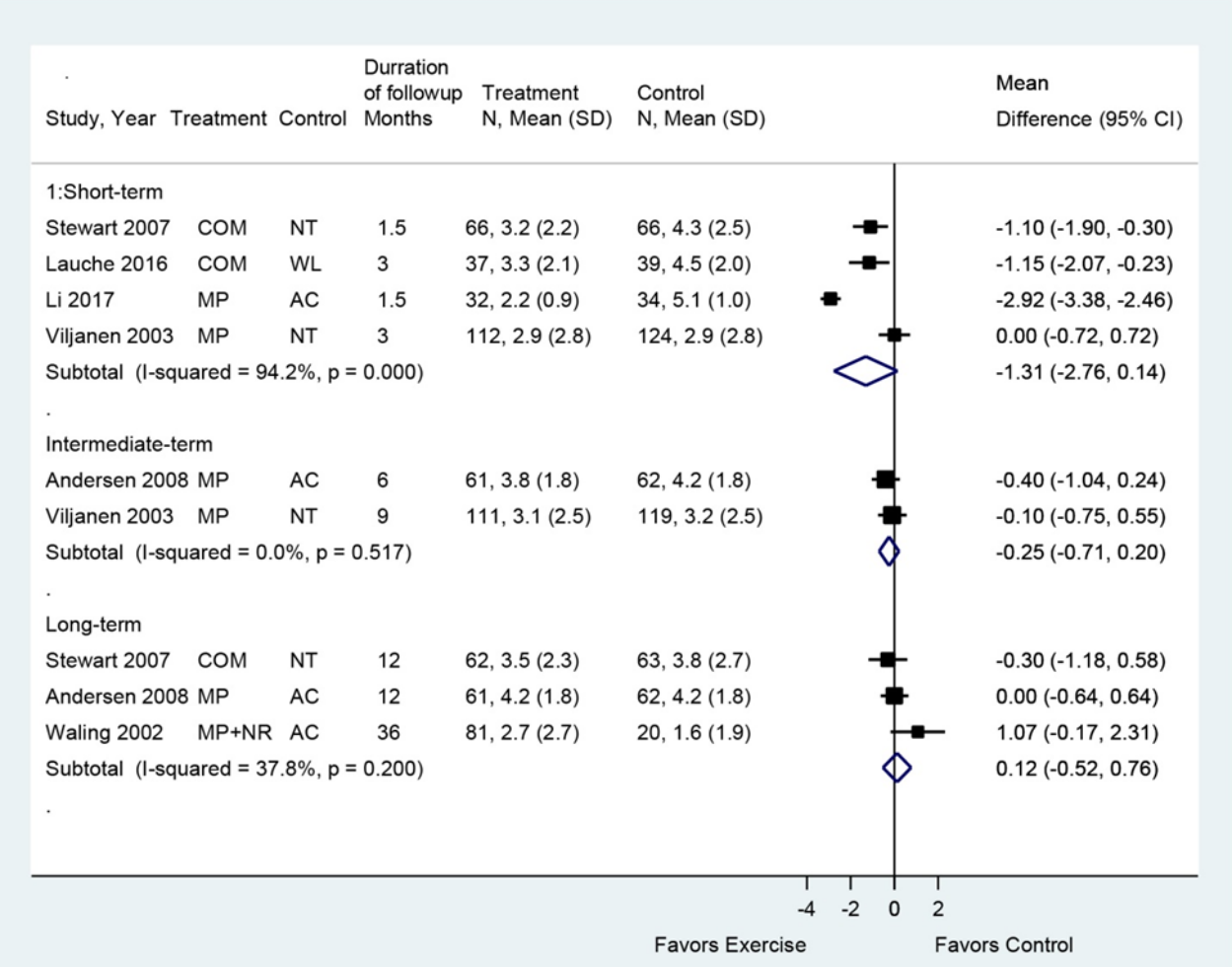
Only two exercise trials reported harms. One reported only mild complaints that included muscle pain with exercise (5%), knee pain (3%), and lumbar spine pain (3%).[37] None required referral to a medical practitioner. In the other, investigators reported no serious harms related to the intervention.[35] One occurrence of minor knee pain was reported in the exercise group.

Figure 26. Exercise versus no treatment or an attention control for chronic neck pain: effects on function



CI = confidence interval; COM = combination exercise therapy; MP = muscle performance exercise; NDI = Neck Disability Index; NDS = neck disability scale; NT = no treatment; SD = standard deviation; SMD = standardized mean difference; WL = waitlist.

Figure 27. Exercise versus no treatment or an attention control for chronic neck pain: effects on pain



AC = attention control; CI = confidence interval; COM = combination exercise therapy; MP = muscle performance exercise; MP+NR = muscle performance plus neuromuscular rehabilitation exercise; NT = no treatment; SD = standard deviation; WL = waitlist

Psychological Therapies for Chronic Neck Pain

Key Points

- No evidence of differences was found in function (NDI, 0−80 scale) or pain (visual analog scale [VAS], 0-10 scale) in the short term (adjusted difference 0.1, 95% CI −2.9 to 3.2 and 0.2, 95% CI −0.4 to 0.8, respectively) or intermediate term (adjusted difference 0.2, 95% CI −2.8 to 3.1 and 0.2, 95% CI −0.3 to 0.8, respectively) from one fair-quality study comparing relaxation training and no intervention or exercise (SOE: low for all). We found no trials with outcomes assessed in the long term.
- We found no evidence comparing relaxation training with pharmacological therapy.
- The only trial of relaxation training did not report harms.

Detailed Synthesis

We found one trial comparing the effects of relaxation training versus no intervention (N=258) or exercise therapy (N=263) in female office workers with chronic neck pain[38] (Table 19 and Appendix D). Relaxation training and muscle performance exercise therapy were done in 30-minute sessions three times per week for 12 weeks, with 1 week of reinforcement training 6 months after randomization. Patients in the no-treatment group were instructed not to change their usual activities. Adherence to the relaxation schedule during the intervention period was 42 percent of the scheduled sessions. The nature of the intervention and control precluded blinding of participants and people administering the interventions; therefore, this trial was rated as fair quality.

Table 19. Chronic neck pain: psychological therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Viljanen, 2003[38] 3 and 9 months Pain duration: 11 years *Fair*	A. Physical therapist guided relaxation training (n=128): progressive relaxation, autogenic training, functional relaxation, and systematic desensitization (goal was to teach correct activation and relaxation of muscles used in daily activities); 3 times per week for 12 weeks, 30 minute sessions B. Physical therapist guided dynamic strengthening exercises of the shoulder and cervical musculature (muscle performance exercises) (n=135): 3 times per week for 12 weeks, 30 minute sessions C. No intervention (n=130)	A vs. B vs. C Age: 43 vs. 45 vs. 44 years Female: 100% Performing physical activity ≥3x/week: 34% vs. 44% vs. 41% Duration of office work: 20 vs. 23 vs. 21 years Sedentary work >6 hours per day: 75% vs. 76% vs. vs. 73% Computer work >6 hours per day: 39% vs. 33% vs. vs. 35% Absent from work due to neck pain: 12% vs. 12% vs. 12% Pain duration: 11 vs. 11 vs. 10 years Neck disability scale[a] (0-80): 29 vs. 29 vs. 26 Pain VAS (0-10): 4.8 vs. 4.8 vs. 4.1 Depression index: 16 vs. 16 vs. 16	A vs. C 3 months Neck disability scale[b]: 15 vs. 14, adjusted difference 0.1 (95% CI −2.9 to 3.2) Pain VAS: 3.0 vs. 2.9, adjusted difference 0.2 (95% CI −0.4 to 0.8) 9 months Neck disability scale[b]: 19 vs. 17, adjusted difference 0.2 (95% CI −2.8 to 3.1) Pain VAS: 3.3 vs. 3.2, adjusted difference 0.2 (95% CI −0.3 to 0.8) A vs. B 3 months Neck disability scale[a]: 15 vs. 15, adjusted difference 0.2 (95% CI −2.8 to 3.2) Pain VAS: 3.0 vs. 2.9, adjusted difference −0.2 (95% CI −0.8 to 0.4) 9 months Neck disability scale[a]: 19 vs. 19; adjusted difference 0.2 (95% CI −2.7 to 3.2) Pain VAS: 3.3 vs. 3.1, adjusted difference −0.2 (95% CI −0.8 to 0.3)	NR

CI = confidence interval; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Neck disability scale was created by investigators from responses to eight questions related to functional limitations due to pain. This scale is not the same as the more common Neck Disability Index (NDI)

Relaxation Training Compared With No Treatment

The one fair-quality trial found no between-group differences in the short term (3 months) or intermediate term (9 months) as measured by a neck disability scale (MD 0.1 on a 0-80 scale, 95% CI −2.9 to 3.2, and MD 0.2, 95% CI −2.8 to 3.1, respectively)[38] (Table 19). The neck disability scale, a nonvalidated instrument, asked whether the participant had pain or difficulty on eight functional activities, with each activity scored from 0 (no pain or hindrance) to 10 (unbearable pain or maximum hindrance), for a total of 80 points. Likewise, there were no differences in pain intensity between groups at the same time frames, (MD 0.2 on a 10-point scale, 95% CI −0.4 to 0.8, and MD 0.2, 95% CI −0.3 to 0.8, respectively). There were no trials evaluating relaxation in the long term.

Relaxation Training Compared With Pharmacological Therapy

We did not find any trials meeting our criteria that compared a relaxation training with pharmacological therapy.

Relaxation Training Compared With Exercise Therapy

The one fair-quality trial found no differences between relaxation training and exercise therapy in the short term (3 months) or intermediate term (9 months) as measured by a neck disability scale described above (MD 0.2 on a 0-80 scale, 95% CI −2.8 to 3.2, and MD 0.2, 95% CI −2.7 to 3.2, respectively)[38] (Table 19). Similarly, there were no differences in pain intensity between groups at the same time frames (MD −0.2 on a 10-point scale, 95% CI −0.8 to 0.4, and MD −0.2, 95% CI −0.8 to 0.3, respectively). There were no trials comparing relaxation with exercise therapy in the long term.

Harms

The trial on relaxation therapy did not report harms.[38]

Physical Modalities for Chronic Neck Pain

Key Points

- Low-level laser therapy was associated with a moderate improvement in short-term function (2 trials, pooled difference −14.98, 95% CI −23.88 to −6.07, I^2=39%, 0-100 scale) and pain (3 trials, pooled difference −1.81 on a 0-10 scale, 95% CI −3.35 to −0.27, I^2=75%) compared with sham (SOE: moderate for function and pain).
- Data from two small, poor-quality trials, one evaluating cervical traction versus attention control (infrared irradiation) and the other electromagnetic fields versus sham, were insufficient to determine effects on function or pain over the short term (SOE: insufficient).
- No trials assessed outcomes in the intermediate term or long term, or compared a physical modality to pharmacological therapy or exercise.
- Harms were poorly reported in trials of low-level laser. Adverse effects occurred with similar frequency in the laser and sham groups in the one trial reporting such effects. The most frequently reported adverse effects included mild (78%) or moderately (60%) increased neck pain, increased pain elsewhere (78%), mild headache (60%), and tiredness (24%) (SOE: low).
- The trials of cervical traction and electromagnetic fields did not report harms.

Detailed Synthesis

A total of five trials (N=53 to 90)[120-124] evaluating physical modalities for the treatment of chronic neck pain met inclusion criteria (Table 20 and Appendixes D and E). Interventions included traction, laser therapy, and electromagnetic field therapy.

One trial (N=79) conducted in Hong Kong compared intermittent cervical traction versus attention control (infrared irradiation).[121] Each treatment was administered for 20 minutes twice weekly for 6 weeks. This trial was considered poor quality due to lack of patient and caregiver blinding, high and unequal attrition (41% in traction group, 58% in control), and dissimilar baseline characteristics between groups.

Three trials (N=53 to 90)[120,122,123] compared low-level laser therapy with sham. The mean duration of pain varied from 4 years in two trials[120,123] to 15 years in a third.[122] Treatment consisted of laser application (wavelength range, 830 to 904 nm) over several myofascial tender points; across the trials, duration ranged from 30 seconds to 3 minutes per tender point and frequency varied from daily to twice weekly over periods of 2 or 7 weeks. One trial was rated good quality[122] and two fair quality.[120,123] Common methodological limitations in the two fair-quality trials included inadequate reporting of treatment allocation and no or unclear blinding of the care provider. In addition, baseline characteristics were not similar in one trial, in which the intervention group tended to have more pain and tenderness and longer duration of symptoms.[120]

One trial (N=81) compared the effects of eighteen 30-minute sessions (3-5 times per week) of low frequency pulsed electromagnetic fields versus sham.[124] The treatment consisted of an electromagnetic coil against the back of the neck while the participants were lying on a pillow. The investigators covered the set of light emitting diodes that pulse to signal the coil being energized in order to blind the participants to the treatment or sham. This trial was rated as poor quality due to several factors: failure to describe the number randomized in each group; inadequate reporting of treatment compliance and information to calculate participant attrition and intent to treat analysis; care provider not blinded to treatment; and baseline characteristics dissimilar between groups.

Table 20. Chronic neck pain: physical modalities

Author, Year, Followup[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Altan, 2005[120] 3 months Pain duration: 4.5 years *Fair*	A. GaAs low-level laser treatment (n=26): over the 3 trigger points bilaterally and 1 point in the taut bands in trapezius muscle bilaterally for 2 min over each point once a day for 2 weeks. Laser wavelength of 904 nm. B. Sham laser treatment (n=27)	A vs. B Age: 43 vs. 43 years Female: 87% vs. 48% Pain duration: 4.7 vs. 4.4 years Pain (VAS 0-10): 6.85 vs. 6.24 Pain (5-point scale, 0-5): 2.35 vs. 2.20	A vs. B <u>3 months:</u> Pain (VAS): 3.17 vs. 3.80, difference −0.63 (95% CI −0.95 to −0.31) Pain (5 point scale): 1.09 vs. 1.16, difference −0.07 (95% CI −0.19 to 0.05)	NR

Author, Year, Followup[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Chiu, 2011[121] 1.5 months Duration of pain: NR *Poor*	A. Cervical Traction (intermittent) (n=39): ranging from 10-20% of patient body weight, holding time 10-25 seconds; resting time 20-50% of holding time; twice/week for 6 weeks; sessions lasting 20 minutes. B. Infrared Irradiation Control (n=40): via infrared lamp positioned so that patients reported minimal warmth over the back of their neck; twice/week for 6 weeks; sessions lasting: 20 minutes.	A vs. B Age: 50.9 vs. 46.8 years Female: 65.2% vs. 76.5% NPQ (0-100%): 46.1 vs. 38.5 NPS (0-10): 5.8 vs. 5.2	A vs. B <u>1.5 months</u> NPQ Disability[b]: 31.4 vs. 29.6; P>0.05, 95% CI 29.66 to 37.50, power=0.15 NPS Pain Severity[b]: 3.5 vs. 2.8; P>0.05, 95% CI 3.29 to 4.50, power=0.17	NR
Chow, 2006[122] 1 month Pain duration: 15 years *Good*	A. Low-level laser therapy (n=45): 2x/week for 7 consecutive weeks, maximum half hour per treatment. Up to 50 tender points in the neck were treated for 30 seconds per point. Laser wavelength of 830 nm. B. Sham laser (n=45)	A vs. B Age: 57 vs. 55 years Female: 64% vs. 67% Pain duration: 17 vs. 13 years Pain (VAS 0-10): 5.9 vs. 4.0	A vs. B <u>1 month</u> NPQ (0-100%): −3.5 vs. −0.6, difference −3.0 (95% CI −5.0 to −0.9) NPAD (0-100): −15.2 vs. −3.1, difference −12.1 (95% CI −19.3 to −4.8) Pain, VAS: −2.7 vs. 0.3, difference 3.0 (95% CI −3.8 to −2.1) MPQ VAS (1-5): −2.1 vs. 0.1, difference −2.2 (95% CI −3.5 to −0.9) Improved pain <−3 (%): 40% vs. 7%, RR 6.0 (95% CI 1.9 to 19.0)	A vs. B <u>1 month</u> SF36 PCS: 3.2 vs. −1.3, difference 4.5 (95% CI 0.7 to 8.2) SF 36 MCS: 2.4 vs. 5.4, difference −2.9 (95% CI −7.2 to 1.3), MPQ sensory (0-33): −3.4 vs. −1.9, difference −1.5 (95% CI −4.5 to 1.5) MPQ affective (0-12): −1.3 vs. −0.7, difference −0.6 (95% CI −2.3 to 1.1)

Author, Year, Followup[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Gur, 2004[123] 2.5 months Pain duration: 43 months *Fair*	A. Active Ga-As low-level laser therapy (n=30): daily for 2 weeks, 3 minutes each myofascial tender point. Laser wavelength of 904 nm. B. Sham laser (n=30)	A vs. B Age: 32 vs. 31 years Female: 82% (total pop only) Pain duration: 43 vs. 43 months Employed: 12% vs. 17% Pain at rest (VAS 0-10): 7.43 vs. 6.87 Pain at movement (VAS 0-10): 7.43 vs. 7.19 NPAD (0-100): 65.36 vs. 68.52 NHP (0-100): 78.9 vs. 75.5 BDI (0-63): 21.56 vs. 20.81	A vs. B 2.5 months NPAD: 41.14 vs. 63.29, difference −22.15 (95% CI −36.7 to −7.6) Pain at rest (VAS): 4.18 vs. 6.29, difference −2.11 (95% CI −3.80 to −0.42) Pain at movement (VAS): 5.26 vs. 7.28, difference −2.02 (95% CI −3.31 to −0.73)	A vs. B 2.5 months BDI: 14.72 vs. 21.38, difference −6.66 (95% CI −13.24 to −0.08) NHP: 56.41 vs. 72.48, difference −16.1 (95% CI −30.9 to −1.3),
Trock, 1994[124] 1 month Pain duration: 7.5 years *Poor*	A. Pulsed electromagnetic fields (n=42 treated): extremely low frequency (<2 A, 120 V) applied with stepwise energy characteristics as follows: 5 Hz, 0-15 gauss for 10 minutes; 10 Hz, 15-25 gauss for 10 minutes; and 12 Hz, 15-25 gauss for 10 minutes. Maximum number of pulses/burst was 20. B. Sham (n=39 treated) Treatments were given for 30 minute periods, 3-5 times per week for 18 treatments.	A vs. B Age: 61 vs. 67 years Female: 71% vs. 67% Weight (lb): 161 vs. 162 Duration of symptoms: 7 vs. 8 years ADL difficulty (0-24) 11.9 vs. 11.5 Pain (0-10): 7.20 vs. 6.23	A vs. B 1 month: ADL difficulty: 3.78 vs. 2.14, difference 1.6 (95% CI −1.5 to 4.8) Pain: 2.59 vs. 1.47, difference 1.12 (95% CI −0.31 to 2.55)	A vs. B 1 month: Patients' assessment of improvement (0-100): 41.2 vs. 40.0, difference 1.2 (95% CI −15.2 to 17.6)

ADL = activity of daily living; BDI = Beck Depression Inventory; BMI = body mass index; CI = confidence interval; Ga-As = Gallium Arsenide; HADS = Hospital Anxiety and Depression Scale; MD = mean difference; MPQ = McGill Pain Questionnaire; NDI = Neck Disability Index; NHP = Nottingham Health Profile; NPAD = Neck Pain and Disability Scale; NPQ = Northwick Park Questionnaire; NPS = numeric pain scale; NR = not reported; PSFS = Patient Specific Functional Scale; RR = risk ratio; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Results of two-way repeated measures analysis of variance (ANOVA)

Physical Modalities Compared With Attention Control or Sham

Traction. One poor-quality trial found no short-term differences in function comparing intermittent cervical traction versus attention control (infrared irradiation) using the Northwick Park Questionnaire (NPQ) (MD −1.8, 95% CI −10.8 to 7.2, 0-100% scale).[121] Likewise, there was no difference in pain intensity between groups (MD −0.7, 95% CI −2.2 to 0.8, 10 point scale). There were no trials evaluating cervical traction in the intermediate term or long term.

Low-Level Laser Therapy. Laser was associated with moderately greater effects compared with sham on short-term function (2 trials, pooled difference −14.98, 95% CI −23.88 to −6.07, I^2=39%, 0-100 scale) (Figure 28)[122,123] and short-term pain (3 trials, pooled difference −1.81, 95% CI −3.35 to −0.27, I^2=75%, 0-10 scale) (Figure 29).[120,122,123] Pain improvement of greater than −3.0 on a 10-point VAS scale was substantially more common with laser therapy in the good-quality trial (RR 6.0, 95% CI 1.9 to 19.0).[122] Quality of life improvement also favored low-level laser as measured by the SF-36 PCS (MD 4.5, 95% CI 0.7 to 8.2)[122] and the Nottingham Health Profile (MD −16.1 on a 0-100 scale, 95% CI −30.9 to −1.3).[123] Measures demonstrating no difference between groups included the SF36 MCS and the McGill Pain Questionnaire component scores[122] (Table 20). There were no trials evaluating laser therapy in the intermediate term or long term.

Electromagnetic Fields. One poor-quality trial found no between-group differences in short-term difficulty with activities of daily living (ADLs) (MD 1.6 , 95% CI −1.5 to 4.8, scale 0-24, nonvalidated measure).[124] The ADL instrument asked whether the participant had pain or difficulty on eight activities scored from 0 (never) to 3 (always), for a total of 24 points. Likewise, there was no difference in pain intensity between groups (MD 1.1, 95% CI −0.3 to 2.6, 0-10 scale) or in patients' assessment of improvement (MD 1.2, 95% CI −15.2 to 17.6, 0-100 scale).[124] There were no trials evaluating electromagnetic fields in the intermediate term or long term.

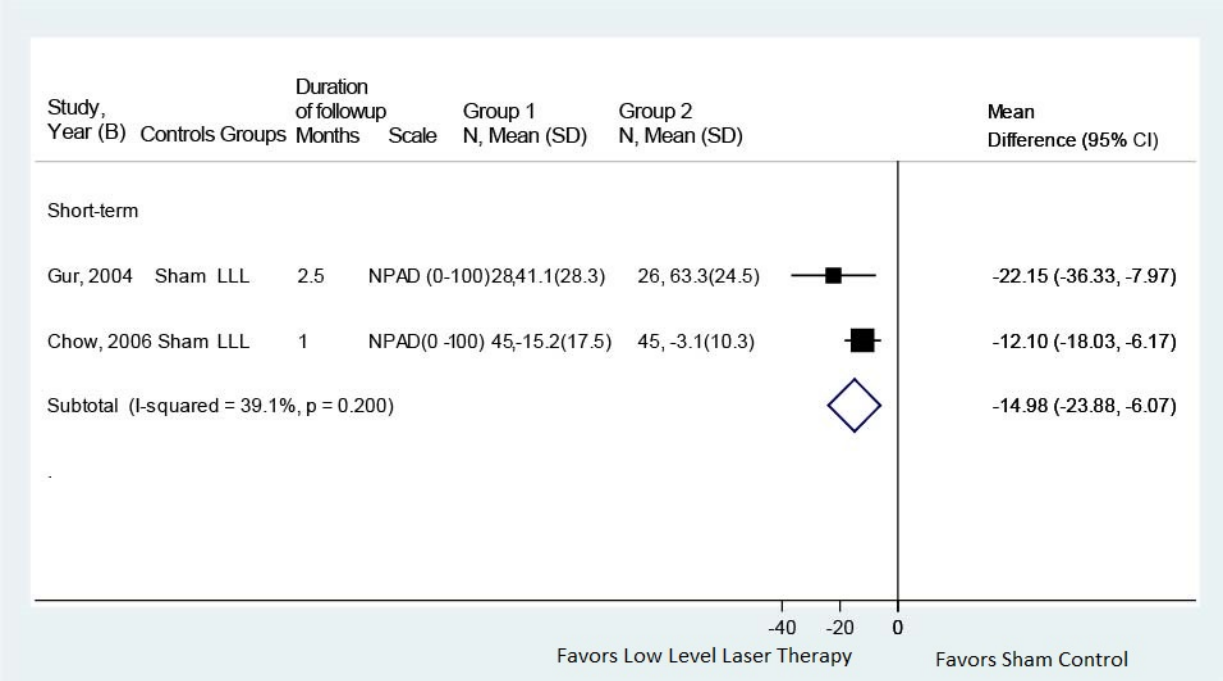
Physical Modalities Compared With Pharmacological Therapy or With Exercise Therapy

We did not find any trials meeting our criteria comparing a physical modality with pharmacological therapy or with exercise.

Harms

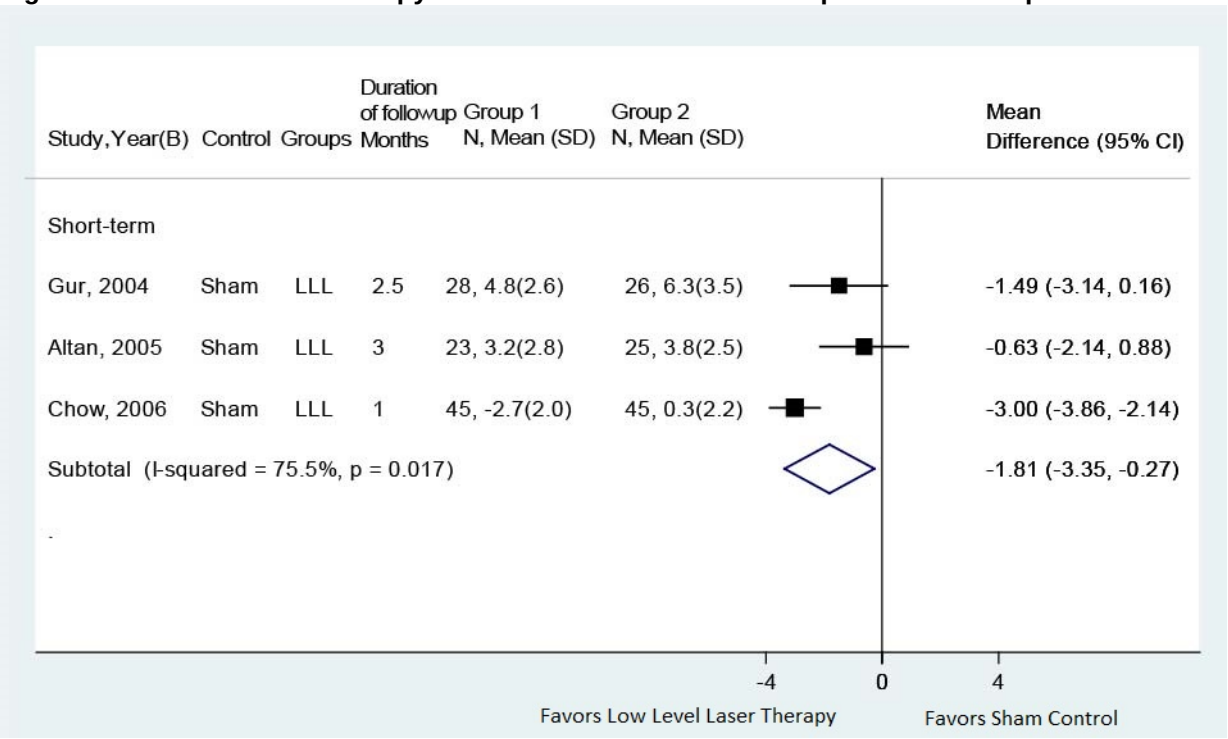
Only one laser trial reported harms.[122] The trial reported a large number of adverse effects with similar frequency in both groups. However, the sham group reported nausea significantly more frequently (42% vs. 20%) while the laser group reported stiffness more frequently (20% vs. 4%). The most frequently reported adverse effects included mild (78%) or moderate (60%) increased neck pain, increased pain elsewhere (78%), mild headache (60%), and tiredness (24%). Harms were not reported by either trial evaluating cervical traction or electromagnetic fields.

Figure 28. Low-level laser therapy versus sham for chronic neck pain: effects on function



CI = confidence interval; LLL = low-level laser therapy; NPAD = Neck Pain and Disability Scale; SD = standard deviation

Figure 29. Low-level laser therapy versus sham for chronic neck pain: effects on pain



CI = confidence interval; LLL = low-level laser therapy; SD = standard deviation

Manual Therapies for Chronic Neck Pain

Key Points

- The effects of massage on function versus self-management attention control were slight and not statistically significant in one trial (N=64) in the short term (≥5 point improvement on the NDI, 39% versus 14%, RR 2.7, 95% CI 0.99 to 7.5) and intermediate term (57% versus 31%, RR 1.8, 95% CI 0.97 to 3.5) (SOE: low for both time periods).
- No clear evidence that massage improved pain in the intermediate term versus exercise (P>0.05, data not reported) in one fair-quality trial (SOE: low).
- Two fair-quality trials reported no serious adverse effects, and more transient nonserious pain or soreness during or after exercise, but not massage (SOE: low).

Detailed Synthesis

Two trials of classical (N=85)[152] or Swedish massage (N=58)[153] met inclusion criteria (Table 21 and Appendix D). One trial compared massage versus attention control (self-care education),[153] and one trial compared massage versus two types of exercise (muscle re-education and strength training targeting the neck and shoulder muscles).[152] Muscle re-education was performed with a newly developed training device strapped to the head and consisted of a plate with 5 exchangeable surfaces that allow for progression of task difficulty. One trial was conducted in Sweden[152] and one in the United States.[153] One trial administered 10 massage treatments over 10 weeks,[153] and the other trial 22 massage treatments over 11 weeks.[152]

Both trials were rated fair quality (Appendix E). Methodological limitations included the inability to blind interventions in both trials, and 21 percent attrition in the trial comparing massage with exercise.[152]

Table 21. Chronic neck pain: manual therapies

Author, Year, Followup, Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Rudolfsson, 2014[152] 6 months Duration of pain: median 84 to 123 months *Fair*	A. Massage, classical (n=36): upper body including the back, neck and shoulders. B. Neck coordination exercise (n=36): performed with a newly developed training device designed to improve the fine movement control of the cervical spine. C. Strength training (n=36): isometric and dynamic exercises targeting the neck and shoulder regions. All 3 interventions consisted of 22 individually supervised single treatment sessions, 30 min each, distributed over 11 weeks	A vs. B vs. C Age: 51 vs. 52 vs. 51 years Female: 100% vs. 100% vs. 100% Weight (kg): 73 vs. 74 vs. 74 Height (cm): 167 vs. 164 vs. 165 Pain duration: 120 vs. 123 vs. 84 months (median) Pain NRS (0-10), 5 vs. 6 vs. 6 (median) NDI: 26 vs. 29 vs. 31 SF-36 PCS (0-100): 43 vs. 39 vs. 39 (median) SF-36 MCS (0-100): 49 vs. 52 vs. 47 (median)	A vs. B: <u>6 months</u> Pain NRS (0-10): 4.0 vs. 3.8, MD 0.2 (95% CI −0.82 to 1.22) A vs. C: <u>6 months</u> Pain NRS (0-10): No data given at 6 month, however, authors state no difference among A, B or C.	NR
Sherman, 2009[153] 2.5 and 6.5 months Duration of pain >1 year: 81% *Fair*	A. Massage (n=32): Swedish and clinical techniques and self-care recommendations; 10 massage treatments over a 10-week period B. Self-care book: (n=32) information on potential causes of neck pain, neck-related headaches, whiplash, recommended strengthening exercises, body mechanics and posture, conventional treatment, complementary therapies for neck pain, and first aid for intermittent flare-ups.	A vs. B Age: 47 vs. 46 years Female: 69% vs. 69% White: 87% vs. 81% Married: 78% vs. 59% Smoker: 9% vs. 6% Pain lasted > 1 year: 81% vs. 81% Symptom bothersome (0-10): 4.8 vs. 4.9 NDI (0-50): 14.2 vs. 14.2 SF-36 PCS (0-100): 46.0 vs. 44.1 SF-36 MCS (0-100): 51.9 vs. 53.1	A vs. B <u>2.5 months</u> NDI, % ≥5 points: 39% vs. 14%, RR 2.7 (95% CI 0.99 to 7.5) NDI (0-50): MD −2.3 (95% CI −4.7 to 0.15) <u>6.5 months</u> NDI, % ≥5 points: 57% vs. 31%, RR 1.8 (95% CI 0.97 to 3.5) NDI: MD: −1.9 (95% CI −4.4 to 0.63)	A vs. B <u>2.5 months</u> Bothersome score (0-10): MD −1.2 (95% CI −2.5 to 0.1) Bothersome improvement ≥30%: 55% vs. 25%, RR 2.1 (95% CI 1.04 to 4.2) SF-36 PCS: 52.8 vs. 53.3, P=0.982 SF-36 MCS: 45.9 vs. 45.3, P=0.444 <u>6.5 months</u> Bothersome score: MD −0.14 (95% CI −1.5 to 1.2) Bothersome improvement ≥30%: 43% vs. 39%, RR 1.1 (95% CI 0.6 to 2.0) SF-36 PCS and MCS: data not given, no statistical difference Medication use: No change in group A, 14% increase in group B

CI = confidence interval; MD = mean difference; NDI = Neck Disability Index; NR = not reported; NRS = numeric rating scale; SF-36 MCS = Short-Form 36 Mental Component Summary; SF-36 PCS = Short-Form 36 Physical Component Summary

[a]Unless otherwise noted, followup time is calculated from the end of the treatment period.

Manual Therapies Compared With an Attention Control

The effects of massage on function versus self-management attention control were small and not statistically significant in one trial (N=64) in the short term (≥5 point improvement on the NDI, 39% versus 14%, RR 2.7, 95% CI 0.99 to 7.5) and intermediate term (57% versus 31%, RR 1.8, 95% CI 0.97 to 3.5).[153] A greater proportion of participants in the massage group reported improvement in a symptom bothersomeness scale (≥30%) in the short term (55% versus 25%; RR 2.2, 95% CI 1.04 to 4.2) but not intermediate term (RR 1.1, 95% CI 0.6 to 2.0). There were no differences between groups in SF-36 PCS and MCS. Medication use did not change in the massage group while it increased in the self-management group (14%).

Manual Therapies Compared With Pharmacological Therapy

No trial of manual therapy versus pharmacological therapy met inclusion criteria.

Manual Therapies Compared With Exercise

One fair-quality study reported no difference in intermediate-term pain comparing massage with neck coordination exercises (difference 0.2, 95% CI −0.82 to 1.22, 0-10 scale) or muscle performance exercises (no data given, P>0.05).[152]

No trial evaluated effects of manual therapies on use of opioid therapies or health care utilization.

Harms

Neither trial reported serious adverse effects. Nonserious mild adverse effects included discomfort or pain during (n=5) or after massage (n=3) in one trial.[153] There were no serious adverse effects in the massage group in the second trial, though there was transient neck or headache pain in the neuromuscular training exercise group (n=10).

Mind-Body Practices for Chronic Neck Pain

Key Points

- Alexander Technique resulted in a small improvement in function in the short term (difference −5.56 on a 0-100% scale, 95% CI −8.33 to −2.78) and intermediate term (difference −3.92, 95% CI −6.87 to −0.97) compared with usual care alone, based on one fair-quality trial (SOE: low).
- There was no clear evidence that basic body awareness therapy improved function in the short term versus exercise in one fair-quality trial (SOE: low).
- There is insufficient evidence from one poor-quality trial to determine the effects of qigong on intermediate-term or long-term function or pain versus exercise; no data were available for short term outcomes (SOE: insufficient).
- Both fair-quality trials reported no serious treatment-related adverse events. The trial evaluating Alexander Technique versus usual care found no clear between-group difference for nonserious adverse events, such as pain and incapacity, knee injury, or muscle spasm (RR 2.25, 95% CI 1.00 to 5.04). The other trial reported no differences between basic body awareness and exercise in any nonserious adverse effect (RR 0.65, 95% CI 0.37 to 1.14) (SOE: low).

Detailed Synthesis

Three trials of mind-body practices met inclusion criteria (Table 22 and Appendix D).[180,187,188] One trial evaluated the Alexander Technique (a method of self-care developed to help people enhance their control of reaction and improve their way of going about everyday activities) plus usual care (N=344),[180] one trial basic body awareness therapy (N=115),[188] and one trial of qigong (N=134).[187] One trial compared mind-body techniques versus usual care[180] and two trials versus individually adjusted cervical and shoulder strengthening and stretching exercises,[187] or group-led exercises for whole body strengthening, aerobic, and coordination exercises.[188] Two trials were conducted in Sweden[187,188] and one in England.[180] The duration of mind-body treatment ranged from 10 to 20 weeks and the number of treatment sessions ranged from 12 to 20. One trial reported outcomes during the intermediate term and long term,[187]one short-term and intermediate-term outcomes,[180] and one short-term outcomes only.[188]

Two of the trials were rated fair quality[180,188] and one trial poor quality[187] (Appendix E). In the two fair-quality trials, the main methodological limitation was the inability to blind interventions. Limitations in the other trial included the inability to blind interventions, high attrition, and unequal loss to followup between groups.

Table 22. Chronic neck pain: mind-body practices

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Lansinger, 2007[187] 6 and 12 months Pain duration: >5 years, 45% *Poor*	A. Qigong (n=72): 10-12 group sessions of 10-15 people done 1-2 times per week over 3 months. Sessions were 1 hour and consisted of information of the philosophy of medical qigong followed by exercises based on the Biyun method B. Exercise (n=67): 10-12 sessions 1-2 times per week over 3 months. Sessions were 1 hour and individualized to target 30%-70% of a person's maximal voluntary capacity, with exercises aiming to maintain/increase circulation, endurance, and strength. All patients: Ergonomic instructions and a pamphlet containing written information on neck pain	A vs. B Age: 45 vs. 43 Female: 73% vs. 67% Duration of neck pain: 3 mos-1 year: 15% vs. 20% >1 year: 38% vs. 37% >5 years: 22% vs. 24% >10 years: 25% vs. 20% Physical activity: No to light exercise: 67% vs. 65% Med to hard exercise: 33% vs. 35% NDI (0-100%), median: 26 vs. 22 Neck pain VAS (0-10), median: 45 vs. 39	A vs. B <u>6 months</u> NDI, median: 22 vs. 18, p>0.05 Neck pain VAS (0-10), median: 2.6 vs. 2.3, p>0.05 <u>12 months</u> NDI, median: 22 vs. 18, p>0.05 Neck pain VAS, median: 2.8 vs. 2.1, p>0.05	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
MacPherson, 2015[180] 1 and 7 months Duration of pain, 7 years *Fair*	A. Alexander Technique group (n=172): up to 20 one-to-one lessons of 30 minutes' duration (600 minutes total) plus usual care, delivered weekly, with the option of being delivered twice per week initially and every 2 weeks later. B. Usual care (n=172) including general and neck pain–specific treatments routinely provided to primary care patients, such as prescribed medications and visits to physical therapists and other health care professionals. Treatment was 12 sessions over 5 months lasting 50 minutes.	A vs. B Age: 52 vs. 54 years Female: 69% vs. 69% White: 93% vs. 89% Employed: 61% vs. 62% Pain duration (median): 60 vs. 96 months NPQ (0-100%): 39.64 vs. 40.46	A vs. B <u>1 month</u> NPQ: 35.35 vs. 40.90, MD −5.56 (95% CI −8.33 to −2.78) <u>7 months</u> NPQ: 37.07 vs. 40.99, MD −3.92 (95% CI −6.87 to −0.97)	A vs. B <u>1 month</u> SF-12v2 physical: data NR, P=NS SF-12v2 mental: data NR, P=NS <u>7 months</u> SF-12v2 physical: 0.68 (95% CI −1.08 to 2.44), P=0.44 SF-12v2 mental: 1.76 (95% CI 0.15 to 3.37), P=0.033

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Seferiadis,[188] 2015 3 months Pain duration: 9.5 years *Fair*	A. Basic body awareness therapy (n=57): 1.5 hour sessions twice a week for 10 weeks. Sessions consisted of exercises based on activities of daily living, meditation, and tai chi inspired exercises aiming to improve posture and increase efficient movement patterns B. Exercise (n=56): 1.5 hour sessions twice a week for 10 weeks. Sessions consisted of 45 minutes of muscle strengthening, 15 minutes of stretching, and 20 minutes of progressive muscle relaxation	A vs. B Age: 47 vs. 49 Female: 66% vs. 77% Duration of symptoms (years): 10 vs. 9 WAD classification: 1: 0% vs. 2% 2: 23% vs. 28% 3: 77% vs. 70% NDI (0-50): 20 vs. 18.8 SF-36v2 physical functioning (0-100): 67.5 vs. 69.7 role-physical (0-100): 33.9 vs. 24.5 bodily pain (0-100): 34.3 vs. 35.2 general health (0-100): 54.7 vs. 48.7 vitality (0-100): 39.5 vs. 35.1 social functioning (0-100): 60 vs. 59.4 role-emotional (0-100): 55.4 vs. 51.7 mental health (0-100): 65.9 vs. 62.7	A vs. B <u>3 months</u> NDI: Difference from baseline −2 (95% CI −3.5 to −0.5) vs. −1 (95% CI −2.5 to 0.4), p>0.05	A vs. B <u>3 months</u> SF-36v2 physical functioning: Difference from baseline 7.1 (95% CI 3.7 to 11.4) vs. 0.5 (95% CI −3.2 to 4.1), p>0.05 SF-36 role-physical: Difference from baseline 17.5 (95% CI 5.9 to 29) vs. 19 (95% CI 9.3 to 28.6), p>0.05 SF-36 bodily pain: Difference from baseline 12.2 (95% CI 6.9 to 17.6) vs. 4.9 (95% CI −0.1 to 9.8), P=0.044 SF-36 general health: Difference from baseline 7.5 (95% CI 2.4 to 12.6) vs. 4.5 (95% CI −0.1 to 9), p>0.05 SF-36 vitality: Difference from baseline 7.3 (95% CI 1.0 to13.6) vs. 5.6 (95% CI −0.5 to 11.6), p>0.05 SF-36 social functioning: Difference from baseline 13.3 (95% CI 6.6 to 19.9 vs. 3.5 (95% CI −3 to 9.9), P=0.037 SF-36 role-emotional: Difference from baseline 9.3 (95% CI −2.3 to 21) vs. 4 (95% CI −8.3 to 16.4), P>0.05 SF-36 mental health: Difference from baseline 2.8 (95% CI −2 to 7.6) vs. 1.2 (95% CI −3.6 to 5.9), p>0.05

CI = confidence interval; MD = mean difference; NDI = Neck Disability Index; NR = not reported; SF-36 =Short-Form 36 Questionnaire; VAS = visual analog scale; WAD = Whiplash Associated Disorders

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Mind-Body Practices Compared With Usual Care

One fair-quality trial found a small improvement in function as measured by the NPQ in favor of the Alexander Technique plus usual care versus usual care alone in the short term (MD −5.56 on a 100% scale, 95% CI −8.33 to −2.78) and intermediate term (MD −3.92, 95% CI −6.87 to −0.97).[180] There were no significant differences between the intervention group and

usual care for the physical component score of the SF-12 v 2 at 1-month or 7-month followup. However, significantly larger improvements in the MCS occurred in the Alexander group versus the usual care group 7 months following treatment (MD, 2.12 on a 0-100 scale, 95% CI 0.42 to 3.82).[180]

Mind-Body Practices Compared With Pharmacological Therapy

No trial of mind-body practice versus pharmacological therapy met inclusion criteria.

Mind-Body Practices Compared With Exercise

There were no differences in function as measured by the NDI between basic body awareness therapy (1 fair-quality study, n=113)[188] in the short term (mean change from baseline −2 versus −1, P>0.05) or qigong (poor-quality study, n=139)[187] in the intermediate term or long term (median 22 versus 18, P>0.05, at each time period) versus exercise therapy. The trial assessing qigong found no difference in pain at 6 or 12 months following treatment (median 2.6 versus 2.3 and 2.8 versus 2.3, P>0.05, respectively).[187] Two of the eight sections of the SF-36v2 favored basic body awareness therapy versus exercise in the short term (bodily pain and social functioning) in the fair-quality trial.[188] No other section of the SF-36v2 demonstrated a difference between groups.

No trial evaluated effects of mind-body practices on use of opioid therapies or health care utilization.

Harms

One trial of basic body awareness therapy reported no serious adverse effects.[188] One patient in the basic body awareness group and four patients in the exercise group reported that they discontinued treatment due to increased neck symptoms or pain in other joints (P=0.363). The event risk for all nonserious adverse events was 0.27 in the body awareness therapy group and 0.40 in the exercise group (RR 0.65, 95% CI 0.37 to 1.14).

Acupuncture for Chronic Neck Pain

Key Points

- Acupuncture was associated with slightly greater effects on short-term and intermediate-term function versus sham acupuncture, a placebo (sham laser), or usual care (short term, 5 trials, pooled SMD −0.40, 95% CI −0.64 to −0.17, I^2=67.7%; intermediate term, 3 trials, pooled SMD −0.19, 95% CI −0.35 to −0.02). One trial reported no difference in function in the long term (SMD −0.23, 95% CI −0.61 to 0.16) (SOE: low for all time periods).
- There was no evidence of differences in pain in studies comparing acupuncture with sham acupuncture or placebo interventions in the short term (4 trials [excluding outlier trial], pooled difference −0.2 on a 0-10 scale, 95% CI −0.59 to 0.05, I^2=2%), intermediate term (3 trials, pooled difference 0.45, 95% CI −0.34 to 1.25, I^2=59%), or long term (1 trial, difference -1.8, 95% CI −1.34 to 0.64) (SOE: low for all time periods).
- There was insufficient evidence from two small poor-quality trials to draw conclusions regarding short-term function or pain for acupuncture versus NSAIDs (SOE: insufficient).

- No serious adverse events were reported in five trials reporting harms. The most commonly reported nonserious adverse events in people receiving acupuncture included numbness/discomfort, fainting, and bruising (SOE: moderate).

Detailed Synthesis

We identified nine trials of acupuncture that met our inclusion criteria[180,196-202,217] (Table 23 and Appendix D). All trials evaluated needle acupuncture to body acupoints; two also evaluated electroacupuncture.[199,202] Control groups included sham acupuncture in five trials,[196-199,201] placebo intervention (sham TENS[200] and sham laser acupuncture[202]) in two trials, usual care in one trial,[180] and pharmacological therapy (Zaltoprofen[217] and Trilisate[196]) in two trials. The duration of acupuncture therapy ranged from 2 weeks to 5 months, and the number of sessions from 5 to 14. Sample sizes ranged from 30 to 355 (total sample=1,245). Across trials, participants were predominately female (from 60% to 90%) with mean ages ranging from 37 to 53 years. One trial was conducted in the United States,[196] one in Turkey,[199] and the rest in Asia[197,198,202,217] or Europe.[180,200,201] One trial reported outcomes through long-term followup,[201] four trials through intermediate-term followup,[180,200-202] and the remainder only evaluated short-term outcomes.[196-199,217]

Seven trials were rated fair quality[180,197-202] and two trials poor quality[196,217] (Appendix E). Common limitations in the fair-quality trials included unclear allocation concealment methods and of care provider blinding; additionally, the poor-quality trials had baseline group dissimilarity (not controlled for) and high attrition.

Table 23. Chronic neck pain: acupuncture

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Birch, 1998[196] 3 months Duration of pain, 7.5 years *Poor*	A. Relevant acupuncture, Japanese technique (n=15): using bilateral needles on hands and feet known to be associated with treatment for neck pain and followed by Infrared lamp. B. Irrelevant acupuncture (n=16): using bilateral needles on hands and feet in areas not associated with treatment for neck pain and followed by light. C. NSAIDs only (n=15): 500mg per day of Trilisate 30 minute treatment twice per week for 4 weeks, then once per week for 4 weeks, total 14 treatments	A vs. B vs. C Age: 41 vs. 38 vs. 39 years Female: 86% vs. 77% vs. 86% Pain duration: 82 vs. 92 vs. 91 months Married: 36% vs. 23% vs. 50% Employed: 86% vs. 69% vs. 77% Pain intensity (0-10) 4.8 vs. 4.7 vs. 4.9	A vs. B <u>3 months</u> SF-MPQ[b] (0-33): 9.0 vs. 15.1, P=NS A vs. C <u>3 months</u> SF-MPQ: 9.0 vs. 18.0, P=NS	NR
Cho, 2014[217] 1 month Duration of pain, NR *Poor*	A. Active acupuncture, traditional Chinese (n=15 randomized/15 analyzed), 3x/week for 3 weeks.(length of time for each intervention not reported) B. Zaltoprofen (80mg) alone (n=15 randomized/15 analyzed) 3x/day for 3 weeks.	A vs. B Age: 38 vs. 39 years Female: 60 vs. 80 NDI (0-50): 22.3 vs. 26.3 Pain VAS (0-10): 6.1 vs. 7.1	A vs. B <u>1 month</u> NDI: 17.3 vs. 17.7, difference −0.40 (95% CI −4.55 to 3.75) Pain VAS: 4.5 vs. 3.8, difference 0.7 (95% CI −0.74 to 2.14)	A vs. B <u>1 month</u> BDI (0-63) : 28.5 vs. 27.2, P=NS SF-36 (0-100): 88.6 vs. 84.3, P=NS EQ-5D (scale unclear): 7.3 vs. 6.7, P=NS

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Ho 2017[197] 1 month Duration of pain: 6 years *Fair*	A. Acupuncture (77 randomized/77 analyzed), 30 sessions of abdominal acupuncture 3 times a week for 2 weeks. The acupuncture points CV12, CV4, KI17, and ST24 were needled for 30 minutes with infrared therapeutic lamp placed 30 cm above the naval. B. Sham acupuncture (77 randomized/77 analyzed), 30 sessions of sham abdominal acupuncture 3 times a week for 2 weeks. Blunt sham needles were nonpenetrative and administered at nonacupuncture points.	A vs. B Age: 46 vs. 45 Female: 81% vs. 83% Pain duration (years): 6.0 vs. 6.0 Use of pain medications: 15% vs. 13% Previous acupuncture use: 42% vs. 44% NPQ, mean: 41.3 vs. 41.0 Pain VAS, mean: 6.4 vs. 6.1 SF-36 PCS, mean: 40.9 vs. 42.7 SF-36 MCS, mean: 42.9 vs. 44.3	A vs. B <u>1 month</u> NPQ, mean Δ (95% CI): −11.9 (−14.6 to −9.2) vs. −3.3 (−5.5 to −1.0), MD −8.7 (95% CI −12.1 to −5.2) P<0.001 Pain VAS, mean Δ (95% CI): −2.4 (−2.8 to −1.9) vs. −0.6 (−0.9 to −0.2), MD −1.8 (95% CI −2.4 to −1.2) P<0.001	A vs. B <u>1 month</u> SF-36 PCS, mean Δ (95% CI): 4.1 (3.0 to 5.3) vs. 1.3 (0.1 to 2.5), MD 2.8 (95% CI 1.2 to 4.5), P=0.003 SF-36 MCS, mean Δ (95% CI): 2.0 (0.5 to 3.5) vs. −0.3 (−2.0 to 1.4), MD 2.3 (95% CI −0.0 to 4.5) P=NR
Liang, 2011[198] 3 months Duration of pain, NR *Fair*	A. Active acupuncture, traditional Chinese, (n=93) B. Sham acupuncture (n=97) Treatment was 3x/week for 3 weeks (9 treatments total) lasting 20 minutes after needling Both groups received infrared	A vs. B Age: 37 vs. 37 years Female: 72% vs. 73% NPQ (0-100%): 32.7 vs. 33.0 Pain VAS (0-10): 5.3 vs. 5.5	A vs. B <u>3 months</u> NPQ: 19.1 vs. 25.5, difference −6.4 (95% CI −9.9 to −2.9) Pain VAS: 2.9 vs. 3.2, difference −0.3 (95% CI −0.75 to 0.15)	A vs. B <u>3 months</u> SF-36 physical functioning (0-100): 84.3 vs. 85.9, P=0.447 SF-36 mental (0-100): 67.1 vs. 61.6, P=0.001
MacPherson, 2015[180] 1 and 7 months Duration of pain, 7 years *Fair*	A. Active acupuncture, traditional Chinese, (n=173): plus usual care 2 weeks later. B. Usual care (n=172): including general and neck pain–specific treatments routinely provided to primary care patients, such as prescribed medications and visits to physical therapists and other health care professionals. Treatment was 12 sessions over 5 months lasting 50 minutes	A vs. B Age: 52 vs. 54 years Female: 69% vs. 69% White: 93% vs. 89% Employed: 61% vs. 62% Pain duration (median): 60 vs. 96 months NPQ (0-100%): 39.64 vs. 40.46	A vs. B <u>1 month</u> NPQ: 35.35 vs. 40.90, difference −5.56 (95% CI −8.33 to −2.78) <u>7 months</u> NPQ: 37.07 vs. 40.99, difference −3.92 (95% CI −6.87 to −0.97)	A vs. B <u>1 month</u> SF-12v2 physical: data NR, P=NS SF-12v2 mental: data NR, P=NS <u>7 months</u> SF-12v2 physical (0-100): MD 0.68 (95% CI 1.08 to 2.44) SF-12v2 mental (0-100): MD 1.76 (95% CI 0.15 to 3.37)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Sahin, 2010[199] 3 months Duration of pain, NR *Fair*	A. Electro-acupuncture (n=15) B. Sham acupuncture (n=16) Treatment was 10 sessions, 3 sessions per week, lasting 30 minutes	A vs. B Age: 39 vs. 35 years Female: 100% vs. 81% University graduate: 54% vs. 94% BMI: 23.9 vs. 24.6 Pain with motion VAS (0-10): 7.38 vs. 6.19 Pain at rest VAS (0-10): 4.00 vs. 5.25	A vs. B 3 months Pain with motion VAS: 4.50 vs. 5.38, difference −0.88 (95% CI −2.70 to 0.94) Pain at rest VAS: 4.00 vs. 3.54, difference 0.46 (95% CI −1.88 to 2.80)	NR
Vas, 2006[200] 6 months Duration pain, 3.8 years *Fair*	A. Active acupuncture, traditional Chinese, (n=61) B. Sham TENS (n=62) Treatment was 5 sessions over 3 weeks lasting 30 minutes	A vs. B Age: 46 vs. 47 years Female: 75% vs. 89% Pain duration: 47 vs. 43 months Pain VAS with motion (0-10): 6.9 vs. 7.2 NPQ (0-100): 52.7 vs. 56.5	A vs. B 6 months (MD from baseline) Pain VAS with motion: 4.1 vs. 2.7, difference 1.4 (95% CI 0.3 to 2.6)	A vs. B 6 months SF-36 PCS: (0-100): 9.3 vs. 5.3, P=0.054 SF-36 MCS: (0-100): 8.0 vs. 5.2, P=0.351 Rescue medication (none or occasional): 87% (39/45) vs. 68% (27/40), RR 1.28 (95% CI 1.01 to 1.64)
White, 2004[201] 2, 6, 12 months Duration pain, 6 years *Fair*	A. Active acupuncture, Western technique based on tender local and distal points, (n=70 randomized/54 analyzed) B. Sham electro-acupuncture (n= 65 randomized/53 analyzed) Treatment was 8 sessions over 4 weeks lasting 20 minutes	A vs. B Age: 54 vs. 53 years Female: 66% vs. 63% Pain duration: 4.8 vs. 7.7 years NDI (0-50): 16.8 vs. 17.2 Pain VAS (0-10): 5.0 vs. 5.4	A vs. B 2 months NDI: 11.0 vs. 12.7, difference −1.7 (95% CI −4.3 to 0.9) Pain VAS: 1.7 vs. 2.3, difference −0.6 (95% CI −1.3 to 0.1) 6 months NDI: 9.9 vs. 10.6, difference −0.7 (95% CI −3.61 to 2.21) Pain VAS: 1.9 vs. 2.1, difference −1.8 (95% CI −1.1 to 0.7) 12 months NDI: 8.9 vs. 10.7, difference −1.8 (95% CI −4.84 to 1.24) Pain VAS: 2.1 vs. 2.4, difference −0.3 (95% CI −1.4 to 0.6)	A vs. B 2 months SF-36 PCS (0-100): 42.5 vs. 43.8, P=NS SF-36 MCS (0-100): 52.5 vs. 50.3, P=NS

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Zhang, 2013[202] 3 and 6 months Duration of pain, 6.3 years *Fair*	A. Electro-acupuncture, traditional Chinese (n=103 randomized/84 analyzed) B. Sham laser acupuncture (n=103 randomized/76 analyzed) via a mock laser pen 2 minutes, with the pen at a distance of 0.5 to 1 cm from the skin. Treatment 3x/week for 3 weeks, 45 min for electro-acupuncture and 2 min per point for sham laser	A vs. B Age: 46 years (whole population) Female: 70% (whole population) NPQ (0-100%): 40.7 vs. 41.1 Pain with motion (0-10): 5.5 vs. 5.2	A vs. B <u>3 months</u> NPQ: mean 32.9 (95% CI 30.3 to 35.4) vs. mean 33.3 (95% CI 30.1 to 36.5), P=0.664 Pain with motion VAS: mean 4.7 (95% CI 4.2 to 5.1) vs. mean 4.5 (95% CI 4.1 to 5.0), P=0.617 <u>6 months</u> NPQ: mean 33.59 (95% CI 30.7 to 36.4) vs. mean 34.3 (95% CI 31.1 to 37.6), P=0.808 Pain with motion: mean 4.7 (95% CI 4.2 to 5.2) vs. mean 4.4 (95% CI 3.9 to 4.8), P=0.813	A vs. B <u>3 months</u> SF-36 PCS (0-100): mean 52.8 (95% CI 53.0 to 53.7) vs. mean 53.3 (95% CI 52.4 to 54.2), P=0.982 SF-36 MCS (0-100): mean 45.9 (95% CI 46.0 to 46.8) vs. mean 45.3 (95% CI 44.2 to 46.4), P=0.444 <u>6 months</u> SF-36 PCS: mean 53.0 (95% CI 52.0 to 53.9) vs. mean 53.2 (95% CI 52.3 to 54.0), P=0.559 SF-36 MCS: mean 45.4 (95% CI 44.5 to 46.3) vs. mean 44,4 (95% CI 43.4 to 45.4), P=0.246

BDI = Beck Depression Inventory; CI = confidence interval; EQ-5D = Euroqol 5-D; MD = mean difference; NDI = Neck Disability Index; NPQ = Northwick Park Neck Pain Questionnaire; NR = not reported; NS = not statistically significant; NSAID = nonsteroidal anti-inflammatory drug; SF-36 MCS = Short Form-36 questionnaire Mental Component Summary; SF-36 PCS = Short Form-36 questionnaire Physical Component Summary; SF-MPQ = McGill Pain Questionnaire Short Form; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Estimated from Figure 1 in Birch et al.[196]

Acupuncture Compared With Sham Acupuncture, Usual Care, or a Placebo Intervention

Acupuncture was associated with slightly greater effects on short-term and intermediate-term function versus sham acupuncture, placebo (sham laser), or usual care (short term, 5 trials,[180,197,198,201,202] pooled SMD −0.40, 95% CI −0.64 to −0.17, I^2=67.7%; intermediate term, 3 trials,[180,201,202] pooled SMD −0.19, 95% CI −0.35 to −0.02, I^2=0.0%) (Figure 30). Trials measured function using the NDI or the NPQ; across trials the SMD ranged from −0.53 to −0.03 in the short term and −0.29 to −0.05 in the intermediate term. None of the trials were rated poor quality. One trial reported no difference in function in the long term (SMD −0.23, 95% CI −0.61 to 0.16).[201]

Acupuncture was associated with slightly greater effect on short-term pain versus controls (5 trials, pooled MD −0.67, 95% CI −1.41 to 0.08, I^2=83.9%), but statistical heterogeneity was large.[197-199,201,202] (Figure 31). Excluding an outlier trial (pooled MD −1.80, 95% CI −2.36 to −1.24)[197] eliminated statistical heterogeneity and resulted in a markedly attenuated effect (MD −0.27, 95% CI −0.59 to 0.05, I^2=2%). Stratified analyses according to the type of control (sham or placebo laser) resulted in similar estimates. Trials reported no differences in pain between acupuncture versus controls in the intermediate term (3 trials, pooled MD 0.45, 95% CI −0.34 to 1.25, I^2=58.5%)[200-202] or long term (1 trial, MD −0.35, 95% CI −1.34 to 0.64).[201]

In general, acupuncture did not improve quality of life compared with sham intervention in the short term or intermediate term as reported in four trials[198,200-202] (Table 23).

No trial evaluated effects of acupuncture on use of opioid therapies or health care utilization.

Acupuncture Compared With Pharmacological Therapy

Two small poor-quality trials evaluated acupuncture versus NSAIDs. One trial (n=27) compared acupuncture three times per week for 3 weeks versus 80 mg of Zaltoprofen alone three times per day for 3 weeks.[217] The other trial (n=30) compared 14 sessions of acupuncture versus 500 mg of Trilisate per day for 8 weeks.[196] In the short term, one trial reported no difference in NDI (MD −0.4, 95% CI −4.6 to 3.8).[217] Both trials reported no difference between groups in pain as measured by the McGill Pain Questionnaire[196] or VAS.[217] One trial found no differences between groups in the Beck Depression Index, the SF-36, or the EQ-5D in the short term[217] (Table 23).

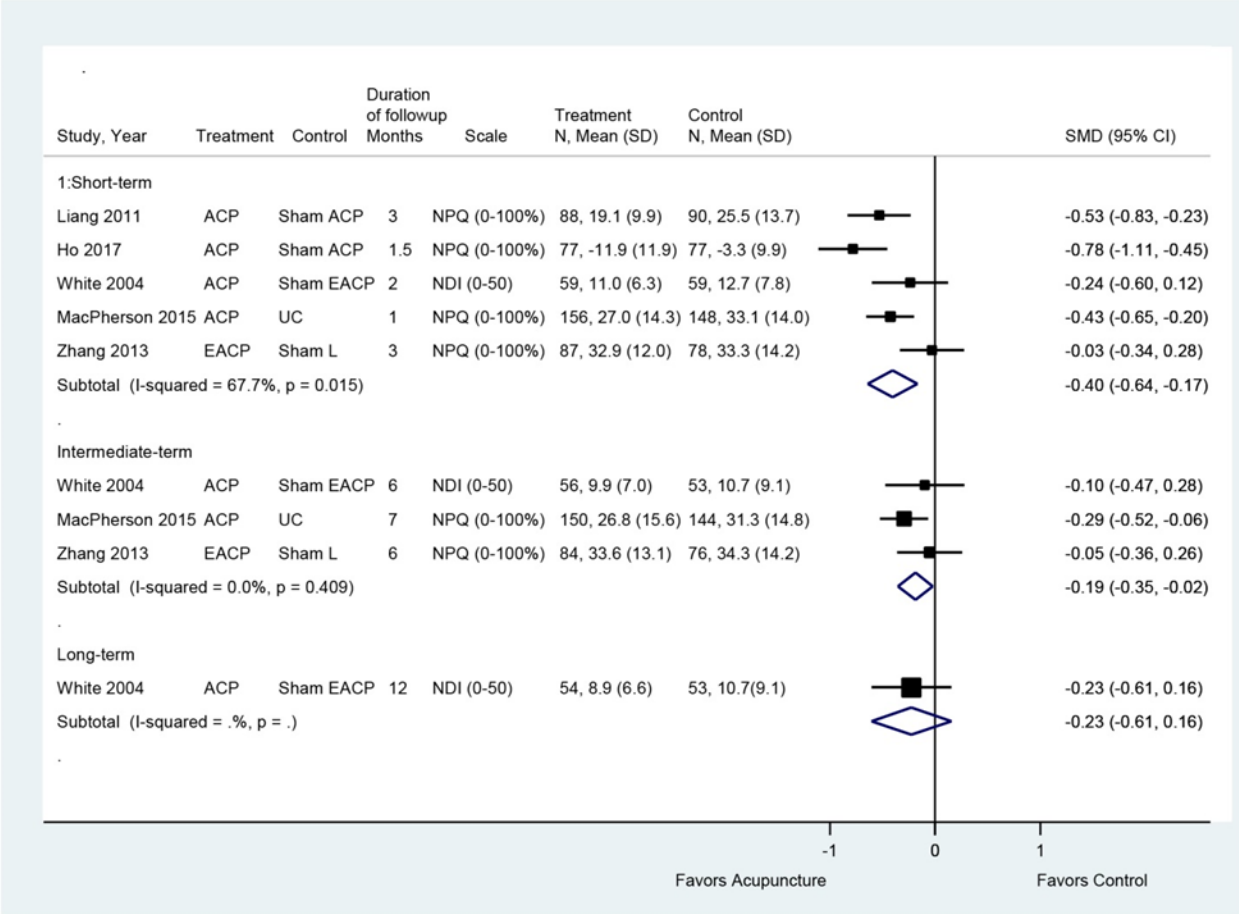
Acupuncture Compared With Exercise Therapy

No trial of acupuncture versus exercise met inclusion criteria.

Harms

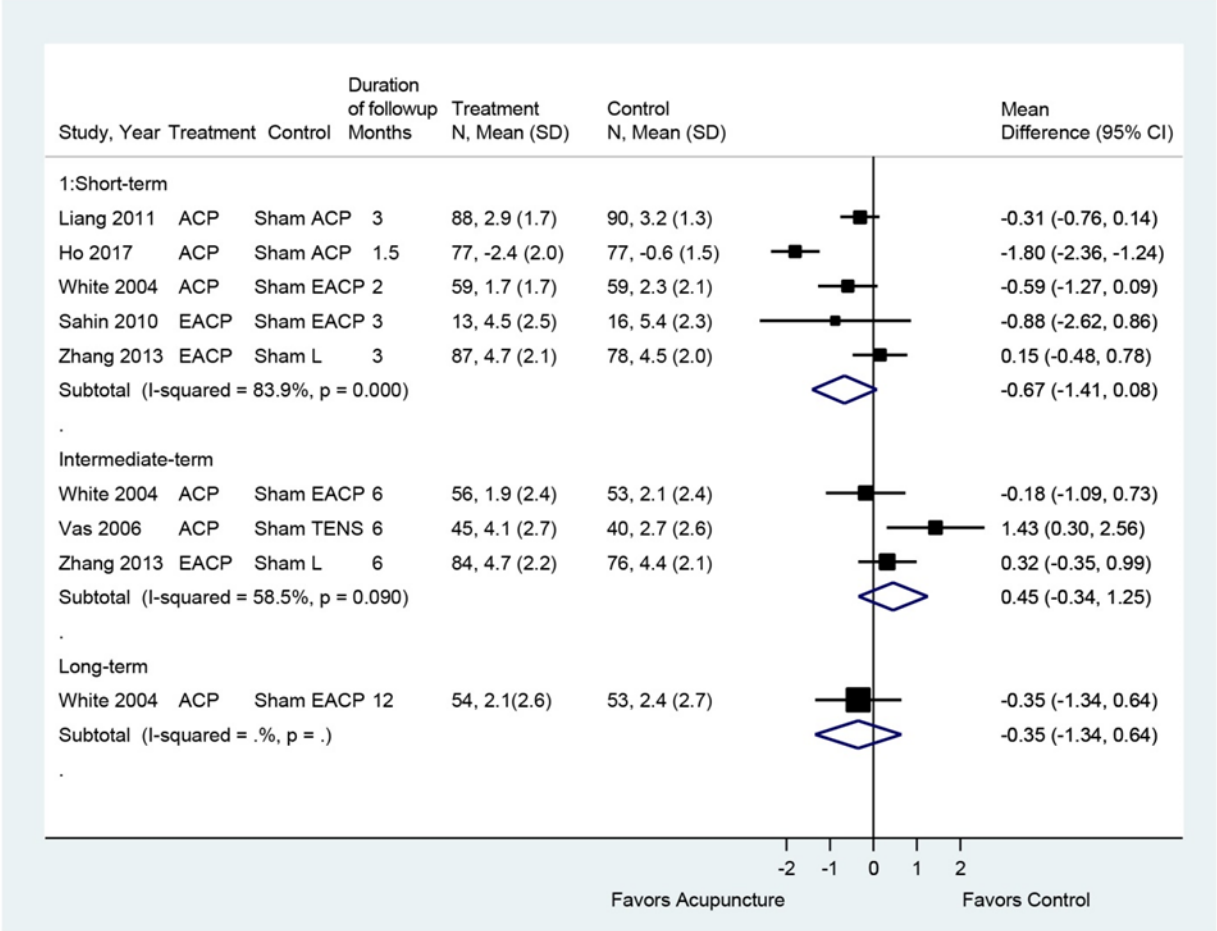
Five of the eight trials assessing acupuncture reported harms.[180,198,200-202] No serious adverse events (defined as involving death, hospitalization, persistent disability, or a life-threatening risk in one trial[180] and undefined in the other four studies) were reported in any trial. The most commonly reported nonserious adverse effects in people receiving acupuncture included numbness/discomfort (2.7%), fainting (1.1%), and bruising (1.1%).

Figure 30. Acupuncture versus sham acupuncture, a placebo intervention, or usual care for chronic neck pain: effects on function



ACP = traditional needle acupuncture; CI = confidence interval; EACP = electroacupuncture; NDI = Neck Disability Index; NPQ = Northwick Park Questionnaire; SD = standard deviation; Sham L = sham laser; SMD = standardized mean difference; UC = usual care

Figure 31. Acupuncture versus sham acupuncture or a placebo intervention for chronic neck pain: effects on pain



ACP = traditional needle acupuncture; CI = confidence interval; EACP = electroacupuncture; SD = standard deviation; Sham L = sham laser; SMD = standardized mean difference; TENS = transcutaneous electrical stimulation; UC = usual care

Key Question 3: Osteoarthritis

Exercise for Osteoarthritis of the Knee

Key Points

- Exercise was associated with slightly greater improvement in function compared with usual care, no treatment, or sham intervention short term (7 trials, pooled SMD −0.25, 95% CI −0.4 to −0.09, I^2=0%), intermediate term (9 trials [excluding outlier trial] pooled SMD −0.78, 95% CI −1.37 to −0.19, I^2=91.4%), and long term (2 trials, pooled SMD −0.24, 95% CI −0.37 to −0.11, I^2=0%) (SOE: moderate for short term; low for intermediate and long term).
- Exercise was associated with a slight improvement in pain short term (7 trials, pooled difference −0.44 on a 0 to 10 scale, 95% CI −0.82 to −0.05, I^2= 35%) versus usual care, no treatment, or sham intervention (SOE: moderate), and with moderately greater effect

on pain in the intermediate term (9 trials, pooled difference −1.61 on a 0 to 10 scale, 95% CI −2.51 to −0.72, I^2=91%) compared with usual care, an attention control, or no treatment (SOE: low). Long term, there was no clear difference between exercise and improvement in pain but data were limited (2 trials, difference −0.24, 95% CI −0.72 to 0.24) (SOE: low).

- No trial evaluated exercise versus pharmacological therapy.
- Harms were not well reported. Across seven trials, one reported minor temporary increase in pain with exercise, four others found no difference in worsening pain versus controls, and one reported no difference in falls or death (SOE: moderate).

Detailed Synthesis

Twenty-one publications from 18 randomized controlled trials[40-60] that evaluated exercise interventions for the treatment of knee OA met the inclusion criteria (Table 24 and Appendix D). Seven trials evaluated muscle performance exercise versus attention control[44,45,47,50,51,59] or no treatment.[42,46,58] In six trials, the interventions consisted of combined exercise approaches compared with usual care,[40,48,49,53,56] an attention control,[57] or no treatment.[43] Muscle performance exercises were a component of 6 trials.[40,43,48,49,53,56,57] One trial had an aerobic exercise arm that consisted of a facility-based, 1-hour walking program three times per week over 3 months, and it used an attention control.[44,50,51] A single trial evaluated a mobility exercise program based on Mechanical Diagnosis and Therapy (MDT) versus a waitlist comparator, where patients were allowed to continue receiving usual care.[54] One trial evaluated gait training (guided strategies to optimize knee movements during treadmill walking with computerized motion analysis with visual feedback) versus usual care.[55] Three trials tested exercise programs as a part of physiotherapy care compared to usual care or sham.[41,52,60] The duration of exercise programs ranged from 2 to 24 weeks; the number of exercise sessions ranged from 4 to 36. No trials comparing exercise with a pharmacological intervention were identified.

Sample sizes ranged from 50 to 786. Across the trials, the majority of patients were female (51% to 88%) with mean ages ranging from 56 to 75 years. Five trials specifically included patients with bilateral knee OA.[42,45-47,59] Five trials were conducted in the United States or Canada,[44,49-51,53-56] five in Europe,[48,52,57,58,60] five in Taiwan,[42,45-47,59] two in Australia or New Zealand,[40,41] and one in Brazil.[43] Most trials had short (6 trials)[40,48,54,55,58,60] or intermediate followup (10 trials).[42,43,45-47,49,55-57,59] Three trials reported long-term outcomes.[49-51,53,57]

Twelve trials were rated fair quality (one at short-term followup[55]),[40,41,44,45,47-54,58] and eight trials poor quality,[42,43,46,56,57,59,60] including one at intermediate-term followup[55] (Appendix E). In the fair-quality trials, the main methodological limitation was a lack of blinding for the patients or care providers. Additional limitations in the poor-quality trials included unclear randomization and allocation concealment methods, unclear use of intention to treat, unclear baseline differences between intervention groups, and attrition not reported or unacceptable.

Table 24. Osteoarthritis of the knee: exercise

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Abbott, 2013[40] 9.75 months Duration of diagnosis: Mean 2.5 to 2.8 years *Fair*	A. Exercise (n=51/29 knee OA): 7 sessions of strengthening, stretching, and neuromuscular control over 9 weeks, with 2 booster sessions at week 16. Individual exercises prescribed as needed. Home exercise prescribed 3 times weekly B. Usual care (n=51/28 knee OA)	A vs. B (total population, includes hip OA) Age: 67 vs. 66 years Female: 52% vs. 58% Percent hip OA: 43% vs. 45% Percent knee OA: 57% vs. 55% Percent both hip OA and knee OA: 20% vs. 26% Baseline WOMAC (0−240): 95.5 vs. 93.8	A vs. B (knee OA only) A vs. C 9.75 months WOMAC mean change from baseline: −12.7 vs. −31.5	None

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Bennell, 2005[41] 3 months Duration of pain: 9.6 vs. 8.7 years *Fair*	<u>A. Neuromuscular Re-education (Physiotherapy) (n=73)</u> Knee taping; exercises to retrain the quadriceps, hip, and back muscles; balance exercises; thoracic spine mobilization; and soft tissue massage. individual sessions lasting 30 to 45 minutes once weekly for four weeks, then fortnightly for eight weeks. Thrice-daily standardized home exercises. <u>B. Control (n=67)</u> Placebo: sham ultrasound and topical nontherapeutic gel. 30 to 45 minutes once weekly for four weeks, then fortnightly for eight weeks.	A vs. B Age: 67 vs. 70 years Female: 68% vs. 66% WOMAC Physical Function (0-68): 27.6 vs. 28.4 WOMAC Pain (0-20): 8.2 vs. 8.0 VAS Pain on movement (0-10): 5.3 vs. 5.2 KPS (0-36): 16.6 vs. 16.4 KPS Frequency (0-30): 23.5 vs. 22.8	A vs. B <u>3 months</u> Responders, global improvement in pain: 59% vs. 50%, P=0.309 Responders, VAS pain: 58% vs. 42%, P=0.069 WOMAC, Physical Function: 20.0 vs. 21.7, MD −0.9 (95% CI −4.4 to 2.7) WOMAC, Pain: 5.8 vs. 6.0, MD −0.4 (95% CI −1.5 to 0.7) VAS pain on movement: 3.2 vs. 3.5, MD −0.5 (95% CI −1.2 to 0.3) KPS, Severity: 13.5 vs. 14.3, MD −1.0 (95% CI −2.5 to 0.6) KPS, Frequency: 19.4 vs. 20.3, MD −1.7 (95% CI −3.5 to 0.1)	A vs. B <u>3 months</u> SF-36, Physical Function (0-100): 50.5 vs. 46.2, MD 4.3 (95% CI −1.8 to 10.4) SF-36, Bodily Pain (0-100): 60.4 vs. 61.8, MD 1.8 (95% CI −6.7 to 10.3) SF-36, Role Physical (0-100): 47.0 vs. 46.5, MD 1.6 (95% CI −11.1 to 14.3) AQoL(−0.04 to 1.0): 0.52 vs. 0.48, MD 0.05 (95% CI 0.01 to 0.10) Withdrawals: 18% (13/73) vs. 3% (2/67); RR 6.0 (95% CI 1.4, 25.5) Group A: Minor skin irritation (48%), increased pain with exercises (22%), pain with massage (1%) Group B: Increased pain (2%), itchiness and pain with application of gel (2%) (All were minor and short-lived)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Chen, 2014[42] 6 months Duration of pain: 10-144 months *Poor*	A. Exercise (n=30): 3 sessions per week for 8 weeks. Sessions consisted of a 20 minutes of hot packs and 5 minutes of passive range of motion exercises on a stationary bike, followed by an isokinetic muscle-strengthening exercise program B. Control (n=30): Details NR	A + B Age: 63 Females: 85% A vs. B Lequesne Index (0-26): 7.8 vs. 8.0 Pain VAS (0-10): 5.5 vs. 5.6	A vs. B 6 months Lequesne Index: 5.4 vs. 7.6, (MD −2.2, 95% CI −3.1 to −1.3) Pain VAS: 4.0 vs. 6.5, (MD −2.5, 95% CI −3.3 to −1.7)	A vs. B 6 months Intolerable knee pain: 10% (3/30) vs. 0% (0/30) RR=infinity, P=0.08
Dias, 2003[43] 6 months Duration of pain: NR *Poor*	A. Exercise (n=25): 12 exercise sessions twice a week for the 6 month study period in addition to three supervised walks of 40 minutes each week. Exercise sessions consisted stretching, concentric and eccentric isotonic progressive resistance exercises, and closed kinetic chain weight-bearing exercises B. Control group (n=25): Subjects were instructed to follow the instructions given at an educational session that all participants attended (see information below) All patients: One-hour educational session consisting of a lecture on disease characteristics, joint protection, pain management, and strategies to overcome difficulties in activities of daily life	A vs. B Age, median: 74 vs. 76 Female: 84% vs. 92% Lequesne Index, median (0-24): 12 vs. 12.5 HAQ, median (0-3): 1 vs. 1	A vs. B 6 months Lequesne Index, median: 4.3 vs. 13, P=0.001 HAQ, median: 0.3 vs. 1.1, P=0.006	A vs. B 6 months SF-36 functional capacity, median (0-100): 77.5 vs. 40, P<0.001 SF-36 physical role limitation, median (0-100): 92.5 vs. 75, P=0.001 SF-36 bodily pain, median (0-100): 100 vs. 0, P=0.002 SF-36 general health, median (0-100): 100.5 vs. 51, P=0.021 SF-36 vitality, median (0-100): 93.5 vs. 87, P=0.027 Adverse Events: NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Ettinger, 1997[44] (index trial) Pennix 2002[51] (substudy looking at baseline depressive symptoms) FAST trial 6 months, 15 months Duration of pain: NR *Fair*	<u>A. Aerobic Exercise Program (n=144)</u> 3-month facility-based walking program of 3 times per week for 1 hour. Each session consisted of a 10-minute warm-up and cool-down phase, including slow walking and flexibility stretches, and a 40-minute period of walking at an intensity equivalent to 50% to 70% of the participants' heart rate reserve. Followed by 15-month home-based walking program. <u>B. Resistance Exercise Program (n=146)</u> 3-month supervised facility-based program, with 3 one-hour sessions per week, and a15-month home-based program. Each session consisted of a 10-minute warm-up and cool-down phase and a 40-minute phase consisting of 2 sets of 12 repetitions of 9 exercises. <u>C. Attention Control (n=149)</u> attended, during the first 3 months, monthly group sessions on education related to arthritis management, including time for discussions and social gathering. Later, participants were called bimonthly (months 4-6) or monthly (months 7-18) to maintain health updates and provide support	A vs. B vs. C Age: 69 vs. 68 vs. 69 years Female: 69% vs. 73% vs. 69% African-American: 24% vs. 28% vs. 26% Baseline function NR	A vs. C <u>Average across all time-points:</u> FAST Physical Disability Scale Total: 1.72 vs. 1.90 Ambulation subscale: 2.22 vs. 2.64 Transfers subscale: 1.75 vs. 1.92 Pain: 2.14 vs. 2.40 B vs. C <u>Average across all time-points:</u> FAST Physical Disability Scale Total: 1.74 vs. 1.90 Ambulation subscale: 2.37 vs. 2.64 Transfers subscale: 1.72 vs. 1.92 Pain: 2.2 vs. 2.40	A vs. B vs. C Adverse Events: Falls- 14% (2/144) vs. 14% (2/146) vs. 0% (0/149); P=0.15 for both A vs. C and B vs. C Death- 0% (0/144) vs. 0% (0/146) vs. 0.7% (1/149) CES-D (<u>average across all time-points)</u> CES-D: 2.12 vs. 2.59 vs. 2.80; A vs. C, P<0.001; B vs. C, P=0.27

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Penninx, 2001[50] FAST trial (same trial as Ettinger 1997 and Pennix 2002 above): substudy in only patients with no baseline ADL disability 6 and 15 months Duration of pain: NR *Fair*	<u>A. Aerobic Exercise Program (n=88)</u> 3-month facility-based walking program of 3 times per week for 1 hour. Each session consisted of a 10-minute warm-up and cool-down phase, including slow walking and flexibility stretches, and a 40-minute period of walking at an intensity equivalent to 50% to 70% of the participants' heart rate reserve. Followed by 15-month home-based walking program. <u>B. Resistance Exercise Program (n=82)</u> 3-month supervised facility-based program, with 3 one-hour sessions per week, and a15-month home-based program. Each session consisted of a 10-minute warm-up and cool-down phase and a 40-minute phase consisting of 2 sets of 12 repetitions of 9 exercises. <u>C. Attention Control (n=80)</u> attended, during the first 3 months, monthly group sessions on education related to arthritis management, including time for discussions and social gathering. Later, participants were called bimonthly (months 4-6) or monthly (months 7-18) to maintain health updates and provide support	A vs. B vs. C Age: 70 vs. 69 vs. 69 years Female: 66% vs. 72% vs. 66% African-American: 25% vs. 21% vs. 28% Disability (scale NR): 1.7 vs. 1.7 vs. 1.6 Pain intensity (1-6): 2.2 vs. 2.1 vs. 2.1	A vs. B vs. C <u>15 months</u> ADL Disability (overall): 36.4% vs. 37.8% vs. 52.5% Disability in transferring from a bed to a chair: 29.5% vs. 36.6% vs. 50.0% Disability in bathing: 12.5% vs. 13.4% vs. 27.5% Disability in toileting: 19.4% vs. 13.4% vs. 25.0% Disability in dressing: 5.7% vs. 7.3% vs. 17.5% Disability in eating: 0% vs. 1.2% vs. 5.0%, P=0.02 <u>15 months</u> ADL Disability (overall) A vs. C: adj RR 0.53 (95% CI 0.33 to 0.85), B vs. C: adj RR 0.60 (95% CI 0.38 to 0.97), Disability in transferring from a bed to a chair A vs. C: adj RR 0.46 (95% CI 0.28 to 0.76) B vs. C: adj RR 0.68 (95% CI 0.42 to 1.09) Disability in bathing A vs. C: adj RR 0.31 (95% CI 0.15 to 0.68) B vs. C: adj RR 0.44 (95% CI 0.21, 0.93) Disability in toileting A vs. C: adj RR 0.58 (95% CI 0.29 to 1.15) B vs. C: adj RR 0.61 (95% CI 0.28 to 1.31) Disability in dressing A vs. C: adj RR 0.20 (95% CI 0.07 to 0.64) B vs. C: adj RR 0.46 (95% CI 0.17 to 1.22) Disability in eating: incidence too small to calculate risks.	A vs. B vs. C <u>15 months</u> Increased severity of knee OA leading to withdrawal: n=3 (not reported by exercise group)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Huang, 2003[46] 10 months Duration of pain: range, 0.33(4 months) to 9 years *Poor*	A. Isokinetic Strengthening (n=33) 3 sessions per week for 8 weeks. 60% of average peak torque the initial dose of isokinetic exercise. An increasing dose program was used in the initial first to fifth sessions (1 set to 5 sets), and a dose of 6 sets was applied from sixth to the twenty-fourth sessions. Each set consists of 5 repetitions of concentric and eccentric contraction in angular velocity 30°/second and 120°/second for extensors, and 5 repetitions of eccentric and concentric contraction in angular velocity 30°/second and 120°/second forflexors. B. Isotonic Strengthening (n=33) The same protocol was used as in the isokinetic exercise. The isotonic muscle strengthening exercise program consisted of 5 repetitions of concentric and eccentric the maximum velocity that the lever arm could achieve. C. Isometric Strengthening (n=33) The same protocol of was used as in the isokinetic exercise. The speed of passive forward or backward motion was set at 30°/second. All intervention groups exercised 3 times weekly for 8 weeks. The patients in all groups also received 20 minutes of hot packs and passive range motion exercise by an electric stationary bike (20 cycles per minute) for 5 minutes to both knees before muscle strengthening exercise. D. Control (n=33) Description NR	A+B+C+D Age: 62 years Female: 70% A vs. B vs. C vs. D Lequesne Index (0-26): 6.9 vs. 7.1 vs. 6.8 vs. 7.2 VAS pain (0-10): 4.8 vs. 4.6 vs. 4.7 vs. 4.6	A vs. D 10 months Lequesne Index: 3.1 vs. 7.6, MD −4.5 (95% CI −5.3 to −3.7), VAS Pain: 2.5 vs. 6.1; P<0.05 B vs. D 10 months Lequesne Index: 3.1 vs. 7.6, MD −3.6 (95% CI −4.4 to −2.8) VAS Pain: 2.0 vs. 6.1; P<0.05 C vs. D 10 months Lequesne Index: 4.8 vs. 7.6, MD −2.8 (95% CI −3.6 to −2.0) VAS Pain: 3.2 vs. 6.1; P<0.05	A vs. B vs. C vs. D 10 months Withdrawals: 3% (1/33) vs. 6% (2/33) vs. 3% (1/33) vs. 18% (6/33) Withdrawals RR (95% CI): A vs. D: 0.17 (0.02, 1.3) B vs. D: 0.33 (0.07,1.53) C vs. D: 0.17 (0.02, 1.3) Stopped therapeutic exercise due to intolerable pain during exercise: 12.1% (4/33) vs. 6.1% (2/33) vs. 6.1% (2/33)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Huang, 2005[47] 10 months Duration of pain: 0.42 (5 months) to 12 years *Fair*	A. Isokinetic Exercise (n=35) 3 times per week for 8 weeks. Began with 60% of the mean peak torque, increasing dose program was used in the first 5 sessions (1 set to 5 sets), and a dose of 6 sets was applied from the sixth to twenty-fourth sessions, with the density rising from 60% to 80% of the mean peak torque as the patient was able. Each set consisted of 5 repetitions of concentric contraction in angular velocities of 30°/second and 120°/second for extensors, and 5 repetitions of eccentric and concentric (Ecc/Con) contractions in angular velocities of 30°/second and 120°/second for flexors. B. Control (n=35) Warm-up exercises only	A+B Age: 65 years Female: 81% A vs. B Lequesne Index(1-26): 7.6 vs. 7.4 VAS pain(0-10): 5.3 vs. 5.4	A vs. B 10 months Lequesne Index: 5.8 vs. 8.1, MD −2.3 (95% CI −3.2 to −1.4) VAS Pain: 3.9 vs. 6.6, P<0.05	A vs. B 10 months Withdrawals 11% (4/35) vs. 11% (4/35) Discontinuation of exercise due to intolerable pain during exercise: 14% (5/35) vs. NA
Huang 2005[45] 10 months Duration of pain: 0.5 (6 mos.) to 11 years *Fair*	A. Isokinetic Exercise (n=30) 3 times per week for 8 weeks. Began with 60% of the average peak torque. Intensity of isokinetic exercise increased from 1 set to 5 sets during the first through fifth sessions and remained at 6 sets for the remaining 6th through 24th sessions. Each set consisted of 5 repetitions of concentric contraction in angular velocities of 30°/s and 120°/s for extensors, and 5 repetitions of eccentric and concentric contractions in angular velocities of 30°/s and 120°/s for flexors. B. Control (n=30) Heat for 20 minutes and 5 minutes of passive range of motion on bike only.	A+B Age: 62 (range, 42-72) years Female: 81% A vs. B Lequesne Index(1-26): 6.7 vs. 7.0 VAS pain(0-10): 4.9 vs. 4.8	A vs. B 10 months Lequesne Index: 5.1 vs. 7.8, MD −2.7 (95% CI −3.8 to −1.6) VAS Pain: 3.5 vs. 6.0; P<0.05	A vs. B 10 months Withdrawals 13% (4/30) vs. 13% (4/30) Discontinuation of exercise due to intolerable pain during exercise: 17% (5/30) vs. NA

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Lund, 2008[48] 3 months Duration of pain: 8.5 vs. 7.8 vs. 4.5 *Fair*	A. Aquatic Exercise (n=27): 2x per week for 8 weeks. warm-up, strengthening and endurance exercise, balance exercise and stretching exercise. Each session lasted 50 min, comprising 10 min warm-up, 20 min resistance exercises, 10 min balance and stabilizing exercises, 5 min lower limb stretches and 5 min cool-down period. Compliance was 92%. B. Land-based Exercise (n=25): 2x per week for 8 weeks. warm-up, strengthening/endurance exercise, balance exercise and stretching exercise. Each session lasted 50 min, comprising 10 min warm-up, 20 min resistance exercises, 10 min balance and stabilizing exercises, 5 min lower limb stretches and 5 min cool-down period. Compliance was 85%. C. Control (n=27): No exercise All 3 groups were asked to continue any other treatment as usual.	A vs. B vs. C Age: 65 vs. 68 vs. 70 years Female: 83% vs. 88% vs. 66% KOOS symptom (0-100): 50.5 vs. 50.9 vs. 50.1 KOOS pain (0-100): 47.1 vs. 41.0 vs. 37.9 KOOS Activities of Daily Living (0-100): 44.7 vs. 40.6 vs. 39.6 KOOS Sport (0-100): 79.1 vs. 75.6 vs. 70.0 KOOS Quality of Life (0-100): 63.7 vs. 57.0 vs. 60.8 VAS Pain at rest (0-100): 29.8 vs. 23.3 vs. 15.5 VAS Pain during walking (0-100): 59.8 vs. 53.0 vs. 48.5	A vs. C 3 months KOOS symptom: 64.1 vs. 63.7; MD 0.5 (95% CI −6.6 to 7.6) KOOS Activities of Daily Living: 63.0 vs. 61.4; MD 1.6 (95% CI −5.7 to 8.9) KOOS sport: 24.2 vs. 23.5; MD 0.7 (95% CI −9.3 to 10.7) KOOS quality of life: 42.8 vs. 41.4; MD 1.7 (95% CI −5.4 to 8.2) KOOS pain: 60.7 vs. 62.6; MD −1.5 (95% CI −8.7 to 5.8) VAS pain at rest: 18.1 vs. 23.8; MD −5.7 (95% CI −13.3 to 2.0) VAS pain: 52.9 vs. 58.3; MD −5.4 (95% CI −16.2 to 5.4) B vs. C 3 months KOOS symptom: 66.1 vs. 63.7; MD 2.4 (95% CI −4.8 to 9.5) KOOS Activities of Daily Living: 63.9 vs. 61.4; MD 2.5 (95% CI −5.0 to 9.9) KOOS sport: 31.6 vs. 23.5; MD 8.1 (95% CI −2.0 to 18.2) KOOS quality of life: 43.1 vs. 41.4; MD 1.7 (95% CI −5.3 to 8.7) KOOS pain: 62.0 vs. 62.6; MD −0.3 (95% CI −7.5 to 7.0) VAS pain at rest: 15.6 vs. 23.8; MD −8.1 (95% CI −15.8 to −0.4) VAS pain walking: 50.1 vs. 58.3; MD −8.2 (95% CI −19.7 to 2.7)	A vs. B vs. C 3 months Withdrawals: 4% (1/27) vs. 20% (5/25) vs. 7% (2/27) A vs. C: RR 0.5 (95% CI 0.05, 5.2) B vs. C: RR 2.5 (95% CI 0.6, 12.7) Increased pain during and after exercise: 11% (3/27) vs. 32% (8/25) vs. NR Swollen knees: 0% (0/27) vs. 12% (3/25) vs. NR Withdrawals due to adverse events: 0% (0/27) vs. 12% (3/25) vs. NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Messier, 2004[49] Rejeski, 2002[53] 3, 6 and18 months Duration of pain: NR *Fair*	A. Exercise (n=80): Three 1-hour sessions per week done at the study facility for 4 months. Option to undergo a 2 month transition phase alternating between facility and home sessions, after which they carried out the program at home. Sessions consisted of 15 minutes of aerobic exercises, 15 minutes of resistance-training, an additional 15 minutes of aerobic exercises, and a 15 minute cool down phase. B. Control (n=78): 1 hour sessions monthly for three months consisting of presentations on OA, obesity, and exercise and a question and answer session. Monthly phone contact was maintained for months 4-6 and bimonthly phone contact was maintained for months 7-18. All subjects: Instructed to continue use of all medications and other treatments as prescribed by their personal physicians	A vs. B Age: 69 vs. 69 Female: 74% vs. 68% WOMAC physical function (0-68): 24.0 vs. 26.0 WOMAC pain (0-20): 6.6 vs. 7.3	A vs. B 6 months WOMAC physical function*: 22.0 vs. 22.0 WOMAC pain: 6.2 vs. 6.2, MD 0.0 (95% CI −0.2 to 0.2) 18 months WOMAC physical function: 21.0 vs. 22.6 WOMAC physical function, mean change: 3.1 vs. 3.4 WOMAC pain: 6.2 vs. 6.0, MD 0.2 (95% CI 0.04 to 0.4)	A vs. B 3 months Accident related to treatment: 1% (1/80) vs. 0% (0/78) 6-18 months (average; reported by Rejeski 2002) SF-36 PCS: 37.1 vs. 34.4 SF-36 PCS, adjusted mean: 37.6 vs. 35.3 SF-36 MCS: 52.9 vs. 53.5 SF-36 MCS, adjusted mean: 54.1 vs. 53.7
Quilty, 2003[52] 2.5 months, 10.5 months Duration of pain: NR *Fair*	A. Combination (Physiotherapy) (n=40) 9 sessions over a 10 week period. Sessions consisted of patellar taping, 7 individualized exercises, posture correction, and footwear advice. All exercises were performed 10 times each, 5 times a day B. Control (n=43): Baseline discussion with the physiotherapist concerning diagnosis, prognosis, footwear, weight reduction, and activity. General exercise was encouraged but no specific quadriceps exercises were advised	A vs. B Age: 69 vs. 67 years WOMAC Function (0-68): 27.4 vs. 27.8 VAS pain (0-100): 51.0 vs. 53.4	A vs. B 2.5 months WOMAC function: 26.5 vs. 27.5; Adjusted MD −0.6 (95% CI −3.7, 2.4) VAS Pain: 42.8 vs. 50.5; Adjusted MD −6.4 (95% CI −15.3, 2.4) 10.5 months WOMAC function: 29.7 vs. 28.3; Adjusted MD 1.7 (95% CI −1.8, 5.2) VAS Pain: 48.1 vs. 54.1; Adjusted MD −4.9 (95% CI −13.6, 3.8)	A vs. B Withdrawals 2% (1/43) vs. 0% (0/44) Adverse Events: None

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Rosedale, 2014[54] 2.5 months Duration of pain: NR *Fair*	A. Exercise (n=120): given end-range exercises in the direction they had responded to, to be performed 10 times every 2 to 3 hours. A nonresponder subgroup was given exercises to strengthen quadriceps and aerobic exercises. All subjects in the exercise group attended 4 to 6 physiotherapy sessions, 2 to 3 assessment sessions lasting up to 1 hour and the rest followup sessions lasting 20 minutes, over a 2 week period. B. Waiting list (n=60): Subjects were followed up in the orthopedic department at the surgeon's discretion and continued receiving their usual care.	A vs. B vs. C Age: 66 vs. 64 Female: 56% vs. 60% Median comorbidities: 3 vs. 3 KOOS function (0-100): 56 vs. 51 KOOS function in sport and recreation(0-100): 22 vs. 20 KOOS pain(0-100): 51 vs. 46 P4 pain scale: 21 vs. 23 KOOS knee symptoms(0-100): 50 vs. 48 KOOS quality of life(0-100): 28 vs. 27	A vs. B 2.5 months KOOS function: 61 vs. 52, (Adj MD 5, 95% CI 1 to 9) KOOS function in sport and recreation: 31 vs. 24, (Adj MD 6, 95% CI 0 to 11) KOOS pain: 56 vs. 46, (Adj MD 7, 95% CI 3 to 11) P4 pain scale: 24 vs. 21, (Adj MD −2, 95% CI −4 to 1) KOOS knee symptoms: 56 vs. 52, (Adj MD 2, 95% CI −2 to 6) KOOS quality of life: 34 vs. 32, (Adj MD 1, 95% CI −3 to 6)	NR
Segal, 2015[55] 3 and 9 months Duration of pain: NR *Fair (3 months)* *Poor (9 months)*	A. Gait Training (n=24): guided strategies to optimize knee movements during treadmill walking; computerized motion analysis with visual biofeedback; individualized home programs from physical therapist; Twice weekly sessions (45 minutes) for 12 weeks (24 total sessions) B. Usual Care (n=18) Usual care for knee OA and were not asked to make changes in their lifestyle (e.g., annual visit to their physician, use of pain medications, knee surgery and/or physical therapy); ask to keep a diary	A vs. B Age: 70 vs. 69 years Female: 76% vs. 53% Race: NR LLFDI basic lower limb function score: 65.8 vs. 63.5 KOOS Pain: 62.7 vs. 59.8 KOOS Symptoms: 60.1 vs. 63.0	A vs. B, between group difference in change score compared with baseline 3 months LLFDI basic lower limb function score: 2.3 (95% CI −1.8 to 6.3) KOOS Pain: 3.7 (95% CI −4.7 to 12.1) KOOS Symptoms: 6.2 (95% CI −2.9 to 15.4) 9 months LLFDI basic lower limb function score: 1.0 (95% CI −7.4 to 9.4) KOOS Pain: 7.2 (95% CI −2.0 to 16.5) KOOS Symptoms: 6.0 (95% CI −6.2 to 18.2)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Sullivan, 1998[56] 10 months Duration of pain: NR *Poor*	A. Exercise (n=52): 3 group sessions of 10-15 subjects per week were done for 8 weeks. Sessions were structured as a hospital-based supervised fitness walking and supportive patient education program. Sessions consisted of stretching and strengthening exercises, expert speakers, group discussions, instructions in safe walking techniques, and up to 30 minutes of walking. At the end of the 8 week treatment period, subjects were encouraged to continue walking and given guidelines for managing individualized programs of fitness walking. B. Usual care (n=50): Subjects continued to receive the standard routine medical care they had been receiving prior to enrollment in the study. Subjects were interviewed weekly during the 8 week treatment period about their functional and daily activities.	A vs. B Age: 71 vs. 68 Female: 77% vs. 90% AIMS physical activity subscale (0-10): 6.3 vs. 6.4 AIMS arthritis impact subscale (0-10): 4.6 vs. 4.5 AIMS pain subscale (0-10): 4.9 vs. 5.5 Pain VAS (0-10): 4.1 vs. 6.3 AIMS general health perception subscale (0-10): NR	A vs. B 10 months AIMS physical activity subscale: 6.1 vs. 6.2, MD −0.1, (95% CI −1.7 to 1.5) AIMS arthritis impact subscale: 3.3 vs. 3.8, MD −0.5, (95% CI −1.8 to 0.8) AIMS pain subscale: 4.6 vs. 5.5, MD −0.9, (95% CI −2.2 to 0.4) Pain VAS: 5.0 vs. 5.4, MD −0.4, (95% CI −2.0 to 1.2) AIMS general health perception subscale: 3.7 vs. 3.3, MD 0.4 (95% CI −1.0 to 1.8)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Thomas, 2002[57] 6 months, 12 months, 18 months, 24 months Duration of pain: NR *Poor*	A. Exercise (n=470): Two year, self-paced program that started with four 30 minute visits in the first 2 months followed by visits every 6 months. Designed to maintain and improve strength of muscles around the knee, range of motion at the knee joint, and locomotor function. 121 of the 470 patients also received attention control which consisted of monthly phone calls by a study researcher that sought to monitor symptoms and offer simple advice on knee pain management. 114 of the 470 patients received the attention control and a placebo tablet in addition to the exercise program. The remaining 235 participate in the exercise program only.* B. Control (n=316): 160 subjects received attention control consisted of monthly phone calls by a study researcher that sought to monitor symptoms and offer simple advice on knee pain management. 78 subjects took a placebo tablet. 78 patients had no contact with the researchers between assessment visits.	A vs. B Age: 62 vs. 62 Female: 63% vs. 66% WOMAC pain score(0-20): 7.15 vs. 7.35	A vs. B 6 months WOMAC physical function, MD (95% CI): NR WOMAC pain, MD (95% CI): −0.6 (−1.0 to −0.2) 24 months WOMAC physical function, MD (95% CI): −2.6 (−4.1 to −1.1) WOMAC pain: −0.82 (−1.3 to −0.3)	A vs. B 6 months HADS: NR SF-36: NR 24 months HADS: NR (NS) SF-36: NR (NS)
Thorstensson, 2005[58] 5 months Duration of pain: NR *Fair*	A. Exercise (n=30): 1 hour group exercise sessions of 2 to 9 participants, twice a week for 6 weeks. Sessions consisted of weight-bearing exercises to increase postural control and to increase endurance and strength in the lower extremity. Patients were given daily exercises to perform at home. B. Control group (n=31): Subjects were told not to make any lifestyle changes. Subjects met with the physical therapist at baseline, at 6 weeks, and at 6 months	A vs. B Age: 55 vs. 57 Female: 50% vs. 52% KOOS ADL (0-100): 69 vs. 71 KOOS Pain (0-100): 60 vs. 64 KOOS Symptoms (0-100): 63 vs. 66 KOOS sports and recreation (0-100): 34 vs. 37	A vs. B 5 months KOOS ADL, mean change: 0.9 vs. −1.9, P=0.61 KOOS pain, mean change: 3.1 vs. −1.1, P=0.32 KOOS symptoms, mean change: 1.0 vs. −3.4, P=0.31 KOOS sports and recreation, mean change: 0.5 vs. −8.3, P=0.32	A vs. B 5 months KOOS QOL, mean change (0-100): 5.1 vs. −2.3, P=0.02 SF-36 PCS, mean change (0-100): 3.0 vs. −0.7, P=0.09 SF-36 MCS, mean change (0-100): 0.7 vs. −0.7, P=0.40 Adverse Events: A vs. B Increased knee pain: 3% (1/30) vs. 0% (0/31)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Weng,[59] 2009 10 months Duration of pain: 42.5 months *Poor*	A. Isokinetic exercise (n=33): 3 sessions a week for 8 weeks. Sessions consisted of sets of concentric and eccentric contractions at varying angular velocities and start and stop angles. Hot packs for 10 minutes and passive range of motion exercises B. No intervention (n=33): Warm-up cycling for 10 minutes. Hot packs for 10 minutes and passive range of motion exercises	A+B Age: 64 Female: 75% A vs. B Lequesne Index (0-24): 7.3 vs. 7.1 Pain VAS (0-10): 4.7 vs. 4.5	A vs. B 10 months Lequesne Index: 6.3 vs. 7.3 Pain VAS: 3.6 vs. 5.0	A vs. B 10 months Treatment related pain causing withdrawal: 9% (3/33) vs. 0% (0/33) RR=infinity, P=0.08
Williamson, 2007[60] 1.5 months Duration of pain: NR *Poor*	A. Combination (Physiotherapy) (n=60): Groups of 6–10 patients, hourly, once a week for 6 weeks. Exercise circuit of static quadriceps contractions; inner range quadriceps contractions; straight leg raises; sit to stands, stair climbing; calf stretches; theraband resisted knee extensions; wobble board balance training; knee flexion/extension sitting on gym ball and free standing peddle revolutions. B. Control (n=61): Usual Care (home exercise and advice leaflet)	A vs. B Age: 70 vs. 70 years Female: 52% vs. 54% OKS (0-48): 39.3 vs. 40.5 WOMAC (unclear scale): 50.2 vs. 51.1 VAS pain (0-10): 6.8 vs. 6.9	A vs. B 1.5 months OKS: 38.8 vs. 40.8 WOMAC: 49.4 vs. 52.3 VAS Pain: 6.4 vs. 7.2	A vs. B 1.5 months HAD Anxiety (0-21): 7.1 vs. 6.5 HAD Depression (0-21): 6.8 vs. 7.1 Withdrawals: 17% (10/60) vs. 0% (0/61) Adverse Events: None

ADL = activity of daily living; AIMS = Arthritis Impact Measurement Scale; AQoL = Assessment of Quality of Life; CES-D = Center for Epidemiologic Studies Depression; CI = confidence interval; HADS = Hospital Anxiety and Depression Scale; HAQ = Health Assessment Questionnaire; ITT = intention-to-treat; KOOS = Knee Injury and Osteoarthritis Outcome Score; KPS = Knee Pain Scale; LLFDI = Late-Life Function and Disability Instrument; MCS = Mental Component Score; MD = mean difference; NA = not applicable; NR = not reported; NS = not significant; OA = osteoarthritis; OKS = Oxford Knee Score; PCS = Physical Component Score; RR = risk ratio; QoL = quality of life; SF-36 = Short-Form-36; VAS, visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Exercise Compared With Usual Care, No Treatment, Sham, or an Attention Control

Functional Outcomes. Exercise was associated with slightly greater short-term impact on function (assessed across various measures) than usual care, no treatment, or sham intervention (7 trials, pooled SMD −0.25, 95% CI −0.4 to −0.09, I^2=0%)[41,48,52,54,55,58,60] (Figure 32). Estimates were similar following exclusion of poor-quality trials and when analyses were stratified by exercise and control type. In the short term, a small improvement in the Knee Injury and Osteoarthritis Outcome Score (KOOS) Sport and Recreation scale (0-100) with exercise

compared with usual care or no treatment was seen (3 trials, pooled MD 5.88, 95% CI 0.80 to 10.96, $I^{2=}$0%, plot not shown).[48,54,58]

Exercise was also associated with moderately greater effect on function (assessed across various measures) than usual care, no treatment, or attention control at intermediate term (10 trials, pooled SMD −1.15, 95% CI −1.85 to −0.46, I^2=93.9%)[42,43,45-47,49,52,55,56,59] (Figure 32). Substantial heterogeneity was present with one outlier trial[43] of combination exercise versus no treatment in elderly patients (median age 75 years) which had higher (worse) baseline Lequesne Index scores compared with other studies and a larger change from baseline scores in the intervention group. Removal of this poor quality trial did not improve heterogeneity but did attenuate the pooled estimate (9 trials, pooled SMD −0.78, 95% CI −1.37 to −0.19, I^2=91.4%). Stratification by exercise type and control type may partially explain the heterogeneity. Muscle performance exercise was associated with a moderately greater effect on function compared with attention control or no treatment (5 trials, pooled SMD −1.44, 95% CI −2.08 to −0.17)[42,45-47,59] and when compared with attention control only (3 trials, pooled SMD −1.12, 95% CI −1.83 to −0.47).[45,47,59] No difference was seen across studies of exercise versus usual care (4 trials, pooled SMD 0.02, 95% CI −0.20 to 0.24).[49,52,55,56]

Analyses confined to trials that evaluated function on the 0-24 point Lequesne Index also suggests a moderately greater effect on function compared with attention control or no treatment (6 trials, pooled MD −3.42, 95% CI −5.49 to −1.35, I^2=97%, plot not shown).[42,43,45-47,59] Again, removal of the poor quality outlier trial[43] did not impact the heterogeneity, but yielded a slightly lower effect estimate (5 trials, pooled MD −2.40, 95 CI −3.32 to −1.44), still consistent with a moderate effect for exercise. Results were similar to this estimate for muscle performance exercise, use of attention control, and when the two fair-quality trials were retained.

One fair-quality trial (n=101 with knee OA)[40] compared combined exercise programs to usual care for intermediate-term function using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The exercise group had improvement in function from baseline, which was not statistically significant (mean change from baseline −12.7, 95% CI −27.1 to 1.7), while the usual care group had no change in function (mean change from baseline 1.6, 95% CI −10.5 to 13.7). Data were insufficient to determine effect size or include in the meta-analysis.

One trial separately analyzed participants free of disability for ADLs at baseline (n=250) and followed them to compare cumulative incidence of disability over 15 months. The aerobic exercise group had decreased risk of disability compared to the attention control group, RR 0.53 (95% CI 0.33, 0.85), as did the muscle performance exercise group compared to the attention control group, RR 0.60 (95% CI 0.38, 0.97).[50]

A small improvement in function long term was seen across two trials of combination exercise compared with usual care, one fair[49] and the other poor quality[57] (pooled SMD −0.24, 95% CI −0.37 to −0.11, I^2=0%), although separately neither trial reached statistical significance (Figure 32).

Pain Outcomes. Exercise was associated with slight improvement in short-term pain compared with usual care, no treatment, or sham in seven trials (pooled difference on a 0-10 scale −0.44, 95% CI −0.82 to −0.05, I^2=35 %) (Figure 33). Six trials were fair quality[41,48,52,54,55,58] and one was poor quality.[60] Across studies comparing exercise with usual care, results were also similar (5 trials, pooled difference −0.53, 95% CI −1.07 to −0.02).[48,52,54,55,60] The estimate was similar following exclusion of the poor-quality trials, but results were no longer significant (5 trials, pooled difference −0.40, 95% CI −0.85 to 0.08). One trial found no difference between exercise

or sham procedure in the percentage of patients who reported clinically relevant reduction in VAS pain (58% versus 42%, P=0.069) or global improvement (59% versus 50%, P=0.309).[41]

Exercise was associated with moderately greater effect on intermediate-term pain compared with usual care, attention control, or no treatment across pain measures (9 trials, pooled difference −1.61, 95% CI −2.51 to −0.72, I^2=91% on a 0-10 scale) across four fair-quality trials[45,47,49,52] and five poor-quality trials[42,46,55,56,59] (Figure 33). Results differed somewhat by type of exercise and type of control. Three trials showed no difference between combination exercise and usual care;[49,52,56] however, a substantial effect on pain was seen across trials comparing muscle performance exercise with an attention control (3 trials, pooled difference −2.18, 95% CI −3.15 to −1.24)[45,47,59] and with no treatment (2 poor quality trials, pooled difference −3.01, 95% CI −4.0 to −1.90).[42,46] Substantial improvement in pain was seen across trials of muscle performance exercise versus attention control or no treatment (5 trials, pooled difference on 0-10 scale −2.53, 95% CI −3.23 to −1.80).[42,45-47,59] Results were no longer significant when four poor-quality trials[42,46,56,59] were excluded (3 trials, pooled difference on a 0-10 scale −1.69, 95% CI −3.74 to 0.30).[45,47,49]

There was no clear difference between exercise and usual care or attention control on long-term pain (pooled difference −0.24 on a 0 to 10 scale, 95% CI −0.72 to 0.24, I^2=54.9%), but data were limited to two trials, the largest of which was of poor quality[49,57] (Figure 33).

Most trials evaluated pain using a traditional 0 to 10 VAS. A small improvement in short-term pain was observed across three trials (2 fair, 1 poor quality, pooled difference −0.51, 95% CI −1.01 to −0.01, I^2=0%),[41,52,60] but was marginally statistically significant. Findings for intermediate-term pain were similar to the above findings across pain measures, showing a moderate improvement in pain (6 trials, pooled difference −2.29, 95% CI −3.02 to −1.55, I^2=78%).[42,45-47,56,59] The pooled estimate was slightly larger when four poor-quality trials[42,46,56,59] were excluded, leaving two fair-quality trials (pooled difference −2.62, 95% CI −3.33 to −1.89).[45,47] Stratification by control type among studies reporting VAS pain yielded similar findings to those across multiple measures. Estimates were similar when analyses were stratified according to the type of exercise. No trial employing VAS reported on long-term pain.

Other Outcomes. Health-related quality of life outcomes had mixed results (Table 24). Two fair-quality trials found no association between exercise and short-term quality of life on the KOOS 0 to 100 scale (pooled difference 1.76, 95% CI −2.45 to 5.97, I^2=0%, plot not shown).[48,54] A fair-quality trial (n=65) reported no differences in mean change for short term SF-36 PCS (mean change of 3.0 [95% CI −5.9 to 16.3] versus −0.7 [95% CI −14.8 to 9.8]) and SF-36 MCS (mean change of 0.7 [95% CI −18.1 to 13.2] vs. −0.7 [95% CI -16.8 to 12.8]).[58] One fair-quality trial (n=158) reported similar health-related quality of life scores between a combined exercise group and usual care using averaged intermediate- and long-term scores. The adjusted mean (standard error [SE]) SF-36 PCS were 37.6 (0.9) vs. 35.3 (0.8), respectively, and adjusted mean (SE) SF-36 MCS were 54.1 (0.8) vs. 53.7 (0.8), respectively.[53] A poor-quality trial (n=50) reported intermediate-term SF-36 scores for individual domains. Functional capacity, physical role, bodily pain, general health, and vitality were slightly improved with exercise versus attention control.[43]

A fair-quality trial (n=438) reported no difference in depressive symptoms compared with attention control (2.59 vs. 2.80, P=0.27) for muscle performance exercise, while aerobic exercise was associated with fewer depressive symptoms on the Center for Epidemiologic Studies Depression (CES-D) questionnaire compared to attention control (2.12 vs. 2.80, P<0.001).[51]

There was insufficient evidence to determine effects of duration of exercise therapy or number of sessions on outcomes. No trials reported on changes in opioid use as a result of exercise programs.

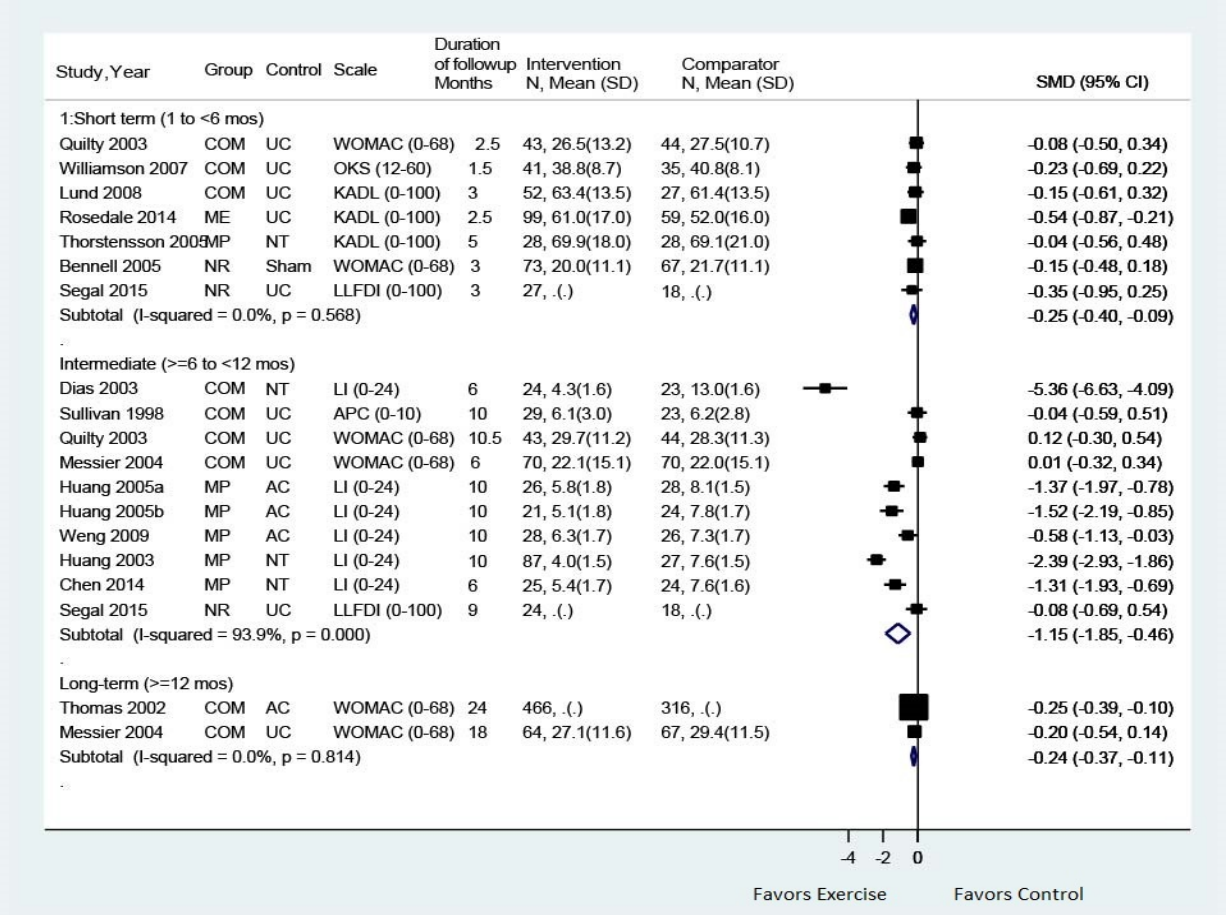
Exercise Compared With Pharmacological Therapy or With Other Nonpharmacological Therapies

No trial of exercise therapy versus pharmacological therapy met inclusion criteria. Findings for exercise versus other nonpharmacological therapies are addressed in the sections for other nonpharmacological therapies.

Harms

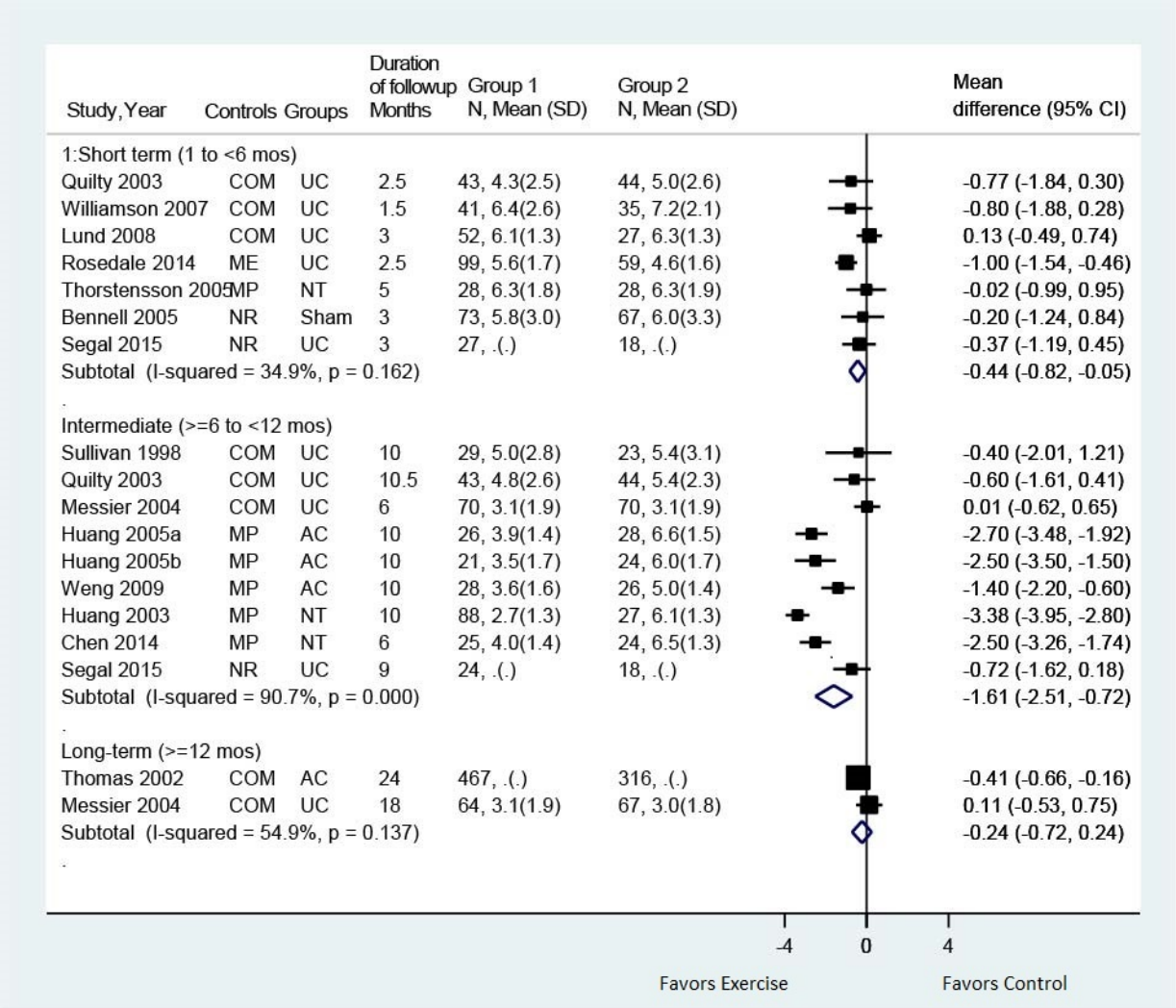
Most trials did not report harms. One trial reported greater temporary, minor increases in pain in the exercise group versus a sham group (RR 14.7, 95% CI 2.0 to 107.7); however, the confidence interval is wide.[41] Four studies found no difference in worsening of pain symptoms with exercise versus comparators.[42,46,58,59] One trial found no difference in falls or deaths.[44]

Figure 32. Exercise versus usual care, no treatment, sham, or an attention control for osteoarthritis of the knee: effects on function



AC = attention control; APC = Arthritis Impact Measurement Scale (AIMS) physical activity component; CI = confidence interval; COM = combination exercise therapy; KADL = Knee Injury and Osteoarthritis Outcome Score (KOOS) ADL subscore; LI = Lequesne Index; LLFDI = Late Life Function and Disability Index Basic Lower Limb Function Score; ME = mobility exercise; MP = muscle performance exercise; NR = neuromuscular reeducation exercise; NT = no treatment; OKS = Oxford Knee Score; SD = standard deviation; SMD = standardized mean difference; UC = usual care; WOMAC = Western Ontario and McMaster's Universities Osteoarthritis Index

Figure 33. Exercise versus usual care, no treatment, sham, or an attention control for osteoarthritis of the knee: effects on pain



AC = attention control; CI = confidence interval; COM = combination exercise therapy; ME = mobility exercise; MP = muscle performance exercise; NR = neuromuscular re-education exercise; NT = no treatment; SD = standard deviation; SMD = standardized mean difference; UC = usual care

Psychological Therapy for Osteoarthritis of the Knee

Key Points

- Two trials of pain coping skills training and CBT versus usual care found no evidence of differences in function (WOMAC physical function, 0-100) or pain (WOMAC pain, 0-100); treatment effects were averaged over short term to intermediate term (difference −0.3, 95% CI −8.3 to 7.8 for function and −3.9, 95% CI −1.8 to 4.0 for pain) and intermediate term to long term (mean 35.2, 95% CI 31.8 to 38.6 vs. mean 37.5, 95% CI 33.9 to 41.2, and mean 34.5, 95% CI 30.8 to 38.2 vs. mean 38.0, 95% CI 34.1 to 41.8), respectively (SOE: low).
- One trial of pain coping skills training versus strengthening exercises found no evidence of differences in WOMAC physical function scores (0-68 scale) at short term (MD 2.0, 95% CI −2.4 to 6.4) or intermediate term (MD 3.2, 95% CI −0.6 to 7.0) or in WOMAC

pain scores (0-20 scale) at short term (MD −0.1, 95% CI −1.2 to 1.0) or intermediate term (MD 0.4, 95% CI −0.8 to 1.6). (SOE: low).

- No serious harms were reported in either trial (SOE: low).

Detailed Synthesis

Three trials (total n=371)[94,95,110] of psychological therapies for knee OA met inclusion criteria (Table 25 and Appendix D). One was conducted in the United States,[95] one in Finland,[94] and one in Australia.[110] Across the trials, participants were predominately female (60% to 72%) with mean ages ranging from 58 to 64 years. Two trials (n=111 for both)[94,95] evaluated group therapy consisting of CBT or pain coping skills training with usual care. The number and duration of psychological sessions varied between the trials (six 2-hour sessions versus eighteen 1-hour sessions, respectively), as did the total duration of therapy (6 and 24 weeks). Usual care was defined as routine care provided by the patient's primary care doctor and was not well-described in either trial. The third trial (n=149)[110] compared pain coping skills training (ten 45-minute sessions) with strengthening exercises (ten 25-minute sessions); all sessions were conducted on an individual basis over a treatment period of 12 weeks. Participants randomized to receive PCST were told to practice skills daily and then as needed during followup; those in the exercise group were instructed to perform exercises four times a week during 12-week intervention and three times a week during the followup period.

Two trials were rated fair quality[94,110] and the other was rated poor quality[95] (see Appendix E for quality ratings). The primary methodological limitation in the fair-quality trials were the inability to effectively blind care providers, outcome assessors, and/or patients. Additional methodological shortcomings in the poor-quality trial included poor treatment compliance and high attrition (32%).

Table 25. Osteoarthritis of the knee: psychological therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Bennell 2016[110] 5 and 9 months Duration of pain: 6 years *Fair*	A. Pain coping skills training (n=74): 10, 45-minute sessions over 12 weeks; consisted of pain education and cognitive and behavioral pain coping skills training B. Exercise (n=75): 10, 25 minute sessions over 12 week; consisted of 6 strengthening exercises.	A vs. B Age, years: 63 vs. 63 Female: 61% vs. 59% Radiographic disease severity: Grade 2: 45% vs. 40% Grade 3: 28% vs. 25% Grade 4: 27% vs. 35% Opioid use: 4% vs. 1% WOMAC physical function (0-68): 35.0 vs. 34.3 WOMAC pain (0-20): 8.7 vs. 8.6 Pain overall VAS (0-100): 58.7 vs. 59.1 Pain with walking VAS (0-100): 61.3 vs. 60.9	A vs. B 5 months WOMAC physical function: 23.4 vs. 21.4, difference 2.0 (95% CI −2.4 to 6.4) WOMAC pain: 6.2 vs. 6.3, difference −0.1 (95% CI −1.2 to 1.0) Pain overall VAS: 35.7 vs. 36.0, difference −0.3 (95% CI −9.0 to 8.4) Pain with walking VAS: 39.1 vs. 42.3, difference −3.2 (95% CI −12.4 to 6.0) 9 months WOMAC physical function: 21.3 vs. 18.1, difference 3.2 (95% CI −0.6 to 7.0) WOMAC pain: 5.8 vs. 5.4, difference 0.4 (95% CI −0.8 to 1.6) Pain overall VAS: 34.8 vs. 34.5, difference 0.3 (95% CI −7.8 to 8.4) Pain with walking VAS: 37.3 vs. 37.5, difference −0.2 (95% CI −9.1 to 8.7)	A vs. B 5 months DASS21 depression scale: 4.3 vs. 5.5, difference −1.2 (95% CI −4.0 to 1.6) DASS21 anxiety scale: 4.0 vs. 4.9, difference −0.6 (95% CI −3.0 to 1.2) AQoL-6D: 0.79 vs. 0.76, difference 0.03 (95% CI −0.02 to 0.09) 9 months DASS21 depression scale: 3.5 vs. 4.9, difference −1.4 (95% CI −3.6 to 0.8) DASS21 anxiety scale: 3.0 vs. 4.6, difference −1.6 (95% CI −3.4 to 0.2) AQoL-6D: 0.81 vs. 0.78, difference 0.03 (95% CI −0.02 to 0.08) Percent of patients using opioids: 10% (7/72) vs. 13% (9/71), RR 0.77 (95% CI 0.3 to 1.9)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Helminen, 2015[94] 31.5 to 10.5 months Duration of pain: 7.8 years *Fair*	Cognitive-Behavioral Training plus usual care (n=55): 2-hour groups sessions, weekly for 6 weeks (6 sessions total); included attention diversion methods (relaxation, imagery, distraction), activity-rest cycling and pleasant activity scheduling, cognitive restructuring, and homework assignments B. Usual Care (n=56)	A vs. B Age: 64.5 vs. 63 years Female: 71% vs. 68% BMI: 30 vs. 30 kg/m^2 Bilateral knee OA: 33% vs. 30% Kellgren-Lawrence grade 2: 60% vs. 61% Duration of Chronicity: 6.6 vs. 8.9 years WOMAC Function (0-100): 53.0 vs. 48.4 WOMAC Pain (0-100): 57.6 vs. 56.4 WOMAC Function: 53.0 (48.1−57.9) vs. NRS pain (0-10), average past week: 6.6 vs. 6.4 NRS pain (0-10), worst past week: 8.0 vs. 7.5 NRS pain (0-10), average 3 months: 6.8 vs. 6.6 NRS pain (0-10), worst 3 months: 8.2 vs. 8.0	A vs. B <u>Post-Treatment Average (1.5 to 10.5 months)</u> WOMAC Function: 36.5 vs. 36.7, MD−0.3 (95% CI −8.3 to 7.8) WOMAC Pain: 35.6 vs. 39.5, MD−3.9 (95% CI −11.8 to 4.0) NRS pain, average past week: 5.0 vs. 4.9, MD 0.02 (95% CI −0.89 to 0.93) NRS pain, worst over week: 6.1 vs. 5.9, MD 0.1 (95% CI −0.8 to 1.1) NRS pain, average 3 months: 5.2 vs. 5.4 MD −0.2 (95% CI −1.0 to 0.6) NRS pain, worst 3 months: 6.4 vs. 6.6, MD −0.1 (95% CI −0.9 to 0.7)	A vs. B <u>Post-Treatment Average (1.5 to 10.5 months)</u> WOMAC Stiffness (0-100): 46.2 vs. 49.0 MD −2.7 (95% CI −11.4 to 5.9) BDI (0−63): 5.8 vs. 5.9, MD −0.1 (95% CI −2.2 to 2.0) BAI (0−63): 8.0 vs. 7.1, MD0.9 (95% CI −1.3 to 3.1) HRQoL, 15D: 0.82 vs. 0.85, MD −0.03 (95% CI −0.06 to 0.00) RAND-36 Physical Functioning: 48.0 vs. 49.4 MD −1.4 (95% CI −10.2 to 7.3) RAND-36 Role-Physical: 44.4 vs. 44.5 MD −0.09 (95% CI −14.4 to 14.3) RAND-36 Bodily Pain: 57.3 vs. 57.4, MD −0.1 (95% CI −8.0 to 7.7) RAND-36 General Health: 53.1) vs. 58.2, MD−5.0 (95% CI −12.3 to 2.3) RAND-36 Vitality: 62.7 vs. 67.5, MD−4.8 (95% CI −12.6 to 3.1) RAND-36 Social Functioning: 75.0 vs. 82.8, MD−7.8 (95% CI −16.4 to 0.81) RAND-36 Role-Emotional: 67.9 vs. 74.7, MD−6.7 (95% CI −20.2 to 6.8) RAND-36 Emotional Well-Being: 75.3 vs. 78.5, MD−3.2 (95% CI −9.5 to 3.1) RAND-36 Health Change: 46.6 vs. 47.4, MD −0.8 (95% CI −9.2 to 7.6)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Somers, 2012[95] 6-12 months Duration of pain: NR *Poor*	A. Pain Coping Skills Training (n=60): 1-hour group sessions, weekly for 12 weeks then every other week for 12 weeks (total of 18 sessions over 24 weeks); consisted of informational lectures, problem solving, skills training, relaxation exercises, homework assignments, and feedback B. Usual Care (n=51)	A vs. B Age: 58 vs. 58 years Female: 67% vs. 78% Caucasian: 62% vs. 61% Mean Duration of Chronicity: NR Kellgren-Lawrence score (0-4): 2.5 vs. 2.3 WOMAC function subscale (0-100): 46.2 vs. 46.1 WOMAC pain subscale (0-100): 42.8 vs. 43.4	A vs. B <u>Post-treatment Average (6-12 months)</u> WOMAC function: 35.2 vs. 37.5, P=NS AIMS physical disability subscale: 1.5 vs. 1.4, P=NS WOMAC pain subscale: 34.5 vs. 38.0, P=NS AIMS pain subscale: 4.4 vs. 4.7, P=NS	A vs. B <u>Post-treatment Average (6-12 months)</u> WOMAC stiffness subscale: 44.5 vs. 46.4, P=NS AIMS psychological subscale: 2.6 vs. 2.5, P=NS

AIMS = Arthritis Impact Measurement Scale; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; CI = confidence interval; HRQoL = health-related quality of life; MD = mean difference; NR = not reported; NRS = numeric rating scale; NS = not statistically significant; OA = osteoarthritis; RR = risk ratio; WOMAC = Western Ontario and McMaster Universities Osteoarthritis index

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Psychological Therapies Compared With Usual Care

Both trials reported outcomes averaged over all post-treatment followup times; the trial of CBT averaged results from 1.5 to 10.5 months post treatment (spanning short to intermediate term)[94] and the trial of pain coping skills training averaged results from 6 to 12 months post treatment (spanning intermediate to long term).[95]

No significant differences in function or pain were found between the psychological therapy and the usual care groups in either trial. Function was measured using the WOMAC physical function subscale (0-100) in both trials, over the short to intermediate term (MD −0.3, 95% CI −8.3 to 7.8)[94] and intermediate to long term (mean 35.2, 95% CI 31.8 to 38.6 vs. mean 37.5, 95% CI 33.9 to 41.2),[95] and using the Arthritis Impact Measurement Scale (AIMS) physical disability subscale in one trial[95] (Table 25). Both trials measured pain using the WOMAC pain subscale (0-100), one trial over short- to intermediate-term followup (MD −3.9, 95% CI −11.8 to 4.0)[94] and the other over intermediate- to long-term followup (mean 34.5, 95% CI 30.8 to 38.2 vs. mean 38.0, 95% CI 34.1 to 41.8).[95] Results were similar for the AIMS pain subscale and the numeric rating scale (NRS) pain scale, reported by one trial each (Table 25). Neither trial reported any differences between groups in any secondary outcome measure.

No trial evaluated effects of psychological therapies on use of opioid therapies or health care utilization.

Psychological Therapies Compared With Pharmacological Therapy

No trial of psychological therapy versus pharmacological therapy met inclusion criteria.

Psychological Therapies Compared With Exercise Therapy

One fair-quality trial[110] of pain coping skills training versus strengthening exercise found no between-group differences in function or pain in the short term (WOMAC physical function, MD

2.0, 95% CI −2.4 to 6.4 on a 0-68 scale and WOMAC pain, MD −0.1, 95% CI −1.2 to 1.0 on a 0-20 scale) or the intermediate term (WOMAC physical function, MD 3.2, 95% CI −0.6 to 7.0 and WOMAC pain, MD 0.4, 95% CI −0.8 to 1.6) (Table 25). Results were similar for overall pain and pain with walking, both measured on a 0-100 VAS. There were also no differences between groups on any other secondary outcome measure including opioid use at short-term or intermediate-term follow up.

Harms

In the two trials of psychological interventions versus usual care,[94,95] no adverse events were observed. In the third trial,[110] fewer participants in the pain coping skills training group compared with the exercise group experienced pain in the knee (3% vs. 31%, P<0.001) and in other body regions (4% vs. 15%, P=0.02) during treatment; during followup, only the frequency of pain in other body areas differed between groups (0% vs. 11%, respectively, P<0.05; knee pain, 7% vs. 10%, P=0.53). Pain was most mostly mild and transient.

Physical Modalities for Osteoarthritis of the Knee

Key Points

Ultrasound

- One fair-quality trial found continuous and pulsed ultrasound was associated with slightly better short-term function (difference −6.2, 95% CI −8.36 to −4.20, and −5.71, 95% CI −7.72 to −3.70 on a 0-24 scale) and short-term pain intensity (difference −3.3, 95% CI −4.64 to −1.96, and −3.37, 95% CI −4.73 to −2.01 on a 0-10 scale) (SOE: low).
- One fair-quality trial found no evidence of differences between continuous and pulsed ultrasound versus sham in intermediate-term function (difference −2.9, 95% CI −9.19 to 3.39 and 1.6, 95% CI −3.01 to 6.22, on a 0-68 scale) or pain (difference −1.6, 95% CI −3.26 to 0.06 and 0.2, 95% CI −1.34 to 1.74, on a 0-20 scale). There was also no difference between groups for VAS pain during rest or on movement (SOE: low).
- No adverse events were reported during the two trials (SOE: low).

Transcutaneous Electrical Nerve Stimulation

- One trial found no evidence of differences between TENS and placebo TENS in intermediate-term function (proportion of patients who achieved a MCID on the WOMAC function subscale [≥9.1], 38% vs. 39%, RR 1.2, 95% CI 0.6 to 2.2; and MD −1.9, 95% CI −9.7 to 5.9 on the 0-100 WOMAC function subscale) or intermediate-term pain (proportion of patients who achieved MCID [≥20] in VAS pain, 56% vs. 44%, RR 1.3, 95% CI 0.8 to 2.0; and MD −5.6, 95% CI −14.9 to 3.6 on the 0-100 WOMAC pain subscale) (SOE: low for function and pain).
- One trial of TENS reported no difference in the risk of minor adverse events (RR 1.06 (95% CI 0.38 to 2.97) (SOE: low).

Low-Level Laser Therapy

- Evidence was insufficient from one small fair-quality and two poor-quality trials to determine effects or harms of low-level laser therapy in the short or intermediate term; No data were available for the long term (SOE: insufficient)

Microwave Diathermy

- There was insufficient evidence to determine short-term effects or harms from one small, fair-quality trial (SOE: insufficient).

Pulsed Short-Wave Diathermy

- There was insufficient evidence to determine effects or harms from one poor-quality trial in the short term or from another poor quality trial in the long term (SOE: insufficient).

Electromagnetic Field

- One fair-quality trial found pulsed electromagnetic fields were associated with slight improvements in function (difference −3.48, 95% CI −4.44 to −2.51 on a 0-85 WOMAC ADL subscale) and pain (difference −0.84, 95% CI −1.10 to −0.58 on a 0-25 WOMAC pain subscale) versus sham short-term but differences may not be clinically significant (SOE: low).
- More patients who received real versus sham electromagnetic field therapy reported throbbing or warming sensations or aggravation of pain (29% versus 7%); however, the difference was not significant (RR 1.95, 95% CI 0.81 to 4.71) (SOE: low).

Superficial Heat

- Evidence was insufficient from one small fair-quality trial to determine effects or harms of trial superficial heat versus placebo in short-term pain (SOE: insufficient).

Braces

- There is insufficient evidence from one poor-quality study to determine the effects of bracing versus usual care for intermediate-term and long-term function or pain (SOE: insufficient).
- Harms were not reported.

Detailed Synthesis

A total of 13 trials[125-137] reported the use of a physical modality for the treatment of knee OA (Table 26 and Appendixes D and E). Physical modalities evaluated included ultrasound, TENS, low-level laser therapy, microwave diathermy, pulsed short-wave diathermy, electromagnetic fields, superficial heat, and bracing. All but one intervention (bracing vs. usual care)[127] were compared to a sham procedure.

Table 26. Osteoarthritis of the knee: physical modalities

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Al Rashoud, 2014[125] 1.5 and 6 months Duration of pain: 11 years *Fair*	A. Low-level laser therapy (n=26), continuous laser (30 mW, 830 nm wavelength) applied to 5 acupuncture points over approximately of 10 sessions B. Placebo laser (n=23), placebo laser applied to 5 acupuncture points over approximately 10 sessions	A vs. B Age: 52 vs. 56 years Female: 62% vs. 65% Baseline pain on movement VAS (0-10): 6.4 vs. 5.9 Baseline Saudi Knee Function Scale (SKFS) (0-112), median: 61.0 vs. 60.0	A vs. B 1.5 months Pain on movement VAS: 3.0 vs. 4.2[b] SKFS, median: 31 vs. 40, median difference −10 (95% CI −23 to −4) P=0.054 6 months Pain on movement VAS: 3.4 vs. 5.2[b] SKFS, median: 31 vs. 51, median difference −21 (95% CI −34 to −7) P=0.006	NR
Battisti, 2004[126] 1 month Duration of pain: 11 years *Poor*	A. Therapeutic Application of Musically Modulated Electromagnetic Field (TAMMEF) (n=30) The anatomical region treated is placed between opposing faces of low frequency electromagnets (3x4 cm). The current from amplifier B feeds a loud speaker that plays music. The music modifies parameters (frequency, intensity, waveform) of the electromagnetic field in time, randomly varying within respective ranges. 15 consecutive daily sessions, 30 minutes each B. Extremely Low Frequency (ELF) (n=30) Similar treatment as Intervention A except the electromagnetic field is stabilized at a frequency of 100Hz in a sinusoidal waveform. 15 consecutive daily sessions, 30 minutes each C. Simulated (Sham) Frequency Field (n=30) Functionally similar operation to the other groups except a simulated (noneffective) field is used, but the patients remain blinded to its effectiveness. 15 consecutive daily sessions, 30 minutes each	A + B + C Age: 58.9 (7.4) Female: 70% Race: NR Mean Duration of Chronicity: 11 (3.1) A vs. B vs. C Mean Lequesne Function Score (0-10)[c]: 3.65 vs. 4.28 vs. 3.48 Mean Lequesne Pain Score (0-10)[c]: 6.88 vs. 6.28 vs. 6.15	A vs. C 1 month Mean Lequesne Functionality: 6.5 vs. 3.83 Mean Lequesne Pain Score: 1.4 vs. 6.85 B vs. C 1 month Mean Lequesne Functionality: 7.1 vs. 3.83 Mean Lequesne Pain Score: 1.4 vs. 6.85	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Brouwer, 2006[127] 6 and 12 months Duration of pain: 6.7 vs. 4.9 years *Poor*	A. Brace (n=60) Patients were fitted with a commercially available knee brace that allowed medial unloading or lateral unloading and also received usual care. Device: Oasys brace, Innovation Sports, Irvine, CA, USA B. Usual Care (n=57) Usual care was identical in both groups and consisted of patient education (adaptation of activities and/or weight loss), and (if needed) physical therapy and analgesic	A vs. B Age[f]: 59.2 Female: 48% vs. 51% Race: NR HSS Knee Function Score (0-100): 64.9 vs. 69.0 VAS Pain Severity (0-10): 6.6 vs. 5.5	A vs. B 6 months HSS Knee Function: difference 3.2 (95% CI −0.58 to 6.98) VAS Pain Severity: difference −0.58 (95% CI −1.48 to 0.32) 12 months HSS Knee Function: difference 3.0 (95% CI −1.05 to 7.05) VAS Pain Severity: difference −0.81 (95% CI −1.76 to 0.14)	A vs. B 6 months EQ-5D: difference 0.01 (95% CI −0.08 to 0.10) 12 months EQ-5D: difference 0.01 (95% CI −0.08 to 0.10)
Cakir, 2014[128] 6 months Duration of pain: Mean 4.0 to 5.1 years *Fair*	A. Continuous ultrasound (n=20), Therapeutic ultrasound given 5 times a week for 2 weeks B. Pulsed ultrasound (n=20), Therapeutic pulsed ultrasound given 5 times a week for 2 weeks C. Sham (n=20), Sham ultrasound given 5 times a week for 2 weeks All patients performed home exercise program 3 days a week for 8 weeks	A vs. B vs. C Age: 57 vs. 58 vs. 57 years Female: 70% vs. 80% vs. 85% WOMAC physical mean function (0-68): 55.7 vs. 52.4 vs. 52.5 WOMAC pain (0-20):15.9 vs. 14.5 vs. 14.9 WOMAC stiffness (0-8): NR Pain at rest VAS (0-10): 57.9 vs. 55.7 vs. 53.6 Pain on movement VAS (0-10): 75.5 vs. 73.0 vs. 72.2 Disease severity VAS (0-10): 73.9 vs. 67.9 vs. 68.4	A vs. C 6 months WOMAC physical function: 32.6 vs. 35.5, difference −2.9 (95% CI −9.2 to 3.4) WOMAC pain: 9.5 vs. 11.1, difference −1.6 (95% CI −3.3 to 0.1) Pain at rest VAS: 21.4 vs. 22.3, difference 1.2 (95% CI −9.1 to 11.5) Pain on movement VAS: 38.7 vs. 38.1, difference 0.6 (95% CI −13.7 to 14.9) Disease severity VAS: 30.0 vs. 29.5, difference 0.5 (95% CI −6.7 to 7.7) B vs. C 6 months WOMAC physical function: 37.1 vs. 35.5, difference 1.6 (95% CI −3.01 to 6.22) WOMAC pain: 11.3 vs. 11.1, difference 0.2 (95% CI −1.34 to 1.74) Pain at rest VAS: 20.2 vs. 22.3, difference −2.1 (95% CI −11.2 to 7.0) Pain on movement VAS: 37.5 vs. 38.1, difference −0.6 (95% CI −16.98 to 15.78) Disease severity VAS: 32.5 vs. 29.5, difference 3.0 (95% CI −3.95 to 9.95)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Fary, 2011[129] 6.5 months Duration of pain: 12 years *Good*	A. Pulsed electrical stimulation (n=34), pulsed electrical stimulator worn 7 hours a day daily for 26 weeks B. Placebo electrical stimulation (n=36), placebo pulsed electrical stimulator worn 7 hours a day daily for 26 weeks	A vs. B Age: 71 vs. 69 years Female: 50% vs. 44% Baseline WOMAC total (0-100): 36 vs. 34 Baseline WOMAC function (0-100): 35 vs. 34 Baseline WOMAC stiffness (0-100): 45 vs. 41 Baseline WOMAC pain (0-100): 35 vs. 36 Baseline pain VAS (0-100): 51 vs. 52	A vs. B 6.5 months Proportion of patients who achieved MCID (≥9.1) in WOMAC function: 38% vs. 39%, RR 1.2 (95% CI 0.6 to 2.2) Proportion of patients who achieved MCID (≥20) in pain VAS: 56% vs. 44%, RR 1.3 (95% CI 0.8 to 2.0) Mean change in WOMAC total: 6 vs. 7, MCD −1.3 (−8.8 to 6.3) Mean change in WOMAC function: 5 vs. 7, MCD −1.9 (95% CI −9.7 to 5.9) Mean change in WOMAC stiffness: 9 vs. 5, MCD 3.7 (95% CI −6.0 to 13.5) Mean change in WOMAC pain: 5 vs. 10, MCD −5.6 (95% CI −14.9 to 3.6) Mean change in pain VAS: 20 vs. 19, MCD 0.9 (95% CI −11.7 to 13.4)	A vs. B 6.5 months Mean change in SF-36 physical component score (0-100): −1.0 vs. −2.6, MCD 1.7 (95% CI −1.5 to 4.8) Mean change in SF-36 mental component score (0-100): −1.2 vs. −2.4, MCD 1.2 (95% CI −2.9 to 5.4)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Fukuda,[130] 2011 12 months Duration of pain: NR *Poor*	<u>A. Low-dose Pulsed Short Wave (PSW) (n=32)</u> Patients administered a precalibrated device to the anterior area of the thigh, 5 cm above superior border of the patella. Device was set to output a specific frequency and pulse duration, with a care provider nearby but without direct input from care provider. Three, 19 minute applications per week for three weeks (9 total) Total Energy: 17 kJ Frequency: 27.12 MHz Mean Power Output: 14.5 W Pulse Duration: 400 microseconds Pulse Frequency: 145 Hz <u>B. High-dose PSW (n=31)</u> Treatment characteristics were identical to Group A except length of treatment (and received total energy) were doubled. Three, 38 min applications per week for three weeks (9 total) Total Energy: 33 kJ <u>C. Sham (n=23)</u> Treatment characteristics were identical to Group A except the device was kept in standby mode without any electrical current applied. Three, 19 min applications per week for 3 weeks (9 total)	A vs. B vs. C Age: 62 vs. 63 vs. 57 Female: 100% Race: NR Knee Injury and Osteoarthritis Outcome Score Symptoms Subscale (0-100): 46.5 vs. 47.0 vs. 42.0 KOOS Daily Activities Subscale (0-100): 45.8 vs. 51.7 vs. 45.7 KOOS Recreational Activities Subscale (0-100): 16.6 vs. 15.3 vs. 18.2 KOOS Pain Subscale (0-100): 37.4 vs. 42.5 vs. 38.0 NRS Pain(0-10): 7.1 vs. 6.7 vs. 7.7 KOOS Quality of Life Subscale (0-100): 26.1 vs. 32.4 vs. 27.8	A vs. C <u>12-months</u> KOOS Symptoms Subscale: 61.6 vs. 40.7, difference 20.9 (95% 8.92 to 32.88) KOOS Daily Activities Subscale: 68.9 vs. 41.6, difference 27.30 (95% 13.73 to 40.87) KOOS Recreational Activities Subscale: 24.6 vs. 11.0, difference 13.6 (95% −0.73 to 27.93) KOOS Pain Subscale: 57.5 vs. 33.0, difference 24.5 (95% 12.12 to 36.88) NRS Pain: 5.7 vs. 7.5, difference −1.8 (95% −3.60 to 0.00) B vs. C <u>12-months</u> KOOS Symptoms Subscale: 54.9 vs. 40.7, difference 14.2 (95% 1.21 to 27.19) KOOS Daily Activities Subscale: 51.9 vs. 41.6, difference 10.30 (95% −1.24 to 21.84) KOOS Recreational Activities Subscale: 15.9 vs. 11.0, difference 4.9 (95% −5.32 to 15.12) KOOS Pain Subscale: 57.6 vs. 33.0, difference 24.6 (95% 14.59 to 34.61) NRS Pain: 5.2 vs. 7.5, difference −2.3 (95% −3.68 to −0.92)	A vs. C <u>12-months</u> KOOS Quality of Life Subscale: 31.8 vs. 33.0 <u>B vs. C</u> <u>12-months</u> KOOS Quality of Life Subscale: 41.2 vs. 33.0 A vs. B vs. C <u>Adverse Events:</u> Went on to have a Total Knee Replacement during 12 month followup: 3.1% (1/32) vs. 6.5% (2/31) vs. 4.3% (1/23)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Giombini, 2011[131] 3 months Duration of pain: 3 years *Fair*	<u>A. Microwave diathermy (n=29)</u> hyperthermic treatment 3 times a week for 4 weeks <u>B. Sham diathermy (n=25)</u> sham hyperthermic treatment 3 times a week for 4 weeks	A vs. B Age: 67 vs. 67 years Female: 66% vs. 68% Baseline WOMAC total (0-1.20): 103.1 vs. 101.3 Baseline WOMAC pain (0-25): 19.2 vs. 18.5 Baseline WOMAC stiffness (0-10): 9.7 vs. 9.7 Baseline WOMAC ADL (0-85): 74.3 vs. 73.1	A vs. B <u>3 months</u> Mean change in WOMAC total: −46.8 vs. −0.4, difference −46.4 (95% CI −58.3 to −34.5) Mean change in WOMAC pain; −8.6 vs. −0.6, difference −8.1 (95% CI −10.7 to −5.3) Mean change in WOMAC ADLs: −33 vs. 0.3, difference −33.2 (95% CI −42.0 to −24.6) Mean change in WOMAC stiffness: −5.2 vs. −0.1, difference −5.1, P<0.01	NR
Hegedus, 2009[132] 2 months Duration of pain NR *Poor*	<u>A. Low-Level Laser Therapy (n=18)</u>: 50 mW, continuous wave laser (wavelength 830 nm). Treatment provided over the femoral and tibial condyles. Total dose of 48 J/cm2 per session. Twice a week for four weeks. <u>B. Placebo (n=17)</u>: Placebo probe (0.5 mW power output) used twice a week for four weeks.	Age: 49 Female: 81% A vs. B Pain VAS (0-10): 5.75 vs. 5.62	A vs. B <u>2 months</u> Pain VAS: 1.18 vs. 4.12, difference −2.94 (no estimate of variability provided or calculable)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Laufer, 2005[133] 3 months Duration of pain: NR *Poor*	A. Low Intensity Pulsed Shortwave Diathermy (n=38) Treatment Protocol: Shortwave diathermy was applied to anterior aspect of the affected knee; Three, 20 min sessions per week for 3 weeks (9 total) Pulse Duration: 82 µs Pulse Frequency: 110 Hz Peak Power: 200 W (mean 1.8W)) B. High Intensity Pulsed Shortwave Diathermy (n=32) Treatment protocol identical to Group A except with a higher intensity (pulse duration and frequency) Pulse Duration: 300 µs Pulse Frequency: 300 Hz Peak Power: 200 W (mean 18W) C. Sham Shortwave Diathermy (n=33) Identical treatment except the apparatus was turned on but the power output was not raised.	A vs. B vs. C Age: 75 vs. 73 vs. 73 Female: 82% vs. 90.6% vs. 67% Race: NR Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Overall: 5.13 vs. 4.60 vs. 5.02 WOMAC Pain: 4.89(3.30) vs. 4.43(3.35) vs. 4.97(3.52); WOMAC Stiffness : 4.87(3.50) vs. 4.25(3.47) vs. 4.92(3.58) WOMAC Activities of Daily Living: 5.16(3.52) vs. 4.69(3.41) vs. 5.05(3.45);	A vs. C 3 months WOMAC Overall: 4.82 vs. 4.60, difference 0.22 (95% CI −1.51 to 1.95) WOMAC Pain: 4.48 vs. 4.33, difference 0.15 (95% CI −1.57 to 1.87) WOMAC Stiffness: 4.43 vs. 3.60, difference 0.83 (95% CI −0.98 to 2.64) WOMAC Activities of Daily Living: 4.98 vs. 4.82, difference 0.16 (95% CI −1.51 to 1.83) B vs. C 3 months WOMAC Overall: 4.56 vs. 4.60, difference −0.04 (95% CI −1.75 to 1.67) WOMAC Pain: 4.09 vs. 4.33, difference −0.24 (95% CI −2.02 to 1.54) WOMAC Stiffness: 3.81 vs. 3.60, 0.21 (95% CI −1.55 to 1.97) WOMAC Activities of Daily Living: 4.8 vs. 4.82, difference −0.02 (95% CI −1.67 to 1.63)	A vs. B vs. C Adverse Events: No adverse reactions to the treatment were reported by the subjects.
Mazzuca, 2004[134] 1 month Duration of pain: NR *Fair*	A. Superficial Heat (sleeve) (n=25) Participants word a cotton and lycra sleeve with a heat retaining polyester and aluminum substrate. Patients were asked to wear the sleeve at least 12 hours each day and to continue their usual pain medication(s). B. Placebo Sleeve (n=24) Placebo sleeves and treatment protocol were identical except placebo sleeves did not contain the heat retaining substrate layer.	A + B Age: 62.7 Female: 77% Race: 67% white WOMAC Function (17-85)[e]: 51.8 (11.8) WOMAC Pain (5-25)[d]: 15.2 vs. 14.7* WOMAC Stiffness (2−10)[e]: 6.5 (1.4)	A vs. B 1 month WOMAC Pain: 13.7 vs. 13.9	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Tascioglu, 2004[135] 6 months Duration of pain: 7 years *Poor*	A. Active laser 3 joule (n=20) continuous laser therapy (50 mW, 830 mm wavelength) applied to 5 painful points 5 days a week for 2 weeks B. Active laser 1.5 joule (n=20) continuous laser therapy (50 mW, 830 mm wavelength) applied to 5 painful points 5 days a week for 2 weeks C. Placebo laser (n=20), sham laser therapy applied to 5 painful points 5 days a week for 2 weeks	A vs. B vs. C Age: 63 vs. 60 vs. 64 years Female: 70% vs. 75% vs. 65% Baseline WOMAC function (0-68):36.6 vs. 38.0 vs. 39.5 Baseline WOMAC stiffness (0-8): 4.1 vs. 4.6 vs. 4.5 Baseline WOMAC pain (0-20): 10.3 vs. 11.6 vs. 9.6 Baseline pain at rest VAS (0-100): 39.1 vs. 41.6 vs. 37.9 Baseline pain at activation VAS (0-100): 68.0 vs. 65.7 vs. 63.9	A vs. C 6 months WOMAC function: 34.8 vs. 38.7, difference −3.8 (95% CI −9.8 to 2.1) WOMAC stiffness: 3.9 vs. 4.2, difference −0.3 (95% CI −1.6 to 0.9) WOMAC pain: 10.4 vs. 9.9, difference 0.6 (95% CI −1.5 to 2.7) Pain at rest VAS: 38.7 vs. 38.9, difference −0.3 (95% CI −9.8 to 9.3) Pain at activation VAS: 66.8 vs. 62.0, difference 4.8 (95% CI −4.9 to 14.5) B vs. C 6 months WOMAC function: 38.5 vs. 38.7 WOMAC stiffness: 4.5 vs. 4.2 WOMAC pain: 11.3 vs. 9.9 Pain at rest VAS: 40.0 vs. 38.9 Pain at activation VAS: 61.8 vs. 62.0	NR
Thamsborg,[136] 2005 1.5 month Duration of pain, 8 years *Fair*	A. Pulsed Electromagnetic Fields (PEMF) (n=42) Two sets of two adjacent coils were placed on the medial and lateral regions of the study knee, with the interspace between the coils being at the level of the koin line. The coils were placed on an insulating bandage of 3-5 mm thickness. 2-hour daily treatment 5 days per week for 6 weeks 30 total Device: ±50V in 50Hz pulses changing voltage in 3 ms intervals. B. Sham Electromagnetic Field (n=41) Patients in the control group were subjected to a noneffective placebo electromagnetic field. No. of Treatments: daily treatment 5 days per week for 6 weeks (30 total Length of Treatments: 2 hours each	A vs. B Age: 60 vs. 60 Female: 47.6% vs. 61% Race: NR WOMAC Activities of Daily Living (0-85): 43.83 vs. 46.49 WOMAC Stiffness (0-10): 5.74 vs. 5.85 WOMAC Joint Pain (0-25): 13.15 vs. 14.49	A vs. B 1.5 months WOMAC Activities of Daily Living: 37.89 vs. 41.3, difference −3.48 (95% CI −4.44 to −2.51) WOMAC Stiffness: 4.81 vs. 5.15, difference −0.34 (95% CI −0.48 to −0.20) WOMAC Joint Pain: 11.40 vs. 12.24, difference −0.84 (95% CI −1.10 to −0.58)	A vs. B Adverse Events: throbbing sensation, warming sensations or aggravation of pain 28.5% (12/42) vs. 14.6% (6/41)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Yildiz,[137] 2015 2 months Duration of pain: Mean 2.8 to 5.1 years *Fair*	A. Continuous ultrasound (n=30), Therapeutic ultrasound given 5 times a week for 2 weeks B. Pulsed ultrasound (n=30), Therapeutic pulsed ultrasound given 5 times a week for 2 weeks C. Sham (n=30), Sham ultrasound given 5 times a week for 2 weeks All patients performed home exercise program 3 days a week for 8 weeks	A vs. B vs. C Age: 56 vs. 55 vs. 58 years Female: 83% vs. 80% vs. 87% Lequesne Index score (0-24): 13.2 vs. 12.9 vs. 12.4 Pain at rest VAS (0-10): NR Pain on movement VAS (0-10): 9.0 vs. 8.6 vs. 8.9	A vs. C 2 months Lequesne Index: 5.5 vs. 11.7, difference −6.2 (95% CI −8.4 to 4.2) Pain at rest VAS: NR Pain on movement VAS: 3.9 vs. 7.2, difference −3.3 (95% CI −4.6 to −2.0) B vs. C 2 months Lequesne Index: 6.0 vs. 11.7, difference −5.7 (95% CI −7.7 to −3.7) Pain at rest VAS: NR Pain on movement VAS: 3.8 vs. 7.2, difference −3.4 (95% CI −4.7 to −2.0)	NR

ADL = activity of daily living; EQ-5D = EuroQol Quality of Life Instrument 5-D; HSS = Hospital for Special Surgery; Hz = hertz; KOOS = Knee Injury and Osteoarthritis Outcome Score; MCID = minimal clinically important difference; MD = difference between means; NR = not reported; NRS = numeric rating scale; RR = risk ratio; SKFS = Saudi Knee Function Score; SF-36 = Short Form 36 Questionnaire; VAS = visual analog scale; W = watts; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; μs = microsecond

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Values estimated from graph

[c] The study separated outcome values out into slight, moderate and severe disease patient groups for each treatment arm. These values are combined values for each intervention groups estimated from graphs in the study.

[d] Values estimated from graph

[e] Separate group baseline values not given for stiffness and function subscales

[f] Age only reported for population as a whole

Two fair-quality randomized controlled trials that evaluated ultrasound for knee OA met the inclusion criteria.[128,137] Both trials required grade 2 or 3 radiographic knee OA using the Kellgren–Lawrence criteria for inclusion. Both trials had a continuous and a pulsed ultrasound group, which they compared to sham ultrasound. Both ultrasound groups received 1 MHz treatments five times per week for 2 weeks at an intensity of either 1 or 1.5 W/cm^2. Sham ultrasound used the same protocols, but the power was switched off. All participants were also instructed to perform a home exercise program of mostly muscle performance exercises three times per week. Compliance with the intervention protocol was not reported. One trial reported short-term outcomes,[137] the other intermediate-term outcomes. The methodological shortcomings were unclear adherence to an intention-to-treat analysis,[137] and unclear blinding of the provider or assessor.[128]

We found one good-quality (n=70) trial that compared active TENS with sham TENS for knee OA.[129] Inclusion criteria required a confirmed diagnosis of knee OA using the American College of Rheumatology criteria. The TENS protocol had patients wear a pulsed TENS device 7 hours daily for 26 weeks. The sham TENS groups followed the same protocol as the active treatment, but the device turned off after 3 minutes. Compliance was unacceptable for time the TENS device was worn.

We identified three small trials (n=30, 49, and 60) that investigated low-level laser therapy versus sham laser for knee OA.[125,132,135] The mean age ranged from 49 to 64 years and most

patients were female (62% to 75%). Two studies included patients meeting the American College of Rheumatology criteria for knee OA.[125,135] Two trials also required an average pain intensity of greater than 3 or 4 on a 0-10 VAS,[125] while the other trial had an additional inclusion criteria of radiographic knee OA of Kellgren–Lawrence grade of 2 or 3.[135] Treatment duration ranged from 2 to 4 weeks and the number of total sessions from eight to ten. Low-level laser therapy protocols differed across the trials with doses ranging from 1.2 to 6 Joules per point (range, 5 to 6 points) and length of irradiation from 40 seconds to 2 minutes; all trials used a continuous laser beam. The sham laser comparison groups followed the same respective protocols, but the device was inactive. One trial was rated fair quality[125] and two poor quality.[132,135] In the fair-quality trial, blinding of the care provider was unclear. The two poor-quality trials suffered from insufficient descriptions of allocation concealment methods, unclear application of intention to treat, lack of clarity regarding patient blinding, and no reporting of or unacceptable attrition.

One small (n=63), fair-quality trial compared microwave diathermy (three 30-minute sessions per week for 4 weeks) to sham.[131] The inclusion criteria required radiographic knee OA of a Kellgren and Lawrence grade 2 or 3. The power was set to 50 watts. Sham diathermy followed the same protocol, but the machine was set to off. Compliance with the treatment regimen for each group was unclear. Methodological limitations of this study included no blinding of the care providers.

Two trials (n=86 and 115) examined pulsed short-wave diathermy compared to sham diathermy.[130,133] The mean age ranged from 62 to 75 years, and the proportion of female participants ranged from 67 to 100 percent. Both trials included patients meeting radiographic criteria for knee OA. Each trial compared two doses of short-wave diathermy to a sham diathermy group; dosages varied by intensity in one trial (mean power output of either 1.8 or 18 Watts for 20 minutes)[133] or by length of session (19 or 38 minutes at 14.5 Watts) in the other.[130] Both trials applied diathermy three times per week for 3 weeks (total of 9 sessions). Each sham diathermy group followed the same treatment protocol, but the electrical current was not applied. Compliance with the treatment regimens was acceptable for both trials. Both trials were rated poor quality due to unclear concealment of treatment allocation, a lack of care provider blinding, and unacceptable attrition.

Two trials (n=90 for both) compared the application of electromagnetic fields to sham interventions for knee OA.[126,136] The mean age of participants was 59 and 60 years, and the proportion of female participants ranged from 48 to 70 percent. The mean duration of chronicity ranged from 9 to 11 years. The good-quality trial enrolled participants meeting the American College of Rheumatology criteria for knee OA.[136] The inclusion criteria was not clearly presented in the poor-quality trial.[126] The intervention group in the good-quality study received 2 hours of pulsed electromagnetic fields 5 days a week for 6 weeks.[136] The poor-quality trial had a musically modulated electromagnetic field group that received 15 daily 30-minute sessions. Music from a connected speaker modulated the parameters of the electromagnetic field. The study also had an extremely low frequency electromagnetic field group that had 15 daily 30 minutes sessions, but the electromagnetic field was set at a frequency of 100 Hz.[126] The sham group in each trial followed the same respective treatment protocol, but used a noneffective electromagnetic field during the sessions. Compliance to the treatment sessions was acceptable in both trials. One trial was rated fair quality[136] and the other was rated poor quality.[126] Methodological limitations in both trials included unclear methods for allocation concealment.

Additionally, in the poor-quality trial, there were baseline dissimilarities between groups, no blinding of patients, providers, or outcome assessors, and attrition was not reported.[126]

A single trial compared superficial heat with placebo (n=52).[134] Participants were included if they had grade 2 or higher using the Kellgren-Lawrence grading for radiographic knee OA. Superficial heat was provided using a knee sleeve with a heat retaining polyester and aluminum substrate. Participants were instructed to wear the sleeve at least 12 hours per day. The placebo sleeves were identical and participants received the same instructions, but the sleeve did not contain the heat retaining substrate; the extent to which patients could be truly blinded is unclear (sleeve may retain body heat and feel warmer). Compliance with wearing the sleeve was acceptable. This trial was rated fair quality due to unclear concealment of treatment allocation, and a lack of clarity regarding whether it was the provider or outcomes assessor that was blinded.

We identified one trial comparing use of a knee brace to usual care (n=118).[127] Inclusion criteria required unicompartmental knee OA, and either a varus or valgus malalignment. Patients in the intervention group were fitted with a commercially available knee brace that allowed medial unloading or lateral unloading. Usual care consisted of patient education and physical therapy and analgesics as needed. Compliance with continued use of the brace was unacceptable. This trial was rated poor quality due to lack of patient, provider, or assessor blinding, and unacceptable attrition.

Physical Modalities Compared With Sham or Usual Care

Ultrasound. One fair-quality trial reported short-term function using Lequesne Index (0-24) and VAS pain (0-10) during activity.[137] Both the continuous ultrasound group and the pulsed ultrasound group had substantially better short-term function versus sham ultrasound (MD −6.2, 95% CI −8.36 to −4.20, and −5.71, 95% CI −7.72 to −3.70, respectively). Continuous and pulsed ultrasound was also associated with substantially less pain during activity compared to sham ultrasound (MD −3.3, 95% CI −4.64 to −1.96, and −3.37, 95% CI −4.73 to −2.01, respectively, on a 0 to 10 scale).

Intermediate-term results at 6 months from the other fair-quality trial showed no difference on the WOMAC Physical Function subscale (0 to 100) between either the continuous or pulsed ultrasound group versus sham ultrasound (MD −4.5, 95% CI −10.34 to 1.34, and −2.9, 95% CI −9.19 to 3.39, respectively).[128] Results for pain intensity were not consistent with regard to ultrasound method. The continuous ultrasound group had slightly less pain on the WOMAC pain scale compared to sham (MD −1.8, 95% CI −3.34 to −0.26), but no statistical difference was seen between pulsed ultrasound and sham (MD −1.6, 95% CI −3.26 to 0.06). There was no difference between either ultrasound group versus sham ultrasound for VAS pain during rest or on movement (Table 26).

Transcutaneous Electrical Nerve Stimulation. No effect was seen for TENS versus placebo TENS for function or pain over the intermediate term for any outcome measured in one good-quality trial.[129] Function was measured via the WOMAC-function subscale (0 to 100); the difference in mean change scores was −1.9 (95% CI −9.7 to 5.9) and the proportion of patients who achieved a MCID ≥9.1 was 38 percent versus 39 percent (RR 1.2, 95% CI 0.6 to 2.2). Pain was measured using a VAS pain scale (difference 0.9 on a scale of 0 to 10, 95% CI –11.7 to 13.4) and the WOMAC pain subscale (difference −5.6 on a 0 to 100 scale, 95% CI –14.9 to 3.6). The proportion of patients who achieved MCID (≥20) in pain VAS was 56 percent versus 44 percent (RR 1.3, 95% CI 0.8 to 2.0). Health-related quality of life measured with the SF-36 was

not different between the two groups for the physical component and mental component score (Table 26).

Low-Level Laser Therapy. One fair-quality trial reported no difference between low-level laser therapy and sham for short-term function based on median Saudi Knee Function Scale scores (range 0-112 with higher scores indicating greater severity), median difference −10 (interquartile range of −23 to −4), P=0.054.[125] There were inconclusive results for intermediate-term function. One fair-quality trial reported the low-level laser therapy group had less functional severity at 6 months compared to sham on the Saudi Knee Function Scale (median difference −21.0, 95% CI −34.0 to −7.0), P=0.006.[125] For the other poor-quality trial, neither the higher dose nor the lower dose low-level laser therapy group differed from sham on the WOMAC physical function (0 to 96) subscale (MD −3.82, 95% CI −9.75 to 2.11 and −0.14, 95% CI −6.59 to 6.31, respectively).[135] However, the evidence was considered insufficient for function.

Low-level laser therapy was associated with moderately less pain over the short term in one fair-quality and one poor-quality trial (pooled difference −2.03, 95% CI −3.74 to −0.33) (Figure 34).[125,132] There was no difference between low-level laser therapy versus sham for intermediate-term pain (pooled difference −0.93, 95% CI −2.82 to 0.96).[125,135] However, the evidence was considered insufficient for pain.

Microwave Diathermy. Data were insufficient from one small, fair-quality trial evaluating microwave diathermy.[131] The microwave diathermy group showed substantial short-term improvement compared with sham for function (difference −33.2 on a 0-85 scale, 95% CI −42.0 to −24.6, WOMAC ADL subscale) and pain (difference −8.1 on a 0-25 scale, 95% CI −10.7 to −5.3, WOMAC pain subscale). Substantial imprecision was noted.

Pulsed Short-Wave Diathermy. Data were insufficient for pulsed short-wave diathermy compared with sham. There was no difference in short-term function or pain for either the low intensity or high intensity group compared to sham diathermy based on the WOMAC in one poor-quality trial.[131] There was no difference on the WOMAC function subscale (0 to 10) between either the low intensity group versus sham (MD 0.16, 95% CI −1.51 to 1.83), or the high intensity group versus sham (MD −0.02, 95% CI −1.67 to 1.63). There was also no difference on the WOMAC pain subscale (0 to 10) for either the low or high intensity group versus sham (MD 0.15, 95% CI −1.57 to 1.87 and −0.24, 95% CI −2.02 to 1.54, respectively).

The other trial found inconsistent results among the high and low dose groups for long-term function using the KOOS (0 to 100).[130] The low dose group had substantially greater improvement on the KOOS-Daily Activities subscale compared to sham (MD 27.30, 95% CI 13.73 to 40.87), but there was no difference between the high dose group and sham on the KOOS-Daily Activities subscale (MD 10.30, 95% CI −1.24 to 21.84). Neither the low or high dose group differed from sham on the KOOS-recreational activities subscale (Table 26). Regarding pain intensity, the low dose group had moderately better pain NRS (0 to 10) that was not statistically significant (MD −1.8, 95% CI −3.60 to 0.00). The high dose group experienced substantially greater pain reduction than the sham group (MD −2.3, 95% CI −3.68 to −0.92).

Electromagnetic Fields. The fair-quality trial found use of pulsed electromagnetic fields did not appear to provide clinically meaningful short-term improvements in function or pain compared with sham, although statistical significance was achieved. The pulsed electromagnetic field

group had better function on the WOMAC ADL subscale (0 to 85) compared with the sham group, (MD −3.48, 95% CI −4.44 to −2.51), and it had lower scores on the WOMAC pain subscale (0 to 25) versus sham (MD −0.84, 95% CI −1.10 to −0.58).[136] Based on estimated values from a graph for the poor-quality trial,[126] each group using electromagnetic fields had better function and substantially less pain in the short term on the Lequesne Index. The musically modulated electromagnetic field group had moderately better Lequesne Function scores (0-10) versus sham (mean of 6.5 vs. 3.8) and substantially lower Lequesne Pain scores (0 to 10) (mean of 1.4 vs. 6.9). The low frequency electromagnetic field group had similar benefits for function (mean of 7.1 vs. 3.83) and pain (mean of 1.4 vs. 6.85, standard deviation and statistical testing not reported), compared with sham.

Superficial Heat. Evidence from one small fair-quality trial was insufficient to determine the effects of superficial heat on short-term pain. WOMAC pain subscale scores were similar between the heat and placebo group at 1 month post treatment (13.7 versus 13.9, respectively).[134]

Brace. Evidence from one small poor-quality trial was insufficient to determine the effects of brace treatment. There was no difference between bracing and usual care for intermediate-term or long-term function, pain, and quality of life outcomes.[127] Function was measured using the Hospital for Special Surgery (HSS) score (MD 3.2, 95% CI −0.58 to 6.98 for intermediate-term function and 3.0, 95% CI −1.05 to 7.05 for long-term function). Pain intensity was assessed using a VAS. The MD was −0.58 (95% CI −1.48 to 0.32) for intermediate-term pain and −0.81 (95% CI −1.76 to 0.14) for long-term pain. Health-related quality of life was measured using the Euro-Qol 5-Dimensions (EQ-5D) (MD 0.01, 95% CI −0.08 to 0.10 for both intermediate-term and long-term health-related quality of life).

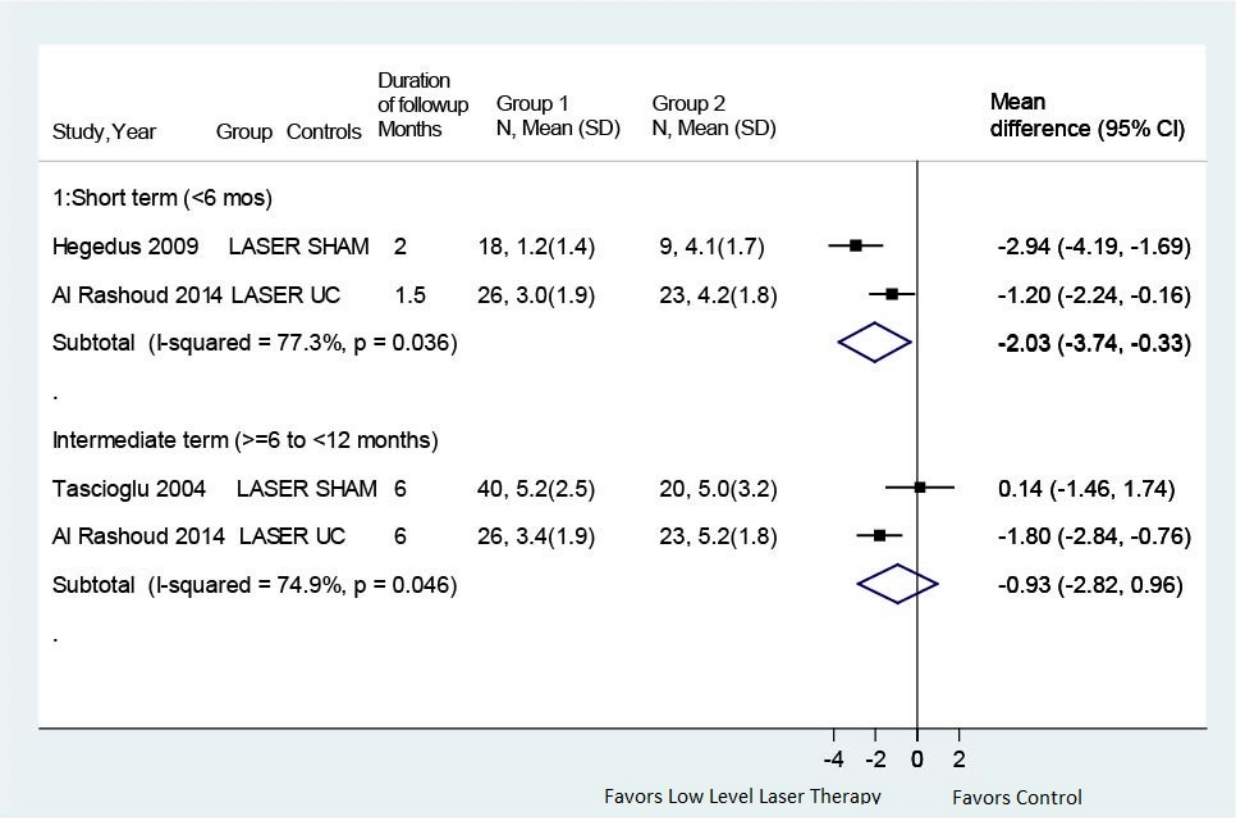
Physical Modalities Compared With Pharmacological Therapy or With Exercise Therapy

No trial of physical modalities versus pharmacological therapy or versus exercise met inclusion criteria.

Harms

In general, harms were poorly reported across the physical modality trials. Six trials (2 of low-level laser therapy,[125,135] 2 of ultrasound therapy,[128,137] 1 of pulsed short-wave diathermy,[133] and 1 of superficial heat[134]) reported that no adverse events or side effects occurred in either group. The good-quality trial that evaluated TENS found no difference between active and sham TENS in the risk of localized, mild rashes (18% vs.17%; RR 1.06, 95% CI 0.38 to 2.97).[129] One trial of microwave diathermy reported two cases of symptom aggravation in the intervention group; the events were transient and neither patient withdrew from the trial.[131] More patients who received real versus sham electromagnetic field therapy reported throbbing or warming sensations or aggravation of pain (29% versus 7%); however, the difference was not significant (RR 1.95, 95% CI 0.81 to 4.71) in one fair-quality trial.[136]

Figure 34. Low-level laser therapy versus usual care or sham for osteoarthritis of the knee: effects on pain



CI = confidence interval; SD = standard deviation; UC = usual care

Manual Therapies for Osteoarthritis of the Knee

Key Points

- There was insufficient evidence from one trial to determine the effects of joint manipulation on intermediate-term function or harms versus usual care or versus exercise due to inadequate data to determine effect sizes or statistical significance (SOE: insufficient).
- There was insufficient evidence from one trial to determine the effects of massage versus usual care on short-term function, pain, or harms, or to evaluate the effect of varying dosages of massage on outcomes (SOE: insufficient).

Detailed Synthesis

Two trials were identified that met inclusion criteria and evaluated manual therapies for the treatment of knee OA[40,154] (Table 27 and Appendixes D and E); both trials required patients to have radiographically established knee OA meeting the American College of Rheumatology criteria.

Table 27. Osteoarthritis of the knee: manual therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Abbott, 2013[40] 9.75 months Duration of diagnosis: 2.6 years *Fair*	A. Manual therapy (n=54/30 knee OA): 7 manual therapy sessions in 9 weeks with 2 additional booster sessions B. Exercise (n=51/29 knee OA), 7 exercise sessions in 9 weeks with 2 additional booster sessions C. Usual care (n=51/28 knee OA)	A vs. B vs. C (total population, includes hip OA) Age: 67 vs. 67 vs. 66 years Female: 49% vs. 52% vs. 58% Percent knee OA: 56% vs. 57% vs. 55% Percent hip OA: 44% vs. 43% vs. 45% Percent both hip OA and knee OA: 22% vs. 20% vs. 26% Baseline WOMAC (0-240): 114.8 vs. 95.5 vs. 93.8	A vs. C (knee OA only) 9.75 months WOMAC mean change from baseline: −31.5 vs. 1.6, P=NR A vs. B 9.75 months WOMAC mean change from baseline: −31.5 vs. −12.7, P=NR	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Perlman,[154] 2012 4 months Duration of pain: NR *Fair*	<u>A1. Massage Therapy Group 1 (MT) (n=25)</u> Participants received a uniform massage protocol designed to address symptoms of OA of the knee with a series of standard Swedish massage strokes, and specified time allocated to various body regions (therapists agreed not to deviate from protocol); one, 30-minute session per week for 8 weeks (8 total sessions) <u>A2. MT Group 2 (n=25)</u> Identical to group A1 except differing 'dosage' of massage; two, 30-min sessions per week for 4 weeks, then once weekly for four weeks (12 total sessions) <u>A3. MT Group 3 (n=25)</u> Identical to group A1 except differing 'dosage' of massage; one, 60-min per week for 8 weeks (8 total sessions) <u>A4. MT Group 4 (n=25)</u> Identical to group A1 except differing 'dosage' of massage; two, 60-min sessions per week for 4 weeks, then once weekly for four weeks (12 total sessions) <u>B. Usual Care (n=25)</u> Participants continued with their current treatment without the addition of massage therapy.	A1 vs. A2 vs. A3 vs. A4 vs. B Age: 70 vs. 62 vs. 63 vs. 64 vs. 64 Female: 60% vs. 72% vs. 76% vs. 68% vs. 76% Race: 92% vs. 88% vs. 76% vs. 80% vs. 88% white WOMAC Total (0-100): 52.9 vs. 50.2 vs. 53.6 vs. 48.0 vs. 53.2 WOMAC Physical Function (0-100): 52.9 vs. 49.5 vs. 49.8 vs. 48.3 vs. 50.5 WOMAC Pain (0-100): 52.3 vs. 42.4 vs. 52.5 vs. 44.4 vs. 46.3 VAS Pain (0-100): 61.2 vs. 64.0 vs. 66.4 vs. 59.2 vs. 57.6	A1 vs. A2 vs. A3 vs. A4 vs. B <u>4 months:</u> WOMAC Total, mean change from baseline (95% CI): −14.3 (−22.9 to −5.7) vs. −7.0 (−15.6 to 1.6) vs. −14.2 (−23.4 to −5.0) vs. −15.1 (−25.1 to −5.1) vs. −6.0 (−12.6 to 0.5) WOMAC Physical Function, mean change from baseline (95% CI): −15.3 (−24.5 to 26.1) vs. −7.4 (−14.8 to 0) vs. −12.1 (−22.0 to −2.1) vs. −14.4 (−23.4 to −5.4) vs. −4.2 (−11.1 to 2.7) WOMAC Pain, mean change from baseline (95% CI): −12.2 (−22.4 to −2.0) vs. −3.9 (−12.7 to 4.9) vs. −13.7 (−23.4 to −4.0) vs. −14.2 (−24.5 to −3.8) vs. −7.5 (−16.0 to 1.1) VAS Pain, mean change from baseline (95% CI): −14.4 (−25.9, −2.8) vs. −14.0 (−24.7 to −3.3) vs. −18.5 (−29.0 to −8.1) vs. −22.8 (−35.5 to −10.1) vs. −11.5 (−21.0 to −2.0)	A1 vs. A2 vs. A3 vs. A4 vs. B <u>4 months:</u> WOMAC Stiffness, mean change from baseline (95% CI): −15.4 (−26.4 to −4.5) vs. −9.6 (−20.6 to 1.3) vs. −16.9 (−28.5 to −5.2) vs. −16.8 (−29.7 to −3.9) vs. −6.4 (−13.2 to 0.4)

CI = confidence interval; NR = not reported; OA = osteoarthritis; VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Arthritis Index

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

One fair-quality trial (N=58 with knee OA) compared manual therapy with usual care (continued routine care from general practitioner and other providers) and with combination exercise.[40] The manual therapy intervention consisted of nine 50-minute sessions. Seven were delivered in the first 9 weeks and two booster sessions at week 16. All participants were prescribed a home exercise program three times per week. Compliance with the intervention was acceptable in all groups, and the methodological shortcoming of this trial was a lack of blinding for the patients and care providers. Only intermediate-term outcomes were reported.

One fair-quality trial (N=125) compared four different dosages of massage therapy with usual care (continued current treatment).[154] The massage protocol consisted of standard Swedish massage strokes applied in each intervention group over 8 weeks. The dosage varied from 240 to 720 minutes based on the frequency (once or twice per week) and duration of massage (30-60 minutes per session). Compliance was acceptable in all groups, and the methodological shortcoming of this trial was a lack of blinding for the patients and care providers in the usual care arm. Only short-term outcomes were reported.

Manual Therapies Compared With Usual Care

Manual Therapy. Data were insufficient from one fair-quality trial (n=58 with knee OA)[40] to evaluate effects of joint manipulation versus usual care over the intermediate term. Although the manual therapy group showed a statistically significant improvement from baseline in function as measured by the WOMAC (mean change −31.5 on a 0-240 scale, 95% CI −52.7 to −10.3), whereas the usual care group showed no improvement (mean change 1.6, 95% CI −10.5 to 13.7), insufficient data was provided to calculate an effect estimate (number of patients with knee OA in each group were not provided). Pain outcomes were not reported.

Massage. Data were insufficient from one fair-quality trial (n=125) to evaluate the short-term effects of massage therapy (4 different dosages) compared with usual care.[154] Function was measured using the WOMAC total and physical function subscale scores (both 0 to 100 scales) and pain was measured using the WOMAC pain subscale and the VAS (both 0 to 10). No significant effects were seen in any outcome measure at 4 months post-massage treatment versus usual care (Table 27). Authors reported a trend for greater magnitude of change in function and pain with higher massage dosages versus lower massage dosages and versus usual care (statistical tests not provided).

Manual Therapies Compared With Pharmacological Therapy

No trial of manual therapy versus pharmacological therapy met inclusion criteria.

Manual Therapies Compared With Exercise Therapy

The trial evaluating manual therapy also included an exercise group that received aerobic warm-up, muscle strengthening, muscle stretching, and neuromuscular control exercises.[40] Both groups showed improvement from baseline in function (WOMAC) over the intermediate term, but the change was statistically significant in the manual therapy group only (mean change of −31.5, 95% CI −52.7 to −10.3 versus −12.7, 95% CI −27.1 to 1.7) for exercise. However, insufficient data was provided to calculate an effect estimate (number of patients with knee OA in each group were not provided). Pain outcomes were not reported.

Harms

No serious treatment-related adverse events occurred in either trial;[40,154] one nontrial-related death was reported in the usual care group in the trial evaluating manual therapy.[40]

Mind-Body Therapies for Osteoarthritis of the Knee

Key Points

- Data were insufficient from two small, unblinded trials to determine the effects or harms of tai chi versus attention control in the short or intermediate terms. No data on long-term outcomes were available (SOE: insufficient).

Detailed Synthesis

Two small trials (n=41 and 40) of tai chi versus attention control in older adults met the inclusion criteria[181,182] (Table 28 and Appendix D). Tai chi was practiced 40 to 60 minutes two or three times per week for 24 or 36 sessions. Attention control consisted of group education classes with one trial[182] including 20 minutes of stretching for sessions 18 to 24. Blinding was not possible in either trial and was the primary methodological limitation in one fair-quality trial.[182] Additional methodological concerns in the other poor-quality trial included unclear concealment of treatment allocation and high attrition[181] (Appendix E).

Table 28. Osteoarthritis of the knee: mind-body therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Brismee, 2007[181] 1.5 months Duration of pain: NR *Poor*	A. Tai chi (n=18) Subjects in the tai chi group attended group tai chi classes for 6 weeks followed by 6 weeks of home video tai chi practice. No. of Treatments: 3/week for 12 weeks (36 total) Length of Treatments: 40 min/session B. Attention Control (n=13) Subjects in the attention control group attended group lectures and discussions covering health-related topics. They did not take part in any further activity past 6 week group period. No. of Treatments: 3/week for 6 weeks (18 total) Length of Treatments: 40 min/session	A vs. B Age: 71 vs. 69 Female: 86.4% vs. 78.9% Race: NR WOMAC Total (26−13)]: 64.6 vs. 59.6 WOMAC Physical Function (17-85): 42.7 vs. 37.6 WOMAC Pain (7−35): 16.5 vs. 16.9 VAS Pain (0−10): 4.7 vs. 4.2 WOMAC Stiffness (2−10): 5.6 vs. 5.1	A vs. B 1.5 months WOMAC Total: 60.28 vs. 57.73m P=NS WOMAC Physical Function: 38.61 vs. 37.58, P=NS WOMAC Pain: 16.39 vs. 16, P=NS VAS Pain: 3.46 vs. 3.19, P=NS WOMAC Stiffness: 5.28 vs. 4.54, P=NS	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Wang, 2009[182] 3 and 9 months Duration of pain: 9.7 years *Fair*	A. Tai chi (n=20) Subjects in the tai chi group attended group tai chi classes where they learned 10 forms from the classic Yang style tai chi. They were also instructed to practice tai chi at least 20 minutes per day at home with a tai chi DVD. Home practice continued after group sessions ended until the 48 week followup. B. Attention Control (n=20) Subjects in the attention control group attended group classes where they received nutritional and medical information paired with 20 minutes of stretching. Instruction to practice at least 20 minutes of stretching exercises per day at home. In both groups, treatments were 2x/week for 12 weeks (24 total), 60 minute sessions	A vs. B Age: 63 vs. 68 Female: 80% vs. 70% Race: NR WOMAC Physical Function (0−1,700): 707.6 vs. 827 WOMAC Pain (0-500): 209.3 vs. 220.4 VAS Patient-Assessed Pain (0−10): 4.2 vs. 4.8 VAS Physician-Assessed Pain (0−10): 4.8 vs. 5.8 WOMAC Stiffness (0-200): 105.7 vs. 120.7	A vs. B 3 months (mean change from baseline) WOMAC Physical Function: −440.5 (95% CI −574.4 to −306.6) vs. −257.3 (95% CI −391.2 to −123.4); difference −183.2 (95% CI −372.6 to 6.2) WOMAC Pain: −131.6 (95% CI −177.4 to −85.7) vs. −64.6 (95% CI −110.5 to −18.7); difference −70.0 (95% CI −131.8 to −2.1) VAS Patient Assessed Pain: −2.4 (95% CI −3.5 to −1.2) vs. −1.7 (−2.9 to −0.5); MD −0.7 (−2.3 to 1.0) VAS Physician Assessed Pain: −2.6 (95% CI −3.3 to −1.9) vs. −2.1 (95% CI −2.8 to −1.3); difference −0.5 (95% CI −1.6 to 0.5) WOMAC Stiffness: −65.0 (95% CI −86.3 to −43.7) vs. −50.2 (95% CI −71.5 to −28.9); difference −14.8 (95% CI −44.9 to 15.3) 9 months WOMAC Physical Function: −405.9 (95% CI −539.8 to −271.9) vs. −300.6 (95% CI −434.5 to −166.6); difference −105.3 (95% CI −294.7 to −84.1) WOMAC Pain: −115.4 (95% CI −161.2 to −69.5) vs. −69.2 (95% CI −115.1 to −23.3); difference −46.2 (95% CI −111.0 to 18.7) VAS Patient Assessed Pain: −1.7 (95% CI −2.8 to −0.5) vs. −1.7 (95% CI −2.9 to −0.5); difference 0.04 (95% CI −1.6 to 1.7) VAS Physician-Assessed Pain: −2.5 (95% CI −3.3 to −1.8) vs. −1.5 (−2.3 to −0.8); difference −1.0 (95% CI −2.1 to 0.02) WOMAC Stiffness: −64.2 (95% CI −85.5 to −42.8) vs. −60.5 (95% CI −81.8 to −39.2); MD −3.7 (95% CI −33.8 to 26.5)	A vs. B 3 months (mean change from baseline) SF-36 PCS (0−100): 10.8 (95% CI 7.3 to 14.3) vs. 6.3 (95% CI 2.8 to 9.8); difference 4.5 (95% CI −0.4 to 9.5) SF-36 MCS (0−100): 4.4 (95% CI −0.11 to 8.9) vs. 4.5 (95% CI 0.0 to 9.0); difference −0.1 (95% CI −6.5 to 6.3) CES-D (0-60): −6.4 (95% CI −9.9 to −2.9) vs. −1.1 (95% CI −4.6 to 2.4); difference −5.3 (95% CI −10.2 to −0.4) 9 months SF-36 PCS: 10.4 (95% CI 6.9 to 13.9) vs. 4.1 (95% CI 0.6 to 7.6); difference 6.3 (95% CI 1.4 to 11.3) SF-36 MCS: 5.8 (95% CI 1.3 to 10.3) vs. 1.0 (95% CI −3.5 to 5.5); difference 4.8 (95% CI −1.6, 11.1) CES-D: −7.3 (95% CI −10.7 to −3.8) vs. 1.7 (95% CI −1.8 to 5.1); difference −8.9 (95% CI −13.8 to −4.0)

AIMS = Arthritis Impact Measurement Scale; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; CI = confidence interval; HRQoL = health-related quality of life; NR = not reported; NRS = numeric rating scale; NS = not statistically significant; OA = osteoarthritis; WOMAC = Western Ontario and McMaster Universities Osteoarthritis index

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Mind-Body Therapies Compared With Attention Control

There is no clear difference between tai chi and an attention control on functional outcomes across the two trials over the short term on a WOMAC physical function 0- to 85-point scale (difference 1.03, 95% CI −9.87 to 11.93)[181] or WOMAC physical function 0- to 1700-point scale (difference −183.2, 95% CI −372.6 to 6.2),[182] or at intermediate term in one of the trials (difference −105.3, 95% CI −294.7 to −84.1, 0 to 1700 scale).[182] Results for short-term pain improvement were inconsistent with no difference between groups on WOMAC pain scale in one trial (difference 0.39 on a 0-35 point scale, 95% CI −4.21 to 4.99)[181] and the other marginally favoring tai chi on 0 to 500 point WOMAC pain scale (difference −67.0, 95% CI −131.8 to −2.1),[182] but demonstrating no difference between the groups in 0 to 10 VAS pain (difference −0.65, 95% CI −2.31 to 1.02).[182] There were no differences between groups at intermediate term in this latter trial (WOMAC pain 0 to 500 scale, difference −183.2, 95% CI −372.6 to 6.2).[182] One trial noted improvement in health-related quality of life (SF-36) in the intermediate term only and depression (CES-D) and self-efficacy in the short and intermediate terms.

Mind-Body Therapies Compared With Pharmacological Therapy or With Exercise Therapy

No trial of mind-body therapy versus pharmacological therapy or versus exercise met inclusion criteria.

Harms

In the two trials of mind-body interventions, harms were poorly reported. One trial reported no serious adverse events[182] and the other reported sporadic complaints of muscle soreness and foot or knee pain.[181]

Acupuncture for Osteoarthritis of the Knee

Key Points

- There was no evidence of differences between acupuncture versus control interventions (sham acupuncture, waitlist, or usual care) on function in the short term (4 trials [excluding outlier trial], pooled SMD −0.05, 95% CI −0.32 to 0.38) or the intermediate term (4 trials, pooled SMD −0.15, 95% CI −0.30 to 0.01, I^2 = 0%) (SOE: low for short term; moderate for intermediate term). Stratified analysis showed no differences between acupuncture and sham treatments (4 trials) but moderate improvement in function compared with usual care (2 trials) short term.
- There was no evidence of differences between acupuncture versus control interventions (sham acupuncture, waitlist, or usual care) on pain in the short term (6 trials, pooled SMD −0.27, 95% CI −0.56 to 0.02, I^2=75%) or clinically meaningful differences in the intermediate term (4 trials, pooled SMD −0.16, 95% CI −0.31 to 0.02, I^2=0%) (SOE: low for short term; moderate for intermediate term). Short-term differences were significant for acupuncture versus usual care but not for acupuncture versus sham acupuncture.
- Data from one poor-quality trial were insufficient to determine the effects of acupuncture versus exercise (SOE: insufficient).
- There was no evidence of differences in risk of serious adverse events between any form of acupuncture and the control group. Worsening of symptoms (7% to 14%) and mild

bruising, swelling, or pain at the acupuncture site (1% to 18%) were most common; one case of infection at an electroacupuncture site was reported (SOE: moderate).

Detailed Synthesis

Nine trials of acupuncture for knee OA were identified that met inclusion criteria[60,203-210] (Table 29 and Appendix D). Four trials evaluated traditional acupuncture,[60,205,207,209] four electroacupuncture,[203,204,206,208] and two laser acupuncture.[205,210] Three trials compared acupuncture with usual care (provision of educational leaflets, instructions to remain on current oral medications, or no changes to their ongoing treatments)[60,203,207] and one trial each to no treatment[205] or to waitlist control.[208] Six trials compared acupuncture with sham procedures, which consisted of inactive laser treatment (red light on but no power applied),[205,210] superficial needling, or acupuncture performed at nonmeridian sites,[204,208,209] or nonpenetrating sham acupuncture.[206] No trials of acupuncture versus pharmacologic therapy or exercise were identified. Sample sizes ranged from 30 to 455 (total sample 1,364). Duration of acupuncture treatment ranged from 2 to 12 weeks, with the number of sessions ranging from 6 to 16. Four studies were conducted in Europe,[60,206,207,209] three in the United States,[203,204,208] and one study each was conducted in Australia[205] and Turkey.[210] Short-term outcomes were reported by six trials[60,203,206,208-210] and intermediate-term outcomes by four;[204,205,207,209] no trial reported outcomes over the long term.

Trials were rated good quality (for the comparison of acupuncture versus sham only).[205,208] Seven trials were rated fair quality (to include the comparison of acupuncture with no treatment/waitlist in the two trials described previously)[203-206,208-210] and two were considered poor quality[60,207] (Appendix E). The primary methodological shortcoming in the fair-quality trials was lack of blinding; additionally, the poor-quality trials suffered from unclear allocation concealment methods and high rates of attrition (30% to 35%).

Table 29. Osteoarthritis of the knee: acupuncture

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Berman, 1999[203] 1 month Duration of pain: mean 7.2 years *Fair*	A. Acupuncture + usual care (n=36): 20 minute treatments, 2/week for 8 weeks using Traditional Chinese Medicine theory; 9 acupoints points (5 local, 4 distal) with elicitation of de qi; electrical stimulation was used at local points (2.5 to 4 Hz, pulses of 1.0 ms); patients asked not to begin any new physiotherapy or exercise programs B. Usual care alone (n=37): asked to remain on their current level of oral therapy throughout the trial	A vs. B Age: 66 vs. 66 Female: 47% vs. 72% Caucasian: 92% vs. 74% BMI: 32 vs. 32 Duration of symptoms: 7.5 vs. 6.9 years WOMAC total (scale unclear): 48.4 vs. 51.4 WOMAC function (scale unclear): 34.3 vs. 34.4 Lequesne Index (0-24): 11.7 vs. 12.3 WOMAC pain (scale unclear): 9.6 vs. 9.9	A vs. B 1 month WOMAC total: 31.6 vs. 50.4, difference −18.9 (95% CI −26.5 to −11.2) WOMAC function: 23.2 vs. 36.8, difference −13.6 (95% CI −19.4 to −7.8) Lequesne Index: 9.3 vs. 12.4, difference −3.1 (95% CI −4.8 to −1.3) WOMAC pain: 5.6 vs. 9.5, difference −4.0 (95% CI −5.5 to −2.4)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Berman 2004 6 months Duration of pain: NR *Fair*	A. Acupuncture (n=186): electrical stimulation at knee acupoints (5 local and 4 distal) at low frequency (8 Hz and square biphasic pulses (0.5 ms puls width) for 20 minutes. B. Sham acupuncture (n=183): modified combined insertion (at sham points in abdominal area) and noninsertion (at 3 local and 4 distal points on the knee) procedure; mock electric stimulation was attached to sham needles at the knee for 20 minutes. Screens at the waist in both groups to facilitated blinding of knee procedures. Both groups received 8 weeks of 2 sessions per week, followed by 2 weeks of 1 session per week, 4 weeks of 1 session every other week, and 12 weeks of 1 session per month. Total of 26 weeks, 25 possible sessions.	A vs. B Age: 65 vs. 66 years Female: 63.2% vs. 61.8% non-Hispanic white: 70% vs. 70.7% Bilateral OA: 25.0% vs. 28.9% Length of diagnosis of OA <5 years: 53.8% vs. 53% 6−10 years: 19.9% vs. 18.0% >10 years: 25.8% vs. 29.0%Using opioids: 5.5% vs. 5.0% WOMAC Function (0-68): 31.31(vs. 31.29 WOMAC Pain (0-20): 8.92 vs. 8.90	A vs. B 6 months Δ from baseline, WOMAC Function: −12.42 (1.12) vs. −9.88 (0.93), P<0.01 Δ from baseline, WOMAC Pain: −3.79 (0.33) vs. −2.92 (0.30), P<0.01	A vs. B 6 months Δ from baseline, SF-36 Physical Health Score: 10.7 (1.6) vs. 8.2 (1.5), P=0.21 Δ from baseline, Patient Global Assessment: 0.45 (0.08) vs. 0.19 (0.09), P=0.02

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Hinman, 2014[205] 9 months Duration of pain: mean 7.2 years *Good (sham)* *Fair (no treatment)*	A. Needle acupuncture (n=70): combination of Western and traditional Chinese acupuncture; maximum of 6 points (4 on study limb and 2 distal points) at initial session, in other sessions points were added at therapist's discretion. Needles were left in while patient rested. B. Laser acupuncture (n=71): combination of Western and traditional Chinese acupuncture; delivered to selected points using standard Class 3B laser devices (measured output 10mW and energy output 0.2 J/point) C. No treatment (n=71): did not receive acupuncture; continued in an observational study, unaware they were in an acupuncture trial D. Sham laser acupuncture (n=70): same as true laser but no laser was emitted, only red nonlaser light at the probe tip lit up. For all acupuncture and sham groups, sessions were 20 minutes in duration, 1-2 times per week for 12 weeks (8 to 12 sessions total)	A vs. B vs. C vs. D Age: 64 vs. 63 vs. 63 vs. 64 years Female: 46% vs. 39% vs. 56% vs. 56% Duration of symptoms ≥ 10 years: 41% vs. 38% vs. 27% vs. 50% Bilateral symptoms: 64% vs. 66% vs. 51% vs. 63% Opioid use: 1% vs. 3% vs. 1% vs. 1% Previous acupuncture for knee pain: 7% vs. 13% vs. 7% vs. 3% WOMAC function (0-68): 31.3 vs. 27.0 vs. 26.1 vs. 27.5 NRS activity restriction (0-10): 5.0 vs. 4.3 vs. 4.1 vs. 4.5 WOMAC pain (0-20): 9.0 vs. 8.3 vs. 7.8 vs. 8.6 NRS average pain overall (0-10): 5.3 vs. 4.9 vs. 5.1 vs. 5.0 NRS pain on walking (0-10): 5.5 vs. 4.8 vs. 4.8 vs. 5.2 NRS pain on standing (0-10): 4.6 vs. 3.8 vs. 4.1 vs. 4.3	A vs. C 9 months WOMAC function: 22.4 vs. 23.6; adjusted difference −3.7 (95% CI −8.2 to 0.8) Activity restriction, NRS: 3.4 vs. 4.1; adjusted difference −1.1 (95% CI −2.1, −0.2) WOMAC pain: 6.7 vs. 7.4; adjusted difference −1.4 (95% CI −2.7 to 0.0) Overall Pain, NRS: 4.0 vs. 4.6; adjusted difference −0.7 (95% CI −1.6 to 0.2) Pain on walking, NRS: 4.1 vs. 4.4; adjusted difference −0.6 (95% CI −1.5 to 0.4) Pain on standing, NRS: 3.7 vs. 4.0; adjusted difference −0.5 (95% CI −1.4 to 0.5) B vs. C 9 months WOMAC function: 22.6 vs. 23.6; adjusted difference −0.6 (95% CI −1.5 to 0.3) Activity restriction, NRS: 3.7 vs. 4.1; adjusted difference −0.4 (95% CI −1.4, 0.5) WOMAC pain: 7.1 vs. 7.4; adjusted difference −0.4 (95% CI −1.8 to 1.0) Overall Pain, NRS: 4.0 vs. 4.6; adjusted difference −0.6 (95% CI −1.5 to 0.3) Pain on walking, NRS: 4.1 vs. 4.4; adjusted difference −0.3 (95% CI −1.2 to 0.7) Pain on standing, NRS: 3.8 vs. 4.0; adjusted difference −0.2 (95% CI −1.1 to 0.8) B vs. D 9 months WOMAC function: 22.6 vs. 21.6; adjusted difference 1.1 (95% CI −4.8 to 7.0) Activity restriction, NRS: 3.7 vs. 3.9; adjusted difference −0.1 (95% CI −1.1 to 1.0) WOMAC pain: 7.1 vs. 6.9; adjusted difference 0.0 (95% CI −1.9 to 1.9) Overall pain, NRS: 4.0 vs. 3.9; adjusted difference 0.0 (95% CI −0.9 to 1.0) Pain on walking, NRS: 4.1 vs. 4.2; adjusted difference 0.0 (95% CI −1.0 to 1.1) Pain on standing, NRS: 3.8 vs. 3.5; adjusted difference 0.5 (95% CI −0.7 to 1.6)	A vs. C 9 months AQoL-6D (−0.04 to 1.00): 0.74 vs. 0.77; adjusted difference: −0.01 (95% CI −0.07 to 0.05) SF−12 PCS (0-100): 41.7 vs. 38.9; adjusted difference 2.3 (95% CI −1.7 to 6.3) SF-12 MCS (0-100): 51.1 vs. 54.4; adjusted difference −0.9 (95% CI −5.2 to 3.4) Opioid use: 0% (0/70) vs. 1% (1/71) B vs. C 9 months AQoL-6D: 0.73 vs. 0.77; adjusted difference: 0.01 (95% CI −0.05 to 0.06) SF-12 PCS: 38.8 vs. 38.9; adjusted difference −0.4 (95% CI −4.4 to 3.6) SF-12 MCS: 52.1 vs. 54.4; adjusted difference −0.9 (95% CI −5.5 to 3.7) Opioid use: 2% (1/71) vs. 1% (1/71) B vs. D 9 months AQoL-6D: 0.73 vs. 0.74; adjusted difference 0.01 (95% CI −0.05 to 0.08) SF-12 PCS: 38.8 vs. 38.2; adjusted difference 0.4 (95% CI -3.8 to 4.5) SF-12 MCS: 52.1 vs. 52.8; adjusted difference −0.6 (95% CI −5.4 to 4.2) Opioid use: 2% (1/71) vs. 0% (0/70)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Jubb, 2008[206] 1 month Duration of pain: mean 10 years *Fair*	A. Acupuncture (n=34): manual acupuncture (10 minutes, total of 9 points; depth of 1-1.5 cm; elicitation of de qi) and electro-acupuncture (10 minutes each on anterior and posterior part of the knee (20 minutes total); low frequency, delivered at 6 Hz at a constant current) B. Sham (n=34): sham needles, did not penetrate the skin; electrical stimulation apparatus produced sound signals but no electrical current. Both groups received 30 minute treatments, 2/week for 5 weeks, with 10 sessions in total	A vs. B Age: 64 vs. 66 years Female: 85% vs. 76% Caucasian: 74% vs. 85% Duration of symptoms: 10 vs. 9.6 years WOMAC function (0-1700): 1028 vs. 979 WOMAC pain (0−500): 294 vs. 261 Total body pain, VAS (0-100): 49 vs. 49 Night pain knee, VAS (0-100): 61 vs. 52 Overall pain knee, VAS (0-100): 63 vs. 53 Weight-bearing pain knee, VAS (0-100): 71 vs. 60 EuroQoL VAS (0-100): 63 vs. 54	A vs. B 1 month WOMAC function: change from baseline, 137 (95% CI 20 to 255) vs. 134 (95% CI 9 to 258); difference, 4 (95% CI −163 to 171) WOMAC pain: change from baseline, 59 (95% CI 16 to 102) vs. 13 (95% CI −22 to 50); difference, 46 (95% CI −9 to 100) Weight-bearing knee pain (VAS), change from baseline, 19 (95% CI 9 to 30) vs. 8 (95% CI -1 to 16); difference, 11 (95% CI −2 to 25) Overall knee pain (VAS), change from baseline, 14 (95% CI 5 to 24) vs. 2 (95% CI −6 to 10); difference, 12 (95% CI −1 to 24) Nighttime knee pain (VAS), change from baseline, 10 (95% CI −1 to 22) vs. 5 (95% CI −3 to 14); difference, 5 (95% CI −9 to 19) General body pain (VAS), change from baseline, 5 (95% CI −5 to 15) vs. −8 (95% CI −1 to 18); difference: 13 (95% CI 0 to 27) EuroQoL-VAS: mean 63 vs. 52, P=0.98	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Lansdown, 2009[207] 9.5 months Duration of pain NR *Poor*	A. Acupuncture + usual care (n=15): once per week for up to 10 weeks, with maximum of 10 sessions, which varied in length and content (mean number of acupoints was 12, range 4-24; de qi was usually elicited; variety of stimulation methods used including tonification and reduction; retention time for needles ranged from 10-30 minutes); auxiliary treatment included moxibustion (3/14, 21%) and acupressure massage (3/14, 21%); life style advice 11/14 (79%) B. Usual care (n=15): any appointments, medications prescribed or over the counter) and interventions sought by participants from any health practitioner	A vs. B Age: 63 vs. 64 years Female: 60% vs. 60% Caucasian: 100% vs. 100% Duration of symptoms: NR WOMAC total (0-96): 31 vs. 37.5 WOMAC function (0-68): 20.5 vs. 26.3 OKS (12-60): 30.9 vs. 30.6 WOMAC pain (0-20): 7.3 vs. 7.4	A vs. B 9.5 months WOMAC total: 24.8 vs. 25.6 (17.6), adjusted difference −2.9 (95% CI 9.5 to −15.4) WOMAC function: 17.4 vs. 17.6, adjusted difference −1.36 (95% CI 8.7, −11.4) WOMAC pain: 4.7 vs. 5.3 (3.9), adjusted difference −1.4 (95% CI 0.8 to −3.6) OKS: 24.5 vs. 28.1; difference −3.6 (95% CI −9.8 to 2.6)	A vs. B 9.5 months (SF-36 scales are 0-100 for all) SF-36 physical functioning: 54.2 vs. 55.6, difference −1.4 (95% CI −21.8 to 19.0) SF-36 social functioning: 81.3 vs. 76.6, difference 4.7 (95% CI −10.6 to 20.0) SF-36 role physical: 71.4 vs. 57.8, difference 13.6 (95% CI −6.3 to 33.5) SF-36 role mental: 79.2 vs. 67.7, difference 11.5 (95% CI −5.8 to 28.8) SF-36 mental health: 73.1 vs. 65.0, difference 8.1 (95% CI −5.4 to 21.6) SF-36 vitality: 58.2 vs. 46.9, difference 11.3 (95% CI −0.22 to 22.8) SF-36 pain: 65.2 vs. 65.9, difference −0.7 (95% CI −15.6 to 14.2) SF-36 general health: 67.7 vs. 62.4, difference 5.3 (95% CI −4.8 to 15.4), EQ5D: 0.66 vs. 0.63, difference 0.03 (95% CI −0.13 to 0.19)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Suarez-Almazo, 2010[208] 1.5 months Duration of pain: mean 8 years *Good (sham)* *Fair (waitlist)*	A. Electro-acupuncture (n=153): Traditional Chinese Medicine points; TENS equipment emitted a dense disperse wave (50Hz, dispersed at 15 Hz, 20 cycles/minute); voltage increased from 5V to 60V until maximal tolerance achieved. Patients rested for 20 minutes with needles retaining and with continuing TENS. B. Sham (n= 302) 40Hz adjustable wave; voltage increased until the patient could feel it and then immediately turned off. Patients rested for 20 minutes with the needles retained, but without TENS stimulation; nonrelevant acupoints used and depth of needle placement was shallow C. Waitlist (n=72)	A vs. B vs. C Age: 65 vs. 65 vs. 64 Female: 66% vs. 65% vs. 58% Caucasian: 70% vs. 68% vs. 65% Mean duration of chronicity: 9.2 vs. 8.6 vs. 11.5 years WOMAC function (0-100): 42.9 vs. 44.6 vs. 40.1 WOMAC pain (0-100): 44.5 vs. 45.0 vs. 44.1 VAS pain (0-100): 58.3 vs. 57.4 vs. 54.6 J-MAP (1-7): 4.4 vs. 4.4 vs. 4.3	A vs. B 1.5 months WOMAC function: 31.2 (vs. 32.1; difference −0.9 (95% CI −4.4 to 2.6) WOMAC pain: 30.8 vs. 31.0; difference −0.2 (95% CI −3.8 to 3.4) VAS pain: 36.2 vs. 36.7; difference −0.5 (95% CI −6.1 to 5.1) J-MAP: 3.3 vs. 3.4; difference −0.1 (95% CI −0.39 to 0.19) A vs. C 1.5 months WOMAC function: 31.2 vs. 41.7; difference −10.5 (95% CI −15.6 to −5.5) WOMAC pain: 30.8 vs. 42.4; difference −11.6 (95% CI −16.5 to −6.7) VAS pain: 36.2 vs. 53.2; difference −17.0 (95% CI −24.7 to −9.3) J-MAP: 3.3 vs. 4.2; difference −0.9 (95% CI −1.3 to −0.5)	A vs. B 1.5 months SF-12 PCS (0-100): 39.5 vs. 38.7; difference 0.8 (95% CI −1.1 to 2.7) SF-12 MCS (0-100): 54.1 vs. 53.2; difference 0.9 (95% CI −0.8 to 2.6) A vs. C 1.5 months SF-12 PCS: 39.5 vs. 35.8; difference 3.7 (95% CI 1.0 to 6.4) SF-12 MCS: 54.1 vs. 51.6; difference 2.5 (95% CI 0.04, 5.0)
Williamson, 2007[60] 1.5 months Duration of symptoms: NR *Poor*	A. Acupuncture (n=60): conducted by a physiotherapist in a group setting (6-10 patients); needles inserted into 7 acupoints until de qi was achieved and left in place for 20 minutes; treatments were once per week for 6 weeks, with 6 sessions in total B. Combination Exercise (Physiotherapy) (n=60): supervised group (6-10 people) exercise comprised of strengthening, aerobic, stretching, and balance training; 60 minutes, once per week for 6 weeks; C. Usual care (n=61): exercise and advice leaflet; told they were enrolled in the "home exercise group"	A vs. B vs. C Age: 72 vs. 70 vs. 70 years Female: 55% vs. 52% vs. 54% BMI: 30.9 vs. 32.8 vs. 32.7 WOMAC total (scale unclear): 50.9 vs. 50.2 vs. 51.1 OKS (12-60): 40.2 vs. 39.3 vs. 40.5 Pain VAS (0-10): 7.3 vs. 6.8 vs. 6.9 HAD Anxiety (0-21): 7.3 vs. 7.5 vs. 6.7 HAD Depression (0-21): 7.1 vs. 7.1 vs. 7.4	A vs. B 1.5 months WOMAC: 48.4 vs. 49.4, difference −1.0 (95% CI −6.7 to 4.7) OKS: 38.1 vs. 38.8, difference −0.7 (95% CI −3.5 to 2.1) Pain VAS: 6.6 vs. 6.4, difference 0.22 (95% CI −0.67 to 1.11) A vs. C 1.5 months WOMAC: 48.4 vs. 52.3, difference −3.9 (95% CI −9.5 to 1.6) OKS: 38.1 vs. 40.8, difference −2.6 (95% CI −5.4 to 0.1) Pain VAS: 6.6 vs. 7.2, difference −0.66 (95% CI −1.45 to 0.12)	A vs. B 1.5 months HAD Anxiety: 6.9 vs. 7.1, difference −0.20 (95% CI −1.89 to 1.49) HAD Depression: 6.7 vs. 6.8, difference −0.03 (95% CI −1.30 to 1.24) A vs. C 1.5 months HAD Anxiety: 6.9 vs. 6.5, difference 0.34 (95% CI −1.11 to 1.8) HAD Depression: 6.7 vs. 7.1, difference, −0.41 (95% CI −1.63 to 0.8)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Witt, 2005[209] 4 and 10 months Duration of pain: mean 9.4 years *Fair*	A. Acupuncture (n=150): semi-standardized; patients received at least 6 local and at least 2 distant Traditional Acupuncture points; elicitation of de qi; needles stimulated manually at least once during each session B. Minimal acupuncture (n=76): superficial insertion of at nonacupuncture sites away from knee; manual stimulation of the needles and provocation of de qi were avoided Both groups underwent 12 sessions of 30 minutes duration, administered over 8 weeks	A vs. B Age: 65 vs. 63 years Female: 70% vs. 65% Duration of symptoms: 9.1 vs. 9.9 years Bilateral OA: 74% vs. 77% Previous acupuncture: 9% vs. 7% WOMAC total (scale unclear): 50.8 vs. 52.5 PDI (Disability) (0-70): 27.9 vs. 27.8 VAS pain (0-100): 64.9 vs. 68.5	A vs. B 4 months WOMAC total: 30.4 vs. 36.3; difference −5.8 (95% CI −12.0 to 0.3) WOMAC physical function: 30.4 vs. 36.5; difference −6.2 (95% CI −12.4 to 0.1) PDI: 18.6 vs. 22.8; difference −4.2 (95% CI −8.3 to −0.0) WOMAC pain: 28.9 vs. 33.8; difference −4.8 (95% CI −11.2 to 1.6) 10 months WOMAC Total: 32.7 vs. 38.4; difference −5.7 (95% CI −12.1 to 0.7) WOMAC physical function: 33.0 vs. 38.9; difference −5.9 (95% CI −12.5 to 0.7) PDI: 20.0 vs. 23.6; difference −3.6 (95% CI −7.7 to 0.5) WOMAC pain: 30.0 vs. 33.5; difference −3.5 (95% CI −10.0 to 3.0)	A vs. B 4 months SF-36 Physical: 35.1 vs. 33.0; difference 2.1 (95% CI −0·5 to 4.8) SF-36 Mental: 52.6 vs. 51.7; difference 0.9 (95% CI 2.3 to 4.2) ADS (Depression): 48.2 vs. 48.7; difference −0·5 (95% CI −3.6 to 2.5) 10 months SF-36 Physical: 35.0 vs. 32.8; difference 2.2 (95% CI −0.6 to 5,1) SF-36 Mental: 52.9 vs. 51.1; difference 1.9 (95% CI −1.3 to 5.1) ADS: 48.6 vs. 49.8; difference −1.2 (95% CI −4.3 to 1.8)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Yurtkuran, 2007[210] 3 months Duration of pain: mean 5.4 years *Fair*	A. Laser acupuncture (n=28): applied to the medial side of the knee to the acupuncture point on the sural nerve; infrared 27 GaAs diode laser instrument (output 4 mW, 10 mW/cm2 power density, 120-sec treatment time and 0.48 J dose per session); irradiation was pulsed (duration of 1 pulse was 200 nanosecond), and only one point was treated with contact application technique. B. Sham laser acupuncture (n=27): performed in the same location and under the same conditions as the true laser acupuncture; patients could see a red light but the machine was turned off Both groups: 20 minutes sessions, 5 days per week for 2 weeks (total duration of therapy was 10 days, 10 sessions total); in addition, all patients received a home-based, standardized exercise program	A vs. B Age: 52 vs. 53 years Female: 96% vs. 96% Duration of symptoms: 5.2 vs. 5.6 months WOMAC total: 66.5 vs. 51.3 WOMAC physical function: 47.5 vs. 35.3 WOMAC pain: 13.7 vs. 11.6 VAS pain on movement (0-10): 6.5 vs. 6.1	A vs. B 2.5 months WOMAC total: 62.4 vs. 50.6, difference 11.8 (95% CI −1.0 to 24.6) WOMAC physical function: 44.2 vs. 35.3, difference 11.9 (95% CI 2.9 to 20.9) WOMAC pain: 13.5 vs. 11.5, difference 2.0 (95% CI −1.3 to 5.3) VAS pain on movement: 5.6 vs. 4.8, difference 0.8 (95% CI −0.9 to 2.5)	A vs. B 2.5 months NHP (0-38): 7.6 vs. 6.4. difference 1.2 (95% CI −2.1 to 4.4)

ADS = Anxiety and Depression Scale; AIMS = Arthritis Impact Measurement Scale; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; CI = confidence interval; HAD = Hospital Anxiety and Depression Scale; HRQoL = health-related quality of life; J-MAP = Joint-specific Multidimensional Assessment of Pain; NHP = Nottingham health profile; NR = not reported; NRS = numeric rating scale; NS = not statistically significant; OA = osteoarthritis; OKS = Oxford Knee Score; SF-36/12 = Short Form 36/12; VAS = Visual Analog Scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis index

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Acupuncture Compared With Usual Care, Waitlist, or Sham

Functional Outcomes. There was no evidence of differences between acupuncture versus control interventions (sham acupuncture, usual care, waitlist, no treatment) on WOMAC function score in the short term (5 trials, pooled SMD −0.18, 95% CI −0.55 to 0.20, I^2=82%)[203,206,208-210] (Figure 35). All trials were considered fair quality. Removal of one outlier trial (Berman 1999)[203] attenuated the effect estimate size (4 trials, pooled SMD −0.05, 95% CI −0.32 to 0.38); results remained insignificant. No differences were found when the results were analyzed by the type of acupuncture used: electroacupuncture (3 trials, pooled SMD −0.34, 95% CI −1.17 to 0.46),[203,206,208] standard needle acupuncture (SMD −0.28, 95% CI −0.55 to 0.00),[209] or laser acupuncture (SMD 0.55, 95% CI −0.01 to 1.10)[210] compared with control interventions. When

stratified by control type no differences were found between any form of acupuncture and sham treatment (4 trials, pooled SMD −0.02, 95% CI −0.28 to 0.39);[206,208-210] however, when acupuncture was compared with waitlist and usual care, estimates suggested moderate improvement in function (2 trials, pooled SMD −0.74, 95% CI −1.40 to −0.24, plot not shown).[203,208] In one small, fair-quality trial[210] of low-level laser acupuncture the authors reported a difference in WOMAC function score that favored the sham control (Table 29).

Similarly, based on WOMAC total score, there were no differences in short-term function between acupuncture and sham, waitlist, and usual care across trials (4 trials, pooled SMD −0.30, 95% CI −0.81 to 0.21, I^2=85%, plot not shown).[60,203,209,210] Removal of one outlier trial (Berman 1999)[203] attenuated the effect estimate size (3 trials, pooled SMD −0.10, 95% CI −0.54 to 0.49); results remained insignificant. Stratification by acupuncture type, control type, and exclusion of one poor-quality trial yielded similar estimates. Results according to other measures of function were mixed. In two small, fair-quality trials authors reported significant results (Table 29), one favoring electroacupuncture compared with usual care based on the Lequesne Index (0 to 24 scale),[203] and the second favoring the sham control comparing low-level laser acupuncture based on the WOMAC total score.[210] Five additional trials reported no differences between acupuncture and any of the control conditions across other measures of function[60,205-207,209] (Table 29).

In the intermediate term, there was no difference between acupuncture versus control conditions (sham acupuncture, usual care, waitlist) on the WOMAC function score (4 trials, pooled SMD −0.15, 95% CI −0.30 to −0.01, I^2=0%)[204,205,207,209] (Figure 35); the estimate using the more conservative proximal likelihood method yielded a SMD of −0.15 (95% CI −0.31 to 0.02). Estimates were similar when stratified by study quality, acupuncture type, and control type; however, sensitivity analyses were limited by the small number of trials. Similarly, no differences in WOMAC total score were found for standard needle acupuncture versus usual care or sham at intermediate-term followup (2 trials, pooled SMD −0.23, 95% CI −0.49 to 0.03, I^2=0%, plot not shown).[207,209] Across other measures of function, no differences were seen at intermediate term between standard needle acupuncture versus sham acupuncture on the Pain Disability Index (MD −3.5 on a 0-70 scale, 95% CI −7.7 to 0 .5) in one fair-quality trial[209] or versus usual care on the Oxford Knee Score (MD 3.6 on a 12 to 60 scale, 95% CI −9.8 to 2.6) in one small poor-quality trial.[207]

No trials reported data on long-term function.

Pain Outcomes. There was no evidence of differences between acupuncture versus control interventions (sham acupuncture, usual care, waitlist) on pain in the short term (6 trials, pooled SMD −0.27, 95% CI −0.56 to 0.02, I^2=75%)[60,203,206,208-210] (Figure 36). All but one trial used the WOMAC pain score. Removal of one outlier trial (Berman 1999)[203] attenuated the effect estimate size (5 trials, pooled SMD −0.15, 95% CI −0.29 to 0.00); results remained insignificant. Estimates were similar after exclusion of one poor-quality trial and for stratification by acupuncture type and for analyses of VAS or NRS instead of WOMAC pain score if more than one pain measure was reported. When stratified by control type, no differences were seen between acupuncture and sham acupuncture (4 trials, pooled SMD −0.06, 95% CI −0.24 to 0.14);[206,208-210] however, when acupuncture was compared with waitlist or usual care, the

estimate suggested moderate effects on pain (2 trials, pooled SMD −0.68, 95% CI −1.28 to −0.15).[203,208]

There were no clinically meaningful differences between acupuncture and control interventions for pain in the intermediate term (4 trials, pooled SMD −0.16, 95% CI −0.31 to −0.02, I^2=0%);[204,205,207,209] individually no trial reached statistical significance (Figure 36). Stratification based on acupuncture type, type of control intervention, and study quality yielded similar results.

No trial reported data on long-term pain.

Other Outcomes. Data on the effects of acupuncture on quality of life were limited (plots not shown). A slight effect favoring acupuncture versus control conditions (sham acupuncture, usual care, waitlist, no treatment) was seen for the SF-12/SF-36 PCS (0-100 scale) in both the short term (2 trials, pooled difference 1.6, 95% CI 0.08 to 3.11, I^2=0%)[208,209] and the intermediate term (2 trials, pooled difference 1.94, 95% CI 0.03 to 3.86, I^2=0%),[205,209] but no difference was seen in the SF-12/SF-36 MCS (0-100 scale) at either timepoint: short term (2 trials, pooled difference 1.14, 95% CI −0.27 to 2.56, I^2=0%)[208,209] and intermediate term (2 trials, pooled difference −0.25, 95% CI −4.05 to 3.54, I^2=70.8%).[205,209] For individual trials, the effects were slight and not statistically significant for either outcome (SF-12 or SF-36 PCS or MCS). There were no differences between acupuncture and control interventions on other quality of life measures or on measures of anxiety or depression over either the short or intermediate term (Table 29).

In one trial,[205] a small (1%) change in opioid use at intermediate term was seen with needle acupuncture (decrease from 1% to 0%), laser acupuncture (decrease from 3% to 2%), and sham acupuncture (decrease from 1% to 0%) while use remained the same in the no treatment group (Table 29).

Acupuncture Compared With Pharmacological Therapy

No trial of acupuncture versus pharmacological therapy met inclusion criteria.

Acupuncture Compared With Exercise Therapy

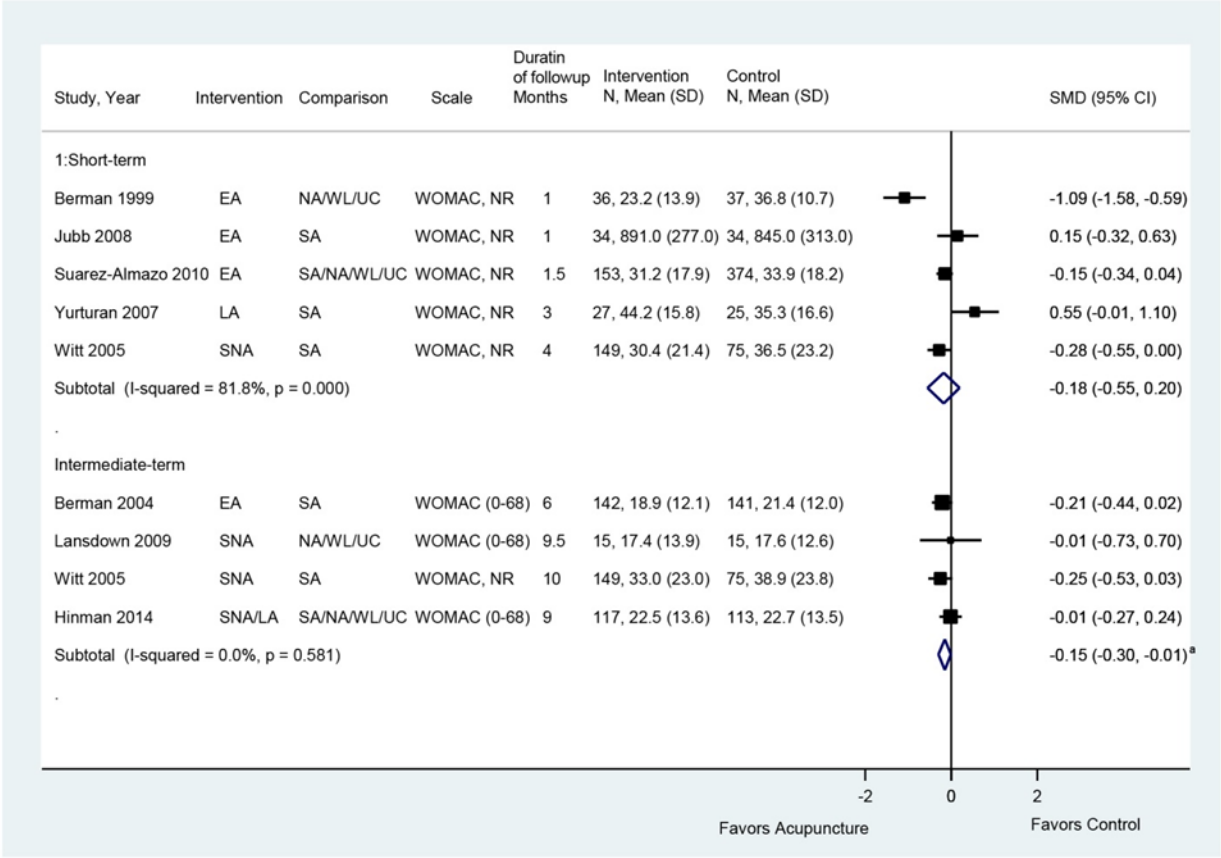
Data were insufficient from one poor-quality trial (n=120)[60] to evaluate the effects of weekly acupuncture versus 60 minutes of combination exercise (strengthening, aerobics, stretching, and balance training) for 6 weeks for knee OA (Table 29 and Appendix D). Methodological limitations included lack of patient or care provider blinding, unclear adherence, unacceptable attrition, and differential loss to followup (Appendix E). There were no differences between groups with regard to function on the Oxford Knee Score questionnaire (difference −0.7, 95% CI −3.5 to 2.1 on 12-60 scale) or WOMAC score (difference −1.0, 95% CI −6.7 to 4.7; scale not provided by author). Similarly there was no difference between treatments for VAS pain on a 0 to 10 scale (difference 0.22, 95% CI −0.67 to 1.11) or for anxiety or depression based on the Hospital Anxiety and Depression Scale.

Harms

All trials reported adverse events. One trial reported similar rates of serious adverse events in patients who received real versus sham acupuncture (2.1% vs. 2.7%, respectively; RR 0.75, 95% CI 0.13 to 4.39), to include hospitalizations and one case of death from myocardial infarction in the control group; none were considered to be related to the study condition or treatment.[209] All other events reported were classified as mild and there was no apparent difference in risk of adverse events between any form of acupuncture and the control groups. The most common

adverse events reported were worsening of symptoms (7% to 14%) in three trials[205,207,208] and mild bruising, swelling, or pain at the acupuncture site (1% to 18%) in five trials.[60,205,207-209] One trial reported one case of an infection at the electroacupuncture site (n=455 for real and sham acupuncture groups).[208] In only one trial did an adverse event (not treatment related) lead to withdrawal: one patient (3%) in the acupuncture group had a flare-up of synovitis (nonseptic).[206]

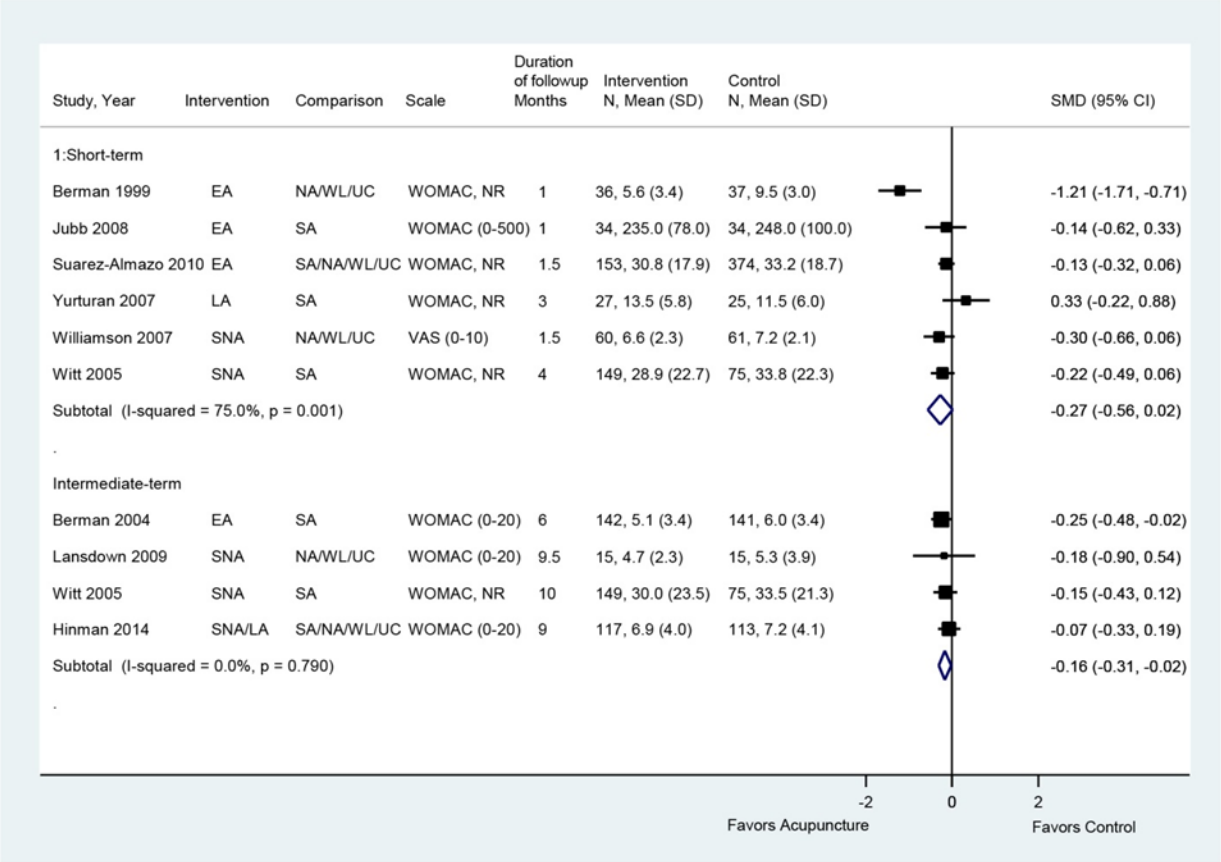
Figure 35. Acupuncture versus usual care, waitlist, sham, or a placebo intervention in osteoarthritis of the knee: effects on function



A = electroacupuncture; LA = laser acupuncture; NR = not reported; SA = sham acupuncture; SNA = standard needle acupuncture; SD = standard deviation; SMD = standardized mean difference; NR = not reported; UC = usual care; WL = waitlist; WOMAC = Western Ontario and McMaster's Universities Osteoarthritis Index

[a] The estimate using the more conservative proximal likelihood method yielded a SMD of −0.15 (95% CI −0.31 to 0.02)

Figure 36. Acupuncture versus usual care, waitlist, sham, or a placebo intervention for osteoarthritis of the knee: effects on pain



EA = electroacupucnture; LA = laser acupuncture; NR = not reported; SA = sham acupuncture; SNA = standard needle acupuncture; SD = standard deviation; SMD = standardized mean difference; NR = not reported; UC = usual care; WL = waitlist; WOMAC = Western Ontario and McMaster's Universities Osteoarthritis Index

Exercise for Osteoarthritis of the Hip

Key Points

- Exercise was associated with a slight improvement in function versus usual care in the short term (3 trials, pooled SMD −0.33, 95% CI −0.53 to −0.12, I^2=0.0%), intermediate term (2 trials, pooled SMD −0.28, 95% CI −0.50 to −0.05, I^2=0.0%), and long term (1 trial, SMD −0.37, 95% CI −0.74 to −0.01) (SOE: low for short and intermediate term, insufficient for long term).
- Exercise tended toward slightly greater improvement in short-term pain compared with usual care (3 trials, pooled SMD −0.34, 95% CI −0.63 to −0.04, I^2=48.2%) but the results were no longer significant at intermediate term (2 trials, pooled SMD −0.14, 95% CI −0.37 to 0.08, I^2=0%) or long term (1 trial, SMD −0.25, 95% CI −0.62 to 0 .11) (SOE: low for short and intermediate term, insufficient for long term).
- Evidence for harms was insufficient in trials of exercise with only two trials describing adverse events. However, no serious harms were reported in either trial (SOE: insufficient).

Detailed Synthesis

Four trials of exercise therapy for hip OA met the inclusion criteria; three were conducted in Europe[61-63] and the other in New Zealand[40] (Table 30 and Appendix D). Three trials evaluated participants with chronic hip pain diagnosed as OA using American College of Radiology criteria[40,61,63] and one assessed participants with hip OA diagnosed clinically who were on a waitlist for hip replacement.[62] Sample sizes ranged from 45 to 203 (total number randomized=477). Across trials, participants were predominately female (>50%) with mean ages ranging from 64 to 69 years. Three trials were conducted in Europe[61-63] and the other in New Zealand.[40]

All trials compared exercise with usual care, defined as care routinely provided by the patient's primary care physician, which could include physical therapy referral. Two trials also provided education about hip OA to all participants.[61,63] The exercise interventions included 8 to 12 supervised sessions of 30 to 60 minutes duration once per week over 8 to 12 weeks; the interventions were comprised of strengthening and stretching exercises (all studies), as well as neuromuscular control exercises in one trial[40] and endurance exercise in another.[63] All trials reported compliance rates with the scheduled exercise sessions between 76 and 88 percent. However, in one trial,[40] although 88 percent of patients completed more than 80 percent of the scheduled sessions, only 44 percent of participants returned logbooks to demonstrate compliance with the recommended home exercises.

Three trials were rated fair quality[40,61,63] and one was rated poor quality[62] (Appendix E). In all trials, the nature of the intervention and control precluded blinding of participants and researchers; patient-reported outcomes were therefore not blinded. Additionally, in the poor-quality trial,[62] concealed allocation was unclear and outcomes were poorly reported, as were attrition rates, which were substantial for pain (68%) and function (73%) outcomes.

Table 30. Osteoarthritis of the hip: exercise

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Abbott, 2013[40] 9.75 months Duration of pain: 9 months *Fair*	A. Exercise therapy (n=51/22 hip OA): 7 sessions of strengthening, stretching, and neuromuscular control over 9 weeks, with 2 booster sessions at week 16. Individual exercises prescribed as needed. Home exercise prescribed 3 times weekly B. Usual care (n=51/23 hip OA): Routine care provided by patient's own GP and other health care providers	A vs. B (total population, includes knee OA) Age: 67 vs. 66 Females: 49% vs. 63% % hip OA: 43.1% vs. 45.1% WOMAC (0-240): 95.5 vs. 93.8	A vs. B (hip OA only) <u>9.75 months</u> WOMAC mean change from baseline: −12.4 vs. 6.6	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Juhakoski, 2011[61] 3, 9, and 21 months Duration of pain: Mean 8.3 to 8.5 years *Fair*	A. Exercise + usual care (n=57): 12 strengthening and stretching exercise sessions of 45 minutes once per week, with 4 booster sessions 1 year later B. Usual care (n=56): normal routine care offered by patient's own GP. All patients attended an hour-long session on basic principles of nonoperative treatment of hip OA	A vs. B Age: 67 vs. 66 years Female: 68% vs. 72% Duration of pain: 8.3 to 8.5 years WOMAC function (0-100): 24.7 vs. 28.9 WOMAC pain (0-100): 21.5 vs. 29.1	A vs. B <u>3 months</u> WOMAC function: 22.6 vs. 30.1, (MD −7.5, 95% CI −13.9 to −1.0) WOMAC pain: 23.4 vs. 28.9 (MD −5.5, 95% CI −13.0 to 2.0) <u>9 months</u> WOMAC function: 24.6 vs. 27.6 (MD −3.0, 95% CI −9.2 to 3.2) WOMAC pain: 22.9 vs. 25.0 (MD −2.1, 95% CI −9.2 to 5.0) <u>21 months</u> WOMAC function: 24.4 vs. 30.0 (MD −5.6, 95% CI −12.9 to 1.7) WOMAC pain: 24.1 vs. 27.9 (MD −3.8, 95% CI −12.0 to 4.4)	A vs. B <u>3 months</u> Weak opioid[b] use (P=0.73): Not using: 82.5% vs. 87.7% 1-6 times/week: 10.5% vs. 8.8% Daily: 7.0% vs. 3.5% <u>9 months</u> Mean doctor visits for hip OA: 0.5 vs. 0.8, P=0.07 Mean physiotherapy visits for hip OA: 1.3 vs. 2.0, P=0.05 Weak opioid[b] use (P=0.12): Not using: 81.0% vs. 93.1% 1-6 times/week: 10.4% vs. 1.7% Daily: 8.6% vs. 5.2% <u>21 months</u> Mean doctor visits (between 9 and 21 month followup) for hip OA: 0.5 vs. 1.1, P=0.05 Mean physiotherapy visits (between 9 and 21 month followup) for hip OA: 0.4 vs. 1.3, P<0.001 Weak opioid[b] use (P=0.70): Not using: 80.7% vs. 85.2% 1-6 times/week: 12.3% vs. 7.4% Daily: 7.0% vs. 7.4%

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Tak,[62] 2005[c] 6 months, 3 years Mean duration of pain: NR *Poor*	A. Exercise (n=45): Eight weekly group sessions of strength training, information on a home exercise program, ergonomic advice, and dietary advice B. Usual care (n=49): Subject-initiated contact with GP. Reference group (n=NR) consisting of weekly stress management sessions for 10 weeks	A vs. B Age: 68 vs. 69 Female: 64% vs. 71% HHS (0-100): 71.1 vs. 71.0 GARS (18-72): 22.8 vs. 25.3 SIP-136 physical (0-100): 7.2 vs. 7.6 Pain VAS (0-10): 3.8 vs. 4.2 HHS pain subscale (0-44): 27.9 vs. 28.8	A vs. B <u>3 months</u> HHS: 75.4 vs. 71.1, (MD 4.3, 95% CI −2.2 to 10.8) GARS: 23.7 vs. 26.3, (MD −2.6, 95% CI −6.0 to 0.8) SIP-136 physical: 5.1 vs. 8.4, (MD −3.3, 95% CI −5.3 to −1.3) Pain VAS: 3.5 vs. 5.1, (MD −1.6, 95% CI −2.6 to −0.6) HHS pain subscale: 29.6 vs. 26.9, (MD −0.9, 95% CI −4.7 to 2.9)	A vs. B <u>3 months</u> QoL VAS (0-10): 5.0 vs. 4.2, (MD 1.4, 95% CI −0.2 to 3.0) HRQoL (7-39): 28.6 vs. 27.3, (MD 0.9, 95% CI −0.4 to 2.2)
Teirlinck, 2016[63] 3 and 9 months Duration of pain: Median 1 year *Fair*	A. Exercise therapy (n=101): 12 sessions over 3 months consisting of strengthening, stretching, and aerobic exercise B. Usual care (n=102): Routine care provided by patient's own GP	A vs. B Age: 64 vs. 67 Females: 62% vs. 55% Pain duration median (IQR): 365 (810) vs. 365 (819) days HOOS function (0-100): 35.4 vs. 32.2 HOOS pain (0-100): 37.6 vs. 38.9 ICOAP constant pain (0-20): 5.4 vs. 5.8 ICOAP intermittent pain (0-24): 8.0 vs. 8.4 ICOAP total pain (0-100): 30.4 vs. 32.2	A vs. B <u>3 months</u> HOOS function: 30.8 vs. 35.3, (Adj MD −2.4, 95% CI −6.7 to 1.9) HOOS pain: 34.4 vs. 37.2, (Adj MD −2.2, 95% CI −6.2 to 1.7) ICOAP constant pain: 4.0 vs. 5.3, (Adj MD −0.9, 95% CI −1.9 to 0.1) ICOAP intermittent pain: 7.0 vs. 7.9 , (Adj MD −0.6, 95% CI −1.7 to 0.6) ICOAP total pain: 24.9 vs. 29.8, (Adj MD −3.3, 95% CI −8.0 to 1.4) <u>9 months</u> HOOS function: 26.8 vs. 34.2, (Adj MD −3.0, 95% CI −6.7 to 0.2) HOOS pain: 31.6 vs. 34.6, (Adj MD −1.6, 95% CI −6.2 to 3.0) ICOAP constant pain: 3.6 vs. 4.7, (Adj MD −0.7, 95% CI −1.7 to 0.4) ICOAP intermittent pain: 6.1 vs. 7.2, (Adj MD −0.6, 95% CI −1.8 to 0.6) ICOAP total pain: 22.2 vs. 27.0, (Adj MD −2.8, 95% CI −7.6 to 2.0)	A vs. B <u>3 months</u> EuroQol 5D−3L (−0.329−1.0): 0.77 vs. 0.76, (Adj MD −0.01, 95% CI −0.06 to 0.04) <u>9 months</u> EuroQol 5D-3L: 0.78 vs. 0.78, (Adj MD −0.01, 95% CI −0.06 to 0.04) Total hip replacements: 6 vs. 9

CI = confidence interval; GARS = gait abnormality rating scale; GP = general practitioner; HHS = Harris Hip Score; HOOS = hip disability and osteoarthritis outcome score; HRQoL = Health Related Quality of Life; ICOA = intermittent and constant pain score; MD = mean difference; NR = not reported; OA = osteoarthritis; QoL = quality of life; SIP-136 = Sickness Impact Profile-136; VAS = visual analog scale; WOMAC= Western Ontario and McMaster Universities Osteoarthritis Index

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period
[b] Authors defined weak opioids as tramadol or codeine
[c] Cluster RCT where clusters were formed from participants selecting a time that best fit their schedule

Exercise Compared With Usual Care

Exercise was associated with a slightly greater effect on function versus usual care in the short term (3 trials, pooled SMD −0.33, 95% CI −0.53 to −0.12, I^2=0.0%),[61-63] intermediate term (2 trials, pooled SMD −0.28, 95% CI −0.50 to −0.05, I^2=0.0%)[61,63] and long term (1 trial, SMD −0.37, 95% CI −0.74 to −0.01)[61] (Figure 37). The intermediate-term findings were consistent with the additional trial not included in the meta-analysis (authors did not provide sufficient data),[40] although the small improvement in function in this trial did not reach statistical significance in those with hip OA. The small number of trials precluded meaningful sensitivity analysis.

Exercise tended toward slightly greater improvement on short-term pain compared with usual care (3 trials, pooled SMD −0.34, 95% CI −0.63 to −0.04, I^2=48%)[61-63] (Figure 38), but not at intermediate term (2 trials, pooled SMD −0.14, 95% CI −0.37 to 0.08, I^2=0%).[61,63] There was moderate heterogeneity between studies and the short-term improvement in pain was observed in only one poor-quality study,[62] whereas the two fair-quality studies did not demonstrate any significant differences in short-term pain relief.[61,63] There were no identifiable differences in methodology between the studies to explain these inconsistent findings, although the poor-quality study only reported pain outcomes for 68 percent of participants, which may have biased results. There was no difference between exercise versus usual care in the long term based on a single study (SMD −0.25, 95% CI −0.62 to 0.11).[61] The small number of trials precluded meaningful sensitivity analysis.

Data on effects of exercise on quality of life were limited and were reported in only two trials.[62,63] One fair-quality trial[63] found no differences in health-related quality of life between groups in the short term and intermediate term and one poor-quality study[62] found no differences between groups in the short term. One fair-quality study found no differences between groups in terms of opioid use at any time point (proportion of patients using tramadol or codeine daily: 7.0% vs. 3.5% at 3 months, 8.6% vs. 5.2% at 9 months, and 7.0% vs. 7.4% at 21 months, P=0.73), but did report slightly fewer followup physical therapy visits in the exercise group in the intermediate and long terms[61] (Table 30).

There was insufficient evidence to determine effects of duration of exercise therapy or number of sessions on outcomes.

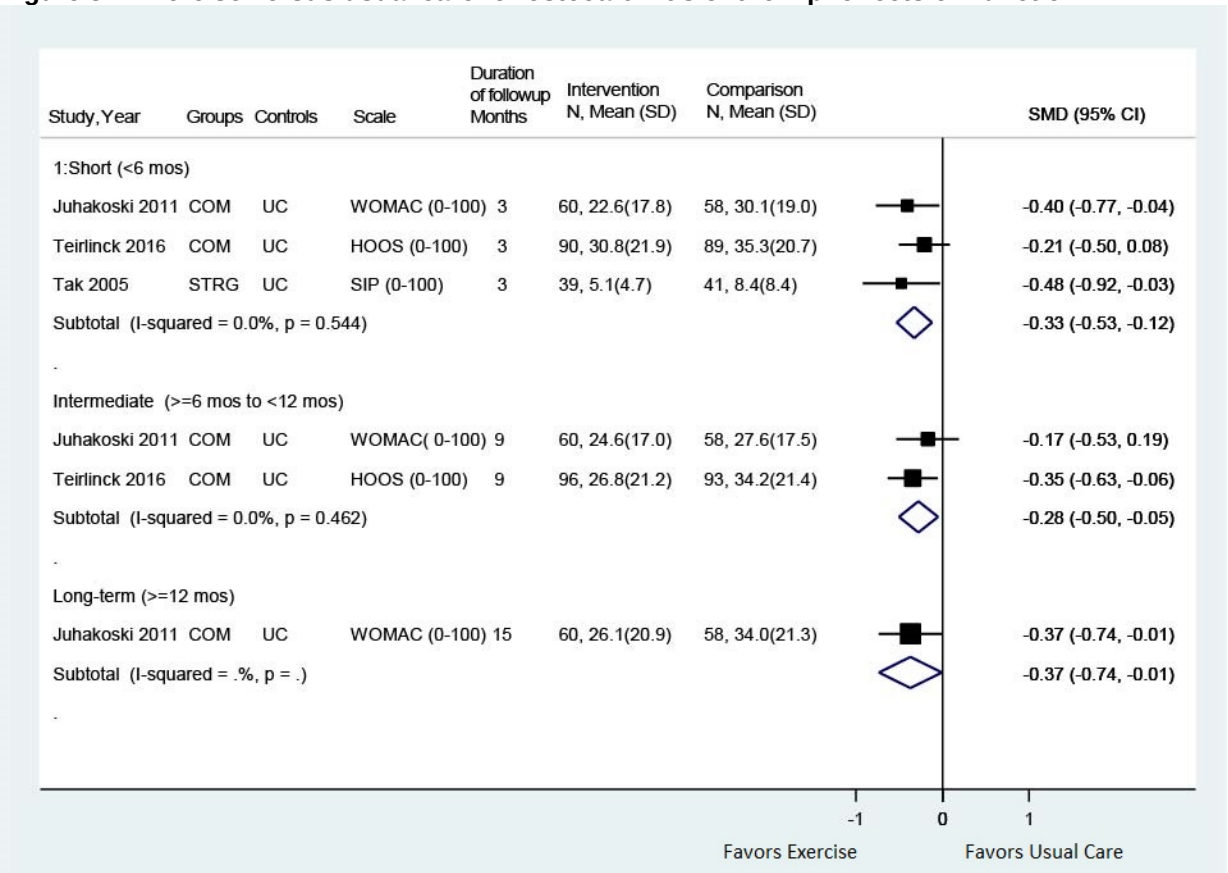
Exercise Compared With Pharmacological Therapy or With Other Nonpharmacological Therapies

No trial of exercise versus pharmacological therapy met inclusion criteria. Findings for exercise versus other nonpharmacological therapies are addressed in the sections for other nonpharmacological therapies.

Harms

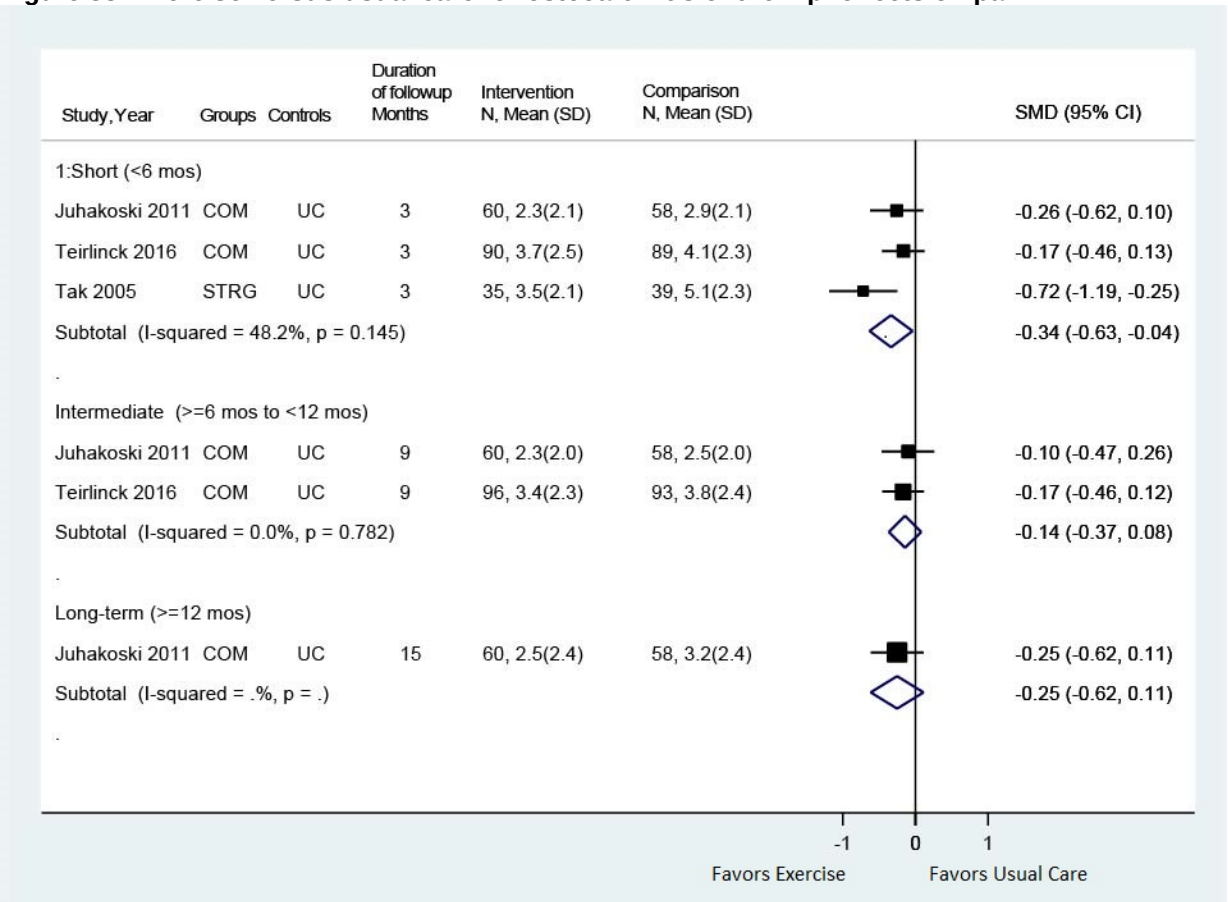
Only two exercise trials reported on harms, and neither reported adverse events in either the exercise group or usual care groups.[40,62]

Figure 37. Exercise versus usual care for osteoarthritis of the hip: effects on function



CI = confidence interval; COM = combination exercise therapy; HOOS = Hip disability and Osteoarthritis Outcomes Score; SD = standard deviation; SIP = Sickness Impact Profile physical function score; SMD = standardized mean difference; STRG = strength training exercise; UC = usual care; WOMAC = Western Ontario and McMaster's Universities Osteoarthritis Index

Figure 38. Exercise versus usual care for osteoarthritis of the hip: effects on pain



CI = confidence interval; COM = combination exercise therapy; SD = standard deviation; SMD = standardized mean difference; STRG = strength training exercise; UC = usual care

Manual Therapies for Osteoarthritis of the Hip

Key Points

- There were insufficient data to determine the effects or harms of manual therapy compared with usual care at intermediate term. No effect size could be calculated (SOE: insufficient).
- Manual therapy was associated with slight improvements in short-term (MD 11.1, 95% CI 4.0 to 18.6, 0-100 scale Harris Hip Score) and intermediate-term (MD 9.7, 95% CI 1.5 to 17.9) function versus exercise (SOE: low).
- Manual therapy was associated with a small effect on pain in the short term (MD −0.72 [95% CI −1.38 to −0.05] for pain at rest and −1.21 [95% CI −2.29 to −0.25] for pain walking) versus exercise (SOE: low). The impact on pain is not clear at intermediate term; there was no evidence of differences in pain at rest (adjusted difference −7.0, 95% CI −20.3 to 5.9 , 0-100 scale) but there was small improvement in pain while walking (adjusted difference −12.7, 95% CI −24.0 to −1.9) (SOE: insufficient).
- No trials evaluated manual therapies versus pharmacological therapy.

- One trial reported that no treatment related-serious adverse events were detected and in the other, no difference in study withdrawal due to symptom aggravation was seen between manual therapy and exercise (RR 1.42, 95% CI 0.25 to 8.16) (SOE: low).

Detailed Synthesis

We identified two trials (n=69 and 109) of manual therapy for hip OA that met inclusion criteria (Table 31 and Appendix D); one was conducted in New Zealand[40] and the other in the Netherlands.[163] Mean patient age ranged from 66 to 72 years and females comprised 49 to 72 percent of the populations. Both trials required a diagnosis of hip OA meeting the American College of Rheumatology (ACR) criteria for inclusion. The duration of manual therapy ranged from 5 to 16 weeks with a total of nine sessions in both groups; in one trial this included seven sessions over the first 9 weeks and two booster sessions at week 16.[40] One trial compared manual therapy to usual care (continued routine care from a general practitioner and other providers)[40] and both trials compared manual therapy to combination exercise programs.[40,163] The number of exercise sessions matched the manual therapy group of that respective study. All participants were prescribed a home exercise program three times per week. One trial reported short-term outcomes[163] and both reported intermediate-term outcomes.

Both trials were rated fair quality (Appendix E). Compliance with the intervention was acceptable in all groups, and the methodological shortcomings of these trials included a lack of blinding for the patients and care providers.

Table 31. Osteoarthritis of the hip: manual therapy

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Abbott, 2013[40] 9.75 months Duration of diagnosis: 2.6 years *Fair*	A. Manual therapy (n=54/24 hip OA): 7 manual therapy sessions in 9 weeks with 2 additional booster sessions B. Exercise (n=51/22 hip OA), 7 exercise sessions in 9 weeks with 2 additional booster sessions C. Usual care (n=51/23 hip OA)	A vs. B vs. C (total population, includes knee OA) Age: 67 vs. 67 vs. 66 years Female: 49% vs. 52% vs. 58% Percent knee OA: 56% vs. 57% vs. 55% Percent hip OA: 44% vs. 43% vs. 45% Percent both hip OA and knee OA: 22% vs. 20% vs. 26% Baseline WOMAC (0-240): 114.8 vs. 95.5 vs. 93.8	A vs. B (hip OA only) 9.75 months WOMAC, mean change from baseline: −22.9 vs. −12.4, P=NR A vs. C (hip OA only) 9.75 months WOMAC, mean change from baseline: −22.9 vs. 6.6, P=NR	None

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Hoeksma, 2004[163] 3 and 6 months Duration of symptoms: mean NR *Fair*	A. Manual therapy (n=56): Sessions consisted of stretching followed by traction manipulation in each limited position (high velocity thrust technique). B. Exercise therapy (n=53): Sessions implemented exercises for muscle functions, muscle length, joint mobility, pain relief, and walking ability and were tailored to the specific needs of the patient. Instructions for home exercises were given. Both groups received 2 sessions per week for 5 weeks (9 sessions in total).	Age: 72 vs. 71 years Females: 68% vs. 72% Symptom duration of 1 month to 5 years: 76% vs. 81% Severe OA on radiography: 45% vs. 38% HHS (0-100): 54 vs. 53 Pain at rest VAS (0-100): 22.5 vs. 23.0 Pain walking VAS (0-100): 34.0 vs. 28.8	A vs. B <u>3 months</u> HHS: 68.4 vs. 56.0, adjusted difference 11.1, 95% CI 4.0 to 18.6 Pain at rest VAS: 19.1 vs. 26.9, adjusted difference −7.2, 95% CI −13.8 to −0.5 Pain walking VAS: 16.4 vs. 23.7, adjusted difference −12.1, 95% CI −22.9 to −2.5 <u>6 months</u> HHS: 70.2 vs. 59.7, adjusted difference 9.7, 95% CI 1.5 to 17.9 Pain at rest VAS: 14.0 vs. 21.6, adjusted difference -7.0, 95% CI −20.3 to 5.9 Pain walking VAS: 17.0 vs. 24.3, adjusted difference −12.7, 95% CI −24.0 to −1.9	A vs. B <u>3 months</u> SF-36 physical function: 45.3 vs. 46.6, adjusted difference −2.1, 95% CI −11.7 to 7.7 SF-36 role physical function: 25.4 vs. 29.8, adjusted difference −23.5 to 10.2 SF-36 bodily pain: 47.4 vs. 46.1, adjusted difference −3.2, 95% CI −13.1 to 6.8 <u>6 months</u> SF-36 physical function: 50.4 vs. 45.3, adjusted difference 3.1, 95% CI −4.1 to 10.5 SF-36 role physical function: 36.7 vs. 32.4, adjusted difference 2.2, 95% CI −16.8 to 21.1 SF-36 bodily pain: 51.4 vs. 49.9, adjusted difference −1.5, 95% CI −11.1 to 7.7

CI = confidence interval; HHS = Harris Hip Score; NR = not reported; OA = osteoarthritis; SF-36 = Short Form 36 Questionnaire; VAS = visual analog scale; WOMAC =Western Ontario and McMaster Universities Arthritis Index
[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Manual Therapies Compared With Usual Care

A single fair-quality trial (n=69 with hip OA)[40] found that manual therapy resulted in an improvement in function at intermediate term using the total WOMAC score (0 to 240) in the manual therapy group (mean change from baseline −22.9, 95% CI −43.3 to −2.6), while the usual care group showed little change from baseline (mean change −7.9, 95% CI −30.9 to 15.3). Lack of information on the number of patients precluded calculation of effect size, and results of statistical testing between groups was not presented.

Manual Therapies Compared With Pharmacological Therapy

No trial of manual therapy versus pharmacological therapy met inclusion criteria.

Manual Therapies Compared With Exercise

One trial found that manual therapy resulted in slightly better short-term function compared with exercise (adjusted MD on the 0-100 scale Harris Hip Score [HHS] of 11.1, 95% CI 4.0 to 18.6). Regarding intermediate-term function, manual therapy conferred a slight benefit in both trials. The adjusted MD on the HHS was 9.7 (95% CI 1.5 to 17.9) in one trial.[163] The other trial compared function using the total WOMAC score (0 to 240), and the manual therapy group experienced a statistically significant improvement from baseline (mean change of −22.9, 95% CI −43.3 to −2.6), while the exercise group did not (mean change −12.4, 95% CI −27.1 to 2.3).[40]

Only one of the trials reported pain outcomes. Manual therapy was associated with slightly better short-term pain at rest and during walking compared to exercise (adjusted MDs on a VAS (0 to 10) of −0.72, 95% CI −1.38 to −0.05, and −1.21, 95% CI −2.29 to −0.25, respectively).[163] Intermediate-term pain results were inconsistent. A moderate effect on VAS pain during walking was seen following manual therapy compared to exercise (adjusted MD −1.27, 95% CI −2.40 to −0.19), but there was no difference for pain at rest (adjusted MD −0.70, 95% CI −2.03 to 0.59).[163]

There was no difference in one trial[163] between manual therapy and exercise for short-term or intermediate-term quality of life measured with the SF-36 physical function, role physical, or bodily pain subscales (Table 31).

Harms

No trial-related serious adverse events were detected in one trial,[40] and there was no difference in symptom aggravation leading to withdrawal (5% vs. 4%; RR 1.42, 95% CI 0.25 to 8.16) in the other trial.[163]

Exercise for Osteoarthritis of the Hand

Key Points

- Data from one poor-quality trial were insufficient to determine the effects or harms (though no serious harms were reported) of exercise versus usual care in the short term (SOE: insufficient).

Detailed Synthesis

One Norwegian trial (n=130) that evaluated the effects of strengthening and range of motion exercise (3 times weekly for 3 months plus 4 group sessions) versus usual care (treatment recommended by the patient's general practitioner) met inclusion criteria[64] (Table 32 and Appendix D). This trial was rated poor quality due to lack of patient blinding, baseline differences in mental health conditions, and large differential attrition between groups (exercise 29% vs. usual care 7%) (Appendix E). Only short-term data was reported.

Table 32. Osteoarthritis of the hand: exercise

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Osteras, 2014[64] 3 months Duration of pain: NR *Poor*	A. Exercise (n=46): ROM/strength exercises, 4 group sessions supplemented by instructions for home exercise 3 times per week for 12 weeks B. Usual care (n=64): Subjects received no particular attention, referral, or treatment from the study.	A vs. B Age: 67 vs. 65 years Females: 89% vs. 91% Fulfillment of ACR criteria for hand OA 91% vs. 91% Self-reported hip OA: 39% vs. 46% Self-reported knee OA: 40% vs. 51% Other rheumatic disease: 13% vs. 15% Severe mental distress: 17% vs. 39% FIHOA (0-30): 10.8 vs. 9.8 PSFS (0-10): 3.5 vs. 3.9 Hand pain NRS (0-10): 4.2 vs. 3.9	A vs. B 3 months FIHOA: 10.9 vs. 10.5; adjusted difference −0.5 (95% CI −1.9 to 0.8) Hand pain NRS: 4.3 vs. 4.3 ; adjusted difference −0.2 (95% CI −0.8 to 0.3) OARSI OMERACT no. of responders: 30% vs. 28% (NS)	A vs. B 3 months PSFS: 4.3 vs. 4.4 ; adjusted difference 0.1 (95% CI −0.7 to 1.0) Patient global assessment of disease activity: 4.2 vs. 4.1; adjusted difference 0.1 (95% CI −0.5, 0.7) Patient global assessment of disease activity affecting ADL: 3.8 vs. 3.8 ; adjusted difference −0.2 (95% CI −0.8 to 0.4)

ACR = American College of Radiology; ADL = activity of daily living; CI = confidence interval; FIHOA = Functional Index for Hand OsteoArthritis; NR = not reported; NRS = numeric rating scale; NS = not statistically significant; OA = osteoarthritis; OARSI OMERACT = Osteoarthritis Research Society International Outcome Measures in Rheumatology; PSFS = patient-specific function scale; ROM = range of motion

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Exercise Compared With Usual Care

Data were insufficient from one poor-quality trial. No differences between exercise and usual care were observed for function according to the Functional Index for Hand OsteoArthritis (adjusted MD −0.5 on a 0-30 scale, 95% CI −1.9 to 0.8), or for pain (adjusted MD −0.2 on a 0 to 10 VAS pain scale, 95% CI −0.8 to 0.3) at 3 months.[64] Similarly, there were no differences between groups in the proportion of OARSI OMERACT responders (30% versus 28%). There were also no differences between groups in any secondary outcome measure, including the patient-specific function scale, hand stiffness, or patient global assessment of disease activity.

The effects of exercise on use of opioid therapies or health care utilization were not reported. There was insufficient evidence to determine effects of duration of exercise therapy or number of sessions on outcomes.

Exercise Compared With Pharmacological Therapy or Other Nonpharmacological Therapies

No trial of exercise versus pharmacological therapy met inclusion criteria. Findings for exercise versus other nonpharmacological therapies are addressed in the sections for other nonpharmacological therapies.

Harms

In this trial,[64] no serious adverse events were reported; 8/130 (6%) patients reported increased pain (3 in hand, 5 in neck/shoulders) but adverse events were not reported by group.

Physical Modalities for Osteoarthritis of the Hand

Key Points

- One good-quality study of low-level laser treatment versus sham found no evidence of differences in function (MD 0.2, 95% CI −0.2 to 0.6) or pain (MD 0.1, 95% CI −0.3 to 0.5) in the short term (SOE: low).
- Data were insufficient from one fair-quality trial to determine effects or harms of heat therapy using paraffin compared to no treatment on function or pain in the short term (SOE: insufficient).
- No serious harms were reported in the trial of low-level laser therapy (SOE: low).

Detailed Synthesis

We identified two trials of physical modality use for hand OA (Table 33 and Appendixes D and E). One good-quality double-blind Canadian trial (N=88)[138] compared three, 20-minute sessions of low-level laser treatment to a sham laser probe over a 6-week period. Identical treatment procedures were used in each group. All participants attended three sham laser treatment sessions prior to randomization to ensure ability to comply with the treatment protocol.

One fair-quality trial (n=56) conducted in Turkey compared 15 minutes of paraffin wrapping 5 days per week for 3 weeks with a no treatment control group.[139] Both groups received information about joint protection strategies. Methodological limitations included lack of patient blinding, unclear compliance with treatment, and poorly reported analyses.

Table 33. Osteoarthritis of the hand: physical modalities

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Brosseau,[138] 2005 4.5 months Duration of pain: NR *Good*	A. Low-level laser therapy (n=42): 3 J/cm^2 applied for 1 second each to the skin overlying the radial, medial and ulnar nerves (total of 15 points irradiated); 3 sessions lasting 20 minutes per week for 6 weeks B. Sham low-level laser therapy (n=46): same procedure as the active treatment but a sham laser probe was used.	A vs. B Age: 64 vs. 65 years Female: 74% vs. 83% Medication use: 60% vs. 61% Diagnosis of OA: 7.5 vs. 8.5 years AUSCAN function (0-4)[b]: 2.2 vs. 2.1 AUSCAN pain (0-4)[b]: 2.4 vs. 2.1 Pain intensity VAS (0-100): 56.9 vs. 49.4	A vs. B 4.5 months AUSCAN function: 1.9 vs. 1.7, difference 0.2 (95% CI −0.2 to 0.6) AUSCAN pain: 1.9 vs. 1.8, difference 0.1 (95% CI −0.3 to 0.5) Pain VAS: NR	A vs. B 4.5 months Patient global assessment: Fully improved: 0% vs. 3% Partially improved: 40% vs. 33.3% No improvement: 60% vs. 52%

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Dilek, 2013[139] 2.25 months Duration of pain: 5.5 years *Fair*	A. Dip-wrap paraffin bath therapy (n=24): patients dip both hands into 50°C paraffin bath 10 times, paraffin left on for 15 minutes, treatment administered 5 days per week for 3 weeks B. Control group (n=22): Details NR; assumed to be no treatment Only paracetamol intake was permitted during the study	A vs. B Age: 59 vs. 60 years Female: 83% vs. 91% AUSCAN function (0-36)[c]: 16.2 vs. 17.1 AUSCAN pain (0-20)[c]: 10.7 vs. 9.8 Pain at rest, median (VAS 0-10): 5.0 vs. 4.0 Pain during ADL, median (VAS 0-10): 7.0 vs. 8.0	A vs. B 2.25 months AUSCAN function: 13.8 vs. 17.8, difference −4.0 (95% CI −8.6 to 0.6) AUSCAN pain: 6.5 vs. 9.5, difference −3 (95% CI −5.5 to −0.5) Pain VAS at rest, median: 0.0 vs. 5.0, P<0.001 Pain VAS during ADL, median: 5.0 vs. 7.0, P=0.05	NR

ADL = activity of daily living; AUSCAN = Australian Canadian Osteoarthritis Hand Index; CI =confidence interval; DFI = Dreiser Functional Index; NR = not reported; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Data for the AUSCAN was presented as an average of all responses, on a 5-point Likert scale (0-4), for both the physical function (9 items) and pain (5 items) subscale

[c] Data for the AUSCAN was presented as a sum of the values across all items within the physical function (9 items) and pain (5 items) subscales; a 5-point Likert scale (0-4) was used to rate each item resulting in score ranges of 0-36 and 0-20, respectively

Physical Modalities Compared With Sham or No Treatment

Low-Level Laser Therapy. In the one good-quality trial of low-level laser treatment versus sham (n=88),[138] there were no differences in short-term function (MD 0.2 on a 0-4 Australian Canadian Osteoarthritis Hand Index [AUSCAN] functional subscale, 95% CI −0.2 to 0.6) or pain (MD 0.1 on a 0-4 AUSCAN pain subscale, 95% CI −0.3 to 0.5) at 4.5 months. Likewise, no difference was seen between groups in improvement based on patient global assessment.

Paraffin Treatment. One fair-quality trial (N =56)[139] of paraffin heat treatment demonstrated no difference compared with no treatment on the AUSCAN function scale (0-36) (MD −4.0, 95% CI −8.6 to 0.6 at short-term [2.25-month] followup). Regarding pain, no clear difference was identified between the groups over the short term as there was inconsistency across measures used and analyses for outcomes were poorly reported; findings were considered insufficient.[139] While heat treatment was slightly favored based on the AUSCAN pain subscale (MD −3 on a 0-20 scale, 95% CI −5.5 to −0.5), it was not statistically significant in the author's intention-to-treat (ITT) analysis (P=0.07). VAS pain at rest suggested more improvement with heat therapy versus control in the ITT analysis (median 0 vs. 5.0 on a 0-10 scale, P<0.001); however, there was no clear difference between groups on VAS pain during ADL (median 5.0 vs. 7.0, P=0.09 for per protocol analysis, P=0.05 for ITT).

No trial evaluated effects of physical modalities on use of opioid therapies or health care utilization.

Physical Modalities Compared With Pharmacological Therapy or With Exercise Therapy

No trial of a physical modality versus pharmacological therapy or versus exercise met inclusion criteria.

Harms

Only the low-level laser therapy trial reported adverse events; no serious harms were reported.[138] One patient (2%) who received low-level laser treatment experienced erythema at the site.

Multidisciplinary Rehabilitation for Osteoarthritis of the Hand

Key Points

- One fair-quality trial of multidisciplinary rehabilitation versus waitlist control found no evidence of differences between groups over the short term in function (adjusted difference 0.49, 95% CI −0.09 to 0.37 on 0-36 scale) or pain (adjusted difference 0.40, 95% CI −0.5 to 1.3 on a 0-20 scale), or with regard to the proportion of OARSI OMERACT responders (OR 0.82, 95% CI 0.42 to 1.61) (SOE: low for all outcomes).
- Data on harms were insufficient, although no serious adverse events were reported in the one trial of multidisciplinary rehabilitation versus waitlist control (SOE: insufficient).

Detailed Synthesis

One fair-quality trial (n=151) compared four, 2.5- to 3-hour group-based sessions, delivered by an occupational therapist and a specialized nurse, consisting of self-management techniques, ergonomic principles, daily home exercises, and splint (optional) versus a waitlist control[224] (Table 34 and Appendix D). Waitlist control consisted of one 30-minute explanation of OA followed by a 3-month waiting period. Effect estimates were adjusted for baseline function or pain, body mass index (BMI), gender, and presence of erosive arthritis. Methodological limitations included lack of patient blinding and unreported compliance to treatment (Appendix E).

Of note, this intervention appeared to focus on functional restoration and while it met our broad definition of multidisciplinary rehabilitation (see footnote in Table 1), it was not consistent with how multidisciplinary rehabilitation is generally delivered clinically.

Table 34. Osteoarthritis of the hand: multidisciplinary rehabilitation

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Stukstette[224] 2013 3 months Duration of pain: 4 years *Fair*	A. Multidisciplinary treatment program (n=75): 4 group based therapy sessions of 2.5-3 hours duration (time period NR), supervised by a specialized nurse and occupational therapist B. Waiting list (n=72) All patients: 30 minute explanation of written information about OA	A vs. B Age: 60 vs. 58 Female: 18% vs. 16% Mean duration of diagnosis: 4 vs. 4 years Proportion taking opioids: 3% vs. 4% AUSCAN function (0-36): 21.0 vs. 21.8 AUSCAN pain (0-20):10.4 vs. 10.2	A vs. B 3 months AUSCAN function: 18.6 vs. 18.8, adjusted MD 0.49 (95% CI −0.09 to 0.37) AUSCAN pain: 9.4 vs. 9.0, adjusted MD 0.40 (95% CI −0.5 to 1.3) OARSI OMERACT responders: 33% vs. 37%, OR 0.82 (95% CI 0.42 to 1.61)	A vs. B 3 months Patient global assessment: 60.4 vs. 66.0, adjusted MD −5.2 (95% CI −11.4, 1.0) SF-36 PCS: 39.8 vs. 39.9, adjusted MD −0.14 (95% CI −1.62 to 1.35) SF-36 MCS: 50.3 vs. 51.6, adjusted MD 0.27 (95% CI −2.13 to 2.67)

AUSCAN = Australian Canadian Osteoarthritis Hand Index; MD = mean difference; NR = not reported; OARSI-OMERACT = Osteoarthritis Research Society International Outcome Measures in Rheumatology; SF-36 MCS = Short-Form 36 Mental Component Summary score; SF-36 PCS = Short-Form 36 Physical Component Summary score

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Multidisciplinary Rehabilitation Compared With Waitlist

No short-term (3 months) differences in function on the AUSCAN functional subscale (adjusted MD 0.49, 95% CI −0.09 to 0.37 on 0-36 scale) or on the AUSCAN pain subscale (adjusted MD 0.40, 95% CI −0.5 to 1.3, scale 0-20) were reported.[224]

There was no difference in the proportion of OARSI OMERACT responders (OR 0.82, 95% CO 0.42 to 1.61) between groups or on any secondary outcome measure, including ADLs (Canadian Occupational Measurement Scales), health-related quality of life (SF-36), arthritis self-efficacy, pain coping, muscle strength, or joint mobility.[224]

The effect of multidisciplinary rehabilitation on use of opioid therapies or health care utilization was not evaluated in any of the included studies.

Multidisciplinary Rehabilitation Compared With Pharmacological Therapy or With Exercise Therapy

No trial of a multidisciplinary rehabilitation program versus pharmacological therapy or versus exercise met inclusion criteria.

Harms

No serious adverse events were reported. One patient reported a swollen hand and increased pain after the second treatment session.[224]

Key Question 4: Fibromyalgia

Exercise for Fibromyalgia

Key Points

- Exercise was associated with slightly greater effects on function compared with attention control, no treatment, or usual care in the short term (7 trials, pooled MD −7.61 on a 0 to 100 scale, 95% CI −12.78 to −2.43, I^2= 59.9%) (SOE: low) and intermediate term (8 trials, pooled MD −6.04, 95% CI −9.05 to −3.03, I^2=0%) (SOE: moderate). There were no clear effects in the long term (3 trials, pooled MD −4.33, 95% CI −10.18 to 1.52, I^2=0%) (SOE: low).
- Exercise had a slightly greater effect on VAS pain (0 to 10 scale) compared with usual care, attention control, or no treatment short term (6 trials [excluding outlier trial], pooled MD −0.89, 95% CI −1.32 to −0.46, I^2=0%), but there were no clear effects at intermediate term (7 trials, pooled MD −0.41, 95% CI −0.87 to 0.05, I^2=9.5%) or long term (4 trials, pooled MD −0.18, 95% CI −0.77 to 0.42, I^2=0%) (SOE: moderate for all time frames).
- There was insufficient evidence from one small, poor-quality trial to determine the effects of aerobic exercise versus pharmacological therapy (paroxetine) on pain in the intermediate term (SOE: insufficient). There was no data on short- or long-term effects.
- Data on harms were insufficient. Most trials of exercise did not report on adverse events at all. One trial reported one nonstudy-related adverse event. Two trials reported no adverse events (SOE: insufficient).

Detailed Synthesis

Twenty-one trials (across 23 publications) of exercise therapy for fibromyalgia met inclusion criteria[65-87] (Table 35 and Appendix D). The exercise interventions varied across the trials and included combinations of different exercise types (11 trials),[66,67,69,72,74,78,80,81,83-86] aerobic exercise (10 trials),[68,70,71,73,75-77,79,81,82,87] muscle performance exercise/strength training (1 trial),[75] and Pilates (1 trial).[65] The duration of exercise therapy ranged from 1 to 8 months across the trials and the total number of exercise sessions ranged from 4 to 96 (at a frequency of 1 to 5 times per week). Many trials also included instruction for home exercise practice. Exercise was compared to usual care in eight trials,[68,69,79-81,85-87] no treatment in six trials,[72-75,78,83,84] attention control in five trials,[65,67,70,71,76,77] and to waitlist,[66] sham (i.e., transcutaneous electrical stimulation),[82] and pharmacological care[82] in one trial each (the latter two groups were separate arms of the same trial). Usual care generally included medical treatment for fibromyalgia and continued normal daily activities (which often specifically excluded the exercise intervention being evaluated). Attention control conditions consisted of fibromyalgia education sessions, social support, instructions in coping strategies, relaxation and stretching exercises, and physical activity planning.

Sample sizes ranged from 32 to 166 across the trials (total number randomized=1,343). Patient mean age ranged from 35 to 57 years, and the majority were female (89% to 100%). Twelve trials were conducted in Europe,[68,72,74,77-81,83-87] five in North America,[67,69-71,73,76] two in Brazil,[66,75] and two in Turkey.[65,82]

Eleven trials were rated fair quality[65,66,68-71,75,77,78,81,85,87] and ten poor quality[67,72-74,76,79,80,82-84,86] (Appendix E). Methodological limitations in the fair-quality trials were primarily related to

unclear allocation concealment methods and lack of blinding (the nature of interventions precluded blinding of participants and researchers). Additionally, poor-quality trials also suffered from unclear randomization methods and high rates of attrition and/or differential attrition.

Table 35. Fibromyalgia: exercise therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Altan, 2009[65] 3 months Pain duration NR *Fair*	A. Pilates (n=25): 1 hour session 3 times per week for 3 months: Pilates postural education, search for neutral position, sitting, antalgic, stretching and, proprioceptivity improvement exercises, and breathing education B. Attention control (n=25): Instructions in home exercise relaxation/stretching program of 1 hour sessions 3 times per week for 3 months All patients: Education session about available diagnosis and treatment of FM	A vs. B Age: 48 vs. 50 years Female: 100% vs. 100% FIQ (0-100): 80.8 vs. 80.1 Pain VAS (0-10): 6.1 vs. 6.3	A vs. B <u>3 months:</u> FIQ: 69.3 vs. 77.6, difference −8.3 (95% CI −21.8 to 5.2) Pain VAS: 5.2 vs. 6.5, difference −1.3 (95% CI −2.6 to 0.03)	A vs. B <u>3 months:</u> NHP (0-100): 224.2 vs. 246.3, difference −22.1 (95% CI −96.0 to 51.8)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Baptista, 2012[66] 4 months Pain duration NR *Fair*	A. Belly dance (n=40): One hour belly dance classes twice a week for 16 weeks (combination exercise) B. Waiting list control (n=40): dance offered at end of the study	A vs. B: Age: 50 vs. 49 years Female: 100% vs. 100% Race: NR FIQ (0-10): 5.9 vs. 6.3 Pain VAS (0-10): 7.7 vs. 7.5	A vs. B <u>4 months</u> FIQ: 4.3 vs. 5.9; difference −1.6 (95% CI −2.45 to −0.75) Pain VAS: 4.7 vs. 7.3; difference −2.6 (95% CI −3.61 to −1.59)	A vs. B <u>4 months</u> BDI (0-63): 23.1 vs. 23.5; difference −0.40 (95% CI −7.09 to 6.29) STAI part 1: 49.4 vs. 51.8; difference −2.40 (95% CI −6.87 to 2.07) STAI part 2: 49.8 vs. 54.1; difference −4.3 (95% CI −8.72 to 0.12) SF-36 function (0-100): 56.3 vs. 39.1; difference 17.2 (95% CI 7.55 to 26.85) SF-36 limitation due to physical aspects (0-100): 36.5 vs. 13.8; difference 22.7 (95% CI 9.06 to 36.34) SF-36 pain (0-100): 46.0 vs. 29.1; difference 16.9 (95% CI 7.62 to 26.18) SF-36 mental (0-100): 52.3 vs. 46.2; difference 6.1 (95% CI −3.89 to 16.09)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Buckelew, 1998[67] 3 and 24 months Duration of symptoms, 11 years *Poor*	A. Combination exercise (n=30): included active range of motion exercises, strengthening exercises, low to moderate intensity aerobic exercise, proper posture and body mechanics instruction, and instructions on use of heat, cold, and massage; one 90 minute session per week for 1.5 months and instructions to train 2 additional times independently per week then 24 months of monthly one-hour groups. B. Attention control (n=30): one 90-180 minute education session weekly for 1.5 months	A vs. B Age: 46 vs. 44 years Female: 93% vs. 90% Duration of symptoms: 12 vs. 10 years Duration of diagnosis: 3.0 vs. 2.5 years AIMS physical activity subscale (0-10): median 4.0 vs. 6.0 Pain VAS (0-10): median 6.3 vs. 5.9	A vs. B <u>3 months</u>: AIMS physical activity subscale: median 4.0 vs. 6.0; median change from baseline 0 vs. 0 Pain VAS: median 5.4 vs. 5.8, median change from baseline −0.8 vs. −0.5 <u>24 months</u> AIMS physical activity subscale: median 4.0 vs. 6.0, median change from baseline 0 vs. 0 Pain VAS: median 5.5 vs. 5.4, median change from baseline −1.2 vs. −0.6	A vs. B <u>3 months</u>: SCL-90-R Global Severity Index (0-90): median 65.5 vs. 65.0, median change from baseline −3 vs. 0 CES-D (0-60): median 13.5 vs. 13.0, median change from baseline −2.5 vs. 3 Sleep scale (0-12), median 8.0 vs. 5.0, median change from baseline 0 vs. 0 <u>24 months</u> SCL-90-R Global Severity Index: median 65.5 vs. 67.0, median change from baseline −2.5 vs. −1 CES-D: median 11.5 vs. 12.0, median change from baseline −3.5 vs. −2 Sleep scale: median 7.5 vs. 6.0, median change from baseline 0 vs. 0

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Clarke-Jenssen, 2014[68] 3 and 12 months Symptom Duration, 14 years *Fair*	A. Aerobic exercise (n=44): conducted on land and in warm water provided in a warm climate; also stretching, relaxation, and education; provided in groups 5 days per week for 4 weeks B. Aerobic exercise (n=44): on land and in warm water provided in a cold climate; also stretching, relaxation, education, provided in groups 5 days per week for 4 weeks C. Usual Care (n=44): no intervention	A vs. B vs. C: Age: 46 vs. 46 vs. 45 years Female: 88% vs. 93% vs. 96% Symptom duration: 17 vs. 13 vs.12 years Pain VAS (mean, 0-10): 6.6 vs. 6.9 vs. 6.6	A vs. C, between-group difference in change from baseline: <u>3 months</u> FIQ: data NR, P=NS Pain VAS: −1.2 (95% CI −2.2 to −0.1) <u>12 months</u> FIQ data NR, P=NS Pain VAS: 0.1 (95% CI −0.9 to 1.1) B vs. C, between-group difference in change from baseline: <u>3 months</u> FIQ: data NR, P=NS Pain VAS: −0.9 (95% CI −1.9 to 0.2) <u>12 months</u> FIQ: data NR, P=NS Pain VAS: 0 (95% CI −1 to 1)	A vs. C, between-group difference in change from baseline: <u>3 months</u> HADS: data NR, P=NS SF-36 Physical: data NR, P=NS SF-36 Mental: data NR, P=NS <u>12 months</u> HADS: data NR, P=NS SF-36 Physical: data NR, P=NS SF-36 Mental: data NR, P=NS B vs. C, between-group difference in change from baseline: <u>3 months</u> HADS: data NR, P=NS SF-36 Physical: data NR, P=NS SF-36 Mental: data NR, P=NS <u>12 months</u> HADS: data NR, P=NS SF-36 Physical: data NR, P=NS SF-36 Mental: data NR, P=NS

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Da Costa, 2005[69] 3 and 9 months Symptom duration, years: 11 years *Fair*	A. Combination Exercise (n=39): aerobic exercise, stretching, and strength exercises; 4 visits (initial 90 minutes, others 30 minutes) over 12 weeks with exercise physiologist; individualized home-based program. B. Usual care (n=41): subjects asked to record exercise activity weekly during the 12-week intervention phase and monthly thereafter.	A vs. B Age, years: 49 vs. 52 Female: 100% vs. 100% Symptom duration: 10.5 vs. 11.2 years FIQ (0-100): 55.1 vs. 48.6 Upper body pain VAS (0-100): 49.5 vs. 47.4 Lower body pain VAS (0-100): 47.0 vs. 47.0	A vs. B, mean change from baseline <u>3 months:</u> FIQ: −7.8 (95% CI −13.9 to −1.7) vs. −0.04 (95% CI −5.2 to 5.1), P=0.05 Pain VAS, upper body: −10.6 (95% CI −17.8 to −3.4) vs. −1.9 (95% CI −6.9 to 3.2), P=0.048 Pain VAS, lower body: −8.21 (95% CI −15.7 to −0.74) vs. −2.0 (95% CI −9.4 to 5.4), P=0.24 <u>9 months</u>: FIQ: −10.1 (95% CI −16.1 to −4.0) vs. −0.024 (95% CI −4.4 to 3.9), P=0.009 Pain VAS, upper body: −7.9 (95% CI −14.3 to −1.4) vs. 2.4 (95% CI 3.7 to 8.5), P=0.02 Pain VAS, lower body: −5.6 (95% CI −13.3 to 2.2) vs. −0.29 (95% CI −8.6 to 8.0), P=0.35	A vs. B, mean change from baseline <u>3 months:</u> SCL 90-R GSI (30−81): −0.02 (95% CI −0.3 to −0.04) vs. −0.07 (95% CI −0.2 to 0.05), P=0.26 <u>9 months</u>: SCL 90-R GSI (30-81): −0.16 (95% CI −0.28 to 0.35) vs. −0.09 (95% CI −0.21 to 0.03), P=0.39
Fontaine, 2010, 2011[70,71] 6 and 12 months Mean duration of fibromyalgia 7.4 years *Fair*	A. Aerobic Exercise (n=30): Lifestyle Physical Activity; 6, 60-minute group sessions over 3 months with the goal to increase moderate-intensity physical exercise by accumulating short bursts of physical activity throughout the day to 30 minutes 5-7 days per week. B. Attention control (n=23): FM education, monthly sessions for 3 months. Included education about FM and social support.	A vs. B Age: 46 vs. 49 years Female: 94% vs. 100% Race, white: 78% vs. 82% Years since diagnosis: 5.9 vs. 9.6 FIQ (scale NR): 67.5 vs. 69.7 Pain VAS (0-100): 54.6 vs. 58.9	A vs. B <u>6 months:</u> FIQ: 65.3 vs. 63.9, difference 1.4 (95% CI −10.0 to 12.8) Pain VAS: 54.9 vs. 49.4, difference 5.5 (95% CI −7.8 to 18.8) <u>12 months:</u> FIQ: 64.4 vs. 65.1, difference −0.7 (95% CI −13.6 to 12.2) Pain VAS: 51.6 vs. 50.9, difference 0.7 (95% CI −12.9 to 14.3)	A vs. B <u>6 months:</u> CES-D (scale NR): 18.1 vs. 19.9, difference −1.8 (95% CI −7.5 to 3.9) <u>12 months:</u> CES-D: 19.8 vs. 20.6, difference −0.8 (95% CI −7.1 to 5.5)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Giannotti, 2014[72] 1 and 6 months Pain duration NR *Poor*	A. Combination exercise (n=21): stretching, strengthening, active and passive mobilization, spine flexibility, and aerobic training plus education 2 days a week (60 minutes per session) for 10 weeks; instructions to perform at home the exercise program at least 3 times per week. B. No intervention (n=20)	A vs. B Age: 53 vs. 51 years Female: 95% vs. 92% FIQ (0-100): 62.7 vs. 59.1 Pain VAS (0-10): 6.1 vs. 6.1	A vs. B <u>1 month:</u> FIQ: 55.5 vs. 50.9, difference 4.6 (95% CI −6.38 to 15.58) Pain VAS: 5.3 vs. 5.5, difference −0.20 (95% CI -1.87 to 1.47) <u>6 months</u> FIQ: 48.8 vs. 56.9, difference −8.1 (95% CI −20.33 to 4.13) Pain VAS: 5.8 vs. 5.4, difference 0.4 (95% CI −1.4 to 2.2)	A vs. B <u>1 month</u> Sleep VAS (0-10): 4.6 vs. 5.0, difference −0.40 (95% CI −2.51 to 1.71) <u>6 months</u> Sleep VAS (0-10): 6.3 vs. 6.1, difference 0.20 (95% CI −2.15 to 2.55)
Gowans, 2001[73] 6 months Duration of symptoms, 9 years *Poor*	A. Aerobic exercise (n=30): 3 pool and walking exercise classes (plus stretching) per week for 6 months B. Control group (n=27): continued ad libitum activity	A vs. B Age: 45 vs. 50 years Female: 89% vs. 87% FIQ (0-80): 57.7 vs. 56.6	A vs. B <u>6 months:</u> FIQ: 48.6 vs. 54.9, p**<0.05; difference −6.3 (95% CI −14.8 to 2.2)	A vs. B <u>6 months:</u> BDI (0-63): 16.9 vs. 21.3, p**<0.05 difference −4.4 (95% CI −10.4 to 1.6), P=0.15 STAI (20-80): 41.3 vs. 51.7, P**<0.05; difference −10.4 (95% CI −18.2 to −2.6), P=0.01
Gusi, 2006[74] 3 months Duration of symptoms, 22 years *Poor*	A. Combination exercise (n=18): 1-hour pool exercise (warm up, aerobic exercise, mobility and lower-limb strength exercises, cool down) 3 times per week for 12 weeks (subjects instructed to avoid physical exercise for the next 12 weeks) B. Control (n=17): Normal daily activities, which did not include any exercise related to those in the therapy.	A vs. B Age, years: 51 vs. 51 Female: 100% vs. 100% Pain VAS (0-100): 63.1 vs. 63.9	A vs. B Change from baseline <u>3 months</u> Pain VAS: −1.6 (95% CI −12.7 to 0.9) vs. 0.9 (95% CI −7.3 to 9.2), P=0.69	A vs. B Change from baseline <u>3 months</u> EQ-5D (0-1): 0.14 (95% CI −0.03 to 0.32) vs. −0.02 (−0.17 to 0.13), P=0.14 EQ-5D Pain/discomfort (1-3): −0.1 (95% CI −0.4 to 0.3) vs. 0 ((95% CI −0.3 to 0.3), P=0.79 EQ-5D Anxiety/depression (1-3): −0.5 (95% CI −0.8 to −0.1) vs. 0 (95% CI −0.2 to 0.2), P=0.01

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Kayo, 2012[75] 3 months Duration of symptoms, 5 years *Fair*	A. Aerobic exercise (n=30): Walking program, 60 minutes 3 times per week for 16 weeks, supervised by physical therapist. B. Muscle strengthening exercise (n=30): 60 minutes 3 times per week for 16 weeks, supervised by physical therapist. C. No treatment (n=30)	A vs. B: Age: 48 vs. 47 vs. 46 years Symptom duration: 4.0 vs. 4.7 vs. 5.4 FIQ total (0-100): 63.1 vs. 67.3 vs. 63.8 Pain VAS (0-10): 8.6 vs. 8.7 vs. 8.4	A vs. C <u>3 months</u> FIQ: 38.5 vs. 57.7; overall group X time interaction P=NS Pain VAS: 4.8 vs. 6.7; overall group X time interaction P=NS B vs. C <u>3 months</u> FIQ: 50.5 vs. 57.7; overall group X time interaction P=NS Pain VAS: 5.9 vs. 6.7; overall group X time interaction P=NS	NR
King, 2002[76] 3 months Duration of symptoms, 8.5 years *Poor*	A. Aerobic exercise (n=30): aerobic land and water activities; three, 10-40 minute supervised exercise sessions per week for 3 months B. Control (n=18): instructions on stretches and coping strategies and contacted 1-2 times during the 3 month treatment period to answer any questions	A vs. B Age: 45 vs. 47 years Female: 100% vs. 100% Duration of symptoms: 7.8 vs. 9.6 years FIQ (0-80): 52.4 vs. 55.2	A vs. B <u>3 months</u> FIQ: 47.5 vs. 51.5, difference −4.0 (95% CI −12.2 to 4.2)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Mannerkorpi, 2009[77] 6-7 months Pain duration NR *Fair*	A. Aerobic exercise (n=81): One 45 minute pool aerobic exercise session per week for 20 weeks, stretching exercise also, plus six 1 hour weekly sessions of strategies to cope with FM symptoms, plan for physical activity for the following week and short relaxation exercise B. Education control (n=85): six 1 hour weekly sessions of strategies to cope with FM symptoms, plan for physical activity for the following week and short relaxation exercise	A vs. B Age: 45 vs. 47 years Female: 100% vs. 100% FIQ (0-100): 61.6 vs. 66.6 FIQ pain subscale (0-100): 67.7 vs. 70.4	A vs. B <u>6-7 months</u> FIQ: mean change from baseline: −3.9 vs. −4.5, P=0.04 FIQ pain: mean change from baseline: −6.5 vs. −2.5, P=0.018	A vs. B <u>6-7 months</u> HADS depression scale (0-21): mean change from baseline −0.4 vs. 0.0, P=0.99 HADS anxiety scale (0-21): mean change from baseline −0.7 vs. 0.4, P=0.15 SF-36 PCS (0-100): mean change from baseline 2.9 vs. 1.3, P=0.13 SF-36 MCS (0-100): mean change from baseline 0.5 vs. 1.3, P=0.15 SF-36 physical functioning (0-100): mean change from baseline 2.2 vs. 1.3, P=0.70 SF-36 role-physical (0-100): mean change from baseline 12.1 vs. 9.3, P=0.72 SF-36 bodily pain (0-100): mean change from baseline 5.0 vs. 3.6, P=0.24
Paolucci, 2015[78] Duration of symptoms: NR 3 months *Fair*	A. Combination exercise (n=19): Low-impact aerobic training, agility training balance and postural exercises, hip flexor strengthening, static stretching, diaphragmatic breathing, and relaxation; 10, 60-minute sessions, twice a week for 5 weeks B. Control (n=18): No rehabilitation interventions, continued normal activities	A vs. B Age: 50 vs. 48 years Female: 100% vs. 100% FIQ total (0-100): 64.8 vs. 63.9	A vs. B <u>3 months:</u> FIQ total: 53.8 vs. 64.3, difference −10.50 (95% CI −17.77, −3.23)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Sanudo, 2010[81] 6 months Pain duration NR *Fair*	A. Combination exercise (n=21): supervised aerobic, muscle strengthening, and flexibility exercises; twice-weekly sessions for 24 weeks B. Aerobic exercise (n=22): warm-up, aerobic exercise, cool down; two, 45-60 minute sessions/week for 6 months C. Usual care control (n=21): medical treatment for FM and continued normal daily activities, which did not include aerobic exercise.	A vs. B vs. C Age: 56 vs. 56 vs. 57 years FIQ (0-100): 62.2 vs. 60.9 vs. 60.5	A vs. C <u>6 months</u> FIQ: mean change from baseline −8.8 vs. NR; P<0.01 B vs. C <u>6 months</u> FIQ: mean change from baseline −8.8 vs. NR; P<0.05	A vs. C <u>6 months</u> BDI (0-63): mean change from baseline −6.4 vs. NR; P<0.01 SF-36 total (0-100): mean change from baseline 8.4 vs. NR; P<0.01 B vs. C <u>6 months</u> BDI: −8.5 vs. NR; P<0.01 SF-36 total: 8.9 vs. NR; P<0.05
Sanudo, 2012[80] 6, 18 and 30 months Pain duration NR *Poor*	A. Combination exercise (n=21): Twice-weekly 45- to 60-minute sessions of exercise (warm up, aerobic exercise, muscle strengthening exercise, flexibility exercises) for 6 months. B. Usual care (n=20): alternated between 6 months of training and 6 months with no exercise intervention (asked not to participate in any structured exercise program) for 30 months.	A vs. B Female: 100% vs. 100% FIQ (0-80): 58.6 vs. 55.6	A vs. B <u>6 months:</u> FIQ: 48.5 vs. 55.4, P<0.0005; difference −6.9 (95% CI −14.35 to 0.55), P=0.07 <u>18 months:</u> FIQ: 45.6 vs. 51.3, P=NR; difference −5.7 (95% CI −14.6 to 3.2), P=0.20 <u>30 months</u> FIQ: 38.5 vs. 49.5, p NS; difference −11.0 (95% CI −19.93 to −2.07), P=0.02	A vs. B <u>6 months:</u> SF-36 (0-100): 49.5 vs. 37.9, P=0.13; difference 4.68 (95% CI .096 to 21.104), P=0.02 BDI (0-63): 14.7 vs. 16.6, P=0.18; difference −1.9 (95% CI −6.5 to 2.7), P=0.41 <u>18 months:</u> SF-36: 51.8 vs. 41.3, P=NR; difference 10.5 (95% CI 0.5 to 20.5), P=0.04 BDI: 14.3 vs. 14.2, P=NR; difference 0.10 (95% CI −5.4 to 5.6), P=0.97 <u>30 months</u> SF-36: 60.5 vs. 42.0, P=NS BDI: 9.7 vs. 17.9, P=NS

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Sanudo, 2015[79] 6 months Pain duration NR *Poor*	A. Aerobic exercise (n=16): consisted of warm up, steady state exercise at 60-65% of predicted maximum heart rate, interval training at 75-80% of predicted maximum heart rate, and cool-down; 2, 45-60 minute sessions per week for 6 months B. Usual care (n=16): normal activities, which did not include structured exercise.	A vs. B Age: 55 vs. 58 years Female: 100% vs. 100% Pain VAS (0-10): 7.4 vs. 7.2	A vs. B <u>6 months:</u> Pain VAS: 6.7 vs. 7.0, difference −0.3 (95% CI −6.3 to 5.7),	A vs. B <u>6 months</u> Anxiety VAS (0-10): 5.7 vs. 7.5, difference −1.8 (95% CI −10.8 to 7.2) Depression VAS (0-10): 5.6 vs. 6.7 (2.2), difference −1.1 (95% CI −10.1 to 7.9) Sleep disturbance VAS (0-10): 7.2 vs. 8.6 (1.9), difference −1.4 (95% CI −8.9 to 6.1)
Sencan, 2004 6 months Duration of pain: 5.4 years *Poor*	A. Exercise group (n=14): 3 40-minute aerobic exercise sessions per week for 6 weeks B. Paroxetine (n=18): 20/mg paroxetine/day for 6 weeks C. Sham (n=20): placebo TENS with electrodes applied to two most painful tender points for 20 minutes, 3 times/week for 6 weeks. All patients instructed to take paracetamol as a rescue medication throughout the study.	A vs. B vs. C Age: 35 vs. 36 vs. 36 years Female: 100% vs. 100% vs. 100% BMI: 24 vs. 24 vs. 15 Duration of symptoms: 4.7 vs. 6.5 vs. 5.1 years VAS (0-10): 6.85 vs. 6.62 vs. 7.70 Beck Depression Index (BDI 0-60): 16.20 vs. 20.80 vs. 18.50	A vs. C 6 months VAS: 4.75 vs. 5.01, difference −0.26 (95% CI −1.46 to 0.94) A vs. B 6 months VAS:4.75 vs. 5.84, difference −1.09 (95% CI −2.37 to 0.19)	A vs. C 6 months BDI: 9.95 vs. 15.15, difference −5.2 (95% CI −7.41 to −2.99) Analgesic Consumption: 1.15 vs. 4.35, difference −3.17 (95% CI −3.79 to −2.55) A vs. B 6 months BDI: 9.95 vs. 10.12, difference −0.17 (95% CI −2.09 to 1.75) Analgesic Consumption: 1.15 vs. 2.40, difference −1.25 (95% CI −1.39 to −1.11)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Tomas-Carus, 2008/2009[83,84] 8 months Symptom duration 20 years *Poor*	A. Combination exercise (n=17): Pool exercise in 1 hour sessions 3 times per week for 8 months (warm up, aerobic exercise, mobility and lower limb strength exercises using water resistance and upper limb strength exercises without water resistance, cool down) B. Control (n=16): normal activities for 8 months, which did not include exercise similar to that in group A.	A vs. B Age: 51 vs. 51 years Female: 100% vs. 100% FIQ Total (0-10): 6.1 vs. 6.3 FIQ Physical Function (0-10): 3.0 vs. 3.7 FIQ Pain (0-10): 5.6 vs. 6.4	A vs. B <u>8 months</u> FIQ Total: 5.2 vs. 6.5, difference −1.3 (95% CI −0.23 to −0.3) FIQ Physical Function: 2.4 vs. 3.7, difference −1.3 (95% CI −2.7 to 0.09) FIQ Pain: 5.3 vs. 6.6, difference −1.3 (95% CI −2.5 to −0.09)	A vs. B <u>8 months</u> FIQ Anxiety (0-10): 4.7 vs. 6.6, difference −1.9 (95% CI −3.7 to −0.1) FIQ Depression (0-10): 4.0 vs. 6.1, difference −2.1 (95% CI −4.1 to −0.1) STAI State Anxiety (20-80): 37.5 vs. 44.4, difference −6.9 (95% CI −13.2 to −0.6) SF-36 physical function (0-100): 54.1 vs. 36.6, difference 17.5 (95% CI 3.4 to 31.6) SF-36 bodily pain (0-100): 51.7 vs. 27.1, difference 24.6 (95% CI 11.6 to 37.6) SF-36 Mental Health (0-100): 67.3 vs. 49, difference 18.3 (95% CI 2.5 to 34.0)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
van Eijk-Hustings, 2013[85] 18 months Pain duration NR *Fair*	A. Aerobic exercise (n=47): two group sessions per week for 12 weeks (warm up, aerobic exercise, resistance training to strengthen muscles, cool down). Subjects were asked to practice exercises at home with videodisc once a week. B. Usual care (n=48): individualized FM education and lifestyle advice within 1-2 consultations, plus care as usual	A vs. B Age: 44 vs. 43 years Female: 100% vs. 98% FIQ total (0-100): 60.0 vs. 55.4 FIQ physical function (0-10): 3.6 vs. 3.4 FIQ Pain (0-10): 6.2 vs. 5.5	A vs. B <u>18 months:</u> FIQ total: 52.0 vs. 56.2, ES=0.22 (95% CI −0.20 to 0.61) FIQ physical function: 3.6 vs. 3.9, ES=0.11 (95% CI −0.29 to 0.52) FIQ pain: 5.2 vs. 5.3, ES=0.05 (95% CI −0.36 to 0.44)	A vs. B <u>18 months:</u> FIQ Depression (0-10): 5.0 vs. 4.2, ES=0.09 (95% CI −0.31 to 0.49) FIQ Anxiety (0-10): 5.0 vs. 4.8, ES=−0.06 (95% CI −0.46 to 0.34) EQ-5D (−0.59 to 1): 0.54 vs. 0.51, ES=0.10 (95% CI −0.31 to 0.50) GP consultations[b]: 1.0 vs. 0.7, ES=−0.10 (95% CI −0.48 to 0.32) Medical specialist consultations[b]: −0.4 vs. 0.2, ES=−0.29 (95% CI −0.58 to 0.22) Physiotherapist consultations[b]: 0.4 vs. 2.8, ES=−0.29 (−0.58 to 0.22) Other paramedical professional consultations[b]: 2.1 vs. 0.2, ES=−0.68 (95% CI −1.00 to −0.18)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
van Santen, 2002[86] 6 months Duration of symptoms: 12 years *Poor*	A. Combination exercise (n=58): group sessions (60 minutes) twice a week for 24 weeks (aerobic exercises, stretching, general flexibility and balance exercises, and isometric muscle strengthening); encouraged to attend a third, unsupervised, 60 minute session weekly and to use sauna or swimming pool after all sessions. B. Usual care (n=29): analgesics NSAIDs, or tricyclic antidepressants, if appropriate; GPs informed that aerobic exercises and relaxation should not be prescribed or encouraged	A vs. B Age: 46 vs. 43 years Female: 100% vs. 100% Duration of symptoms: 9.7 vs. 15.4 years SIP physical score (mean, 0-100): 11.3 vs. 9.8 SIP total score (mean, 0-100): 14.4 vs. 11.4 AIMS (mean, 0-10): 1.9 vs. 5.4 Pain VAS (mean, 0-100): 66.8 vs. 62.4	A vs. B, mean change from baseline <u>6 months:</u> SIP physical score: −1.7 (95% CI −3.7 to 0.3) vs. −0.6 (95% CI −2.9 to 1.7), P=NS SIP total score: −1.9 (95% CI −3.9 to 0.1) vs. −1.4 (95% CI −3.4 to 0.6) P=NS AIMS: 0.1 (95% CI −0.6 to 0.8) vs. 0.8 (95% CI −1.8 to −0.2), P=NS Pain VAS: −5.5 (95% CI −10.9 to −0.1) vs. 1.3 (95% CI −4.5 to 7.1), P=NS	A vs. B, mean change from baseline <u>6 months:</u> SCL-90-R Global Severity Index (scale unclear): −6.8 (95% CI −20.1 to 6.5) vs. −8.1 (95% CI −19.8 to 3.6), P=NS SIP psychosocial score (0-100): −3.2 (95% CI −6.2 to 0.2) vs. −3.5 (95% CI -7.0 to 0.0), P=NS Patient global assessment (1-5): 0.5 (95% CI 0.2 to 0.8) vs. 0.5 (95% CI 0.2 to 0.8), P=NS
Wigers, 1996[87] 48 months Duration of symptoms: 10 years *Fair*	A. Aerobic exercise (n=20): sessions consisted of training to music (further details not given) and aerobic games; 45 minute group sessions 3 times a week for 14 weeks B. Treatment as usual (n=20)	A vs. B Age: 43 vs. 46 years Female: 90% vs. 95% Duration of symptoms: 9 vs. 11 years Pain VAS (0-100): 72 vs. 65	A vs. B <u>48 months:</u> Pain VAS: 68 vs. 69, difference −1.0 (95% CI −16.3 to 14.4)	A vs. B <u>48 months</u> Depression VAS (0-100): 32 vs. 30, difference 2.0 (95% CI −18.8 to 22.8) Global subjective improvement: 75% vs. 12%, RR 5.9 (95% CI 1.5 to 22.2)

AIMS = Arthritis Impact Measurement Scale; BDI = Beck Depression Inventory; CES-D: Center for Epidemiologic Studies Depression Scale Revised; CI = confidence interval; EQ5D = EuroQoL 5 Dimensions; ES = effect size; FIQ = Fibromyalgia Impact Questionnaire; FM = fibromyalgia; GP = general practitioner; HADS = Hospital Anxiety and Depression Scale; NHP = Nottingham Health Profile; NR = not reported; NS = not statistically significant; NSAID = nonsteroidal anti-inflammatory drug; SCL-90-R = Symptom Checklist-90-Revised; SF-36 = Short-Form 36 Questionnaire; SIP = Sickness Impact Profile; STAI = State-Trait Anxiety Inventory; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Total number of consultations over a period of 2 months prior to measurement

Exercise Compared With Usual Care, Waitlist, an Attention Control, or No Treatment

Functional Outcomes. Exercise was associated with a slightly greater effect on short-term function compared with usual care, an attention control, or no treatment based on Fibromyalgia Impact Questionnaire (FIQ) total scores (7 trials, pooled MD −7.61 on a 0 to 100 scale, 95% CI −12.78 to −2.43, I^2= 59.9%)[65,66,69,72,75,76,78] (Figure 39). The estimate across fair-quality trials (i.e., not including the poor-quality trials) was somewhat higher (5 trials, pooled MD −9.91, 95% CI −15.75 to −4.07).[65,66,69,75,78]

Exercise was associated with slightly greater effects on intermediate-term function versus controls for FIQ total score (8 trials, pooled MD on 0-100 scale, −6.04, 95% CI −9.05 to −3.03.10, I^2= 0%)[69,71-73,77,80,81,83] (Figure 39). Estimates were slightly smaller across the fair-quality trials only (4 trials, pooled MD −4.04, 95% CI −7.90 to −0.03).[69,71,77,81] Stratification by exercise type yielded similar results for combination exercise (7 trials, pooled MD −5.75, 95% CI −9.29 to −2.54),[69,71,72,77,80,81,83] but there was no clear difference between aerobic exercise and no treatment or usual care (2 trials, pooled MD −8.13, 95% CI −16.24 to 0.28).[73,81] Estimates were consistent with a slightly greater effect of exercise on function when compared with usual care (3 trials, pooled MD −6.13, 95% CI −11.71 to −1.06)[69,80,81] or no treatment (3 poor quality trials, pooled MD −9.97, 95% CI −16.24 to −3.45),[72,73,83] but there was no clear difference in two fair-quality trials using attention controls (pooled MD −3.25, 95% CI −99.32 to 5.20).[71,77]

Exercise had a small effect on long-term function compared with controls but results were no longer statistically significant based on the FIQ total score (3 trials, pooled MD on 0 to 100 scale, −4.33, 95% CI −10.18 to 1.52, I^2= 0%)[71,80,85] (Figure 39). There were no clear differences in estimates when analyses were stratified according to the type of exercise (2 trials of combination exercise, pooled MD −4.45, 95% CI −14.39 to 6.24),[71,80] type of comparison (2 trials of usual care, pooled MD −5.34, 95% CI −13.4 to 2.32),[80,85] or after the exclusion of one poor-quality trial (2 trials, pooled MD −3.11, 95% CI −11.26 to 5.86).[71,85] Findings are based on a small number of trials.

Pain Outcomes. Exercise had a moderately greater effect on pain (0 to 10 VAS) in the short term compared with usual care, attention control, or no treatment (7 trials, pooled MD −1.07, 95% CI −1.73 to −0.41, I^2=58.7%)[65-67,69,72,74,75] (Figure 40). Substantial heterogeneity was noted with one outlier trial of belly dance (combination exercise) versus waitlist control, reporting substantially higher estimates.[66] Excluding the outlier trial reduced heterogeneity and led to an effect size consistent with a small effect (6 trials, pooled MD −0.89, 95% CI −1.32 to −0.46, I^2=0%). Estimates were similar when stratified by exercise type and control type. Across the fair-quality trials, the estimate was somewhat larger (4 trials, pooled MD −1.44, 95% CI −2.4 to −0.49, including the outlier).[65,66,69,71,75]

There was no effect of exercise on VAS pain at intermediate term (7 trials, pooled MD −0.41 on a 0-10 scale, 95% CI −0.87 to 0.05, I^2= 9.5%)[69,71,72,79,82,83,86] (Figure 40). Removal of poor-quality trials[72,79,82,83] and stratification by exercise and control types yielded similar estimates (MDs ranged from −0.10 to −0.71) with no clear difference identified.

There was no effect of exercise on pain long term (4 trials, pooled MD −0.18 on a 0-10 scale, 95% CI −0.77 to 0.42, I^2=0%)[67,71,85,87] (Figure 40). Similar estimates were obtained and no clear differences were seen following exclusion of one poor quality-trial or for the comparisons of aerobic exercise with usual care or combination exercise with attention control; pooled differences ranged from −0.5 to −0.26.

Other Outcomes. Data on the effects of exercise on anxiety, depression, and quality of life were often poorly reported (Table 35) and results are mixed. Exercise had no clear effect in the short term on measures of mental health, depression, anxiety, psychological distress, or sleep disturbance VAS across five trials,[65-69] with only one small poor-quality trial favoring exercise on the EuroQol 5-Dimensions (EQ-5D) anxiety/depression scale.[74] Similarly, exercise had no clear effect on quality of life.

At intermediate term, exercise was associated with a small improvement in depression measured by the Beck Depression Inventory (BDI) compared with no treatment or usual care (4 trials, pooled MD −4.86 on a 0-63 scale, 95% CI −7.55 to −2.17, I^2= 33.1%, plot not shown);[73,80-82] three of the four trials were poor quality. Results were similar for aerobic exercise (3 trials, pooled MD −5.34, 95% CI −8.42 to −3.03) but no difference between groups was seen in the pooled estimate for the two trials using combination exercise or when any exercise was compared with usual care only (2 trials). Across various other measures, exercise had no clear effect on depression in five trials,[67,68,71,77,79] however one poor-quality trial favored exercise based on the FIQ depression subscale versus usual care.[83] Results for anxiety were mixed: two trials (one fair- and one poor-quality)[77,79] reported no difference between groups while two small, poor-quality trials reported a greater improvement in anxiety on the State-Trait Anxiety Inventory (STAI) and the FIQ anxiety subscale with exercise versus usual care.[73,83] Exercise was associated with improved quality of life (SF-36) in three small trials,[80,81,84] but not in a fourth larger fair-quality trial[77] (Table 35). Exercise had no clear effect on psychological problems in two trials[67,69] or sleep in three trials.[67,72,79] One trial reported no between-group difference in analgesic consumption by 6 months, although patients who underwent aerobic exercise showed a significant reduction from baseline use.[82]

Long term, exercise had no clear effect on measures of depression, anxiety, or psychological problems in all but one poor-quality trial.[80] This same trial also reported improvement in SF-36 total scores, whereas one larger fair-quality trial did not.[68] No differences between groups in health care utilization were seen in the 2 months prior to the final measurement at 18 months in one trial[85] (Table 35).

Exercise Compared With Pharmacological Therapy

One small, poor-quality trial (N=32 analyzed) comparing 1.5 months of aerobic exercise (40 minutes on bicycle ergometer three times per week) versus paroxetine 20 mg daily found no between-group difference in pain on VAS at intermediate-term followup (MD −0.26 on a 0-10 scale, 95% CI −1.46 to 0.94). Regarding secondary outcomes, no differences were seen for depression (BDI) or mean analgesic consumption over the intermediate term, although the exercise group showed a greater reduction from baseline in analgesic use compared with the paroxetine group.

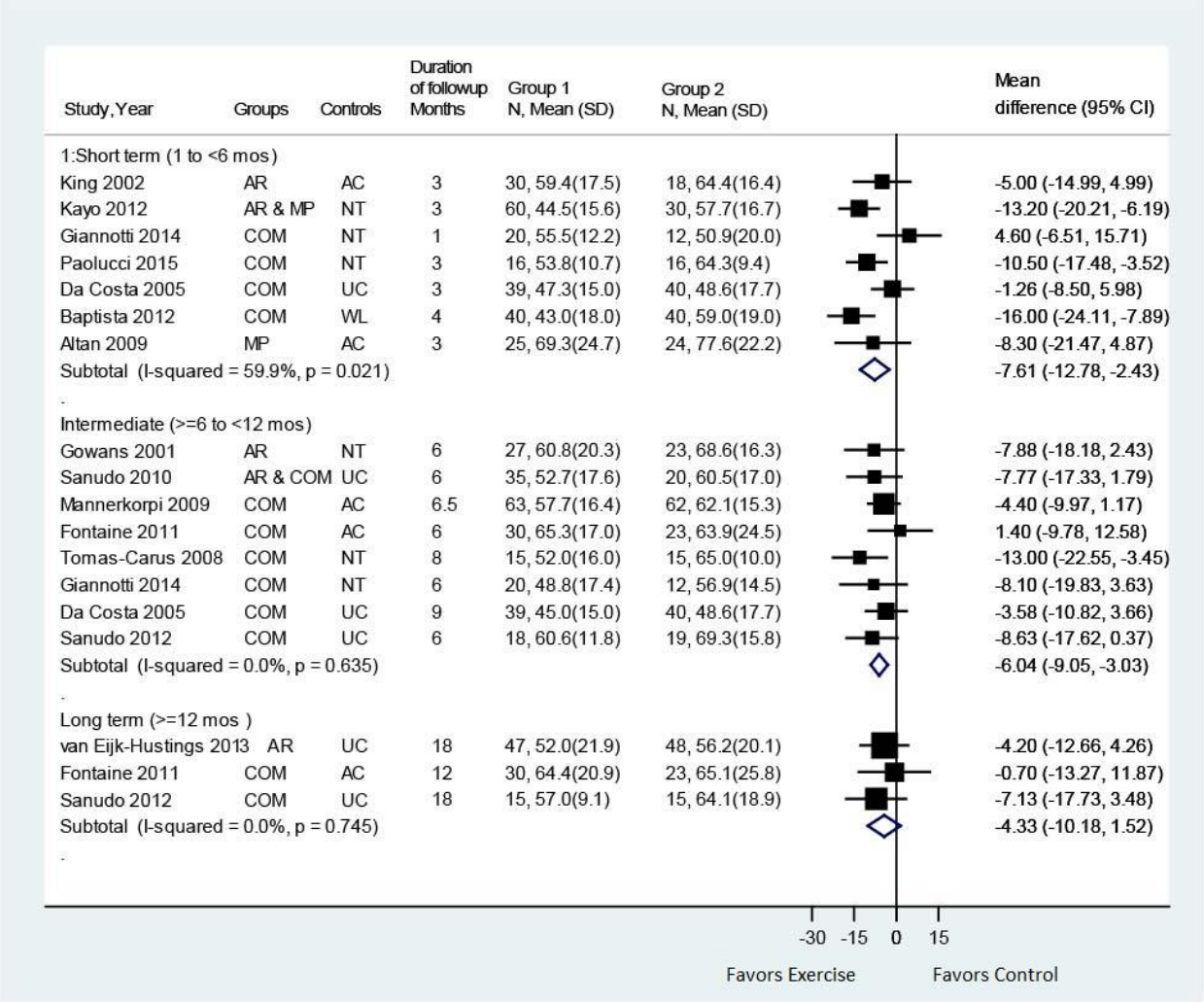
Exercise Compared With Other Nonpharmacological Therapies

Findings for exercise versus other nonpharmacological therapies are addressed in the sections for other nonpharmacological therapies.

Harms

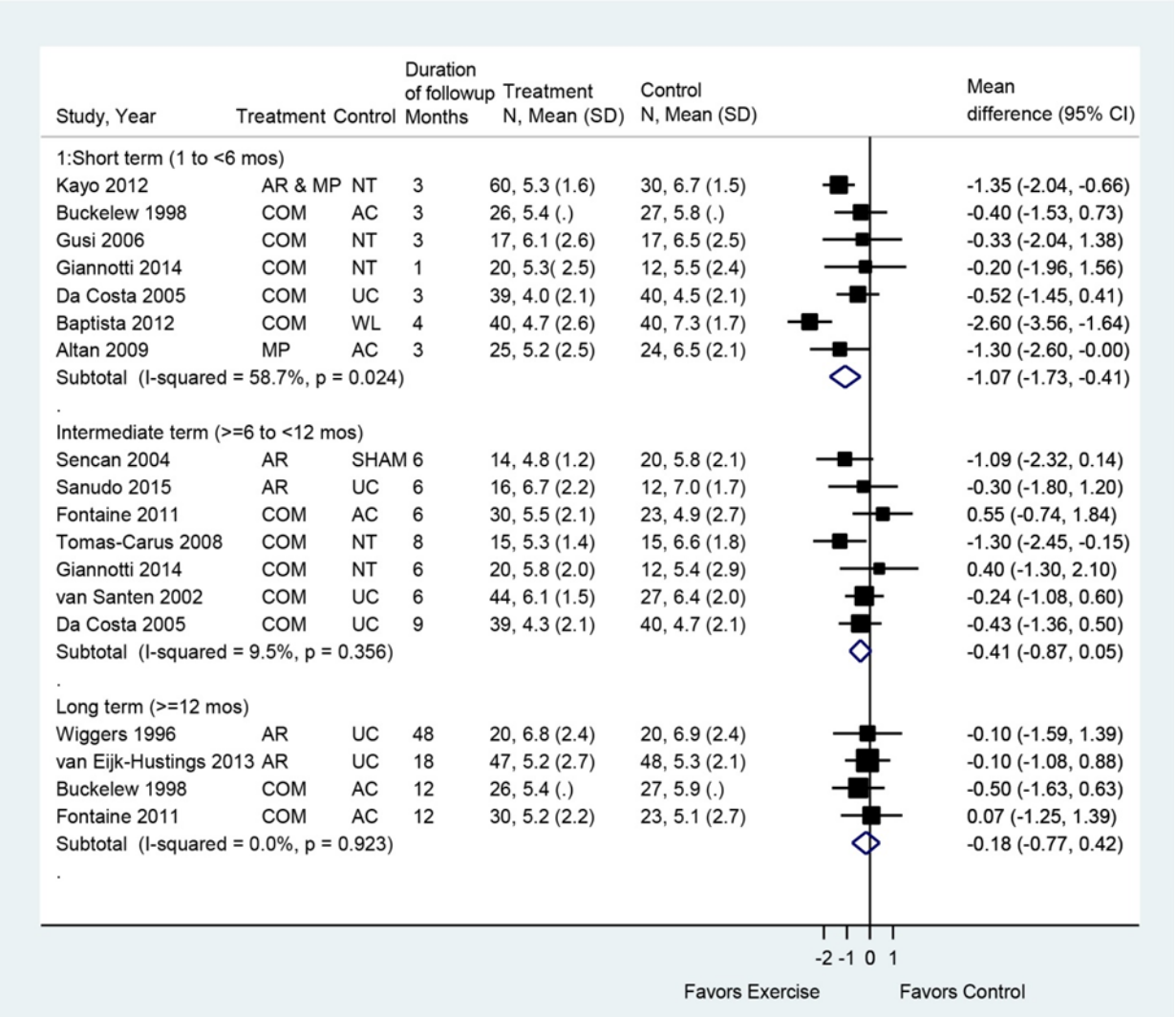
Most trials of exercise did not report on adverse events at all. One trial reported one nonstudy-related adverse event.[74] Two trials reported no adverse events.[75,78]

Figure 39. Exercise versus usual care, no treatment, waitlist, or an attention control for fibromyalgia: effects on function



AC = attention control; AR = aerobic exercise; AR & COM = aerobic exercise in one arm and combination exercise in another arm; AR & MP = aerobic exercise in one arm and muscle performance exercise in another arm; CI = confidence interval; COM = combination exercise therapy; MP = muscle performance exercise; MP+NR = muscle performance plus neuromuscular rehabilitation exercise; NT = no treatment; SD = standard deviation; UC = usual care; WL = waitlist

Figure 40. Exercise versus usual care, no treatment, waitlist, or attention control for fibromyalgia: effects on pain



AC = attention control; AR = aerobic exercise; AR & MP = aerobic exercise in one arm and muscle performance exercise in another arm; CI = confidence interval; COM = combination exercise therapy; MP = muscle performance exercise; MP+NR = muscle performance plus neuromuscular rehabilitation exercise; NT = no treatment; SD = standard deviation; UC = usual care; WL = waitlist

Psychological Therapies for Fibromyalgia

Key Points

- CBT was associated with a slightly greater effect on function (FIQ Total Score) compared with usual care or waitlist in the short term (2 trials, pooled MD −10.67, 95% CI −17 to −4.30, $I^{2=}$0%, 0-100 scale). The pooled estimate at intermediate term was not statistically significant due to heterogeneity, however, individual trials showed a greater effect than usual care, and a third trial using the 0 to 10 FIQ Physical Impairment Scale showed a greater effect of CBT than attention control (MD −1.8, 95% CI −2.9 to −0.70); evidence from two poor-quality trials was insufficient to determine effects on long-term function (SOE: low for short term and intermediate term, insufficient for long term).

- CBT was associated with a slight improvement in pain (on a 0-10 scale) compared with usual care or waitlist in the short term (3 trials, pooled MD −0.78, 95% CI −1.30 to −0.17), but not in the intermediate term (2 trials, pooled MD −0.44, 95% CI −1.30 to 0.01); evidence from one poor-quality trial was insufficient to determine effects on long-term pain (SOE: low for short term and intermediate term, insufficient for long term).
- Data were insufficient to determine the effects of EMG biofeedback on function and pain compared with attention controls in the short and long term (1 poor-quality trial) and with usual care in the intermediate term (1 poor-quality trial), and for the impact of guided imagery versus attention control in the short term (1 poor-quality trial) (SOE: insufficient for all comparisons and time points).
- CBT was associated with a slight benefit compared with pharmacological treatment (pregabalin, duloxetine) for function (MD −4.0 on the 0-100 FIQ, 95% CI −7.7 to −0.27), but not for pain (MD 0.2 on a 0-100 VAS, 95% CI −4.0 to 4.4) at intermediate term (SOE: low).
- There was insufficient evidence to determine the impact on pain and function for the following: CBT versus pharmacological treatment (amitriptyline) over the short term (fair-quality trial) and EEG biofeedback versus pharmacological treatment (escitalopram) over the short and intermediate term (poor-quality trial) (SOE: insufficient); long-term data were not reported.
- There was insufficient evidence to determine the effects of psychological therapies versus exercise on function and pain in the short term (1 small trial of biofeedback), intermediate term (2 trials of CBT and biofeedback) and long term (3 trials of CBT, biofeedback, and relaxation for function; 4 trials of CBT [2], biofeedback, and relaxation for pain). All trials were considered poor quality (SOE: insufficient for function and pain at all time points).
- Data on harms were insufficient. Adverse events were poorly reported across the five poor-quality trials but were overall minor and occurred at similar frequencies between groups. In one trial, however, fewer patients who received stress management (4.8%) compared with usual care (50%) withdrew from the trial, citing increased depression and worsening of symptoms, respectively (SOE: insufficient).

Detailed Synthesis

A total of 14 trials of psychological therapy for fibromyalgia met our inclusion criteria: nine trials (across 10 publications) featured a CBT component,[87,96-100,102,103,106,112] three trials included biofeedback (electromyography [EMG] or electroencephalography [EEG]),[67,86,107] and one trial each included relaxation training[111] or guided imagery[101] (Table 36 and Appendix D). The various psychological interventions were compared with usual care, waitlist control or attention control groups (10 trials),[67,86,87,96-103] pharmacological therapy (3 trials),[96,106,107] or exercise therapy (5 trials).[67,86,87,111,112]

The majority of subjects in all the trials were female (range 90% to 100%) and mean ages ranged from 32 to 52 years. Sample sizes ranged between 32 and 169 subjects (total sample=1,167). Therapy duration and frequency in CBT trials ranged from 6 weekly sessions to 20 sessions over 14 weeks. CBT was delivered in groups in eight studies[96,98-100,102,103,106,112] and by telephone[97] in another. All CBT studies except two were of CBT as traditionally delivered for the treatment of pain problems. The two exceptions were a study of Acceptance and Commitment Therapy (ACT), and a Stress Management Therapy (SMT) intervention that spent

equal time between presentations on stress mechanisms and training on pain coping and relaxation strategies; however, the interventions were similar enough to standard CBT to be included in this analysis. Session lengths ranged from 30 minutes up to 120 minutes. In the five trials of biofeedback and associated interventions, therapy duration ranged from 4 to 16 weeks and was delivered individually in the three biofeedback trials and in groups for the remaining two trials. The frequency ranged from one to five times per week with sessions as short as 25 minutes and as long as 3 hours. Short-term outcomes (<6 months) were reported by three CBT studies[97,99,102,106] and three biofeedback trials.[67,101,107] Intermediate outcomes (6 to <12 months) were reported by four CBT trials[96,98,100,112] and one trial of biofeedback.[86] Long-term outcomes (≥12 months) were reported by four CBT trials[87,100,103,112] and two biofeedback trials.[67,111] Studies were conducted in Brazil, the Netherlands, Norway, Spain, Sweden, Turkey, and the United States.

Of the nine CBT trials, three were considered fair quality,[96,99,102,106] while the remaining six were rated poor quality[87,97,98,100,103,112] (Appendix E). Among the remaining trials of biofeedback, relaxation, and guided imagery interventions, all were rated poor quality.[67,86,101,107,111] Methodological shortcomings included lack of blinding in fair-quality and poor-quality trials, and unclear allocation concealment methods, poor compliance, and high attrition in the poor-quality trials. The nature of the intervention types precluded blinding of participants in all trials.

Table 36. Fibromyalgia: psychological therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Alda,[96] 2011 6 months Years since diagnosis: 12.9 vs. 11.2 vs.11.7 *Fair*	A. CBT (n=57): 10-12 week program; 10 weekly 90-minute group sessions of cognitive restructuring and training in cognitive and behavioral coping strategies. B. Recommended pharmacological treatment (n=56): pregabalin (300-600 mg/day); duloxetine (60-120 mg/day) for patients with major depressive disorder. C. Usual care (n=56): standard care offered by general practitioners at subjects' health centers who received a guide for the treatment of FM in primary care.	A vs. B vs. C Age: 46 vs. 47 years vs. 47 years Females: 95% vs. 93% vs. 96% Race NR FIQ (mean, 0-100): 65.9 vs. 66.4 vs. 64.5 Pain VAS (mean, 0-100): 64.2 vs. 68.1 vs. 64.7	A vs. B <u>6 months</u>: FIQ: 48.8 vs. 52.8; MD −4.0 (95% CI −7.730 to −0.270) Pain VAS: 40.7 vs. 40.5; MD 0.2 (95% CI −3.996 to 4.396) A vs. C <u>6 months:</u> FIQ: 48.8 vs. 53.3, MD −4.5 (95% CI −7.91 to −1.09) Pain VAS: 40.70 vs. 44.3, MD −3.6 (95% CI −7.617 to 0.417)	A vs. B <u>6 months</u>: HAM-D (0-50): 7.9 vs. 8.2; MD −0.3 (95% CI −1.226 to 0.626) HAM-A (0-50): 7.3 vs. 7.4; MD −0.1 (95% CI −1.247 to 1.047) A vs. C <u>6 months</u>: HAM-D: 7.9 vs. 8.6, MD −0.7 (95% CI −1.719 to 0.319) HAM-A: 7.3 vs. 7.6, MD −0.3 (95% CI −1.361 to 0.761)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Ang, 2010[97] 1.5 months Duration of fibromyalgia, years: 11.8 vs. 12.3 *Poor*	A. CBT (n=17): 6 weekly 30-40 minute sessions of telephone-delivered CBT (activity pacing, pleasant activity scheduling, relaxation, automatic thoughts and pain, cognitive restructuring, and stress management) B. Usual care (n=15): customary care from subject's treating physician	A vs. B Age: 51 vs. 47 years Female: 100% vs. 100% White: 81% vs. 80% FIQ total (mean, 0-100): 62.2 vs. 67.8 FIQ Physical Impairment (PI) (0-10): 5.6 vs. 5.4 FIQ Pain (0-10): 7.6 vs. 7.8	A vs. B <u>1.5 months:</u> Proportion of patients with clinically meaningful improvement from baseline FIQ total (14%): 33% vs. 15%, RR 2.2 (95% CI 0.5 to 9.3) mean change from baseline: FIQ PI: −0.6 vs. 0.5, adjusted P=0.13; FIQ Pain: −0.6 (1.6) vs. −0.3 (1.7), adjusted P=0.60	A vs. B <u>1.5 months:</u> PHQ-8 (0-24): mean change from baseline −0.9 (5.2) vs. 0.0 (4.1), adjusted P=0.80; overall effect size=0.60

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Buckelew 1998[67] 3, 12, and 24 months Duration of symptoms, years: 11.6 vs. 10.0 vs. 11.6 *Poor*	A. Electromyographic biofeedback and relaxation training (n=29): 1 session for 1.5-3 hours per week for 6 weeks and instructions to train 2 additional times independently per week. Subjects were taught cognitive and muscular relaxation strategies. 6-week individual training was followed by 2-year group maintenance phase of one-hour groups once per month. B. Attention control (n=30): 1 session for 1.5-3 hours per week for 6 weeks. Subjects received educational information on diagnosis and treatment of FM and general health topics information. This was followed by one hour groups once per month for 2 years. C. Combination Exercise (n=30): 1 session for 1.5 hours per week for 6 weeks and instructions to train 2 additional times independently per week. Sessions consisted of active range of motion exercises, strengthening exercises, low to moderate intensity aerobic exercise, proper posture and body mechanics instruction, and instructions on the use of heat, cold, and massage. 6-week individual training was followed by 2-year group maintenance phase of one-hour groups once per month.	A vs. B vs. C Age: 44 vs. 44 vs. 46 years Female: 97% vs. 90% vs. 93% Race NR AIMS physical activity subscale (median, 0-10): 6.0 vs. 6.0 vs. 4.0 Pain VAS (median, 0-10): 5.8 vs. 5.9 vs. 6.3	A vs. B <u>3-months:</u> AIMS physical activity subscale, median (median change from baseline): 6.0 (0) vs. 6.0 (0), NS Pain VAS, median (median change from baseline): 5.2 (−0.2) vs. 5.8 (−0.5), NS <u>24-months:</u> AIMS physical activity subscale, median (median change from baseline): 6.0 (0) vs. 6.0 (0), NS Pain VAS, median (median change from baseline): 5.2 (−1.1) vs. 5.4 (−0.6), NS A vs. C <u>3 months:</u> AIMS physical activity subscale, median (median change from baseline): 6.0 (0) vs. 4.0 (0), p≤0.05 Pain VAS, median (median change from baseline): 5.2 (−0.2) vs. 5.4 (−0.8), NS <u>24 months:</u> AIMS physical activity subscale, median (median change from baseline): 6.0 (0) vs. 4.0 (0), p≤0.05 Pain VAS, median (median change from baseline): 5.2 (−1.1) vs. 5.5 (−1.2), NS	A vs. B <u>3-months:</u> SCL-90-R Global Severity Index, median (median change from baseline): 65.0 (-2) vs. 65.0 (0), NS CES-D, median (median change from baseline): 10.0 (-2) vs. 13.0 (3), NS Sleep scale, median (median change from baseline): 7.0 (0) vs. 5.0 (0), NS <u>24-months:</u> SCL-90-R Global Severity Index, median (median change from baseline): 64.0 (−1) vs. 67.0 (−1), NS CES-D, median (median change from baseline): 10.0 (-2) vs. 12.0 (-2), NS Sleep scale, median (median change from baseline): 6.0 (-2) vs. 6.0 (0), NS A vs. C <u>3 months:</u> SCL-90-R Global Severity Index, median (median change from baseline): 65.0 (−2) vs. 65.5 (−3), NS CES-D, median (median change from baseline): 10.0 (−2) vs. 13.5 (−2.5), NS Sleep scale, median (median change from baseline): 7.0 (0) vs. 8.0 (0), NS <u>24 months:</u> SCL-90-R Global Severity Index, median (median change from baseline): 64.0 (-1) vs. 65.5 (−2.5), NS CES-D, median (median change from baseline): 10.0 (−2) vs. 11.5 (−3.5), NS Sleep scale, median (median change from baseline): 6.0 (−2) vs. 7.5 (0), NS

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Castel,[98] 2012 3 and 6 months A vs. B Pain duration, years: 13.6 vs. 11.6 *Poor*	A. CBT plus usual pharmacological care (n=34): CBT conducted in groups (except for one individual session); 14 weekly 2 hour sessions. CBT included education about FM and pain, autogenic training, cognitive restructuring, CBT for insomnia, assertiveness training, activity pacing, pleasant activity scheduling, goal setting, and relapse prevention. B. Usual care (n=30): usual pharmacological care, including analgesics, antidepressants, anticonvulsants, and myorelaxants	A vs. B Age: 50 vs. 49 years Female: 94% vs. 100% White: 100% vs. 100% FIQ (scale NR): 62.7 vs. 66.1 Pain NRS (0-10): 6.1 vs. 6.9	A vs. B <u>3 months:</u> Proportion of patients with MCSD (14% improvement from baseline): FIQ: 55.9% vs. 20%; OR 5.1 (95% CI 1.7 to 15.6); RR 2.8 (95% CI 1.3 to 6.1) Pain: 14.6% vs. 10%; RR 1.5 (95% CI 0.4 to 5.7) FIQ: 52.8 vs. 66.3; MD -13.5 (95% CI -15.5 to -11.5) Pain NRS: 5.9 vs. 6.8; MD −0.9 (95% CI -1.1 to −0.7) <u>6 months:</u> Proportion of patients with MCSD: FIQ: 58.8% vs. 20%; OR 5.7 (95% CI 1.9 to 17.8); RR 2.9 (95% CI 1.4 to 6.3) Pain: 17.6% vs. 13.3%; RR 1.3 (95% CI 0.4 to 4.2) FIQ: 50.5 vs. 68.5; MD −18.0 (95% CI −20.095 to −15.905) Pain NRS: 5.7 vs. 6.8; MD −1.1 (95% CI −1.333 to −0.867)	A vs. B <u>3 months:</u> HADS (scale NR): 15.4 (1.3) vs. 22.3 (1.4); MD −6.9 (95% CI −7.685 to −6.115) MOS Sleep quantity (scale NR): 6.9 (0.2) vs. 5.5 (0.3); MD 1.4 (95% CI 1.254 to 1.546), p <0.0001 MOS Sleep index problems (scale NR): 40.1 (1.6) vs. 28.8 (1.7); MD 11.3 (95% CI 10.340 to 12.260) <u>6 months:</u> HADS: 15.7 (1.3) vs. 23.7 (1.4); MD −8.0 (95% CI −8.785 to −7.215) MOS Sleep quantity: 6.7 (0.2) vs. 5.6 (0.3); MD 1.1 (95% CI 0.954 to 1.25) MOS Sleep index problems: 39.9 (1.5) vs. 28.0 (1.6); MD 11.9 (95% CI 10.998 to 12.802)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Falcão, 2008[106] 3 months Disease duration, years: 3.5 vs. 3.7 *Fair*	A. CBT plus Amitriptyline (n=30): amitriptyline 12.5/mg per day during first week, then increase dose to 25 mg/day. Those with intolerance or side effects to amitriptyline were given cyclobenzaprine 5 mg/day in the first week and then 10 mg/day. Routine medical visits once a week for 10 weeks for brief discussions with the doctors. Immediately after each visit, they had a group CBT session, consisting of progressive relaxation training with electromyographic biofeedback, cognitive restructuring, and stress management. B. Amitriptyline only (control) (n=30): amitriptyline 12.5/mg per day during first week, then increase dose to 25 mg/day. Those with intolerance or side effects to amitriptyline were given cyclobenzaprine 5 mg/day in the first week and then 10 mg/day. Routine medical visits once a week for 10 weeks for brief discussions with the doctors.	A vs. B Age: 45 vs. 46 years Female: 100% vs. 100% Caucasian: 80% vs. 77% FIQ (0-100): 64.9 vs. 69.6 Pain VAS (0-10): 6.9 vs. 7.0	A vs. B <u>3 months</u>: FIQ: 38.7 vs. 42.8; MD −4.1 (95% CI −18.765 to 10.565) Pain VAS: 4.4 vs. 5.1; MD −0.7 (95% CI −2.841 to 1.441)	A vs. B <u>3 months</u>: BDI (0-63): 10.6 vs. 15.6; MD −5.0 (95% CI −11.122 to 1.122) STAI-State scale (20-80): 45.8 (2.5) vs. 46.8 (2.3); MD −1.0 (95% CI −2.351 to 0.351) SF-36 Physical Capacity (0-100): 59.6 vs. 54.0; MD 5.6 (95% CI −11.905 to 23.105) SF-36 Pain (0-100): 48.4 vs. 45.5; MD 2.9 (95% CI −10.783 to 16.583) SF-36 Mental Health (0-100): 69.9 vs. 56.2; MD 13.7 (95% CI 0.070 to 27.330)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Jensen 2012,[99] Wicksell 2013[102] 3-4 months Time since FM onset, years: 10.5 vs. 11.8 *Fair*	A. Acceptance and Commitment Therapy (ACT) (n=25): 12 weekly 90-minute group sessions: exposure to personally important situations and activities previously avoided due to pain and distress, training to distance self from pain and distress. B. Waiting list control (n=18)	A vs. B Age: 45 vs. 47 years Female: 100% vs. 100% FIQ (0-100): 49.3 vs. 48.7 PDI (scale NR): 40.0 vs. 39.0 Pain VAS (0-100): 61 vs. 65.0 Pain NRS (0-10): 4.2 vs. 4.3	A vs. B <u>3-4 months</u> FIQ: 37.4 vs. 45.7, Cohen's d=0.66 (95% CI −0.06 to 1.37); MD −8.3 (95% CI −17.056 to 0.456) PDI: 28.1 vs. 38.1, Cohen's d=0.73 (95% CI −0.00 to 1.44); MD −10.0 (95% CI −19.740 to −0.260) Pain VAS: means NR but group X time interaction P=0.26 Pain NRS: 3.9 vs. 4.8, Cohen's d= 0.82 (95% CI 0.08 to 1.54); MD −0.90 (95% CI −1.674 to −0.126)	A vs. B <u>3-4 months</u> BDI (0-63): 10.7 vs. 16.4, Cohen's d=0.64 (95% CI −0.08 to 1.35); MD −5.7 (95% CI −12.044 to 0.644) STAI-State: 39.8 vs. 45.4; Cohen's d=0.55 (95% CI −0.17 to 1.26); MD −5.6 (95% CI −12.751 to 1.551) SF-36 Mental: 46.0 vs. 34.7, Cohen's d=1.06 (95% CI 0.28 to 1.82); MD 11.3 (95% CI 3.761 to 18.839) SF-36 Physical (0−100): 28.4 vs. 31.1, Cohen's d=0.28 (95% CI −0.45 to 1.00); MD −2.7 (95% CI −9.401 to 4.001),
Kayiran 2010[107] 4 to 5 months Duration of symptoms: 5 years *Poor*	A. EEG Biofeedback (Neurofeedback) (n=20): 5 sessions based on sensorimotor rhythm training protocol per week for 4 weeks. Each session consisted of 10 sensorimotor rhythm training periods lasting for 3 minutes for a total of 30 minutes B. Escitalopram (n=20): 10 mg/day for 8 weeks (control group)	A vs. B Age: 32 vs. 32 years Female: 100% vs. 100% FIQ (mean, 0−100): 70 vs. 74* Pain VAS (mean, 0−10): 8.9 vs. 9.1	A vs. B <u>4-5 months</u>: FIQ: 19 vs. 48*, P=NR Pain VAS: 2.6 vs. 5.3; MD −2.7 (95% CI −3.7 to −1.7)	A vs. B <u>4-5 months</u>: HAM-D (0-50): 6.3 vs. 13.4; MD −7.1 (95% CI −9.1 to −5.1) BDI (0-63) : 4.7 vs. 12.3; MD −7.6, 95% CI −9.7 to −5.5) HAM-A (0-56): 7.1 vs. 15.2; MD −8.1 (95% CI −11.0 to −5.2) BAI (0-63): 7.2 vs.. 16.7; MD −9.5 (95% CI −13.9 to −5.1) SF-36*: Physical functioning (0-100): 77 vs. 65, P<0.05 Bodily pain: 70 vs. 45, P<0.05 Role-physical (0-100): 90 vs. 43, P<0.05 Role-emotional (0-100): 95 vs. 51, P<0.05 Social functioning (0-100): 76 vs. 65, P<0.05 General mental health (0-100): 74 vs. 59, P<0.05 General health (0-100): 72 vs. 28, P<0.05 Vitality (0-100): 70 vs. 50, P<0.05

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Larsson 2015[111] 13 to 18 months Duration of symptoms: 10 years *Poor*	A. Relaxation therapy (n=63): Two group sessions of 5-8 subjects per week for 15 weeks. The intervention was preceded by an individual meeting covering instructions and allowing for adjustments to the intervention. The sessions lasted 25 minutes and consisted of autogenic training guided by physiotherapist and were followed by stretching. B. Resistance exercise (Strength) (n=67): Two group sessions of 5-7 subjects per week for 15 weeks. The intervention was preceded by an individual meeting going over instructions on the intervention, testing, and modifications of specific exercises. Sessions were based on a resistance exercise program aiming to improve muscle strength, focusing on large muscle groups in the lower extremity.	A vs. B Age: 52 vs. 51 Female: 100% vs. 100% FIQ (0-100): 61.1 vs. 60.5 Pain VAS (0-100): 52.4 vs. 49.3 PDI (0-70): 35.0 vs. 35.3	A vs. B <u>13-18 months</u> FIQ: 55.4 vs. 57.1, (MD −1.7, 95% CI −9.3 to 5.9) Pain VAS: 52.1 vs. 49.2, (MD 2.9, 95% CI −5.5 to 11.3) PDI: 33.7 vs. 33.0, (MD 0.7, 95% CI −4.0 to 5.4)	A vs. B <u>13-18 months</u> SF-36 PCS (0-100): 32.0 vs. 32.2, (MD −0.2, 95% CI −3.8 to 3.4) SF-36 MCS (0-100): 40.0 vs. 39.2, (MD 0.8, 95% CI −4.6 to 6.2) Patient global impression of change (mean, 1-7): Values NR but difference was NS

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Redondo, 2004[112] 6 and 12 months Pain duration NR *Poor*	A. CBT (n=21): 1, 2.5 hour session per week for 8 weeks. Sessions included information about chronic pain and FM, relaxation techniques, and pain coping strategies training. B. Combination Exercise (n=19): 5, 45-minute sessions per week for 8 weeks. Each week included 1 session of aquatic exercises, 2 sessions of flexibility and endurance exercises, and 2 sessions of cardiovascular exercises. All subjects: Offered ibuprofen or diclofenac, 25 mg of amitriptyline a day, and acetaminophen.	A vs. B Age NR Female: 100% vs. 100% FIQ total (mean, 0-80): 52.0 vs. 52.0 FIQ pain (mean, 0-10): 7.3 vs. 6.8 FIQ depression (mean, 0-10): 5.2 vs. 5.3 FIQ anxiety (mean, 0-10): 6.4 vs. 6.3	A vs. B <u>6 months:</u> FIQ total: 47.4 vs. 48.0, (MD −0.6, 95% CI −12.6 to 11.4) FIQ pain: 5.9 vs. 6.9, (MD −1.0, 95% CI −2.8 to 0.8) <u>12 months:</u> FIQ: 47.8 vs. 47.7; (MD 0.1, 95% CI −10.5 to 10.7) FIQ pain: 6.3 vs. 6.6; (MD −0.3, 95% CI −2.0 to 1.3)	A vs. B <u>6 months:</u> FIQ depression (0-10): 5.2 vs. 5.3, (MD −0.1, 95% CI −2.6 to 2.4) FIQ anxiety (0-10): 6.0 vs. 5.8, (MD 0.2, 95% CI −2.2 to 2.6) BAI: 25.2 vs. 22.1, (MD 3.1, 95% CI −5.1 to 11.3) BDI (0-63): 17.1 vs. 15.0, (MD 2.1, 95% CI −6.6 to 10.8) SF-36 physical functioning (0-100): 52.2 vs. 43.9, (MD 8.3, 95% CI −6.4 to 23.0) SF-36 physical role (0-100): 22.4 vs. 18.3, (MD 4.1, 95% CI −21.2 to 29.4) SF-36 bodily pain (0-100): 31.4 vs. 32.9, (MD −1.5, 95% CI −16.1 to 13.1) SF-36 social functioning (0-100): 66.4 vs. 66.9, (MD −0.5, 95% CI −21.6 to 20.6) SF-36 emotional role (0-100): 68.4 vs. 66.0, (MD 2.4, 95% CI −28.2 to 33.0) SF-36 mental health (0-100): 48.9 vs. 51.8, (MD −2.9, 95% CI −19.3 to 13.5) <u>12 months:</u> FIQ depression: 5.4 vs. 4.9; (MD 0.5, 95% CI −2.0 to 3.0) FIQ anxiety: 6.0 vs. 5.8; (MD 0.2, 95% CI −2.1 to 2.5) BAI: 20.0 vs. 20.0; (MD 0.0, 95% CI −7.4 to 7.4) BDI: 13.0 vs. 13.6; (MD −0.6, 95% CI −7.9 to 6.7) SF-36 physical functioning: 38.9 vs. 41.6; (MD −2.7, 95% CI −19.5 to 14.1) SF-36 physical role: 26.1 vs. 31.0; (MD −4.9, 95% CI −27.9 to 18.1) SF-36 bodily pain: 33.8 vs. 34.3; (MD −0.5, 95% CI −20.9 to 19.9) SF-36 social functioning: 60.7 vs. 57.2; (MD 3.5, 95% CI −17.2 to 24.2) SF-36 emotional role: 66.7 vs. 58.7; (MD 8.0, 95% CI −19.2 to 35.2) SF-36 mental health: 56.5 vs. 53.8; (MD 2.7, 95% CI −19.1 to 24.5)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Thieme, 2006[100] 6 and 12 months Duration of symptoms, years: 9.1 vs. 8.7 *Poor*	A. CBT (n=42): 2-hour group sessions weekly for 15 weeks. Sessions focused on changing patients' thinking and problem-solving, stress and pain coping strategies, and relaxation exercises performed during and between sessions. B. Attention control (n=40): 2-hour group sessions weekly for 15 weeks: general discussions about medical and psychosocial problems of fibromyalgia.	A vs. B Age: 49 vs. 47 years Female: 100% vs. 100% FIQ physical impairment (mean, 0-10): 4.4 vs. 4.2 WHYMPI pain intensity (mean, 0-6): 4.2 vs. 3.8	A vs. B <u>6 months</u> FIQ physical impairment: 3.0 vs. 4.8; MD −1.8 (95% CI −2.899 to −0.701) WHYMPI pain intensity: 3.7 vs. 4.1; MD −0.4 (95% CI −0.841 to 0.041) <u>12 months</u> FIQ physical impairment: 3.4 vs. 5.2; MD −1.8 (95% CI −2.855 to −0.745) WHYMPI pain intensity: 3.2 vs. 4.1; MD −0.9 (95% CI −1.537 to −0.263)	A vs. B <u>6 months</u> WHYMPI affective distress: 2.6 vs. 4.0; MD −1.4 (95% CI −1.952 to −0.848) <u>12 months</u> WHYMPI affective distress: 2.6 vs. 4.2; MD −1.6 (95% CI −2.172 to −1.028)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Van Santen 2002[86] Post 6-month intervention Duration of symptoms, years: 10.1 vs. 15.4 vs. 15.4 *Poor*	A. Electromyographic biofeedback (n=56): Progressive muscle relaxation and frontalis EMG biofeedback; 30-minute individual sessions 2 times per week for 8 weeks; subjects encouraged to practice at home twice daily for the 8 weeks then for 16 more weeks. Subjects randomized to education aimed at compliance with biofeedback training (6 90-minute sessions over 24 weeks). B. Usual care (n=29): General physicians informed not to prescribe or encourage aerobic exercises and relaxation. Intervention duration: 6 months C. Combination Exercise (n=58): 60-minute group sessions of twice a week for 24 weeks; aerobic exercises, postural strengthening, general flexibility and balance exercises, and isometric muscle strengthening; subjects encouraged to attend third, unsupervised, 60-minute session and to use sauna or swimming pool after sessions.	A vs. B Age: 44 vs. 43 vs. 46 years Female: 100% vs. 100% vs. 100% Race NR SIP Physical score (0-100): 11.4 vs. 9.8 vs.11.3 Pain VAS (0-100): 59.1 vs. 62.4 vs. 66.8 AIMS (0-10): 3.1 vs. 5.4 vs. 1.9 SIP Total score (0-100): 14.0 vs. 11.4 vs. 14.4 SIP Psychosocial score (0-100): 15.8 vs. 18.1 vs. 16.3	A vs. B <u>6-months:</u> SIP physical score, mean change: −1.6 (95% CI −3.4 to 0.2) vs. −0.6 (95% CI −2.9 to 1.7) SIP total score, mean change: −2.3 (95% CI −4.3 to −0.3) vs. −1.4 (95% CI −3.4 to 0.6) AIMS, mean change: 0.4 (95% CI −0.1 to 0.9) vs. 0.8 (95% CI −1.8 to −0.2) SIP total score, mean change: −2.3 (95% CI −4.3 to −0.3) vs. −1.4 (95% CI −3.4 to 0.6) Pain VAS, mean change: −0.6 (95% CI −6.5 to 5.3) vs. 1.3 (95% CI −4.5 to 7.1) A vs. C <u>6-months:</u> SIP physical score, mean change: −1.6 (95% CI −3.4 to 0.2) vs. −1.7 (95% CI −3.7 to 0.3), NS SIP total score, mean change: −2.3 (95% CI −4.3 to −0.3) vs. −1.9 (95% CI −3.9 to 0.1) AIMS, mean change: 0.4 (95% CI −0.1 to 0.9) vs. 0.1 (95% CI −0.6 to 0.8) Pain VAS, mean change: −0.6 (95% CI −6.5 to 5.3) vs. −5.5 (95% CI −10.9 to −0.1), NS	A vs. B <u>6-months:</u> SIP psychosocial score, mean change: −3.7 (95% CI −4.9 to −2.5) vs. −3.5 (95% CI −7.0 to 0.0) Patient global assessment of well-being, mean change: 0.3 (95% CI 0.0 to 0.6) vs. 0.5 (95% CI 0.2 to 0.8) A vs. C <u>6-months:</u> SIP psychosocial score, mean change: −3.7 (95% CI −4.9 to −2.5) vs. −3.2 (95% CI −6.2 to 0.2) Patient global assessment of well-being, mean change: 0.3 (95% CI 0.0 to 0.6) vs. 0.5 (95% CI 0.2 to 0.8)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Verkaik, 2014[101] 1.5 months Duration of symptoms, NR *Poor*	A. Guided imagery (n=33): Two 1.5 hour group sessions of 6-12 subjects. The first sessions consisted of group discussion, the theoretical background of guided imagery, and instructions to practice at least one exercise daily for 4 weeks. Each exercise was a CD and contained relaxation techniques, music, positive imagery, and pain management techniques. The second group session took place after the 4 weeks and consisted of a group discussion. B. Attention control (n=37): Two 1.5 hour group sessions of 6-12 subjects held 4 weeks apart. Group sessions were a group discussion and did not contain any information or training on guided imagery.	A vs. B Age: 47 vs. 48 Female: 100% vs. 97% FIQ(0-100): 53.7 vs. 56.4 Pain VAS (0-10): 5.9 vs. 5.8	A vs. B <u>1.5 months</u> FIQ: 54.2 vs. 53.0, MD 1.2, 95% CI −0.2 to 2.6) Pain VAS: NR	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Wigers, 1996[87] 48 months Fibromyalgia duration A vs. B vs. C Mean: 11 vs. 9 years *Poor*	A. Stress management (n=20): 90 minute group sessions of 10 patients done 2 times a week for 6 weeks followed by 1 session per week for the next 8 weeks. Sessions consisted of equal portions of presentations stress mechanisms and strategies for improving quality of life, group discussions on patients' experiences of stress and coping with pain, and relaxation training aimed at helping cope with stress and pain. B. Usual care (n=20): Subjects continued treatments they had been using at baseline. C. Aerobic exercise (n=20): 45 minute group sessions of 10 patients done 3 times a week for 14 weeks. The exercise program involved the whole body and aimed to minimize eccentric muscle strain. Sessions consisted of training to music (further details not given) and aerobic games.	A vs. B Age: 44 vs. 46 vs. 43 years Female: 90% vs. 95% vs.. 90% Pain VAS (0-100): 72 vs. 65 vs. 72	A vs. B <u>48 months</u> Pain VAS: 70 vs. 69, (MD 1, 95% CI −12.6 to 14.6) A vs. C <u>48 months</u> Pain VAS: 70 vs. 68, (MD 2, 95% CI −11.6 to 15.6)	A vs. B <u>48 months</u> Depression VAS (0-100): 40 vs. 30, (MD 10, 95% CI −8.9 to 28.9) Global subjective improvement: 47% (6/13) vs. 12% (2/16), (RR 3.7, 95% CI 0.9 to 15.3) A vs. C <u>48 months</u> Depression VAS: 40 vs. 32, (MD 8, 95% CI −11.9 to 27.9) Global subjective improvement: 47% (6/13) vs. 75% (11/15), (RR 0.6, 95% CI 0.3 to 1.2)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Williams, 2002[103] 12 months Fibromyalgia duration, 8.6 years *Poor*	A. Group CBT plus Usual Care (n=76): 6 1-hour group sessions over 4-week period: progressive muscle relaxation, imagery, activity pacing, pleasant activity scheduling, communication skills and assertiveness training, cognitive restructuring, stress management and problem-solving. B. Usual Care (n=69): Standard pharmacological management (typically low-dose tricyclic antidepressant medication, analgesics, and/or antidepressants) plus suggestions to engage in aerobic fitness.	A + B Age, mean, years: 47.7 Females: 90% Race: White non-Hispanic 88%, black non-Hispanic 9%, Hispanic 2%, Asian American 1% MPQ-Sensory (scale NR): 14.8 MPQ-Affective pain score (scale NR): 4.6	A vs. B 12 months Mean (SD): NR Proportion of subjects who improved more than 12 points from baseline on MPQ-Sensory scale: 3.9% vs. 7.2%; RR 0.54 (95% CI 0.14 to 2.2)	A vs. B 12 months Mean (SD) NR Proportion of subjects who improved more than 6.5 points from baseline on SF-36 PCS Score: 25% vs. 11.6%, OR 2.9; RR 2.2 (95% CI 0.98 to 4.99) Proportion of subjects who improved more than 5 points from baseline on MPQ-Affective scale: 9.2% vs. 8.7%, RR 1.1 (95% CI 0.37 to 3.0)

AIMS = Arthritis Impact Measurement Scales; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; CBT = cognitive-behavioral therapy; CES-D = Center for Epidemiologic Studies Depression Scale; CI = confidence interval; FIQ = Fibromyalgia Impact Questionnaire; HAM-D = Hamilton Rating Scale for Depression; HAM-A = Hamilton Anxiety Rating Scale; HADS = Hospital Anxiety and Depression Scale; MCSD = Minimal Clinically Significant Difference; MD = mean difference; MPQ = McGill Pain Questionnaire; PDI = Pain Disability Index; PHQ = Patient Health Questionnaire; PI = Physical Impairment; RR = risk ratio; SCL-90-R = Symptoms Checklist 90-Revised; SD = standard deviation; SIP = Sickness Impact Profile; SF-36 = Short-Form 36 questionnaire; SF-36 PCS = Short-Form 36 Physical Component Summary Score; SF-36 MCS = Short-Form 36 Mental Component Summary Score; STAI = State-Trait Anxiety Inventory; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Psychological Therapies Compared With Usual Care or Sham

Ten trials compared psychological interventions versus usual care, waitlist, or attention control.[67,86,87,96-103] All but one trial[99,102] were considered poor quality.

Functional Outcomes. Across types of psychological therapies, results for function were not consistent over the short term (Table 36). One trial reported that significantly more patients in the CBT group attained a clinically important improvement (≥14% on the FIQ total, 0-100 scale) from baseline compared with usual care (RR 2.8, 95% CI 1.3 to 6.1),[98] while another smaller trial did not (RR 2.2, 95% CI 0.5 to 9.3).[97] CBT was associated with a small improvement in function compared with usual care or waitlist in the short term (2 trials, pooled MD −10.67, 95% CI −17 to −4.30, I^2=0%, FIQ total score, 0-100 scale)[98,99,102] (Figure 41), but no differences were seen in trial each of guided imagery (FIQ total, 0 to 100 scale, MD 1.2, 95% CI −0.2 to 2.6)[101] and EMG biofeedback (median change from baseline 6.0 for both groups, Arthritis Impact Measurement Scales [AIMS] physical activity subscale, 0-10 scale)[67] versus attention control.

At intermediate term, one trial reported that substantially more CBT patients achieved a clinically important difference (≥14% on the FIQ total, 0-100 scale) compared with usual care (RR 2.9, 95% CI 1.9 to 17.8).[98] Individual trials showed CBT had a statistically greater effect on

function than usual care at intermediate term based on FIQ total score; however, the pooled estimate was not statistically significant due to heterogeneity (2 trials, pooled MD −10.36, 95% CI −23.52 to 2.80, I^2=84.5%, 0-100 scale)[96,98] (Figure 41). Findings from an additional trial suggested a greater effect of CBT on function compared with attention control based on a 0 to 10 FIQ Physical Impairment Scale (MD −1.8, 95% CI −2.9 to −0.70).[100] There was no clear difference between biofeedback and usual care on function according to the Sickness Impact Profile (SIP) physical score in one trial (mean change −1.6, 95% CI −3.4 to 0.2 versus −0.6, 95% CI −2.9 to 1.7, respectively, on a 0-100 scale).[86]

Data from three poor-quality trials were insufficient to determine the long-term effects of psychological therapies on function. One trial found no difference between CBT and usual care in the proportion of participants achieving a clinically meaningful change of 12 points from baseline on the McGill Pain Questionnaire (MPQ) Sensory Scale (RR 0.54, 95% CI 0.14 to 2.2).[103] A second trial reported that CBT resulted in greater improvement compared with attention control on the FIQ Physical Impairment Scale (MD −1.8 on a 0-10 scale, 95% CI −2.85 to −0.745).[100] A trial of biofeedback versus usual care reported median change in the AIMS Physical Activity subscale of 6.0 in both groups.[67]

Pain Outcomes. Psychological therapies (CBT and EMG biofeedback) were associated with a small improvement in pain compared with usual care, waitlist, or attention control at short-term followup (4 trials, pooled MD −0.74, 95% CI −1.20 to −0.28, I^2=0%)[67,97-99,102] (Figure 42); the estimate was similar when only trials of CBT were considered (3 trials, pooled MD −0.78, 95% CI −1.30 to −0.17, plot not shown).[97-99,102] When stratified by type of control (usual care), estimates were also similar, but results were no longer statistically significant. Psychological therapies (CBT, EMG biofeedback) were also associated with a small improvement in pain compared with usual care at intermediate term (3 trials, pooled MD −0.67, 95% CI −1.21 to −0.31, I^2=36.7%)[86,96,98] (Figure 42). Estimates were similar when the two CBT trials were pooled, but no longer statistically significant. Long term, there was no clear difference between psychological therapies (CBT or biofeedback) and attention control or usual care (2 trials, pooled MD 0.04, 95% CI −0.77 to 0.84, I^2=0%);[67,87] however, evidence across the two poor-quality trials was considered insufficient (Figure 42).

Other Outcomes. Results were mixed across trials for effects of CBT or ACT on secondary outcomes (Table 36). Only two trials were of fair quality.

In one fair-quality trial of ACT versus waitlist there were no differences between groups over the short term on the following: BDI, STAI-State scale or SF-36 PCS; ACT was associated with improvement in the SF-36 MCS.[99,102]

Another fair-quality trial reported intermediate-term outcomes and found no differences in either the Hospital Anxiety and Depression Scale (HAM-D) or Hamilton Anxiety Rating Scale (HAM-A) for the comparison of CBT versus usual care.[96] Across the poor-quality trials results were mixed across various secondary outcomes measures (Table 36).

Two poor-quality studies compared EMG biofeedback to attention control conditions; neither found differences on secondary outcomes including the Symptoms Checklist 90-Revised Global Severity Index, SIP psychosocial score, global assessment of well-being, Center for Epidemiologic Studies Depression Scale (CED-S), and a sleep scale.[67,86]

Psychological Therapies Compared With Pharmacological Therapy

Two fair-quality[96,106] and one poor-quality trial[107] compared a psychological therapy with pharmacological treatment. Two trials reported functional outcomes over the short term with differing results. No clear effect was seen for CBT (plus amitriptyline) compared with amitriptyline alone at 3 months in one fair-quality trial (MD −4.1, 95% CI −18.8 to 10.6 on the FIQ total score [0 to 100] scale).[106] One poor-quality trial, comparing EEG biofeedback with escitalopram, reported better mean FIQ total scores in the biofeedback group at 4 to 5 months followup (19 versus 48, 0 to 100 scale), but did not provide enough data to calculate an effect estimate.[107] Intermediate-term function was reported by one fair-quality trial, which found a small benefit for CBT compared with pregabalin (plus duloxetine as needed) on the FIQ at 6 months (difference −4.0 on a 0-100 scale, 95% CI −7.7 to −0.27).[96]

The pattern for pain outcomes was similar over the short term. No differences were seen between groups in the trial of CBT versus amitriptyline (difference −0.7 on a 0-10 VAS, 95% CI −2.8 to 1.4),[106] whereas a moderate effect was seen for EEG biofeedback compared with escitalopram (difference −2.7 on a 0-10 VAS, 95% CI −3.7 to −1.7) in the poor-quality trial.[107] At intermediate-term, VAS pain scores were similar between the CBT and pregabalin groups in the third trial (difference 0.2 on a 0-100 scale, −4.0 to 4.4).[96] It is unclear how many patients in the pharmacological group received concomitant duloxetine for major depressive disorder.

Regarding secondary outcomes, EEG biofeedback was associated with significantly better outcomes on various measures of anxiety, depression, and quality of life compared with escitalopram over short-term followup in the poor-quality trial,[107] whereas the two fair-quality trials evaluating CBT (versus amitriptyline and versus pregabalin)[96,106] found no differences between groups over the short or intermediate term, with the exception of SF-36 Mental Health scores at short-term followup in one trial (difference 13.7 on a 0-100 scale, 95% CI 0.07 to 27.3).[106]

Psychological Therapies Compared With Exercise

Five poor-quality trials compared psychological interventions with exercise; two trials evaluated compared CBT,[87,112] two trials evaluated biofeedback,[67,86] and one evaluated relaxation training[111] (Table 36).

Data were insufficient from one poor-quality trial to determine the effects of biofeedback versus combination exercise on function. The trial reported improved function based on the AIMS physical activity subscale (median change from baseline 6.0 versus 4.0, P<0.05).[67] Intermediate-term data from two poor-quality trials were insufficient to determine effects of psychological therapies on function and no clear differences in function were seen for CBT (MD −0.6, 95% CI −12.6 to 11.4 on 0-100 FIQ total score)[112] or biofeedback (mean change −1.6, 95% CI −3.4 to 0.2 vs. −0.6, 95% CI −2.9 to 1.7 on 0-100 SIP Physical score)[86] versus combination exercise. Similarly, no clear differences between psychological therapies and exercise were seen across three trials at longer term and evidence was considered insufficient. Results from two trials were not statistically significant (CBT vs. combination exercise [MD 0.1, 95% CI −10.5 to 10.7 on 0-100 FIQ total scale][112] and relaxation training versus strength training [MD −1.7, 95% CI −9.3 to 5.9, on 0-100 FIQ Total Score]).[111] The third trial of biofeedback versus combination exercise reported improvement in function, but limited data were provided (median change from baseline, 6.0 versus 4.0, P<0.05).[67]

Data were insufficient from one poor-quality trial to determine the effects of biofeedback versus combination exercise pain (median change from baseline, 5.2 vs. 5.4 on 0-10 VAS).[67] Across two poor-quality trials at intermediate term, no clear differences were seen for CBT (MD

−1.0, 95% CI −2.8 to 0.8)[112] or biofeedback (mean change −0.6, 95% CI −6.5 to 5.3 vs. −5.5, 95% CI −10.9 to −0.1, P=NS)[86] compared with combination exercise; evidence was considered insufficient. There were no clear differences between any of the psychological therapies and exercise for pain on a 0 to 10 scale across four trials long term, including CBT versus combination exercise (MD 0.3, 95% CI −2.0 to 1.3)[112] or aerobic exercise (difference 2, 95% CI −11.6 to 15.6),[87] biofeedback versus combination exercise (median change: 5.2 vs. 5.5, P=NS),[67] and relaxation training versus strength training (difference 2.9, 95% CI −5.5 to 11.3).[111]

There were generally no significant differences on measures of mental health, depression or anxiety, or on SF-36 scales, at any time frame across five poor-quality trials.[67,86,87,111,112] Some trials did not provide data for determination of effect sizes between treatment groups or report results of significance tests (Table 36).

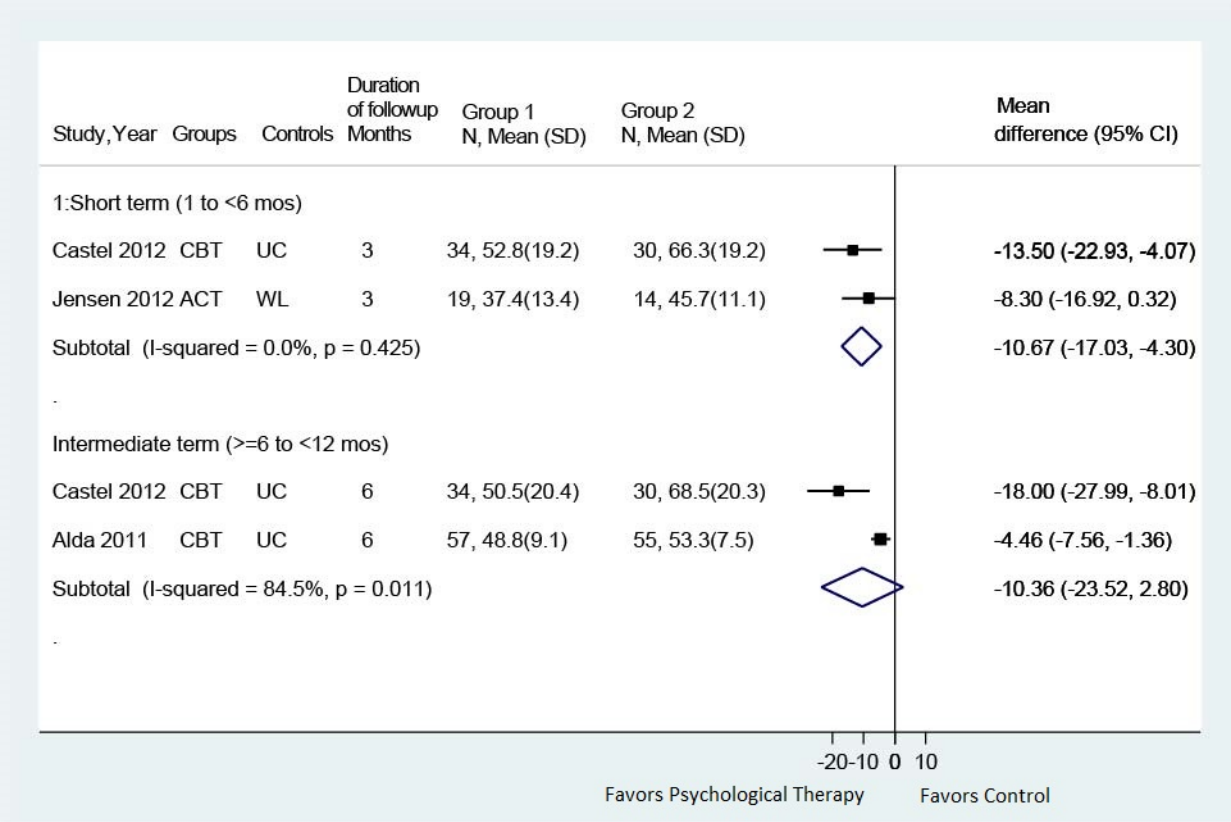
Harms

Only five trials (1 fair-quality and 4 poor-quality) reported harms, which were poorly described in general. Two trials compared CBT with usual care; one trial reported no withdrawals due to adverse events in the CBT group compared with two (3.6%) in the control group (not further described)[96] and the other trial reported two withdrawals, one in each group, because the nociceptive flexion reflex test being used was too painful.[97] One trial comparing CBT with attention control reported that 4.8 percent (due to depression) versus 50 percent (due to worsening of symptoms) of patients, respectively, withdrew from the study.[100] One trial compared stress management to usual care and reported one withdrawal due to cancer (unrelated to the treatment) in the intervention group compared with no withdrawals or adverse events in the control.[87]

One of the above trials also compared CBT to pharmacological therapy (pregabalin) and reported no withdrawals due to adverse events in the CBT group compared with three (5.5%) in the control group, two due to digestive problems and one due to dizziness.[96]

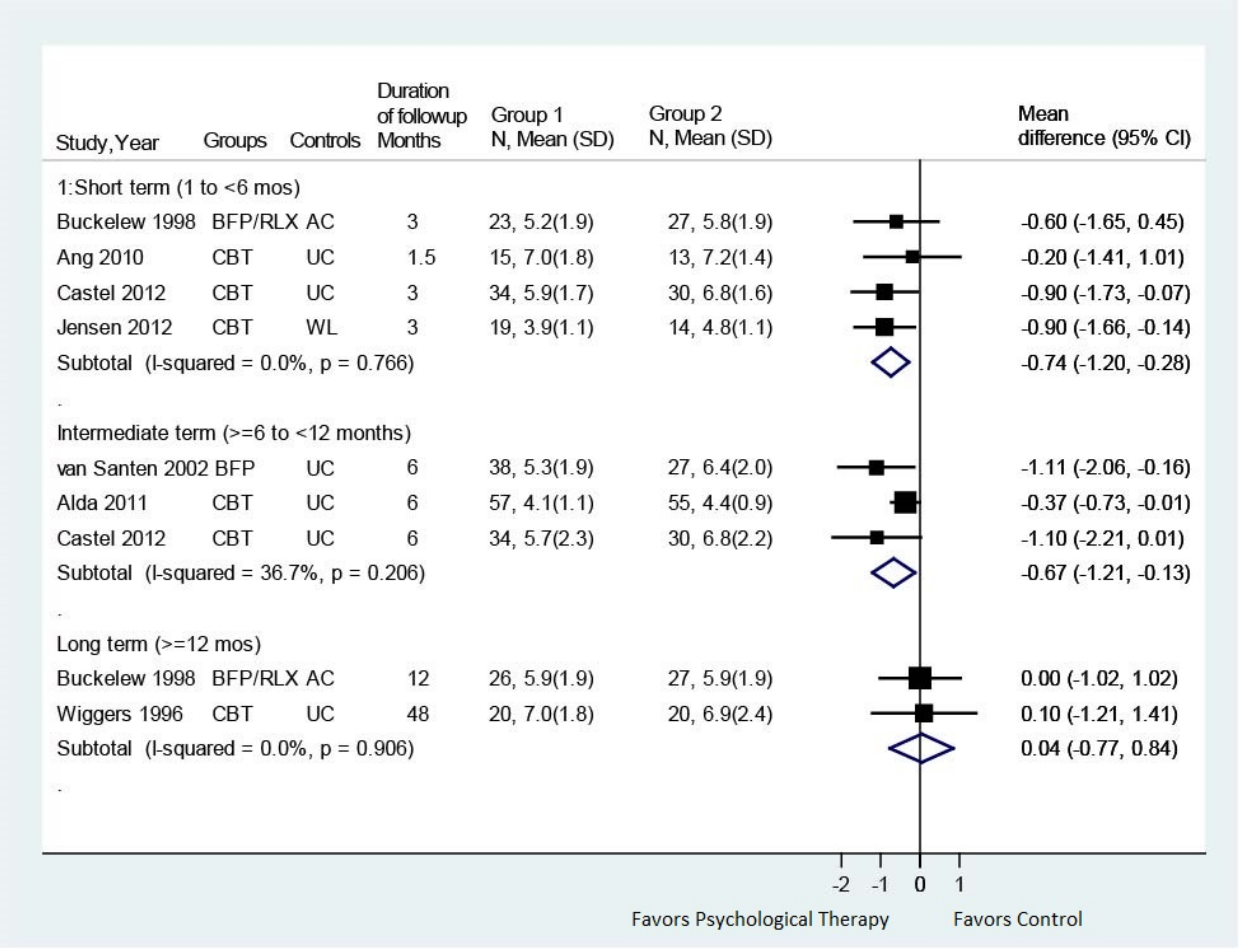
Two trials compared psychological therapies with exercise. One trial reported no adverse effects with relaxation therapy, but five (7.5%) adverse effect reports following strengthening exercises (due to increased pain), resulting in three withdrawals from the trial.[111] The other trial reported one withdrawal due to cancer (unrelated to the treatment) in the intervention group compared with three withdrawals in the exercise group (1 death, 1 gastritis, 1 ischialgia).[87]

Figure 41. Psychological therapies versus usual care or waitlist for fibromyalgia: effects on function



ACT = Acceptance and Commitment Therapy; CBT = cognitive-behavioral therapy; CI = confidence interval; SD = standard deviation; UC = usual care; WL = waitlist

Figure 42. Psychological therapies versus usual care, waitlist, or attention control for fibromyalgia: effects on pain



AC = attention control; BFP = Biofeedback; BFP/RLX = Biofeedback with a Relaxation component; CBT = cognitive-behavioral therapy; CI = confidence interval; SD = standard deviation; UC = usual care; WL = waitlist

Physical Modalities for Fibromyalgia

Key Points

- One fair-quality parallel trial found no evidence of differences between magnetic mattress pads compared with sham or usual care in intermediate-term function (MD on the 0 to 80 scale FIQ −5.0, 95% CI −14.1 to 4.1 vs. sham and −5.5, 95% CI −14.4 to 3.4 vs. usual care) or pain (MD −0.6, 95% CI −1.9 to 0.7 and −1.0, 95% CI −2.2 to 0.2, respectively on a 0 to 10 NRS) (SOE: low). Data from one small, poor-quality crossover trial were insufficient to determine the effects of a magnetic mattress versus sham on function and pain in the short term (SOE: insufficient).
- There were no differences in adverse events between the functional and sham magnetic mattress pad groups (data not reported); none of the events were deemed to be related to the treatments (SOE: low).

Detailed Synthesis

Two trials,[140,141] one parallel and one cross-over design, evaluating the efficacy of magnetic fields for the treatment of fibromyalgia met inclusion criteria (Table 37 and Appendix D). In both trials, the majority of patients were female (93% and 100%) with mean ages of 45 and 50 years; symptom duration was 6 years in one trial and was not reported by the other trial. Due to the differences in trial designs we could not pool the data; therefore, these trials are reported separately.

One parallel trial (n=119),[140] conducted in the United States, compared two different magnetic mattress pads (one with a low, uniform magnetic field of negative polarity and the other a low, static magnetic field that varied spatially and in polarity) versus sham (mattress pads with demagnetized magnets) and versus usual care (management by primary care provider). All pads were used for 6 months and outcomes were measured immediately post-treatment. This trial was rated fair quality due to deviations from the randomization protocol and unacceptable attrition rate (21%) (Appendix E).

A second small, crossover trial (N=33)[141] evaluated the effects of an extremely low frequency magnetic mattress compared with a sham mattress (no magnetic field delivered). The trial was conducted in Italy. The intervention periods were 1 month and the washout period between the first and second period was 1 month; no further information was provided about the washout period. Outcomes were measured 1 month after the end of each treatment cycle (i.e., at the beginning of the second treatment cycle, after a 1 month washout, and 1 month after the end of the second treatment cycle).This trial was rated poor quality for the following reasons: unclear randomization sequence generation and allocation concealment, and loss-to-followup of greater than 20% through the second treatment period; additional sources of bias in this crossover trial include no details regarding handling of missing data and no analysis of carryover effect.

Table 37. Fibromyalgia: physical modalities

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Alfano, 2001[140] 6 months Duration of pain: >3 months (mean NR) *Fair*	A. Magnetic mattress pad designed to expose body to a uniform magnetic field of negative polarity (n=37) B. Magnetic mattress pad exposing body to magnetic field that varied spatially and in polarity (n=33) C. Sham magnetic field (n=32): combined group of 2 sham magnetic mattress pads; identical in appearance to real magnetic pads but contained demagnetized magnets. D. Usual care (n=17): maintain current treatment under PCP, refrain from new treatments Treatment period was 6 months for all groups.	A vs. B vs. C vs. D Age: 44 vs. 47 vs. 46 vs. 45 years Female: 92% vs. 87% vs. 96% vs. 100% FIQ (0-80): 51.6 vs. 55.5 vs. 51.5 vs. 53.9 Pain intensity FIQ NRS (0-10): 7.1 vs. 7.0 vs. 6.7 vs. 7.0	A + B vs. C <u>Post 6-month intervention</u> FIQ: 42.9 vs. 47.9, difference −5.0 (95% CI −14.1 to 4.1) Pain intensity NRS: 5.6 vs. 6.2, difference −0.6 (95% CI −1.9 to 0.7) A + B vs. D <u>Post 6-month intervention</u> FIQ: 42.9 vs. 48.4, difference −5.5 (95% CI −14.4 to 3.4) Pain intensity NRS: 5.6 vs. 6.6, difference −1.0 (95% CI −2.2 to 0.2) A vs. C <u>Post 6-month intervention</u> FIQ: 38.3 vs. 47.9, difference −9.6 (95% CI −20.0 to 0.8) Pain intensity NRS: 4.8 vs. 6.2, difference −1.4 (95% CI −2.8 to 0.05) B vs. C <u>Post 6-month intervention</u> FIQ: 47.4 vs. 47.9, difference −0.5 (95% CI −11.2 to 10.2) Pain intensity NRS: 6.3 vs. 6.2, difference 0.1 (95% CI −1.4 to 1.6) A vs. D <u>Post 6-month intervention</u> FIQ: 38.3 vs. 48.4, difference −10.1 (95% CI −21.9 to 1.7) Pain intensity NRS: 4.8 vs. 6.6, difference −1.8 (95% CI −3.4 to −0.2) B vs. D <u>Post 6-month intervention</u> FIQ: 47.4 vs. 48.4, difference −1.0 (95% CI −13.0 to 11.0), Pain intensity NRS: 6.3 vs. 6.6, difference −0.3 (95% CI −2.0 to 1.4)	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Paolucci 2016 1 month Duration of pain: *Poor*	A. Extremely low-frequency magnetic field first (n=16): 3 thirty minute sessions per week for 4 weeks (12 sessions total). Patients laid on a bed with multi-low-frequency mattress that delivered a magnetic field at an intensity of 100 uT and a multifrequency of 1 to 80 Hz. B. Sham extremely low-frequency magnetic field first (n=17): 3 thirty minute sessions per week for 4 weeks (12 sessions total). Patients laid on a bed with multi-low-frequency mattress but no magnetic field was delivered. Washout period: 1 month	A vs. B Age, years: 50 vs. 51 Female: 100% vs. 100% Fibromyalgia duration, years: 7 vs. 5 FIQ: 58.7 (11.3) vs. 57.2 (12.3) FIQ pain: NR Pain VAS: 4.9 (1.4) vs. 4.8 (1.2) FAS (0−10): 6.1 (1.7) vs. 6.4 (1.4) HAQ (0-3): 0.7 (0.3) vs. 1.1 (0.8)	A vs. B, mean (SD) <u>1 month</u> FIQ: 19.2 (7.3) vs. 57.9 (12.5), P<0.001 Percent change from baseline in FIQ: −67.3% (9.9%) vs. 2.9% (7.4%), P<0.001 FIQ pain: values NR, P<0.001 Pain VAS: 2.2 (1.0) vs. 5.3 (1.3), P<0.001 Percent change from baseline in pain VAS: −54.1% (19.9%) vs. 6.3% (16.0%), P<0.001 FAS: 3.2 (1.2) vs. 6.1 (1.7), P<0.001 Percent change from baseline in FAS: −46.5% (17.3%) vs. −4.5% (20.8%), P<0.001 B vs. A (after cross-over) <u>1 month</u> FIQ: 25.1 (8.5) vs. 53.9 (8.7), P<0.001 Percent change from baseline in FIQ: −56.0% (9.4%) vs. −8.1% (16.5%), P<0.001 Pain VAS: 3.1 (1.6) vs. 4.6 (1.3), P=0.02 Percent change from baseline in pain VAS: −39.7% (26.0%) vs. −9.1% (15.1%), P=0.006 FAS: 3.5 (1.9) vs. 6.2 (1.0), P=0.002 Percent change from baseline in FAS: −46.9% (22.8%) vs. −1.2% (15.4%), P<0.001	A vs. B <u>1 month</u> HAQ: 0.3 (0.2) vs. 1.1 (0.9), P=0.03 Percent change from baseline in HAQ: NR B vs. A (after cross-over) <u>1 month</u> HAQ: 0.7 (0.7) vs. 0.8 (0.3), P=0.41 Percent change from baseline in HAQ: NR

CI = confidence interval; FAS = Fibromyalgia Assessment Status; FIQ = Fibromyalgia Impact Questionnaire; HAQ = Health Assessment Questionnaire; NR = not reported; NRS = numeric rating scale; PCP = primary care physician; SD = standard deviation; VAS = Visual Analog Scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Physical Modalities Compared With Usual Care or Sham

The magnetic mattress pads offered no intermediate-term benefit for either function or pain compared with both sham and usual care in the one parallel trial.[140] The MD between groups on the 0 to 80 scale FIQ at 6 months was −5.0 (95% CI −14.1 to 4.1) (versus sham) and −5.5 (95% CI −14.4 to 3.4) (usual care). Regarding pain, the between-group differences were −0.6 (95% CI −1.9 to 0.7) and −1.0 (95% CI −2.2 to 0.2), respectively, on a 0 to 10 NRS. When the intervention groups were considered separately, only the magnetic mattress pad designed to expose the body to a uniform magnetic field of negative polarity resulted in lower FIQ and NRS

pain scores compared with controls; however, the MDs between groups were not statistically significant.

The crossover trial[141] reported statistically significant improvement in both function and pain favoring the magnetic mattress 1 month after the end of both treatment periods (i.e., over the short term); however, the evidence is considered insufficient. For patients that received magnetic therapy during the first and second (i.e. after crossing-over) treatment periods, mean FIQ scores were 19.2 and 25.1 on a 0-100 scale, respectively, compared with 57.9 and 53.9 for those receiving sham during the same treatment periods (P<0.001 for both). For VAS pain, respective scores were 2.2 and 3.1 versus 5.3 and 4.6 on a 0-10 scale (P<0.001 for both). Results were similar for both the Fibromyalgia Assessment Scale and the Health Assessment Questionnaire (Table 37).

Physical Modalities Compared With Pharmacological Therapy or Exercise

No trial of physical modality versus pharmacological therapy or versus exercise met inclusion criteria.

Harms

In the parallel trial, there were no differences in adverse events between the magnetic mattress pad and sham pad groups.[140] Type of adverse events was not reported, but none of the events were judged to be due to magnetic treatments. The crossover trial only stated that no side effects were recorded during the study.[141]

Manual Therapies for Fibromyalgia

Key Points

- Myofascial release therapy was associated with a slightly greater effect on intermediate-term function as measured by the FIQ (mean 58.6 ± 16.3 vs. 64.1 ± 18.1 on a 100 point scale, P=0.048 for group by repeated measures ANOVA), but not long-term function (mean 62.8 ± 20.1 vs. 65.0 ± 19.8 on the FIQ, 0-100 scale, P=0.329), compared with sham in one fair-quality trial (SOE: low). Short-term function was not reported.
- There was insufficient evidence to determine the effects of myofascial release therapy on short-term pain (1 poor-quality trial) and intermediate-term pain (1 fair-quality and 1 poor-quality trial) compared with sham; there were inconsistencies in effect estimates between the intermediate-term trials (SOE: insufficient).
- Myofascial release therapy was associated with slightly greater improvement in long-term pain compared with sham based on the sensory (mean 18.2 ± 8.3 vs. 21.2 ± 7.9 on a 0-33 scale, P=0.038 for group by repeated measures ANOVA) and evaluative (mean 23.2 ± 7.6 vs. 26.7 ± 6.9 on a 0-42 scale, P=0.036) domains of the MPQ in one fair-quality trial; there were no differences for the affective domain of the MPQ or for VAS pain (SOE: low).
- Data were insufficient for harms; however, no adverse effect occurred in one fair-quality trial (SOE: insufficient)

Detailed Synthesis

Two trials (n=64, 94)[155,156] evaluating myofascial release therapy versus sham therapy for fibromyalgia met inclusion criteria (Table 38 and Appendix D). Mean patient ages were 48 and 55 years. Baseline pain history characteristics were poorly described in both trials. The duration

of myofascial release therapy was 20 weeks in both trials; sessions ranged in length from 60 to 90 minutes and were conducted twice or once a week, respectively. The sham conditions included short-wave and ultrasound electrotherapy or sham (disconnected) magnotherapy. Both trials reported intermediate-term outcomes; short-term and long-term outcomes were also reported by one trial each. One trial was rated fair quality and the other poor quality (Appendix E). Unclear allocation concealment methods and lack of blinding were the major methodological shortcoming in both trials. Additionally, the poor-quality trial did not describe the randomization process employed.

Table 38. Fibromyalgia: manual therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Castro-Sanchez, 2011a[155] 6 and 12 months Duration of pain, NR *Fair*	A. Myofascial Release (n=47): myofascial release (across 10 pain regions) administered by a physiotherapist; 60 minutes sessions twice weekly for 20 weeks B. Sham short-wave and ultrasound electrotherapy (n=47): both applied to the cervical, dorsal and lumbar regions using disconnected equipment; 30 minute sessions (10 minutes each region), twice weekly for 20 weeks	A vs. B Age: 55 vs. 54 years Female: NR Race: NR Mean duration of pain: NR FIQ total (0-100): 65.0 vs. 63.9 Pain (FIQ, 0-10): 9.2 vs. 8.9 Pain (VAS, 0-10): 9.1 vs. 8.9 MPQ sensory dimension (0-33): 19.3 vs. 19.9 MPQ affective dimension (0-12): 5.6 vs. 4.9 MPQ evaluative (sensory + affective) dimension (0-45): 24.9 vs. 25.3	A vs. B <u>6 months</u> FIQ Total: 58.6 vs. 64.1, P=0.048 FIQ pain: 8.5 vs. 8.0, P=0.042 VAS pain: 8.25 vs. 8.94, P=0.043 MPQ sensory: 17.3 vs. 20.7, P=0.042 MPQ affective: 4.5 vs. 5.2, P=0.042 MPQ evaluative: 21.9 vs. 26.2, P=0.022 <u>12 months</u> FIQ Total: 62.8 vs. 65.0, P=0.329 FIQ pain: 8.8 vs. 8.7, P=0.519 VAS pain: 8.74 vs. 8.92, P=0.306 MPQ sensory: 18.2 vs. 21.2, P=0.038 MPQ affective: 4.8 vs. 5.1, P=0.232 MPQ evaluative: 23.2 vs. 26.7, P=0.036 P-values are from authors' ANOVA[b]	A vs. B <u>6 months</u> Clinical Global Impression Severity Scale (Likert, 1-7): 5.3 vs. 6.0, P=0.048 Clinical Global Impression Improvement Scale (Likert, 1-7): 5.6 vs. 6.3, P=0.046 <u>12 months</u> Clinical Global Impression Severity Scale: 5.5 vs. 6.2 P=0.147 Clinical Global Impression Improvement Scale: 5.8 vs. 6.5, P=0.049 P-values are from authors' ANOVA[b]

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Castro-Sanchez, 2011b[156] 1 and 6 months Duration of pain, NR *Poor*	A. Massage-Myofascial Release (n=32): Massage-Myofascial release therapy (across 18 pain regions) administered by a physiotherapist; weekly 90-minute session for 20 weeks. B. Sham magnotherapy (n=32): weekly 30-minute session of disconnected magnotherapy (applied on cervical and lumbar area for 15 minutes each) for 20 weeks.	A vs. B Age: 49 vs. 46 years Female: 94% vs. 96% Race: NR Mean duration of pain: NR Pain Intensity (VAS, 0-10)[c]: 9.1 vs. 9.6	A vs. B <u>1 month</u> VAS pain[c]: 8.4 vs. 9.4, P<0.043 <u>6 months</u> VAS pain[c]: 8.8 vs. 9.7, P=NS P-values are from authors' ANOVA[b]	A vs. B <u>1 month</u> STAI state anxiety (20-80)[c]: 21.5 vs. 22, P=NS STAI trait anxiety (20-80)[c]: 25.1 vs. 26.3, P=NS BDI (0-63)[c]: 2.1 vs. 2.5, P=NS SF-36 physical function (0-100): 46.8 vs. 49.6, P=0.049 SF-36 physical role (0-100): 24.6 vs. 29.0, P=0.047 SF-36 bodily pain (0-100): 75.1 vs. 89.9, P=0.046 SF-36 general health (0-100): 66.8 vs. 68.4, P=0.093 SF-36 vitality (0-100): 61.6 vs. 59.2, P=0.055 SF-36 social function (0-100): 60.6 vs. 63.6, P=0.081 SF-36 emotional role (0-100): 50.5 vs. 47.0, P=0.057 SF-36 mental health (0-100): 75.0 vs. 78.3, P=0.082 PSQI, sleep duration, P=0.041[d]: patients with severe problems, 60% vs. 83%; moderate problems, 37% vs. 10%; and no problems, 3% vs. 7% <u>6 months</u> BDI[c]: 2.3 vs. 2.5, P=NS STAI state anxiety[c]: 22.0 vs. 23.0, P=NS STAI trait anxiety[c]: 25.8 vs. 26.2, P=NS SF-36 physical function: 48.2 vs. 51.2, P=0.281 SF-36 physical role: 25.5 vs. 27.5, P=0.213 SF-36 body pain: 75.6 vs. 77.8, P=0.293 SF-36 general health: 67.5 vs. 68.1, P=0.401 SF-36 vitality: 62.2 vs. 58.9, P=0.312 SF-36 social function: 61.3 vs. 63.9, P=0.088 SF-36 emotional role: 49.1 vs. 46.9, P=0.219 SF-36 mental health: 76.5 vs. 80.0, P=0.126 PSQI, sleep duration, P=0.047[d]: patients with severe problems, 57% vs. 93%; moderate problems, 37% vs. 0%; and no problems, 7% vs. 7% P-values are from authors' ANOVA[b]

ANOVA = repeated-measures analysis of variance; BDI = Beck Depression Inventory; FIQ = Fibromyalgia Impact Questionnaire; MPQ = McGill Pain Questionnaire; NR = not reported; NS = not statistically significant; PSQI = Pittsburgh sleep quality index; SF-36 = Short-Form 36 health questionnaire; STAI = State-Trait Anxiety Inventory; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Changes in scores were analyzed by using a 2 (groups: experimental and placebo) X 4 (time points: baseline, immediately postintervention, at 1 and 6 months) repeated-measures analysis of variance
[c] Values estimated from figures in the article.
[d] For all other dimensions of the PSQI (subjective sleep quality, sleep latency, habitual sleep efficiency, sleep disturbance, daily dysfunction), there were no statistically significant difference between groups in the proportion of patients experiencing severe, moderate or no problems in the authors' analysis of variance (ANOVA).

Myofascial Release Therapy Compared With Sham

Myofascial release therapy was associated with a slightly greater effect on intermediate-term function compared with sham as measured by the FIQ (58.6 ± 16.3 vs. 64.1 ± 18.1 on a 100 point scale, P=0.048 for group by time repeated measures ANOVA) in one fair-quality trial[155]; this effect did not persist to the long term (62.8 ± 20.1 vs. 65.0 ± 19.8, P=0.329, at 12 months). Function was not reported over the short term.

Regarding pain outcomes, one poor-quality trial reported a small effect for myofascial release compared with sham therapy over the short term (8.4 vs. 9.4 on a 0-10 VAS at 1 month, P=0.048 for group by time repeated measures ANOVA).[156] Intermediate-term results were inconsistent across the trials as measured on a 0 to 10 VAS pain scale with one fair-quality trial reporting a slightly greater effect for myofascial release versus sham (8.25 ± 1.13 vs. 8.94 ± 1.34, P=0.043)[155] at 6 months and the other (poor quality) reporting no significant difference between groups (8.8 vs. 9.7, P=not significant) (Figure 43).[156] Additional pain measures were reported over the intermediate-term by the fair-quality trial, all of which showed a small benefit in favor of myofascial release: FIQ pain (8.5 ± 0.7 vs. 8.0 ± 1.3, P=0.042 for group by time repeated measures ANOVA) and the McGill Pain Questionnaire (MPQ) sensory (17.3 ± 7.8 vs. 20.7 ± 7.1 on a 0-33 scale, P=0.04), affective (4.5 ± 2.9 vs. 5.2 ± 3.8 on a 0-12 scale, P=0.04) and evaluative (21.9 ± 7.2 vs. 26.2 ± 6.8 on a 0-42 scale, P=0.02) dimensions.[155] This effect persisted at long-term followup for the sensory and evaluative dimension of the MPQ only; no differences were seen between groups regarding VAS pain of the affective dimension of the MPQ at long term following in this trial (Table 38).

Depression, anxiety, and sleep outcomes were evaluated in one poor-quality trial, with significant improvement seen in the myofascial release versus the sham group on some subscales of the Short-Form-36 and on the sleep duration subscale of the Pittsburgh Sleep Quality Index (PSQI) over the short-term,[156] but no differences between groups on the STAI or Beck Depression Index (Table 38); at intermediate followup, only PSQI sleep duration remained significantly improved following myofascial release versus sham.

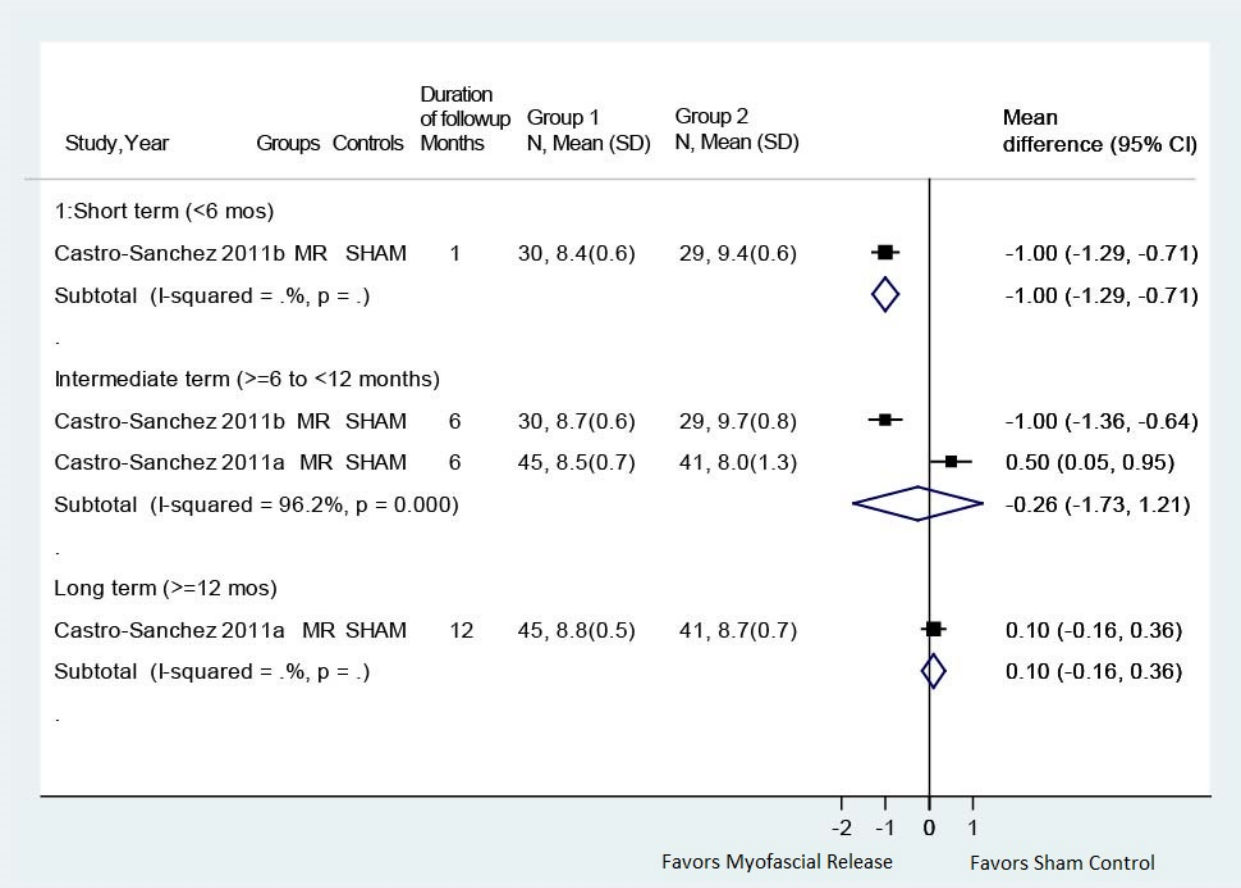
Manual Therapy Compared With Pharmacological Therapy or Exercise

No trial of manual therapy versus pharmacological therapy or versus exercise met inclusion criteria.

Harms

In one trial, no patient experienced an adverse effect (details not reported).[155] There was no information on harms reported by the other trial.

Figure 43. Myofascial release versus sham for fibromyalgia: effects on pain



CI = confidence interval; MR = myofascial release; SD = standard deviation

Mindfulness-Based Stress Reduction Therapy for Fibromyalgia

Key Points

- No clear short-term effects of mindfulness-based stress reduction (MBSR) were seen on function compared with waitlist or attention control (MD 0 to 0.06 on a 0-10 scale) in two trials (one fair and one poor quality) (SOE: moderate).
- No clear short-term effects of MBSR on pain (MD 0.1 on a 0-100 VAS pain scale in one poor quality trial; MD −1.38 to −1.59 on the affective and −0.28 to −0.71 on the sensory dimension [scales not reported] of the Pain Perception Scale in one fair-quality trial) compared with waitlist or attention control in two trials (SOE: moderate). Intermediate-term and long-term outcomes were not reported.
- No trial of MBSR versus pharmacological therapy or versus exercise met inclusion criteria.
- Harms were not reported.

Detailed Synthesis

We identified two trials (3 publications) of mindfulness-based stress reduction (MBSR) for fibromyalgia that met inclusion criteria (Table 39 and Appendix D).[170-172] One study was conducted in the United States[170,172] and the other in Germany.[171] In both trials, MBSR was modeled after the program developed by Kabat-Zinn. The intervention lasted 8 weeks, with

weekly 2.5-hour sessions, daily homework assignments, and a single 7-hour session. Sample sizes ranged from 91 to 177, age ranged from 48 to 53 years, and all participants were female. Both studies compared MBSR versus waitlist control; the German study[171] also compared MBSR to an attention control group that consisted of education, relaxation, and stretching. Both studies reported only short-term outcomes.

One study was considered fair quality[171] and the other was considered poor quality[170,172] (Appendix E). Methodological shortcomings in both studies were the lack of long-term followup and the inability to blind patients and providers. The poor-quality study also had a high rate of overall attrition as well as differential attrition between the groups.

Table 39. Fibromyalgia: mindfulness-based stress reduction therapy

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Cash 2015,[170] Sephton 2007[172,b] 2 months Duration of pain NR *Poor*	<u>A. Mindfulness-based Stress Reduction (n=51)</u> 8-week group-based program with one 2.5 hour session/week including instruction in techniques, meditation, and simple yoga positions to encourage relaxation. Participants were asked to complete daily practices with workbook and audiotapes for 45 min a day for 6 days a week. <u>B. Waitlist control group (n=39)</u> Participants were offered the intervention program only after the conclusion of the study and followup.	A vs. B Age: 48 vs. 48 years Female: 100% vs. 100% Caucasian: 94% vs. 93% FIQ Physical Functioning (0-10): 1.3 vs. 1.2 Pain VAS (0-100): 68.1 vs. 69.2 FIQ Severity (0-100)[c]: 67.5 vs. 62.5	A vs. B <u>2 months:</u> FIQ Physical Functioning: 1.2 vs. 1.2; difference 0.0 (95% CI −0.32 to 0.32) Pain VAS: 65.2 vs. 65.1; difference 0.1 (95% CI −9.96 to 10.16) FIQ Severity[c]: 62.0 vs. 66.7; difference −4.7 (95% CI -12.24 to 2.84)	A vs. B <u>2 months</u> BDI Total[b]: 13.3 vs. 14.8; difference −1.5 (95% CI −4.76 to 1.76) BDI Cognitive Subscale[b]: 5.3 vs. 6.4; difference −1.1 (95% CI −2.98 to 0.78) BDI Somatic Subscale[b]: 7.4 vs. 7.7; difference −0.3 (95% CI −1.73 to 1.13) PSS: 20.2 vs. 20.8; difference −0.60 (95% CI −3.37 to 2.17) SDQ: 8.4 vs. 9.5; difference −1.10 (95% CI −2.58 to 0.38) FSI: 5.5 vs. 6.0; difference −0.50 (95% CI −1.28 to 0.28)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Schmidt, 2011[171] 2 months Duration of fibromyalgia, years: 14 years *Fair*	<u>A. Mindfulness-based Stress Reduction (n=53)</u> 8-week group-based program with one 2.5 hour session/week and one 7 hour all-day session covering training in specific exercises and topics of mindfulness practices. Participants were asked to complete daily practices of 45-60 minutes each <u>B. Active-control Intervention (n=56)</u> Controlled for nonspecific aspects of the MBSR program with similar meeting structure and format to MBSR treatment arm. Equivalent levels of social support and weekly topical education was provided along with Jacobson Progressive Muscle Relaxation training and fibromyalgia-specific gentle stretching exercises. Participants were asked to complete daily homework assignments with the same duration as MBSR group. <u>C. Waitlist (n=59)</u> Received no active treatment but were offered either intervention at the conclusion of the followup period.	A vs. B vs. C Age: 53 vs. 52 years Female: 100% (all female study) Race: NR A vs. C FIQ Total (0-10): 5.8 vs. 5.7; PPS Affective (scale unclear): 35.5 vs. 34.8 PPS Sensory (scale unclear): 22.4 vs. 22.6	A vs. B <u>2 months</u> Proportion of Patients with >14% improvement in FIQ scores (MCID): 30% vs. 25%; RR 1.21 (95% CI 0.79 to 1.82) FIQ: 5.23 vs. 5.33; MD −0.10 (95% CI −0.84 to 0.64) PPS Affective: 30.79 vs. 32.17; MD −1.38 (95% CI −4.79 to 2.03) PPS Sensory: 21.16 vs. 21.87; MD −0.71 (95% CI −2.77 to 1.34) A vs. C <u>2 months</u> Proportion of Patients with >14% improvement in FIQ scores (MCID): 30% vs. 22%; RR 1.37 (95% CI 0.83 to 1.94) FIQ: 5.23 vs. 5.29; MD −0.06 (95% CI −0.75 to 0.63) PPS Affective: 30.79 vs. 32.38; MD −1.59 (95% CI −5.01 to 1.83) PPS Sensory: 21.16 vs. 21.44; MD −0.28 (95% CI −2.30 to 1.74)	A vs. B <u>2 months</u> Proportion of Patients who saw Clinically Relevant Improvement (score of <23) in CES-D scores: 28% vs. 23%; RR 0.53 (95% CI 0.54 to 1.12) CES-D: 21.70 vs. 22.55; MD −0.85 (95% CI −4.66 to 2.96) STAI Trait Subscale: 47.86 vs. 48.44; MD −0.58 (95% CI −4.42 to 3.26) Proportion of Patients with PSQI score <5 indicates good sleep): 17%vs. 7%; RR 2.38 (95% CI 0.85 to 2.34) PSQI: 10.01 vs. 10.25; MD −0.24 (95% CI −1.71 to 1.23) FMI: 37.66 vs. 35.14; MD 2.52 (95% CI 0.04 to 5.00) GCQ: 42.63 vs. 43.91; MD −1.28 (95% CI −6.51 to 3.95) PLC: 12.83 vs. 12.16; MD 0.67 (95% CI −0.60 to 1.94) A vs. C <u>2 months</u> Proportion of Patients who saw Clinically Relevant Improvement (score of <23) in CES-D scores: 28% vs. 19%; RR 1.52 (95% CI 0.85 to 2.04) CES-D: 21.7 vs. 24.0; MD −2.3 (95% CI −5.96 to 1.36) STAI Trait Subscale: 47.9 vs. 49.2; MD −1.32 (95% CI −5.02 to 2.38 Proportion of Patients with PSQI score <5 indicates good sleep): 17% vs. 10%; RR 1.67 (95% CI 0.80 to 2.14) PSQI: 10.0 vs. 10.4; MD −0.36 (95% CI −1.8 to 1.1) FMI: 37.7 vs. 36.1; MD 1.5 (95% CI −0.9 to 3.91) GCQ: 42.6 vs. 45.3; MD −2.7 (95% CI −7.8 to 2.5) PLC: 12.8 vs. 12.3; MD 0.5 (95% CI −0.7 to 1.7)

BDI = Beck Depression Inventory; CES-D = Center for Epidemiological Studies Depression Scale; CI = confidence interval; FSI= Fatigue Symptom Inventory; FIQ = Fibromyalgia Impact Questionnaire; FMI = Freiburg Mindfulness Inventory; GCQ = Giessen Complaint Questionnaire; MCID = minimal clinically important difference; MD = mean difference; PLC = Profile for the Chronically Ill; PPS = Pain Perception Scale; PSQI = Pittsburgh Sleep Quality Index; PSS = Perceived Stress Scale; RR = risk ratio; SDQ = Stanford Sleep Disorders Questionnaire; STAI = State-Trait-Anxiety-Inventory; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Sephton is the same population as Cash 2015 but the focus of the study was on depression (Beck Depression Inventory).

[c] FIQ symptom severity is comprised of visual analog ratings of pain, fatigue, morning sleepiness, stiffness, anxiety, and depression

Mindfulness-Based Stress Reduction Therapy Compared With Waitlist or Attention Control

There were no clear short-term effects of MBSR on any function or pain measure reported compared with waitlist or attention control. Both trials compared MBSR to waitlist and reported function using the FIQ, one reporting the physical function subscale (difference 0 on a 0-10 scale, 95% CI −0.32 to 0.32)[170] and the other reporting the total score (difference −0.06 on a 0-10 scale, 95% CI −0.75 to 0.63).[171] The latter fair-quality trial also reported the proportion of patients who achieved a 14percent or greater improvement in FIQ total scores: 30 percent versus 22 percent, RR 1.37 (95% CI 0.83 to 1.94).[171] Regarding pain, one trial reported a MD 0.1 (95% CI −9.96 to 10.16) on a 0 to 100 VAS pain scale[170] between the MBSR and waitlist groups, while the other reported pain using the affective (difference −1.59, 95% CI −5.01 to 1.83) and sensory (difference −0.28, 95% CI −2.30 to 1.74) domains of the Pain Perception Scale (scale not reported).[171] Estimates for function and pain were similar for the comparison of MBSR versus attention control in the fair-quality trial[171] (Table 39).

Secondary outcomes (measures of depression, anxiety, sleep, fatigue) did not differ significantly between MBSR and waitlist or attention control in either trial[170-172] (Table 39). The fair-quality trial compared medication use (analgesics, anti-depressants, and sleep medication) between baseline and short-term followup; only antidepressant medication was reduced significantly from baseline (46% to 35%, P=0.01) but there was no group effect (data not reported).[171]

Mindfulness-Based Stress Reduction Therapy Compared With Pharmacological Therapy or Exercise

No trial of MBSR versus pharmacological therapy or versus exercise met inclusion criteria.

Harms

Neither trial reported harms.

Mind-Body Therapy for Fibromyalgia

Key Points

- Over the short-term, two trials of mind-body practices reported slight improvement in function for qigong compared with waitlist (MD −7.5, 95% CI −13.3 to −1.68) and for tai chi compared with attention control (MD −23.5, 95% CI −30 to −17) based on 0 to 100 scale total FIQ score; heterogeneity may be explained by duration and intensity of intervention and control condition. Significantly more participants in the tai chi group also showed clinically meaningful improvement on total FIQ (RR 1.6, 95% CI 1.1 to 2.3) consistent with a slight effect (SOE: low).
- Qigong and tai chi were associated with moderately greater improvement in pain (0-10 scale) compared with waitlist and attention control in the short term (2 trials, pooled MD −1.54, 95% CI −2.67, −0.41, I^2=75%). Significantly more participants in the tai chi group also showed clinically meaningful improvement on VAS pain (RR 2.0, 95% CI 1.1 to 3.8) consistent with a slight effect (SOE: low).
- No evidence in the intermediate or long term.
- Data for harms were insufficient. However, one trial reported two adverse events (in two patients) judged to be possibly related to qigong practice: an increase in shoulder pain

and plantar fasciitis; neither participant withdrew from the study. In the trial of tai chi, no adverse events were reported. (SOE: insufficient)

Detailed Synthesis

Two trials[183,184] that evaluated mind-body therapies for fibromyalgia met inclusion criteria (Table 40 and Appendix D). Across trials, the participants were predominately female (87% to 96%), with mean ages between 51 to 52 years. Prior to study enrollment, participants in both trials were being treated with several drugs from major analgesic and adjuvant drug groups such as analgesics/NSAIDs (53% to 73%), antidepressants (35% to 48%), and anticonvulsants (21% to 27%); in one trial, approximately 30 percent of participants were taking opioids and many participants had tried a variety of other therapies (including acupuncture, chiropractic, naturopathic/homeopathic/osteopathic therapies, massage therapy, and psychological therapies).[183]

One trial compared qigong (3 consecutive half-day training sessions, then weekly practice/review sessions for 8 weeks plus daily at-home practice for 45 to 60 minutes) to a waiting list control condition.[183] The other trial compared tai chi (60-minute sessions twice per week for 12 weeks) to an attention control condition (40 minutes of wellness education and 20 minutes of supervised stretching exercises).[184] In both trials, patients were instructed to continue the practice at home throughout the followup period. In the tai chi study, the average percent of sessions attended during the 12-week intervention was 77 percent for the tai chi group and 70 percent for the control group.[184] In the qigong trial, the mean self-reported practice time per week for all participants who completed the trial was 4.9 hours at 2 months, 2.9 hours at 4 months, and 2.7 hours at 6 months. [183]

Both trials were rated fair quality (Appendix E). Due to the nature of the intervention and control groups, blinding was not possible in the two studies. Other methodological concerns included differential attrition between groups in the qigong trial (qigong 19% vs. waitlist 4% at 6 months).[183]

Table 40. Fibromyalgia: mind-body therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Lynch, 2012[183] (N=100) 4 months Duration of fibromyalgia, mean: 9.6 years *Fair*	A. Qigong (n=53) Chaoyi Fanhuan Qigong; Three consecutive half-day training sessions then weekly practice/review sessions for 8 weeks plus daily at-home practice for 45 to 60 minutes. B. Waitlist (n=47) Continued with usual care; offered qigong after the trial ended	A vs. B Age: 53 vs. 52 years Female: 94% vs. 98% Previous opioid therapy: 42% vs. 30% Current opioid therapy: 36% vs. 23% Current NSAID therapy: 49% vs. 57% FIQ (0-100): 65.5 vs. 61.8 NRS pain (0-10): 6.5 vs. 6.6 SF-36 PCS (0-100): 30.0 vs. 32.6 SF-36 MCS (0-100): 38.1 vs. 40.4 PSQI (0-21): 13.8 vs. 13.1	A vs. B 4 months Mean change from baseline: FIQ: −16.1 vs. −4.8; difference −11.3 (95% CI −19.3 to −3.3) NRS pain: −1.21 vs. −0.27; difference −0.9 (95% CI −1.7 to −0.1)	A vs. B 4 months Mean change from baseline: SF-36 PCS: 4.6 vs. 0.2; difference 4.4 (95% CI 1.5 to 7.3) SF-36 MCS: 4.4 vs. 0.7; difference 3.7 (95% CI −0.3 to 7.7) PSQI: −3.3 vs. −1.1; difference −2.2 (95% CI −3.6 to −0.8)
Wang, 2010[184] (N=66) 3 months Duration of fibromyalgia pain: 11 years *Fair*	A. Tai chi (n=33) Classic Yang style tai chi; at home practice for at least 20 minutes a day; encouraged to maintain tai chi practice using an instructional video. B. Attention control (n=33) 40 minutes of education then 20 minutes of supervised stretching (upper body, trunk, and lower body); plus 20 minutes of daily at-home stretching Both groups had 60-minute sessions twice a week for 12 weeks and continued regular medications and routine activities.	A vs. B Age: 50 vs. 51 years Female: 85% vs. 88% Analgesic use: 88% vs. 73% FIQ (0-100): 62.9 vs. 68.0 VAS pain (0-10): 5.8 vs. 6.3 CES-D (0-60): 22.6 vs. 27.8 SF-36 PCS (0-100): 28.5 vs. 28.0 SF-36 MCS (0-100): 42.6 vs. 37.8 PSQI (0-21): 13.9 vs. 13.5	A vs. B 3 months Proportion with clinically meaningful improvement: FIQ[b]: 81.8% vs. 51.5%; RR 1.6 (95% CI 1.1 to 2.3) VAS pain[c]: 54.5% vs. 27.3%; RR 2.0 (95% CI 1.1 to 3.8) Mean change from baseline: FIQ: −28.6 vs. −10.2; difference −18.3 (95% CI −27.1 to −9.6) VAS pain: −2.4 vs. −0.7; difference −1.7 (95% CI −2.7 to −0.8)	A vs. B 3 months Proportion with clinically meaningful improvement: CES-D[d]: 69.7% vs. 39.4%; RR 1.8 (95% CI 1.1 to 2.9) SF-36 PCS[e]: 51.5% vs. 15.2%; RR 3.4 (95% CI 1.4 to 8.1) SF-36 MCS[f]: 48.5% vs. 24.2%; RR 2.0 (95% CI 1.0 to 4.0) PSQI[g]: 45.5% vs. 18.2%; RR 2.5 (95% CI 1.1 to 5.6) Mean change from baseline: CES-D: −6.5 vs. −2.4; difference −4.1 (95% CI −8.2 to 0.1) SF-36 PCS: 8.4 vs. 1.5; difference 7.0 (95% CI 2.9 to 11.0) SF-36 MCS: 8.5 vs. 1.2; difference 7.3 (95% CI 1.9 to 12.8) PSQI: −4.2 vs. −1.2; difference −3.0 (95% CI −5.2 to −0.9)

CES-D = Center for Epidemiologic Studies Depression index; CI = confidence interval; FIQ = Fibromyalgia Impact Questionnaire; NRS = numeric rating scale; NSAIDs = nonsteroidal anti-inflammatory drugs; PSQI = Pittsburgh Sleep Quality Index; RR = risk ratio; SF-36 MCS = Short-Form-36 Mental Component Summary; SF-36 PCS = Short-Form-36 Physical Component Summary; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period
[b] A reduction of ≥8.1 points from baseline on the FIQ was considered a clinically meaningful improvement
[c] A reduction of ≥2 points from baseline on the VAS was considered a clinically meaningful improvement
[d] A reduction of ≥6 points from baseline on the CES-D was considered a clinically meaningful improvement
[e] An increase of ≥6.5 points from baseline on the SF-36 PCS was considered a clinically meaningful improvement
[f] An increase of ≥7.9 points from baseline on the SF-36 MCS was considered a clinically meaningful improvement
[g] A reduction of >5 points from baseline on the PSQI was considered a clinically meaningful improvement

Mind-Body Therapies Compared With Waitlist or Attention Control

Short-term improvement in function on 0 to 100 scale total FIQ score was reported for qigong (slight improvement, MD −7.5, 95% CI −13.3 to −1.68)[183] and for tai chi (substantial improvement, MD −23.5, 95% CI −30 to −17)[184] compared with waitlist or attention control. Substantial heterogeneity (I^2=92%), precluded meaningful pooling for this outcome (Figure 44). Significantly more participants in the tai chi group also showed clinically meaningful improvement (reduction of ≥8.1 points from baseline) on total FIQ (RR 1.6, 95% CI 1.1 to 2.3) consistent with a slight effect. Tai chi and qigong were associated with a moderate improvement in pain (0 to 10 scale) compared with wait list or attention control (2 trials, pooled difference −1.54, 95% CI −2.67 to −0.41, I^2 = 75%) (Figure 45). Significantly more participants in the tai chi group also showed clinically meaningful improvement (reduction of ≥2 points from baseline) in VAS pain (RR 2.0, 95% CI 1.1 to 3.8) consistent with a slight effect. Heterogeneity may in part be due to differences in duration and intensity of the intervention.

Mind-body therapy resulted in significant improvement in most secondary outcomes measured. Participants who received tai chi group showed clinically meaningful improvement in depressive symptoms as measured by the Center for Epidemiological Studies-Depression scale (RR 1.8, 95% CI 1.1 to 2.9), in sleep quality as measured by the Pittsburg Sleep Quality Index (PSQI) (RR 2.5, 95% CI 1.1 to 5.6), and in quality of life as measured by the SF-36 PCS (RR 3.4, 95% CI 1.4 to 8.1) and MCS (RR 2.0, 95% CI 1.0 to 4.0) compared with controls; similar results were seen for mean followup scores on these measures (Table 40).[184] In the second trial,[183] compared to a waitlist control, qigong resulted in significantly improved quality of life as measured by the SF-36 PCS (difference in change from baseline 4.4, 95% CI 1.5 to 7.3) and in sleep quality as measured by the PSQI (difference in change from baseline −2.2, 95% CI −3.6 to −0.8). The change in SF-36 MCS scores did not differ between groups.

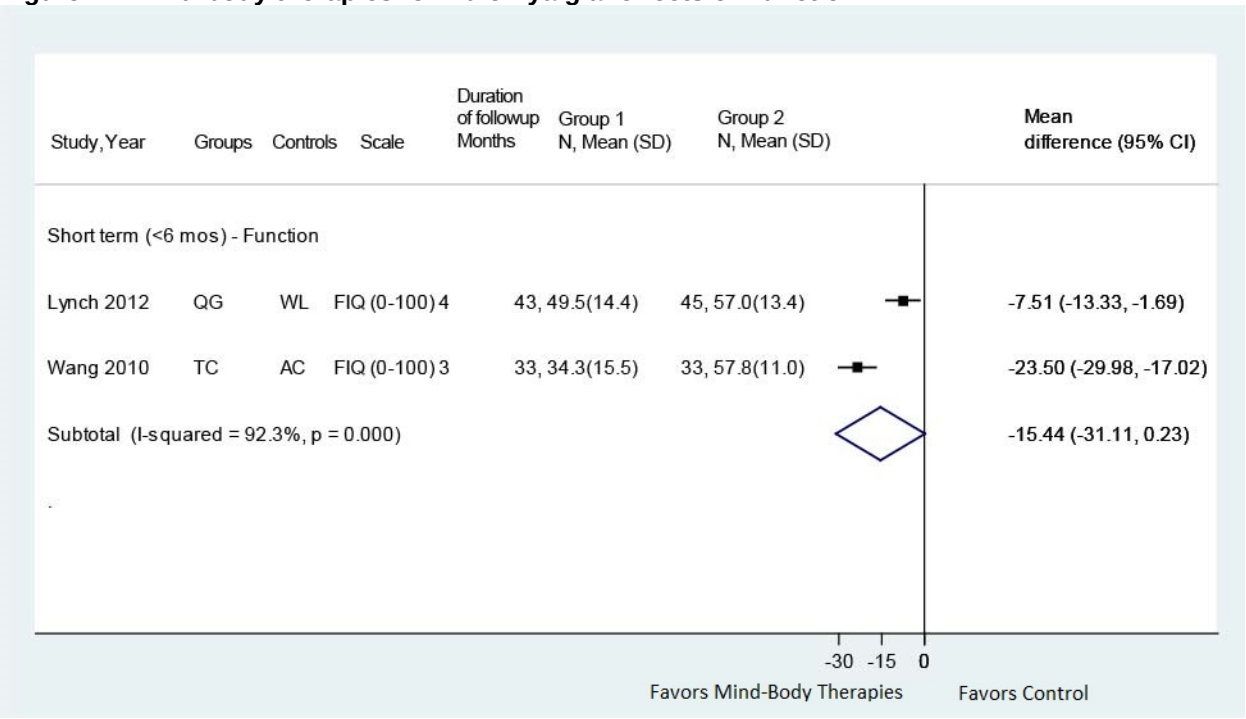
Mind-Body Therapies Compared With Pharmacological Therapy or Exercise

No trials comparing mind-body therapies with pharmacological therapy or with exercise met inclusion criteria.

Harms

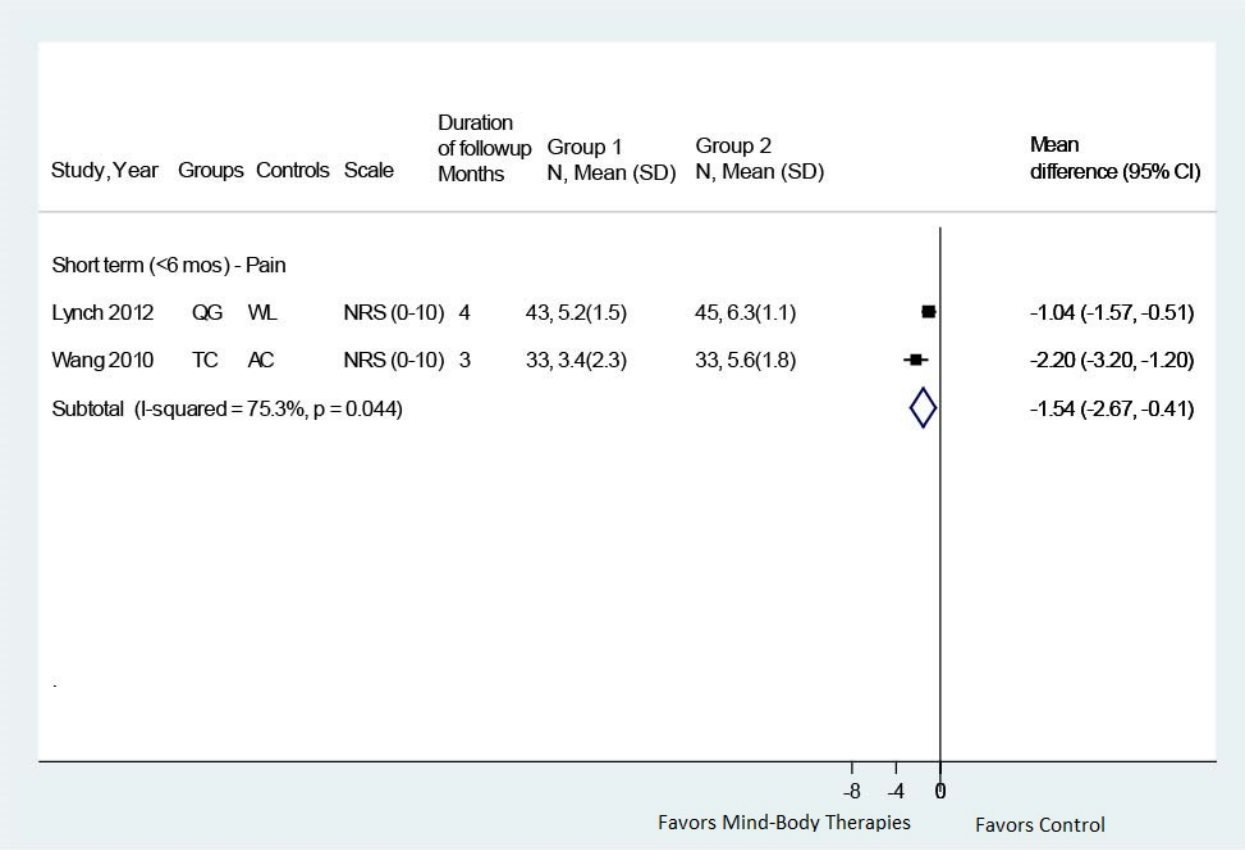
In the trial of qigong,[183] there were two adverse events judged to be possibly related to the practice. One participant reported an increase in shoulder pain and another experienced plantar fasciitis; neither participant withdrew from the study. In the trial of tai chi, no adverse events were reported.[184]

Figure 44. Mind-body therapies for fibromyalgia: effects on function



AC = attention control; CI = confidence interval; FIQ = Fibromyalgia Impact Questionnaire; QG = qigong; SD = standard deviation; TC = tai chi; WL = waitlist

Figure 45. Mind-body therapies for fibromyalgia: effects on pain



AC = attention control; CI = confidence interval; QG = qigong; SD = standard deviation; TC = tai chi; WL = waitlist

Acupuncture for Fibromyalgia

Key Points

- Acupuncture was associated with slightly greater improvements in function based on 0 to 100 FIQ Total Score compared with sham acupuncture in the short term (2 trials, pooled MD −8.63, 95% CI −12.12 to −5.13, I^2=0%) and intermediate term (2 trials, pooled MD −9.41, 95% CI −13.96 to −4.85, I^2=27.4%) (SOE: moderate).
- There was no clear effect of acupuncture on pain (0 to 10 scale) versus sham acupuncture in the short term (3 trials, pooled MD −0.13, 95% CI −1.06 to 0.79, I^2=72%) or intermediate term (3 trials, pooled MD −0.53, 95% CI −1.15 to 0.09, I^2=45.5%) (SOE: low).
- No data on long-term effects were reported.
- Discomfort and bruising were the most common adverse events. Discomfort was substantially more common for acupuncture or sham needling (61% to 70%) compared with simulated acupuncture (29%). Vasovagal symptoms and aggravation of fibromyalgia symptoms were less common (4%, 2.5 of sessions) (SOE: moderate).

Detailed Synthesis

Three trials of acupuncture for fibromyalgia were identified that met inclusion criteria; one was conducted in Spain[213] and two were conducted in the United States[211,212] (Table 41 and Appendix D). Two trials evaluated traditional Chinese needle acupuncture[211,213] and the third evaluated acupuncture with electrical stimulation.[212] All three studies compared acupuncture to sham. One study[211] employed three different types of sham treatments (needling for an unrelated condition, sham needling, and simulated acupuncture), one used sham needling[212] and one used simulated acupuncture.[213] Sample sizes ranged from 50 to 164 (total sample=314), mean ages from 47 to 53 years, and the proportion of females ranged from 95 percent to 100 percent. The duration of acupuncture treatment ranged from 3 to 12 weeks, with the total number of sessions ranging from six to 24. All studies reported short-term and intermediate-term outcomes; no trial had long-term followup.

All three studies were considered good quality (Appendix E). Limitations of all studies were lack of long-term followup and that the person administering acupuncture was not blinded to treatment allocation.

Table 41. Fibromyalgia: acupuncture

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Assefi, 2005[211] 3 and 6 months Mean duration of pain: 9 to 12 years *Good*	A. Acupuncture (n=25): in accordance with Traditional Chinese Medicine B. Sham Acupuncture (n=24): Needling for Unrelated Condition C. Sham Acupuncture (n=24): Sham Needling D. Sham Acupuncture (n=23): Simulated Acupuncture Treatment protocol: 24 sessions (2/week for 12 weeks)	A vs. B vs. C vs. D Mean age: 46 vs. 46 vs. 49 vs. 48 years Female: 88% vs. 96% vs. 100% vs. 96% Race (white): 96% vs. 88% vs. 96% vs. 92% Mean duration of pain: 12 vs. 9 vs. 9 vs. 10 years Pain Intensity VAS (0-10): 7.0 vs. 6.9 vs. 6.8 vs. 7.3	A. vs. B vs. C vs. D <u>3 months</u> Pain Intensity VAS[b]: 6.0 vs. 5.4 vs. 5.4 vs. 4.5 <u>6 months</u> Pain Intensity VAS[b]: 5.7 vs. 6.0 vs. 5.2 vs. 5.2 A vs. B+C+D <u>Across all timepoints[c]</u> Pain intensity VAS: adjusted MD 0.5, (95% CI −0.3 to 1.2)	A. vs. B vs. C vs. D <u>3 months</u> SF-36 PCS (0-100)[b]: 31 vs. 39 vs. 31.5 vs. 40 SF-36 MSC (0-100)[b]: 46 vs. 46.5 vs. 48.5 vs. 47 Sleep Quality VAS (0-10)[a]: 4.3 vs. 4.1 vs. 5.2 vs. 5.5 Overall Well-Being VAS (0-10)[b]: 4.9 vs. 4.9 vs. 5.0 vs. 6.3 <u>6 months</u> SF-36 PCS[b]: 31 vs. 36 vs. 31. vs. 39 SF-36 MCS[b]: 43 vs. 45 vs. 50 vs. 46.5 Sleep Quality VAS[b]: 4.3 vs. 3.4 vs. 5.4 vs. 5.5 Overall Well-Being VAS[b]: 4.6 vs. 4.6 vs. 5.7 vs. 5.7 A vs. B+C+D <u>Across all time-points[c]</u> SF-36 PCS: adjusted MD −0.4 (95% CI −2.3 to 1.5) SF-36 MCS: adjusted MD −1.5, (95% CI −4.0 to 1.0) Sleep Quality VAS: adjusted MD −0.5, (95% CI −1.3 to 0.2) Overall Well-Being VAS: adjusted MD −0.3, (95% CI −1.0 to 0.3)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Martin, 2006[212] 1 and 7 months Duration of pain: NR *Good*	A. Acupuncture (n=25) B. Sham Acupuncture: Sham Needling (n=25) Treatment protocol: 6 treatments over 2 to 3 weeks	A vs. B Age: 48 vs. 52 years Female: 100% vs. 96% Race: 96% vs. 100% white FIQ total (0-80): 42.4 vs. 44.0 FIQ Physical Function (0-10): 4.1 vs. 3.6 MPI Interference (scale NR): 42.6 vs. 36.9 MPI General Activity Level (scale NR): 55.7 vs. 56.6 MPI Pain Severity (scale NR): 40.4 vs. 43.0 FIQ Pain (0-10): 6.2 vs. 6.5	A vs. B <u>1 month</u> FIQ Total: 34.8 vs. 42.2, MD −4.9 (95% CI −8.7 to −1.2) FIQ Physical Function: 3.7 vs. 3.3, MD –0.4 (95% CI –1.1 to 0.3) MPI Interference: 38.3 vs. 34.9, MD 0.1 (95% CI –3.4 to 3.6) MPI General Activity Level: 55.4 vs. 58.3, MD –1.2, (95% CI –3.8 to 1.4) MPI Pain Severity: 34.2 vs. 41.6, MD –4.6 (95% CI –8.7 to –0.5) FIQ pain: 4.7 vs. 5.9, MD –0.8, (95% CI –1.8 to 0.2) <u>7 months</u> FIQ Total: 38.1 vs. 42.7, MD –4.3 (95% CI –7.7 to –0.9) FIQ Physical Function: 3.5 vs. 3.3, MD –0.3 (95% CI –0.9 to 0.3) MPI Interference: 37.7 vs. 35.5, MD 0.1 (95% CI –3.2 to 3.4) MPI General Activity Level: 58.1 vs. 59.5, MD –0.6 (95% CI –3.1 to 1.8) MPI Pain Severity: 37.3 vs. 41.4, MD –3.8 (95% CI –7.5 to –0.2) FIQ Pain: 5.5 vs. 6.4, MD –0.7 (95% CI –1.5 to 0.3)	A vs. B <u>1 month</u> FIQ Anxiety (0-10): 2.6 vs. 5.1, MD –1.1 (95% CI –2.0 to –0.2) FIQ Depression (0-10): 2.0 vs. 3.7, MD –0.7 (95% CI –1.6 to 0.3) FIQ Sleep (0-10): 5.9 vs. 6.8, MD –0.7 (95% CI –1.8 to 0.5) FIQ Well-Being (0-10): 4.6 vs. 3.1, MD 0.8 (95% CI –0.4 to 2.0) <u>7 months</u> FIQ Anxiety: 3.3 vs. 4.8, MD –1.1 (95% CI –1.9 to –0.2) FIQ Depression: 2.2 vs. 3.6, MD –0.7 (95% CI –1.6 to 0.2) FIQ Sleep: 6.1 vs. 6.3, MD –0.3 (95% CI –1.3 to 0.6) FIQ Well-Being: 3.8 vs. 3.6, MD 0.4 (95% CI –0.6 to 1.4)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Vas,[213] 2016 3.75 and 9.75 months Duration of pain: NR *Good*	A. Acupuncture (n=82) B. Sham Acupuncture: Simulated Acupuncture (n=82) Treatment protocol: One 20 min session per week for 9 weeks. Participants also received pharmacological treatment as prescribed by GP.	A vs. B Age: 52.3 vs. 53.2 years Female: 100% vs. 100% FIQ (0-100): 71.7 vs. 70.1 Pain Intensity VAS (0-100): 79.3 vs. 75.8	A vs. B <u>3.75 months</u> FIQ % mean relative change: −25.0 vs. −11.2, Cohen's d=0.58 Pain Intensity VAS % mean relative change: −23.6 vs. −16.6, Cohen's d=0.28 <u>9.75 months</u> FIQ % mean relative change (%): −22.2 vs. −4.9, Cohen's d=0.80, Pain intensity VAS % mean relative change: −19.9 vs. −6.2, Cohen's d=0.62	A vs. B <u>3.75 months</u> HDRS % mean relative change: NR SF-12 MCS % mean relative change: 30.6 vs. 13.9, Cohen's d=0.38 SF-12 PCS % mean relative change: 37.0 vs. 15.5, Cohen's d=0.56 <u>9.75 months</u> HDRS % mean relative change: −19.1 vs. −5.9, Cohen's d=0.22 SF-12 PCS % mean relative change: 37.2 vs. 11.4, Cohen's d=0.58 SF-12 MCS % mean relative change: 23.0 vs. 9.4, Cohen's d=0.36

CI = confidence interval; FIQ = Fibromyalgia Impact Questionnaire; GP = general practitioner; HDRS = Hamilton Depression Rating Scale; MCS = Mental Component Score; MD = mean difference; MPI = Multidimensional Pain Inventory; NR = not reported; PCS = Physical Component Score; SF-12 = Short-Form-12; SF-36 = Short-Form 36; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Outcome values were estimated from graphs.

[c] Authors combined the three sham control groups and calculated the adjusted least-square mean difference between the acupuncture group and combined control groups. Treatment-by-time interaction was not included in the models; therefore data reflects results across all time-points.

Acupuncture Compared With Sham

Acupuncture was associated with slightly greater improvement in function compared with sham acupuncture based on the FIQ Total Score (0 to 100) at short-term followup (2 trials, pooled difference −8.63, 95% CI −12.12 to −5.13, I^2=0%) and intermediate-term followup (2 trials, pooled difference on 0-100 scale, −9.41, 95% CI −13.96 to −4.85, I^2=27.4%) across the same trials[212,213] (Figure 46). There was, however, no clear effect of acupuncture on pain (0 to 10 scale) versus sham acupuncture in the short term (3 trials, pooled difference −0.13, 95% CI −1.06 to 0.79, I^2=72%) or intermediate term (3 trials, pooled difference −0.53, 95% CI −1.15 to 0.09, I^2=45.5%)[211-213] (Figure 47). All trials were considered good quality.

Results for secondary outcomes across two trials of acupuncture versus sham were inconsistent, with each reporting effects in the opposite direction. In the trial of acupuncture versus three different types of sham acupuncture,[211] there was no significant benefit of acupuncture versus the combined sham groups on the SF-36 MCS score, a measure of sleep quality, or a measure of overall well-being. In the trial of six acupuncture treatments over 2 to 3 weeks, there was a benefit for true versus sham acupuncture at 1 and 7 months on the FIQ subscale of anxiety, but not depression, sleep, or well-being.[212] In the trial of one 20-minute session per week for 9 weeks plus pharmacological treatment as prescribed by a general practitioner, there was a benefit for true versus sham acupuncture at 1 month for the SF-12 MCS

scale (mean relative change 30.6%, 95% CI 19.7 to 41.5 vs. 13.9%, 95% CI 5.4 to 22.5), Cohen's d=0.38, P=0.01), and at 9.75 months for the Hamilton Rating Scale for Depression (mean relative change −19.1%, 95% CI −34.2 to −3.9 vs. −5.9%, 95% CI −16.6 to −4.8, Cohen's d=0.22, P=0.01) and the SF-12 Mental Component scale (mean relative change, 23.0%, 95% CI 13.7 to 32.4 vs. 9.4%, 95% CI 1.9 to 16.9, Cohen's d=0.36, P=0.01).[213]

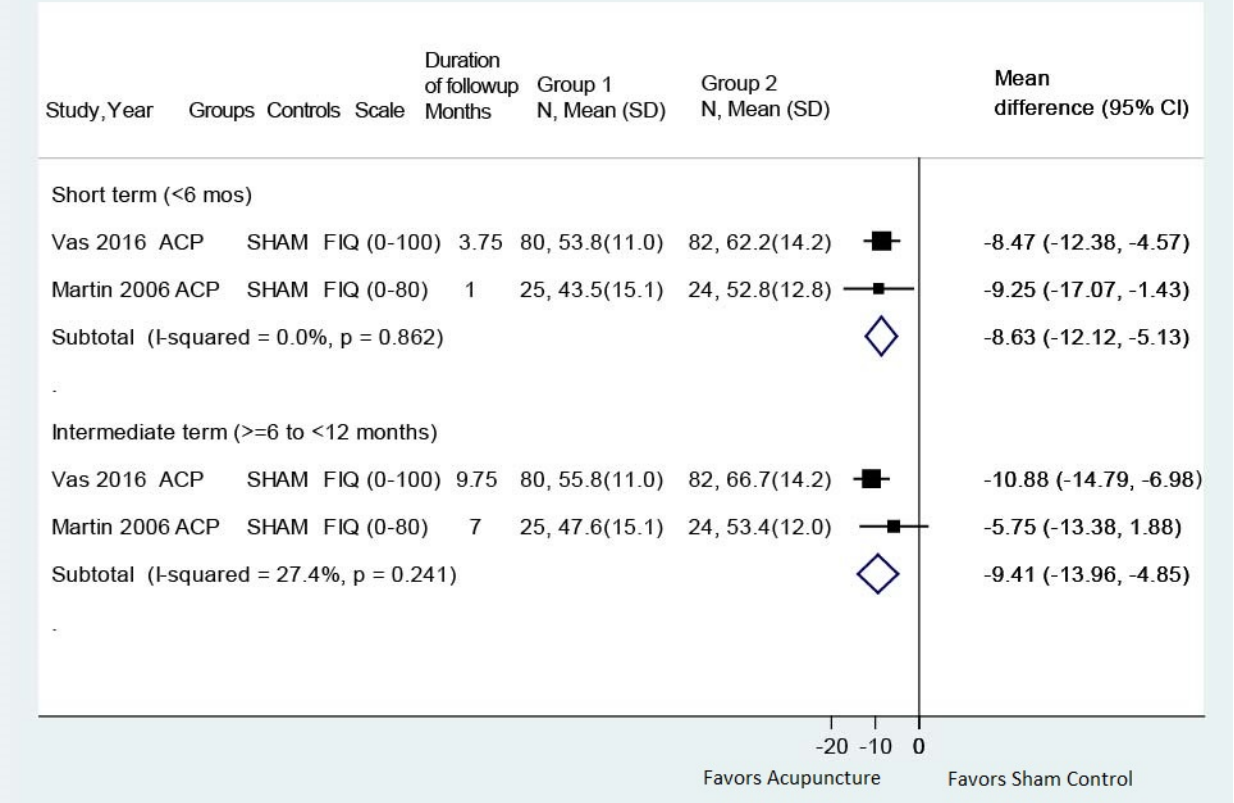
Acupuncture Compared With Pharmacological Therapy or Exercise

No trial of acupuncture versus pharmacological therapy or versus exercise met inclusion criteria.

Harms

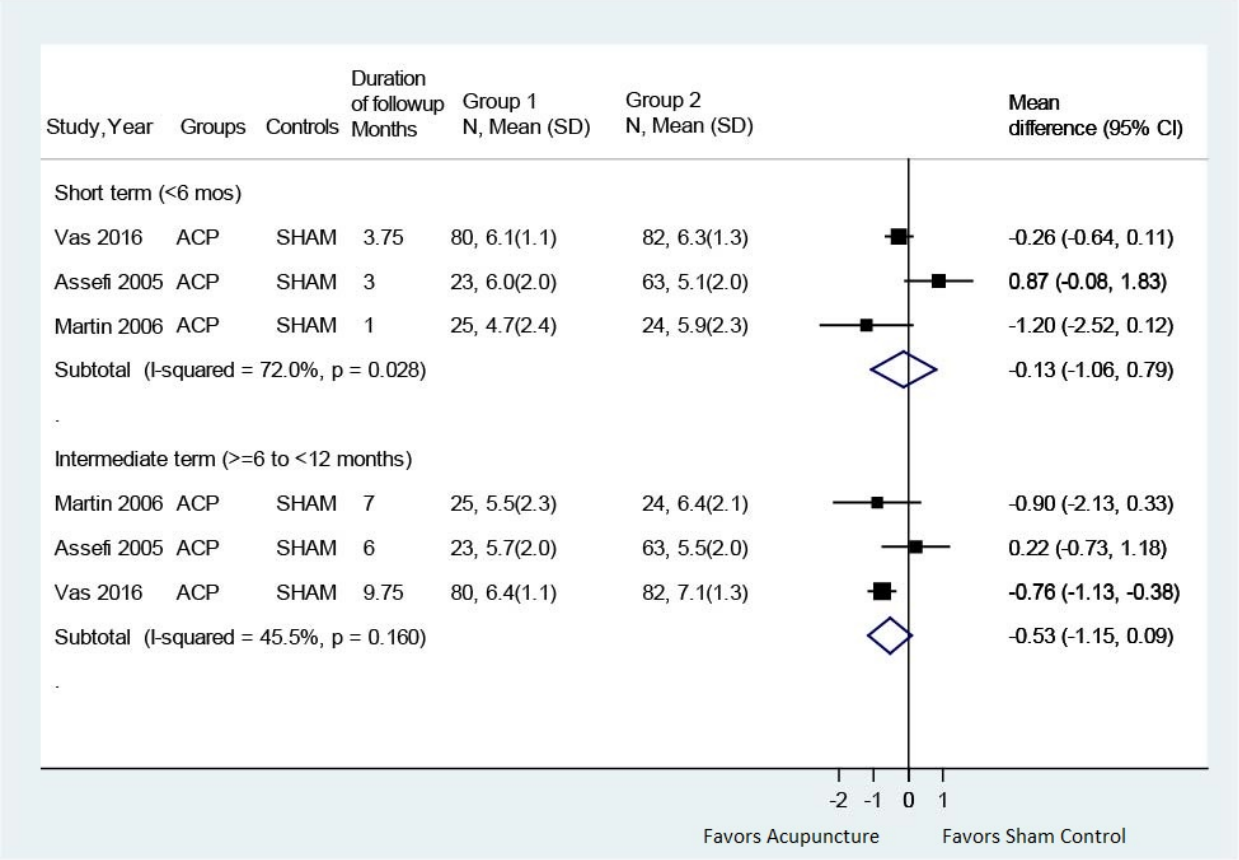
Discomfort and bruising were the most common reported adverse events. In one trial,[211] 89 of 96 treated (true or sham acupuncture) participants reported adverse events; 35 of 96 (37%) reported discomfort at needle insertion sites, 29 of 96 (30%) reported bruising, 3 of 96 (3%) reported nausea, and 1 of 96 (0.3%) felt faint at some point during the study. For patients assigned to simulated acupuncture, 5 of 19 (29%) had significantly less discomfort than those in directed acupuncture (14 of 23, 61%), acupuncture for unrelated condition (15 of 22, 70%) or sham needling (14 of 22, 64%); P=0.02. In one trial,[212] 2 of 50 (4%) experienced mild vasovagal symptoms and 1 of 50 (2%) experienced a pulmonary embolism believed to be unrelated to treatment. Mild bruising and soreness were reported to be more common in the true acupuncture group, but rates were not reported. In one study,[213] 2.6 percent of sessions led to aggravation of fibromyalgia symptoms and 0.5 percent led to headache. In the true acupuncture group, pain, bruising, and vagal symptoms presented after 4.7 percent of sessions.

Figure 46. Acupuncture versus sham for fibromyalgia: effects on function



ACP = acupuncture; CI = confidence interval; FIQ = Fibromyalgia Impact Questionnaire; SD = standard deviation

Figure 47. Acupuncture versus sham for fibromyalgia: effects on pain



ACP = acupuncture; CI = confidence interval; SD = standard deviation

Multidisciplinary Rehabilitation for Fibromyalgia

Key Points

- More multidisciplinary treatment participants experienced a clinically meaningful improvement in FIQ total score (≥14% change) compared with usual care at short (odds ratio [OR] 3.1, 95% CI 1.6 to 6.2), intermediate (OR 3.1, 95% CI 1.5 to 6.4) and long term (OR 8.8, 95% CI 2.5 to 30.9) in one poor-quality trial. Multidisciplinary treatment was associated with a slight improvement in function (based on a 0-100 FIQ total score) versus usual care or waitlist in the short-term (3 trials, pooled MD −6.52, 95% CI −12.84 to −0.21, I^2=67.3%), and versus usual care at intermediate term (3 trials, pooled MD −7.84, 95% CI −11.43 to −4.25, I^2=18.2%) and long term (2 trials, pooled MD −8.42, 95% CI −13.76 to −3.08, $I^{2=}$24.9%) (SOE: low for short, intermediate and long term).
- Multidisciplinary treatment was associated with a slight improvement in pain compared with usual care or waitlist at intermediate term (3 trials, pooled MD −0.68, 95% CI −1.07 to −0.30, I^2 = 0%); there were no clear differences compared with usual care or waitlist in the short term (2 trials [excluding an outlier trial], pooled MD on a 0-10 scale −0.24, 95% CI −0.63 to 0.15, I^2 = 0%) or with usual care in the long term (2 trials, pooled MD −0.25, 95% CI −0.68 to 0.17, I^2 = 0%) (SOE: low for short, intermediate and long-term).

- There was no evidence of an effect for multidisciplinary pain treatment versus aerobic exercise at long term in one fair-quality trial for function (MD −1.10, 95% CI −8.40 to 6.20, 0-100 FIQ total score) or pain (MD 0.10, 95% CI −0.67 to 0.87, 0-10 FIQ pain scale) (SOE: low).
- Data were insufficient for harms. However, one poor-quality study reported on adverse events stating that 19% of participants randomized to multidisciplinary treatment withdrew (versus 0% for waiting list) and 2 of these 16 patients gave increased pain as the reason. Reasons for other withdrawals were not given and there was not systematic reporting of adverse events (SOE: insufficient).

Detailed Synthesis

We identified six trials (across 8 publications) of multidisciplinary treatments that met inclusion criteria (Table 42 and Appendix D); five were conducted in Europe[85,225-230] and one in Turkey.[231] Across trials, sample sizes ranged from 66 to 203 (total randomized=959) and participants were predominantly (>90%) female with mean ages between 40 to 50 years. The multidisciplinary treatments included physical therapy or exercise training in all trials, as well as CBT and pharmacological therapy (2 trials),[226,229] CBT and an educational program (1 trial),[231] sociotherapy, psychotherapy, and creative arts therapy (1 trial),[85] relaxation exercises (1 trial),[228] and education and group discussions (1 trial).[225] All trials compared multidisciplinary treatment with usual care or waitlist; in addition, one trial compared it with exercise.[85] Treatment duration ranged from 2 to 12 weeks and the frequency of sessions from once a week to daily (total number of sessions ranged from 12 to 24 with durations between 1.5 to 5 hours). One of the trials included two intervention arms.[231] The long-term multidisciplinary arm (2 days of education and exercise followed by 10 weeks of CBT) was determined to be most consistent with interventions employed by the other trials and was included in the pooled estimates below; results for the short-term group (2 days of education, exercise, and CBT programs) were similar to those of the long-term group and can be found in Table 42. Three trials reported outcomes over the short term (3 to 5.5 months),[225,226,231] three over the intermediate term (6 months),[226,228,229] and two over the long term (12 and 18 months).[85,226]

Three trials were judged to be of fair quality[85,225,231] and three trials were rated poor quality[226,228,229] (Appendix E). The nature of the intervention precluded blinding of participants and of people administering the treatments. Additional methodological shortcomings in the poor quality trials included unclear allocation concealment methods and unacceptable rates of overall attrition (21% to 43%) and differential attrition between groups (12% to 13%).

Table 42. Fibromyalgia: multidisciplinary rehabilitation

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Amris, 2014[225] 5.5 months Duration of pain: median 10 to 11 years *Fair*	A. Multidisciplinary treatment (n=84), 3 to 5 hours of education, sleep hygiene, group discussions, and physical therapy per day over 2 weeks B. Wait list (n=86)	A vs. B Age: 44 vs. 44 years Female: 100% vs. 100% Baseline Fibromyalgia Impact Questionnaire Total (FIQ, 0-100): 64.0 vs. 65.7 Baseline FIQ pain VAS (0-10): 7.1 vs. 7.4	A vs. B <u>5.5 months</u> Change in FIQ total from baseline: −1.3 vs. −1.4, difference 0.1 (95% CI −3.6 to 3.8) Change in FIQ pain VAS from baseline: 0.1 vs. −0.1, difference 0.2 (95% CI −0.3 to 0.7)	A vs. B <u>5.5 months</u> Change in Generalized Anxiety Disorder-10 from baseline (scale NR): −0.8 vs. −0.5, difference −0.2 (95% CI −2.0 vs. 1.5) Change in Major Depression Inventory from baseline (0-50): −1.7 vs. −0.5, difference −1.3 (95% CI −3.3 to 0.8) Change in SF-36 physical component score from baseline (0-100): 1.4 vs. 0.8, difference 0.6 (95% CI −1.0 to 2.1) Percent responders in SF-36 physical component score: 27% vs. 23% Change in SF-36 mental component score from baseline (0-100): 2.3 vs. 1.2, difference 1.1 (95% CI −1.5 to 3.8) Percent responders in SF-36 mental component score: 27% vs. 27% Change in SF-36 physical functioning from baseline (0-100): 1.1 vs. 1.6, difference −0.5 (95% CI −3.9 to 3.0)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Castel, 2013[226] Salvat 2017[230] 3, 6 and 12 months Duration of pain: Mean 10.8 to 12.5 years *Poor*	A. Multidisciplinary treatment (n=53), conventional pharmacological treatment, 24 sessions of group CBT and physical therapy over 12 weeks. B. Usual care (conventional pharmacological treatment) (n=35), including analgesics, antidepressants, benzodiazepines, and nonbenzodiazepine hypnotics	A vs. B Age: 49 vs. 49 years Female: 100% vs. 100% Baseline FIQ (0-100): 64.6 vs. 66.6 Baseline pain NRS (0-10): 6.8 vs. 7.1	A vs. B <u>3 months</u> FIQ: 55.5 vs. 64.6, difference −9.1 (95% CI −14.9 to −3.3) Proportion with clinically significant FIQ improvement (≥14% change): 48% vs. 23%, OR 3.1 (95% CI 1.6 to 6.2) Pain NRS: 6.4 vs. 6.8, difference −0.40 (95% CI −0.98 to 0.18) Proportion with clinically significant NRS pain improvement (≥30% change): 14% vs. 11% <u>6 months</u> FIQ: 55.8 vs. 67.8, difference −12.0 (95% CI −18.2 to −5.8) Proportion with clinically significant FIQ improvement (≥14% change): 42% vs. 19%, OR 3.1 (95% CI 1.5 to 6.4) Pain NRS: 6.4 vs. 7.0, difference −0.60 (95% CI −1.2 to 0) Proportion with clinically significant NRS pain improvement (≥30% change): 16% vs. 5%, OR 3.3 (95% CI 1.0 to 10.8) <u>12 months</u> FIQ: 58.8 vs. 69.6, difference −10.8 (95% CI −16.8 to −4.8) Proportion with clinically significant FIQ improvement (≥14% change): 27% vs. 4%, OR 8.8 (95% CI 2.5 to 30.9) Pain NRS: 6.7 vs. 7.1, difference −0.40 (95% CI −0.94 to 0.14) Proportion with clinically significant NRS pain improvement (≥30% change): 8.6% vs. 0%, OR 0.5 (95% CI 0.4 to 0.6)	A vs. B <u>3 months</u> HADS (0-42): 15.2 vs. 20.6, difference −5.4 (95% CI −8.2 to −2.6) MOS sleep scale (scale NR): 40.5 vs. 31.2, difference 9.3 (95% CI 6.1 to 12.5) WONCA, mean (95% CI): total score: 23.7 (22.5 to 25.0) vs. 26.5 (25.1 to 27.9), P<0.005; physical function: 2.71 (2.51 to 2.95) vs. 3.20 (2.95 to 3.41), P=NR; daily activities: 2.88 (2.70 to 3.05) vs. 3.20 (3.00 to 3.39), P=NR <u>6 months</u> HADS: 16.2 vs. 21.5, difference −5.3 (95% CI −8.1 to −2.5) MOS sleep scale: 38.7 vs. 29.0, difference 9.7 (95% CI 6.6 to 12.8) WONCA, mean (95% CI): total score: 23.6 (22.4 to 24.9) vs. 27.3 (25.9 to 28.6), P<0.005; physical function: 2.69 (2.48 to 2.90) vs. 3.38 (3.12 to 3.60), P=NR; daily activities: 2.97 (2.80 to 3.15) vs. 3.28 (3.10 to 3.47), P=NR <u>12 months</u> HADS: 17.1 vs. 22.8, difference −5.7 (95% CI −8.7 to −2.7) MOS sleep scale: 36.3 vs. 28.8, difference 7.5 (95% CI 4.3 to 10.7) WONCA, mean (95% CI): total score: 23.5 (22.1 to 24.8) vs. 26.4 (24.9 to 27.9), P<0.005; physical function: 2.72 (2.49 to 2.96) vs. 3.33 (3.05 to 3.62), P=NR daily activities: 2.87 (2.69 to 3.06) vs. 3.32 (3.10 to 3.55), P=NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Cedraschi, 2004[228] 6 months Duration of pain: Mean 8.4 to 9.5 years *Poor*	A. Multidisciplinary treatment (n=84): 12 group pool sessions of physiotherapy, relaxation exercises, and exercise over 6 weeks B. Usual care (n=80) Regular care, including physical therapy, drug treatment and, in some cases, psychotherapy.	A vs. B Age: 49 vs. 50 years Female: 93% vs. 93% FIQ total (0-10): 5.5 vs. 5.6 FIQ physical function (0-10): 4.2 vs. 4.5 FIQ pain (0-10): 6.3 vs. 6.0 FIQ depression (0-10): 5.5 vs. 5.9 FIQ anxiety (0-10): 6.4 vs. 7.1 Regional Pain Score (0-105): 63.9 vs. 67.0	A vs. B <u>6 months</u> FIQ total: 4.9 vs. 5.5, difference −0.6 (95% CI −1.1 to −0.09) FIQ physical function: 4.3 vs. 4.8, difference −0.5 (95% CI −1.3 to 0.3) FIQ pain: 6.1 vs. 6.6, difference −0.5 (95% CI −1.2 to 0.2) Regional Pain Score: 62.6 vs. 68.4, difference −5.8 (95% CI −12.1 to 0.5)	A vs. B <u>6 months</u> Psychological General Wellbeing Index total (0-110): 51.1 vs. 43.8, difference 7.3 (95% CI 0.2 to 14.3) Psychological General Wellbeing Index anxiety (0-25): 13.0 vs. 10.3, difference 2.7 (95% CI 0.6 to 4.8) Psychological General Wellbeing Index depression (0-15): 9.0 vs. 7.7, difference 1.3 (95% CI −0.1 to 2.7) SF-36 physical function (0-100): 42.2 vs. 43.9, difference −1.7 (95% CI −8.6 to 5.2) FIQ depression: 4.6 vs. 6.1 FIQ anxiety: 5.1 vs. 6.7, difference −1.6 (95% CI −2.6 to −0.6)
Martin, 2012[229] 6 months Duration of pain: Mean 14 to 15 years *Poor*	A. Multidisciplinary treatment (n=54), conventional pharmacological treatment, 12 sessions of CBT, education, and physiotherapy over 6 weeks B. Usual care (conventional pharmacological treatment) (n=56), included amitriptyline, paracetamol, and tramadol	A vs. B Age: 49 vs. 52 years Female: 91% vs. 91% FIQ total (0-100): 76.3 vs. 76.2 FIQ physical functioning (0-10): 5.5 vs. 5.4 FIQ pain (0-10): 7.5 vs. 7.5	A vs. B <u>6 months</u> FIQ total: 70.3 vs. 76.8, difference −6.5 (95% CI -12.3 to −0.7) FIQ physical function: 5.2 vs. 5.9, difference −0.7 (95% CI -1.4 to −0.04) FIQ pain: 7.2 vs. 8.2, difference -1.0 (95% CI -1.7 to −0.3)	A vs. B <u>6 months</u> Hospital Anxiety and Depression Scale anxiety (HADS, 0-21): 13.4 vs. 12.8, difference 0.66 (95% CI −1.02 to 2.34) HADS depression (0-21): 9.8 vs. 10.2, difference −0.43 (95% CI −2.00 to 1.14)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Saral 2016[231] 6 months; 4 months based on intervention group[b] Duration of pain: 7.5 years *Fair*	A. Long term interdisciplinary group (n=22): educational program (1 full day), exercise program (1 full day), and CBT (1, 3-hour session per week for 10 weeks); plus home strengthening and stretching exercises and relaxation B. Short term interdisciplinary group (n=22): education, exercise, and CBT over 2 full days; plus home strengthening and stretching exercises and relaxation C. Usual care (n=22): Patients continued current medical treatments, normal daily living, and current physical activity levels	A vs. B vs. C Age, years: 38 vs. 43 vs. 44 Female: 100% vs. 100% vs. 100% Symptom duration, months: 69 vs. 113 vs. 88 FIQ (0-100): 71.6 vs. 67.7 vs. 65.5 Pain VAS (0-10): 8.2 vs. 7.6 vs. 7.5	A vs. C 4 months[b] FIQ: 53.9 vs. 65.5, difference −11.6 (95% CI −21.9 to −1.29) Percent change from baseline in FIQ: −22.1% vs. 3.2% Pain VAS: 5.1 vs. 7.6, difference −2.5 (95% CI −3.78 to −1.22) Percent change from baseline in VAS pain: −38.3% vs. 1.5% B vs. C 4 months[b] FIQ: 54.5 vs. 65.5, difference −11.0 (95% CI −19.5 to −2.5) Percent change from baseline in FIQ: −18.9% vs. 3.2% Pain VAS: 5.8 vs. 7.6, difference −1.8 (95% CI −2.6 to −1.0) Percent change from baseline in VAS pain: −22.8% vs. 1.5%	A vs. C 4 months[b] BDI: 16.6 vs. 18.7, difference −2.1 (95% CI −8.2 to 4.0) SF-36 PCS: 39.9 vs. 34.3, difference 5.6 (95% CI 0.61 to 10.6) SF-36 MCS: 40.7 vs. 37.6, difference 3.1 (95% CI −4.1 to 10.3) Sleep VAS: 3.0 vs. 4.9, difference −1.9 (95% CI −3.8 to −0.04) B vs. C 4 months[b] BDI: 15.0 vs. 18.7 (9.5), difference −3.7 (95% CI −10.2 to 2.8) SF-36 PCS: 39.6 vs. 34.3, difference 5.3 (95% CI −0.03 to 10.6) SF-36 MCS: 40.2 vs. 37.6, difference 2.6 (95% CI −4.0 to 9.2) Sleep VAS: 3.1 vs. 4.9 difference −1.8 (95% CI −3.6 to 0.02)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Van Eijk-Hustings, 2013[85] 18 months Duration of pain: Mean of 6.1 to 7.1 years *Fair*	A. Multidisciplinary intervention (n=108), 36 days of sessions of sociotherapy, physiotherapy, psychotherapy, and creative arts therapy over 12 weeks B. Aerobic exercise (n=47): 24 sessions over 12 weeks C. Usual care (n=48), education and lifestyle advice in addition to usual care	A vs. B vs. C Age: 41 vs. 39 vs. 43 years Female: 93% vs. 100% vs. 98% FIQ physical function (0-10): 4.2 vs. 3.6 vs. 3.4 FIQ total (0-100): 64.5 vs. 60.0 vs. 55.4 FIQ pain (0-10): 6.3 vs. 6.2 vs. 5.5	A vs. B[c] <u>18 months</u> FIQ physical function: 3.6 vs. 3.6, difference 0 (95% CI −0.79 to 0.79) FIQ total: 50.9 vs. 52.0, difference −1.10 (95% CI −8.40 to 6.20) FIQ pain: 5.3 vs. 5.2, difference 0.10 (95% CI −0.67 to 0.87) A vs. C <u>18 months</u> FIQ physical function: 3.6 vs. 3.9, ES 0.12 (−0.22 to 0.46) FIQ total: 50.9 vs. 56.2, ES 0.25 (95% CI −0.09 to 0.59) FIQ pain: 5.3 vs. 5.3, ES −0.01 (95% CI −0.35 to 0.34)	A vs. B[c] <u>18 months</u> FIQ Depression: 3.9 vs. 5.0, difference −1.1 (95% CI −2.2 to 0.01) FIQ Anxiety: 4.7 vs. 5.0, difference −0.30 (95% CI −1.41 to 0.81) EQ-5D (−0.59 to 1): 0.6 vs. 0.5, difference 0.01 (95% CI −0.10 to 0.12) GP consultations[d]: 0.9 vs. 1.0, difference −0.10 (95% CI −0.89 to 0.69) Medical specialist consultations[d]: 0.3 vs. 0.4, difference −0.10 (95% CI −0.43 to 0.23) Physiotherapist consultations[d]: 2.6 vs. 0.4, difference 2.20 (95% CI 0.69 to 3.71) Other paramedical professional consultations[d]: 1.0 vs. 2.1, difference −1.10 (95% CI −2.21 to 0.01) A vs. C <u>18 months</u> FIQ depression: 3.9 vs. 4.2, ES 0.10 (95% CI −0.24 to 0.44) FIQ anxiety: 4.7 vs. 4.8, ES 0.03 (95% CI −0.31 to 0.37 EQ-5D: 0.55 vs. 0.51, ES 0.12 (95% CI −0.22 to 0.46) GP consultations[d]: 0.9 vs. 0.7, ES=−0.11 (95% CI −0.45 to 0.23) Medical specialist consultations[d]: 0.3 vs. 0.2, ES=−0.14 (95% CI −0.48 to 0.20) Physiotherapist consultations[d]: 2.6 vs. 2.8, ES=0.04 (95% CI −0.30 to 0.38) Other paramedical professional consultations[d]: 1.0 vs. 0.2, ES=−0.28 (95% CI −0.62 to 0.06)

CBT = cognitive behavioral therapy; CI = confidence interval; ES = effect size; EQ-5D = EuroQol-5D; FIQ = Fibromyalgia Impact Questionnaire; GP = general practitioner; HADS = Hospital Anxiety and Depression Scale; MOS = Medical Outcomes Study; NR = not reported; OR = odds ratio; SF-36 = Short-Form 36; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Long term multidisciplinary group was followed up at 4 months from end of intervention and the short term multidisciplinary and control groups were followed up at 6 months from end up intervention

[c] Authors did not provide effect estimates for the comparison of multidisciplinary rehabilitation versus exercise; mean differences were calculated by the EPC

[d] Total number of consultations over a period of 2 months prior to measurement

Multidisciplinary Rehabilitation Compared With Usual Care or Waitlist

Clinically important FIQ improvement (≥14% change) was significantly more common for multidisciplinary treatment compared with usual care at short- (odds ratio [OR] 3.1, 95% CI 1.6 to 6.2), intermediate- (OR 3.1, 95% CI 1.5 to 6.4) and long-term followup (OR 8.8, 95% CI 2.5 to 30.9) in one poor-quality trial.[226] Multidisciplinary treatment for fibromyalgia was associated with a small improvement in function versus usual care or waitlist based on a 0 to 100 FIQ total score in the short term (3 trials, pooled MD −6.52, 95% CI −12.84 to −0.21, I^2 =67.3%),[225,226,231] and versus usual care in the intermediate term (3 trials, pooled MD −7.84, 95% CI −11.43 to −4.25, I^2=18.2%)[226,228,229] (Figure 48). The short-term estimate for trials of multidisciplinary treatment versus usual care only was similar (2 trials, pooled MD −9.74, 95% CI −16.38 to −3.83).[226,231] The slightly smaller effect of multidisciplinary rehabilitation versus usual care persisted over the long term (2 trials, pooled MD on 0-100 scale −8.42, 95% CI −13.76 to −3.08, $I^{2=}$24.9%).[85,226] Only one poor-quality trial reported short-term, intermediate-term, and long-term effects on function, showing a significant result for each time frame.[226]

Clinically important improvement in pain (≥30% change on a 0-10 scale) was more common for multidisciplinary treatment compared with usual care at intermediate-term followup in one poor-quality trial, OR 3.4 (95% CI 1.0 to 10.8)[226]; no statistical differences were seen between groups at short- or long-term followup. There were no clear effects of multidisciplinary treatment for fibromyalgia on pain versus usual care or waitlist in the short term (3 trials, pooled MD on a 0-10 scale −0.83, 95% CI −1.85 to 0.18, I^2=83.6%),[225,226,231] but statistical heterogeneity was very large (Figure 49). Excluding an outlier trial (MD −2.50, 95% CI −3.73 to −1.27)[231] reduced the statistical heterogeneity and resulted in an attenuated effect (pooled MD −0.24, 95% CI −0.63 to 0.15, I^2=0%). At intermediate term, multidisciplinary treatment was associated with a slightly smaller effect on pain compared with usual care (3 trials, pooled MD 0−10 scale −0.68, 95% CI −1.07 to −0.30, I^2=0%).[226,228,229] Long term, there were no clear effects of multidisciplinary treatment on pain versus usual care (2 trials, pooled difference −0.25, 95% CI −0.68 to 0.17, I^2=0%).[85,226] Only one poor-quality trial reported short-, intermediate-, and long-term effects on pain, showing a significant result for each time frame.[226]

Results were mixed across the six trials for effects of multidisciplinary treatment on secondary outcomes. Three trials were fair quality. [85,225,231] Across the three fair-quality trials, there were no significant differences between multidisciplinary treatment and usual care or waitlist on measures of anxiety (Generalized Anxiety Disorder−10, FIQ anxiety subscale) in two trials[85,225] and depression (Major Depression Inventory, FIQ depression subscale, BDI) in three trials[85,225,231] over short-term or long-term followup. Regarding quality of life, two of these trials reported no differences between groups on the SF-36 PCS and MCS and the EQ-5D[85,225] while the third reported significant improvement on the SF-36 PCS but not the MCS.[231] One trial reported no difference in health care utilization between groups during the 2 months prior to the final measurement at 18 months.[85]

Multidisciplinary Rehabilitation Compared With Pharmacological Therapy

No trial of multidisciplinary rehabilitation versus pharmacological therapy met inclusion criteria.

Multidisciplinary Rehabilitation Compared With Exercise

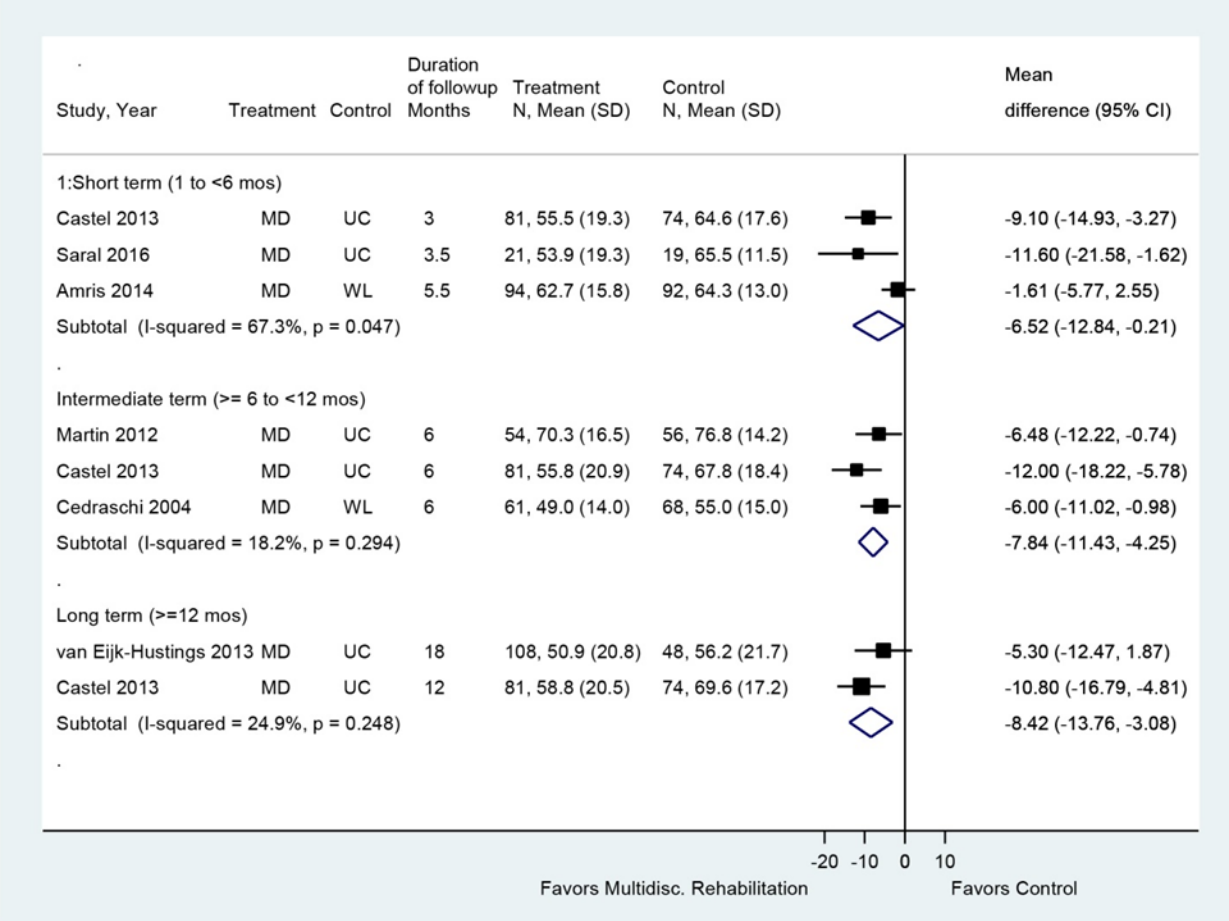
There was no clear effect of multidisciplinary pain treatment versus aerobic exercise at long term in one fair-quality trial[85] for physical function on the FIQ physical function scale (difference 0 on a 0−10 scale, 95% CI −0.79 to 0.79) or the FIQ total score (difference −1.10 on

a 0−100 scale, 95% CI −8.40 to 6.20). Similarly, there were no significant differences on the FIQ pain scale (difference 0.10 on a 0−10 scale, 95% CI −0.67 to 0.87), secondary outcomes of quality of life, depression or anxiety, or health care utilization, with the exception of physiotherapist consultations, which was higher for the multidisciplinary group in the 2 months prior to the final measurement at 18 months (Table 42).

Harms

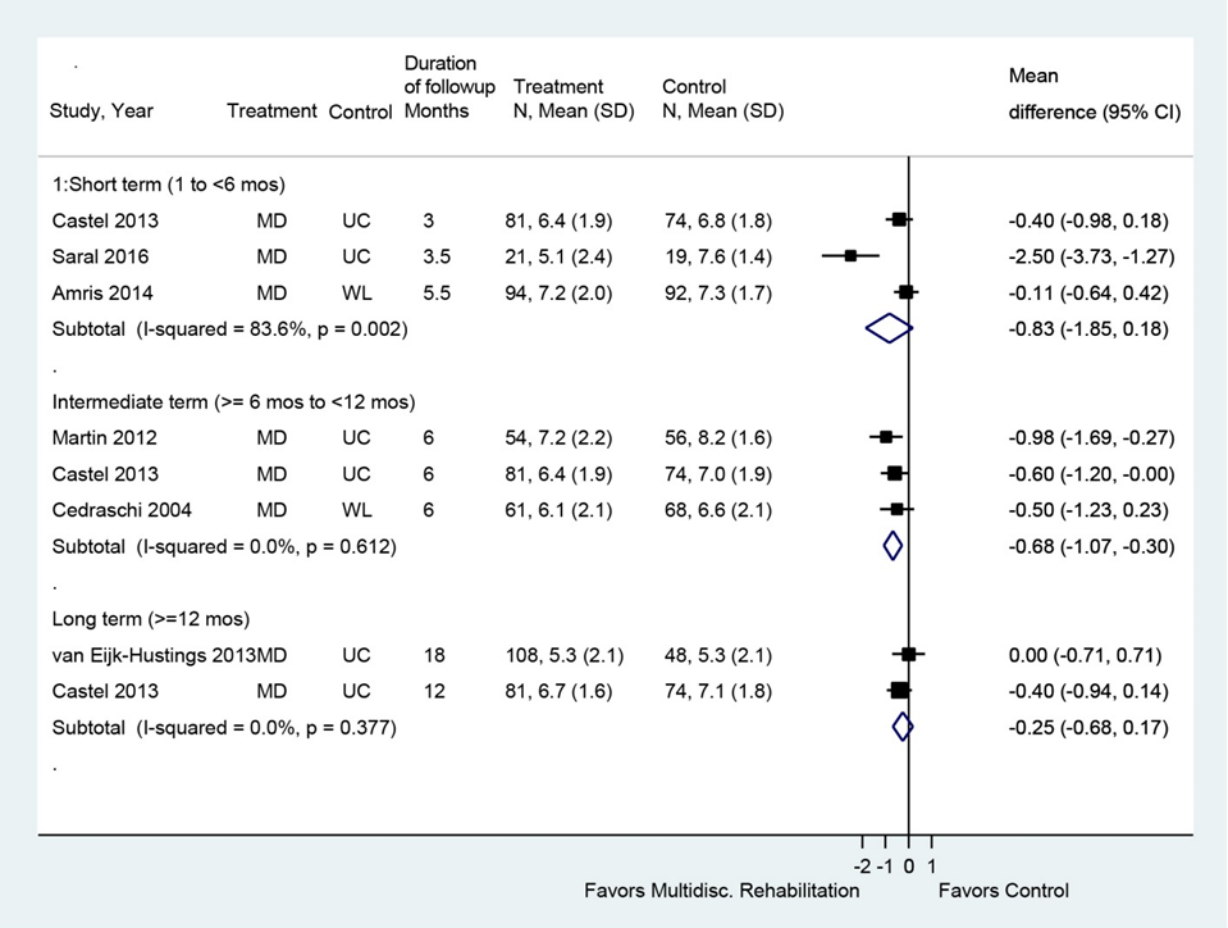
Adverse events were poorly reported by the included trials. One trial that compared multidisciplinary treatment (group pool sessions of physiotherapy, relaxation exercises, and exercise) with usual care (physical therapy, drug treatment and, in some cases, psychotherapy)[228] reported that 16 of 84 (19%) multidisciplinary participants withdrew (versus 0% for waiting list) and two of these gave increased pain as the reason. Reasons for other withdrawals were not given and there was not systematic reporting of adverse events.

Figure 48. Multidisciplinary rehabilitation versus usual care or waitlist for fibromyalgia: effects on function



CI = confidence interval; MD = multidisciplinary rehabilitation; SD = standard deviation; UC = usual care; WL = waitlist

Figure 49. Multidisciplinary rehabilitation versus usual care or waitlist for fibromyalgia: effects on pain



CI = confidence interval; MD = multidisciplinary rehabilitation; SD = standard deviation; UC = usual care; WL = waitlist

Key Question 5: Chronic Tension Headache

Psychological Therapies for Chronic Tension Headache

Key Points

- There is insufficient evidence from three poor quality trials to determine the effects of psychological therapies (CBT, relaxation) on short-term or intermediate-term function or pain compared with waitlist, placebo or attention control (SOE: insufficient).
- There is insufficient evidence from two poor-quality trials to determine the effects of CBT on short-term or intermediate-term function or pain compared with antidepressant medication (SOE: insufficient).
- No long-term outcomes were reported and no trials comparing psychological therapies to biofeedback were identified that met inclusion criteria.
- Data were insufficient for harms. Results were mixed across two poor-quality trials comparing CBT with antidepressant medication, with one trial reporting a lower risk of "at least mild" adverse events in the CBT group (0% vs. 59%), four of which led to

withdrawal from the trial, and the second trial reporting a similar low risk of withdrawal due to adverse events (2% to 6% across groups to include placebo) (SOE: insufficient).

Detailed Synthesis

Three trials, all conducted in the United States,[104,105,108] of CBT for chronic tension headache met inclusion criteria (Table 43 and Appendix D). Sample sizes ranged from 41 to 150; the mean age across trials varied from 32 to 42 years and most participants were female (56% to 80%). Duration since the onset of headache pain ranged from 10.7 to 14.5 years. All trials either excluded patients with concomitant migraines or required that they suffer from no more than one migraine per month. Two trials also specifically excluded patients with medication overuse (analgesic-abuse) headaches and required that patients be free from prophylactic headache medication upon study entry.[105,108]

All three trials evaluated some variation of stress management therapy/cognitive coping skills training with a relaxation component; one trial (n=77) also included an additional relaxation only arm.[104] In two trials (n=41, 150), patients received three 60-minute sessions of CBT and training in home-based relaxation,[105,108] and in the third trial (n=77), patients underwent 11 sessions (1-2 per week) of CBT plus progressive muscle relaxation training (session duration varied from 45 to 90 minutes).[104] In all trials, the interventions were administered by a psychologist or counselor over a 2-month period. Two trials compared CBT with placebo (placebo pill),[105] attention control (pseudomeditation/body awareness training)[104] and waitlist (monitoring via phone and clinical visits) control groups.[104] Two trials compared CBT with amitriptyline (25-75 mg/day).[105,108] All trials reported short-term results; one trial also provided outcomes at intermediate-term followup.[105]

All three trials were considered poor quality (Appendix E) due to lack of blinding and large differential attrition between groups (in one trial, overall attrition was also substantial[105]). Additionally, randomization, concealment, and intention-to-treat processes were unclear in one trial.[108]

Table 43. Chronic tension headache: psychological therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Blanchard, 1990[104] (n=77) 1 month Duration of pain: mean 14.2 years *Poor*	A. Cognitive Stress Coping Training + PMR (n=17): 11, 45-90 minute sessions once or twice per week for 8 weeks B. PMR alone (n=22): 10, 30-70 minute sessions twice weekly for 3 weeks followed by once weekly for 3 weeks with a final session at week 8 C. Pseudomeditation (attention control) (n=19): body awareness and mental control training; 11 sessions over 8 weeks, 40-45 minutes each D. Waitlist (n=19): monitoring via phone, clinical visits and patient diaries.	A vs. B vs. C vs. D Age: 38 vs. 43 vs. 39 vs. 37 years Female: 56% vs. 58% vs. 45% vs. 66% Mean duration of chronicity: 13.0 vs. 13.9 vs. 15.3 vs. 14.3 years Headache Index Scores: mean 5.82 vs. 5.63 vs. 5.23 vs. 5.05 Medication Index Scores: mean 39.8 vs. 16.9 vs. 12.1 vs. 24.0	A vs. C <u>1 month</u> ≥50% improvement (i.e., reduction) in headache frequency: 62.5% vs. 43.7%; RR 1.43 (95% CI 0.81 to 1.97) Headache Index Scores: 3.2 vs. 4.6; difference −1.4 (95% CI −4.3 to 1.5) A vs. D <u>1 month</u> ≥50% improvement (i.e., reduction) in headache frequency: 62.5% vs. 20.0%; RR 3.13 (95% CI 0.91 to 2.45) Headache Index Scores: 3.2 vs. 4.5; difference −1.3 (95% CI −3.9 to 1.4) B vs. C <u>1 month</u> ≥50% improvement (i.e., reduction) in headache frequency: 31.6% vs. 43.7%; RR 0.72 (95% CI 0.65 to 1.69) Headache Index Scores: 3.8 vs. 4.6; difference −0.8 (95% CI −3.2 to 1.6) B vs. D <u>1 month</u> ≥50% improvement (i.e., reduction) in headache frequency: 31.6% vs. 20%; RR 1.58 (95% CI 0.75 to 2.11) Headache Index Scores: 3.8 vs. 4.5; difference −0.6 (95% CI −2.7 to 1.5)	A vs. C <u>1 month</u> Medication Index Scores: 20.7 vs. 8.3; difference 12.4 (95% CI −6.8 to 31.6) A vs. D <u>1 month</u> Medication Index Scores: 20.7 vs. 22.5; difference −1.8 (95% CI −23.8 to 20.2) B vs. C <u>1 month</u> Medication Index Scores: 9.8 vs. 8.3; difference 1.5 (95% CI −6.8 to 9.8) B vs. D <u>1 month</u> Medication Index Scores: 9.8 vs. 22.5; difference −12.7 (95% CI −25.6 to 0.21)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Holroyd, 1991[108] (n=41) 1 month Duration of pain: mean 10.7 years *Poor*	A. CBT (n=19): three, 1 hour sessions over 8 weeks B. Amitriptyline therapy (n=17): Individualized dosage at 25, 50, or 75 mg/day for 8 weeks	A + B Age: 32.3 years Female: 80% A vs. B % of Headache-free days: 18.0 vs. 18.5 Headache Index scores (0−10): 2.17 vs. 2.04 Headache Pain Peak scores (0−10): 6.41 vs. 6.36	A vs. B <u>1 month</u> Proportion with >66% reduction in headaches (substantial improvement): 37% vs. 18%; RR 2.09 (95% CI 0.79 to 2.23) Proportion with 33-66% reduction in headaches (moderate improvement): 53% vs. 35%; RR 1.49 (95% CI 0.80 to 2.03) % of Headache-free days: 54.7 vs. 42.3; difference 12.4 (95% CI −8.06 to 32.86) Headache Index scores: 0.96 vs. 1.49; difference −0.53 (95% CI −1.14 to 0.08) Headache Peak scores: 4.33 vs. 4.55; difference −0.22 (95% CI −1.70 to 1.26)	A vs. B <u>1 month</u> BDI (0-63): 5.16 vs. 5.56; difference −0.4 (95% CI −3.96 to 3.16) STPI Anxiety (20-80): 18.37 vs. 19.06; difference −0.69 (95% CI −3.99 to 2.62) STPI Anger (20-80): 19.47 vs. 17.44; difference 2.03 (95% CI −1.98 to 6.04) WPSI (scale NR): 16.05 vs. 20.50; difference −4.45 95% CI −9.78 to 0.87) Analgesic Tablets: 0.26 vs. 0.82; difference −0.56 (95% CI −1.16 to 0.04)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Holroyd, 2001[105] (n=150) 1 and 6 months Duration of pain: mean 11.8 years *Poor*	A. Stress Management Therapy + Placebo (n=34): three, 1 hour sessions B. Placebo (n=26) Treatment Protocol: identical to group C C. Antidepressant Medications (n=44): Low starting dose (12.5 mg/day increased to 25mg, then 50mg) with the possibility to switch to nortriptyline	A vs. B vs. C Age: 37 vs. 38 vs. 36 years Female: 80% vs. 79% vs. 66% Caucasian: 91% vs. 98% vs. 98% Duration of pain: 12.3 vs. 11.1 vs. 11.9 years Headache frequency, days/month: 26.5 vs. 26.1 vs. 25.1 Headache Index (0−10): 2.8 vs. 2.7 vs. 2.8 Days/month with at least moderately severe headache (≥5 on 0−10 scale): 13.5 vs. 13.5 vs. 14.1	A vs. B <u>1 month</u> Days/month with at least moderately severe headache: MD 2.5 (95% CI −0.1 to 5.2) Headache Disability Inventory (0−100): MD 7.3 (95% CI 1.6 to 13.0) Headache Index: MD 0.46 (95% CI 0.02 to 0.89) <u>6 months</u> Patients who experienced ≥50% reductions in Headache Index Scores: 35% vs. 29%; RR 1.18 (95% CI 0.79 to 1.79) Days/month with at least moderately severe headache: MD 5.1 (95% CI 2.3 to 8.0) Headache Disability Inventory: MD 9.3 (95% CI 3.5 to 15.1) Headache Index: MD 0.79 (95% CI 0.30 to 1.28) A vs. C <u>1 month</u> Days/month with at least moderately severe headache: MD −3.5 (95% CI −6.1 to −0.9) Headache Disability Inventory: MD 0.1 (95% CI −5.6 to 5.7) Mean Headache Index: MD −0.54 (95% CI −0.97 to −0.012) <u>6 months</u> Patients who experienced >50% reductions in Headache Index Scores: 35% vs. 38%; RR 0.92 (95% CI 0.71 to 1.54) Days/month with at least moderately severe headache: MD 0.1 (95% CI −2.7 to 2.9) Headache Disability Inventory: MD 2.4 (95% CI −3.3 to 8.0) Headache Index: MD −0.13 (95% CI −0.61 to 0.35)	A vs. B <u>1 month</u> Weighted analgesic use: MD −1.7 (95% CI −12.0 to 8.6) <u>6 months</u> Weighted analgesic use: MD 11.8 (95% CI 1.5 to 22.1) A vs. C <u>1 month</u> Weighted analgesic use: MD −19.4 (95% CI −29.5 to −9.3) <u>6 months</u> Weighted analgesic use: MD −6.2 (95% CI −16.2 to 3.8)

BDI = Beck Depression Inventory; CBT = cognitive-behavioral therapy; CI = confidence interval; MD = mean difference; NR = not reported; PMR = Progressive Muscle Relaxation; RR = risk ratio; SD = standard deviation; STPI = State-Trait Personality Inventory; VAS = visual analog scale; WPSI = Wahler Physical Symptom Inventory

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Psychological Therapy Compared With Waitlist, Placebo, or Attention Control

There was insufficient evidence from three poor-quality trials to draw conclusions regarding the effects of psychological therapies compared with waitlist, placebo, or attention control over the short term or intermediate term.

CBT plus placebo was associated with a slightly greater effect on both short-term and intermediate-term function compared with placebo alone as measured by the Headache Disability Inventory (HDI) (scale 0−100) in one trial (MD 7.3, 95% CI 1.6 to 13.0 at 1 month and 9.3, 95% CI 3.5 to 15.1 at 6 months.[105] Long-term function was not reported.

Various pain measures were reported across trials. In general, CBT (plus relaxation), but not relaxation alone, appeared to have a small effect on short-term pain compared with waitlist, placebo, or attention control (Table 43). CBT plus relaxation was associated with a slight improvement in pain on the Headache Index (HI) at 1 month compared with waitlist, attention control, or placebo across two trials (pooled SMD −0.40, 95% CI −0.74 to −0.07, I^2=0%)[104,105] (Figure 51). Relaxation only conferred no benefit for short-term pain compared with waitlist or attention control in one of these trials (difference −0.21 on a 0-20 HI scale, 95% CI −0.78 to 0.36).[104] Almost twice as many patients who received CBT plus relaxation achieved at least a 50 percent improvement in headache frequency compared with usual care or waitlist (risk ratio [RR] 1.94, 95% CI 1.03 to 3.66) over the short term in one trial; however, there was no difference between groups when the intervention was relaxation alone (RR 0.98, 95% CI 0.42 to 2.26)[104] (Figure 50). One trial reported similar favorable results regarding pain over the intermediate-term for CBT plus placebo compared with placebo alone, with the exception of "success" (≥50% improvement from baseline in HI score), which did not differ between groups (Table 43).[105]

Medication use did not differ significantly between the CBT and relaxation therapy groups and waitlist, placebo, or attention control groups over the short-term in two trials.[104,105] Over the intermediate-term, CBT plus placebo resulted in a significant reduction in analgesic use compared with placebo alone (difference 11.8, 95% CI 1.5 to 22.1).[105]

Psychological Therapy Compared With Pharmacological Therapy

There was insufficient evidence from two poor-quality trials to draw conclusions regarding the effect of CBT versus pharmacological therapy through intermediate-term followup.

There was no effect for CBT plus placebo versus antidepressant medication over the short-term or intermediate-term for function as measured by the HDI (scale 0−100) in one trial (MD 0.1, 95% CI −5.6 to 5.7 at 1 month and 2.4, 95% CI −3.3 to 8.0 at 6 months).[105] Long-term function was not reported.

Regarding short-term pain, two trials reported HI index scores with differing results. One trial found that CBT plus placebo resulted in less improvement compared with antidepressant medication at 1 month (SMD 0.50, 95% CI 0.11 to 0.89),[105] whereas the other trial showed an improvement with CBT versus amitriptyline by 1 month, although the difference did not reach statistical significance (SMD −0.59, 95% CI −1.26 to 0.08)[108] (Figure 51); due to the significant heterogeneity between groups we did not use the pooled estimate. There were no significant differences between CBT and pharmacological treatment for any other pain outcome reported over the short term in both trials[105,108] or over the intermediate-term in one trial[105] (Table 43).

Short-term results were mixed regarding medication use with one trial reporting no difference between CBT and amitriptyline[108] and the other reporting a significant difference between groups favoring antidepressant therapy[105]; however, this difference did not persist to the intermediate term in the latter trial (Table 43).

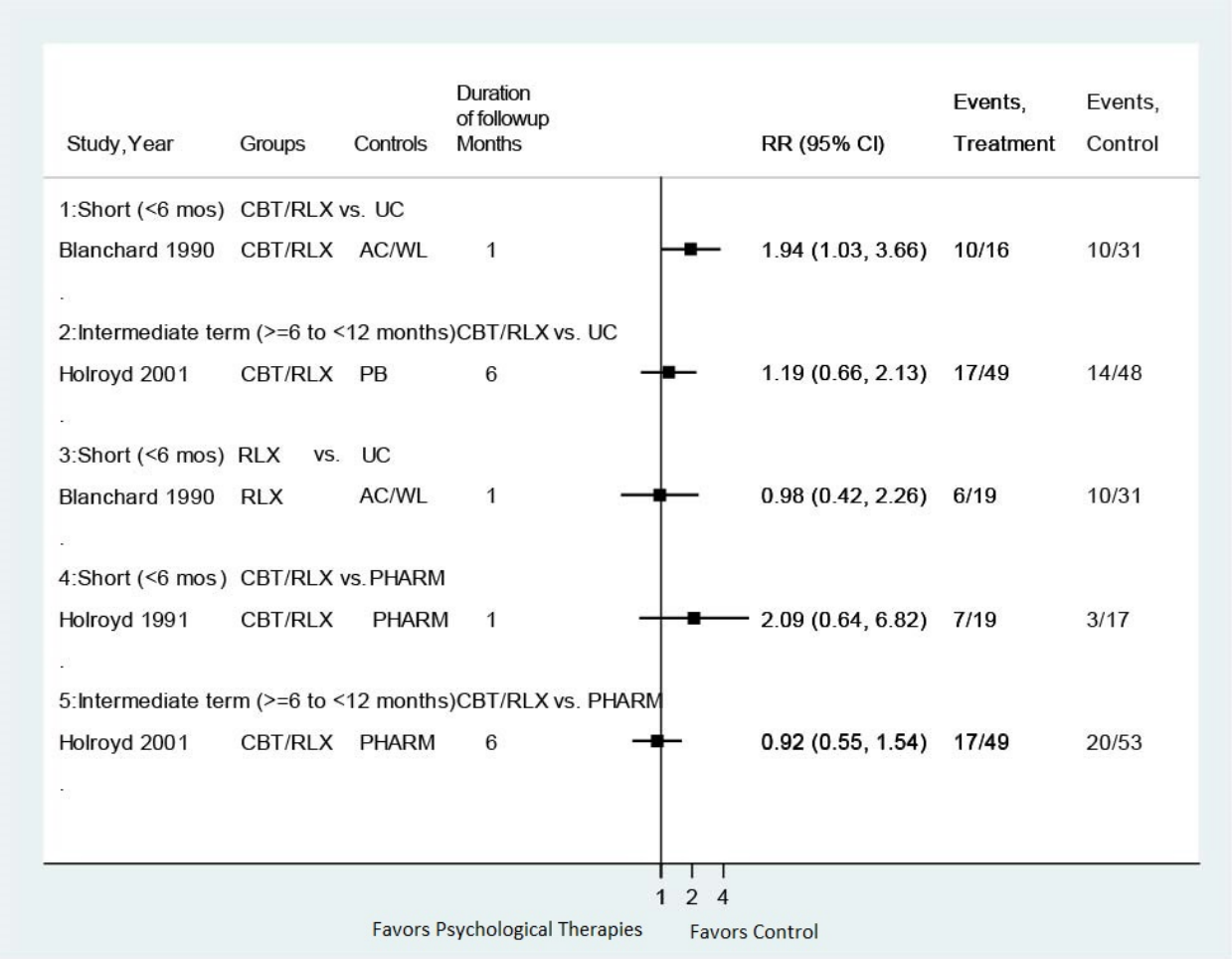
Psychological Therapy Compared With Biofeedback

No trial of psychological therapy versus biofeedback met inclusion criteria.

Harms

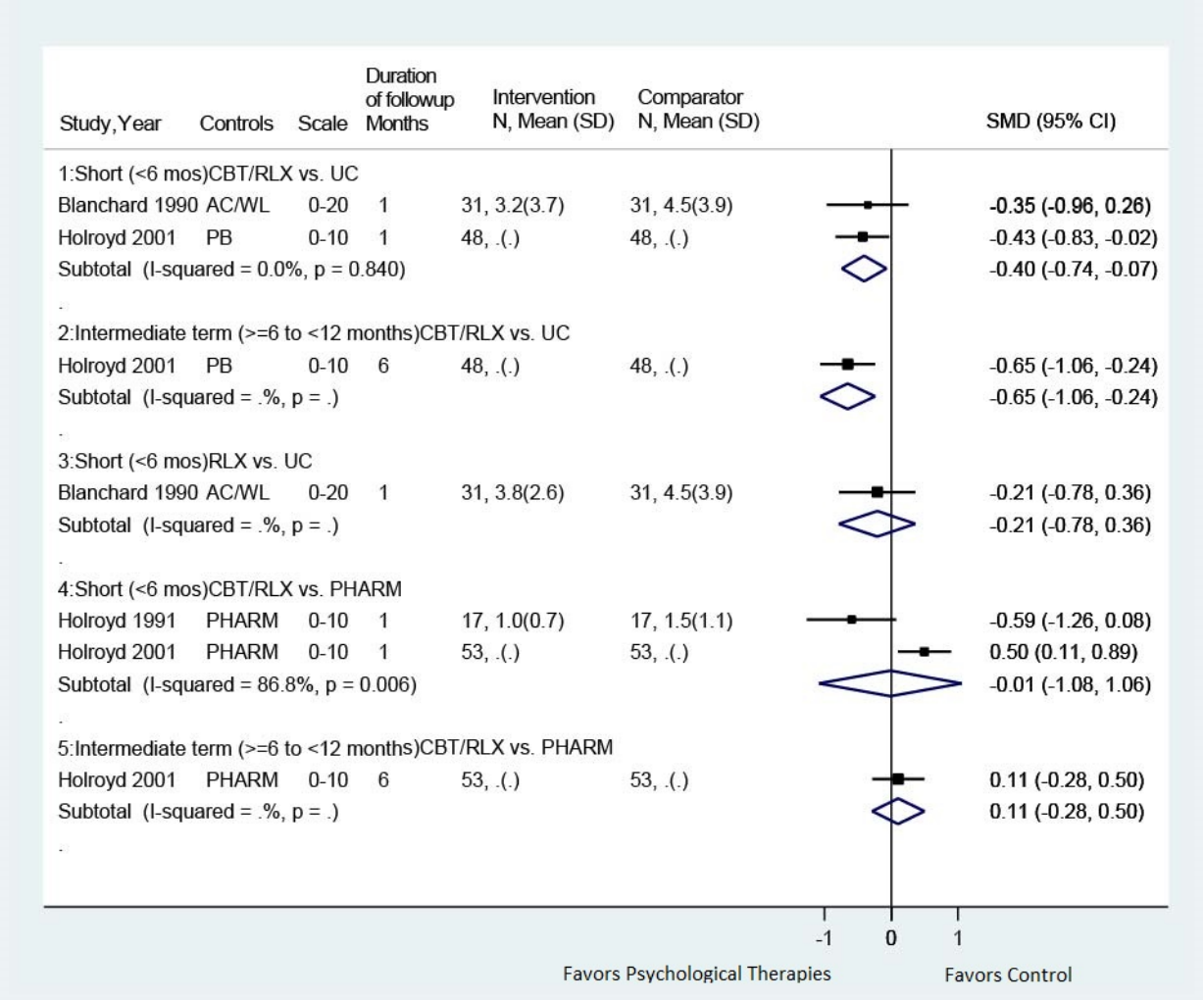
Harms were reported by the two poor-quality trials comparing CBT with antidepressant medication,[108] and with placebo in one.[105] No patient who underwent CBT experienced an adverse effect versus 10 of 17 (59%) of those who took medication in one trial;[108] six events were classified as mild, two as moderate, and two as substantial (no further details provided). Four of these patients withdrew from the trial. The risk of withdrawal due to adverse events was similar across groups in the second trial: CBT (2%) versus antidepressant medication (2%) and placebo (6%); no other information was provided.[105]

Figure 50. Psychological therapies versus waitlist, attention control, placebo intervention, or pharmacological treatment for chronic tension headache: effects on pain (success)



AC/WL = an attention control arm and a waitlist arm; CBT = cognitive-behavioral therapy; CBT/RLX = cognitive-behavioral therapy with a relaxation component; CI = confidence interval; PB = placebo (pill); PHARM = standard pharmacological therapy; RLX = relaxation therapy; RR = risk ratio; UC = usual care

Figure 51. Psychological therapies versus waitlist, attention control, placebo intervention, or pharmacological treatment for chronic tension headache: effects on pain (mean difference)



AC/WL = an attention control arm and a waitlist arm; CBT = cognitive-behavioral therapy; CBT/RLX = cognitive-behavioral therapy with a relaxation component; CI = confidence interval; PB = placebo (pill); PHARM = standard pharmacological therapy; RLX = Relaxation therapy; SMD = standardized mean difference; UC = usual care

Physical Modalities for Chronic Tension Headache

Key Points

- There is insufficient evidence from one poor-quality trial to determine the effects occipital transcutaneous electrical stimulation (OTES) on short-term term function or pain compared with sham (SOE: insufficient).
- No longer-term outcomes were reported and no trials comparing physical modalities to pharmacological therapy or to biofeedback were identified that met inclusion criteria.
- Data were insufficient for harms; however, no adverse events occurred in either the real or the sham OTES group in one poor-quality trial (SOE: insufficient).

Detailed Synthesis

Only one Italian trial[142] was identified that investigated the efficacy of occipital transcutaneous electrical stimulation (OTES) versus sham (Table 44 and Appendix D). Patients were excluded if they had undergone prophylactic treatment in the prior 2 months or had previous treatment with OTES. Acute medications use was permitted during the study period, but other methods of pain control or new preventive treatments were prohibited. At baseline, 46 percent of patients were overusing medications. Identical devices and procedures were used for both the real and the sham OTES, and treatment consisted of 30-minute sessions, three times per day for two consecutive weeks. Limited information on the timing of outcomes was provided, but it was assumed that data was collected at 1 and 2 months post-treatment. This trial was rated poor quality due to unclear randomization sequence, failure to control for dissimilar proportion of females between groups, and no reporting of attrition (Appendix E). The focus of the trial was on allodonia, which was not of interest to this report.

Table 44. Chronic tension headache: physical modalities

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Bono, 2015[142] (N=83) 1 month, 2 months Duration of pain: >2 years (mean NR) *Poor*	A. Occipital TES (n=54): Electro-stimulator generated biphasic impulses via electrodes placed on occipital region bilaterally; pulse width: 250 µs; frequency: 40 Hz; intensity 20 mA. B. Sham (n=29): Same device and procedure, but no current was delivered. Treatment protocol: 30 minute sessions 3 times daily for two consecutive weeks (42 sessions total)	A vs. B Age: 42 vs. 40 years Female: 81% vs. 66% Race: NR Headache frequency: mean 29.0 days/month Medication overuse: 43% vs. 52% MIDAS (0-21+): 63 vs. 50 VAS pain (0−10): 8 vs. 8	A vs. B <u>1 month</u> Patients who achieved >50% reduction in headache days: 85% vs. 7%; RR 12.4 (95% CI 3.2 to 47.3) <u>2 months</u> MIDAS: 16 vs. 51; difference −35.0 (95% CI −42.6 to −27.4) VAS pain (0−10): 3 vs. 8; difference −5.0 (95% CI −5.8 to −4.2) Proportion of patients still overusing medications: 7% vs. 48%; RR 0.15 (95% CI 0.06 to 0.42)	A vs. B <u>2 months</u> BDI-II: 7 vs. 8; difference −1.0 (95% CI −2.2 to 0.2) HAM-A: 6 vs. 7; MD −1.0 (95% CI −1.9 to −0.1)

BDI-II = Beck Depression Inventory-II; CI = confidence interval; HAM-A = Hamilton Anxiety Rating Scale; Hz = Herta; mA = milliamps; MIDAS = Migraine Disability Assessment Questionnaire; NR = not reported; RR = risk ratio; SD = standard deviation; TES = transcutaneous electrical stimulation; VAS = visual analog scale; µs = microsecond

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

Physical Modalities Compared With Sham

There was insufficient data from one poor-quality trial to determine the short-term effects of OTES compared with sham.[142] OTES resulted in greater improvement in function at 2 months as measured by the Migraine Disability Assessment Questionnaire (MD −35.0, 95% CI −42.6 to −27.4, scale 0-21+) and in pain intensity as measured by visual analog scale (VAS) (difference

−5.0 on a 0−10 scale, 95% CI −5.8 to −4.2) The proportion of patients who achieved a 50 percent or greater reduction in headache days also favored OTES (RR 12.4; 95% CI 3.2 to 47.3). Measures of depression and anxiety were both somewhat better following OTES compared with sham at 2 months, however, the between-group difference was only statistically significant for anxiety (Table 44). The proportion of patients overusing medications at 2 months was also significantly lower in the OTES group.

Physical Modalities Compared With Pharmacological Therapy or Biofeedback

No trial of physical modalities versus pharmacological therapy and versus biofeedback met inclusion criteria.

Harms

Authors report that neither adverse events nor side effects occurred in either the real or the sham OTES group in one poor-quality trial.[142]

Manual Therapies for Chronic Tension Headache

Key Points

- Spinal manipulation therapy was associated with slight to moderate improvements, respectively, compared with usual care in function (difference −5.0, 95% CI −9.02 to −1.16 on the Headache Impact Test, scale 36-78 and difference −10.1, 95% CI −19.5 to −0.64 on the Headache Disability Inventory, scale 0 to 100) and pain intensity (difference −1.4 on a 0-10 NRS scale, 95% CI −2.69 to −0.16) over the short term in one fair-quality trial (SOE: low). Approximately 25 percent of the patients had comorbid migraine.
- There is insufficient evidence from one poor-quality trial to determine the effects of spinal manipulation therapy on short-term pain compared with amitriptyline (SOE: insufficient).
- No longer-term outcomes were reported and no trials comparing physical modalities to pharmacological therapy or to biofeedback were identified that met inclusion criteria.
- No adverse events occurred in the trial comparing spinal manipulation to usual care, but significantly fewer adverse events were reported following manipulation versus amitriptyline in the other poor-quality trial (4.3% vs. 82.1%; RR 0.05, 95% CI 0.02 to 0.16). The risk of withdrawal due to adverse events was not significantly different (1.4% vs. 8.9%; RR 0.16, 95% CI 0.02 to 1.33). Common complaints were neck stiffness in the manipulation group and dry mouth, dizziness, and weight gain in the medication group (SOE: low).

Detailed Synthesis

Two trials (n=82 and n=150)[157,158] that evaluated spinal manipulation therapy (SMT) for the treatment of chronic tension headache met inclusion criteria (Table 45 and Appendix D). The majority of patients in both trials were female (61% to 78%) with mean ages ranging from 40 to 42 years and a mean headache duration of 13 years. Both trials included patients with comorbid migraine as long as their headache problem was determined by a physician to be predominantly tension-type in nature (this included 26% of patients in one trial;[157] proportion not reported in the other trial). In one trial, patients were specifically excluded if they met the criteria for medication overuse or if they had received manual therapy in the 2 months prior to enrollment.[157] At

baseline, prophylactic medication use was common. Current or past use of other treatments was not reported.

One Dutch trial compared a maximum of nine, 30-minute sessions of SMT over 8 weeks with usual care (information, reassurance and advice, discussion of lifestyle changes, and analgesics or NSAIDs provided by a general practitioner).[157] The second trial, conducted in the United States, compared 12 SMT sessions of 20 minutes over a 6-week treatment period versus amitriptyline (maximum dose 30 mg/day).[158] Both trials reported only short-term outcomes. One trial was rated fair quality[157] and one poor quality[158] (Appendix E). Due to the nature of the interventions, blinding of patients and researchers was not possible. Additionally, the poor trial had a high rate of differential attrition (7% SMT and 27% amitriptyline).

Table 45. Chronic tension headache: manual therapies

Author, Year, Followup,[a] Pain Duration, Study Quality	**Intervention**	**Population**	**Function and Pain Outcomes**	**Other Outcomes**
Boline, 1995[158] 1 month Duration of pain: 13.5 years *Poor*	A. Spinal Manipulative Therapy (n=70): short-lever, low-amplitude, high-velocity thrust techniques on cervical, thoracic or lumbar spinal segments. Moist heat and light massage preceded manipulation; 12, 20 minute sessions (2 per week for 6 weeks) B. Amitriptyline (n=56): dose titration of amitriptyline for 6 weeks. Nighttime, daily doses began at 10mg/day for first week, then increased to 20mg/day in the second, followed by 30mg/day in the third week and after; continued use of OTC medications as-needed.	A vs. B Age: 41 vs. 42 years Female: 54% vs. 70% Race: NR Daily headache intensity (0-20)[b]: 5.6 vs. 5.0 Weekly headache frequency (0-28)[c]: 12.4 vs. 10.8	A vs. B <u>1 month</u> Daily headache intensity[b]: adjusted means 3.8 vs. 5.2; difference 1.4 (95% CI 0.3, 2.3) Weekly headache frequency[c]: adjusted means 7.6 vs. 11.8; difference 4.2 (95% CI 1.9, 6.5)	A vs. B <u>1 month</u> SF-36 Function Health Status Global Score (% points): adjusted means 78.8 vs. 73.9; difference 4.9 (95% CI 0.4, 9.4) OTC medication usage: adjusted means 1.3 vs. 2.2; difference 0.9 (95% CI 0.3, 1.5)

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Castien, 2011[157] 4.5 months Duration of pain: 13 years *Fair*	A. Spinal Manipulation (n=38) combination of 3 approaches at the therapist discretion: mobilizations of the cervical and thoracic spine, craniocervical muscle exercises and posture correction; maximum of 9, 30-minute sessions over 2 months B. Usual Care (n=37) 2-3 general practitioner visits over 2 months	A vs. B Age, years: 40 vs. 40 years Female: 78% vs. 78% Race: NR Mean frequency of headache (days/month): 24 vs. 24 NSAID use: 29% (mean 3 pills/week); Analgesic use: 59% (mean 1.5 pills/week) HIT-6 (36-78): 62.6 vs. 61.2 HDI (0-100): 39.6 vs. 44.2 Pain intensity, NRS (0-10): 6.3 vs. 5.7	A vs. B <u>4.5 months</u> Proportion of patients with ≥50% reduction in headache frequency: 81.6% vs. 40.5%; RR 2.01 (95% CI 1.32 to 3.05) HIT-6, mean change from baseline: −10.6 vs. −5.5; difference 5.0 (95% CI −9.02 to −1.16) HDI, mean change from baseline: −20.0 vs. −9.9; difference −10.1 (95% CI −19.5 to −0.64) Headache frequency (days/14 days), mean change from baseline: −9.1 vs. −4.1; difference −4.9 (95% CI −6.95 to −2.98) Pain intensity mean change from baseline: −3.1 vs. −1.7; difference −1.4 (95% CI −2.69 to −0.16) Headache duration (hrs./day), mean change from baseline: −7.0 vs. −3.5; difference −3.5 (95% CI −7.71 to −0.63)	A vs. B <u>4.5 months</u> Resource use, proportion who used: ≥1 sick leave day: 7.9% vs. 32.4%; RR 0.23 (95% CI 0.07 to 0.79) Any additional health care: 13.2% vs. 59.4%; RR 0.22 (95% CI 0.09 to 0.52) Additional physical therapy: 2.6% vs. 40.5%; RR 0.06 (95% CI 0.01 to 0.47) Additional medical specialist care: 2.6% vs. 16.2%; RR 0.16 (95% CI 0.02 to 1.28) Additional "other" health care": 7.8% vs. 2.7%; RR 2.9 (95% CI 0.3 to 26.8)

CI = confidence interval; HDI = Headache Disability Index; HIT-6 = Headache Impact Test-6; NR = not reported; NR = not reported; NRS = numeric rating scale; NSAID = nonsteroidal anti-inflammatory drugs OTC = over-the-counter; RR = risk ratio; SF-36 = Short-Form-36 Questionnaire; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Headache intensity was calculated as the total ratings per period and divided by the number of days per period

[c] Headache frequency was calculated by summing all headache ratings 2 and above for the month

Manual Therapies Compared With Usual Care

Only short-term data from one fair-quality trial were reported. SMT resulted in small to moderate improvements in function compared with usual care at 4.5 months post-treatment as measured by the Headache Disability Inventory (HDI, scale 0 to 100) and the Headache Impact Test (HIT-6, scale 36 to 78), respectively (MD between groups in change scores from baseline, −10.1, 95% CI −19.5 to −0.64 and −5.0, 95% CI −9.02 to −1.16).[157] Regarding pain outcomes, twice as many patients who received SMT experienced a ≥50% reduction from baseline in the number of headache days (per 2 weeks) compared with usual care: 81.6% versus 40.5%; RR 2.0 (95% CI 1.3, 3.0).[157] Similarly, a statistically greater reduction in the number of headache days (MD between groups in change scores from baseline, −4.9; 95% CI −6.95 to −2.98) and in headache pain intensity (MD in change scores from baseline, −1.4 on a 0 to 10 NRS scale, 95% CI −2.69 to −0.16) was seen following SMT. Given that 29 percent of SMT patients and 22

percent of usual care patients had comorbid migraine, it is unclear how the coexistence of these headache types may have affected the outcome.

The proportion of patients who used any additional health care services (e.g., physical therapy, medical specialists, other) was statistically lower in the SMT group compared with the usual care group (Table 45).[157] Authors report no statistically significant differences between treatments in analgesic or NSAID use; data were not provided.

Manual Therapies Compared With Pharmacological Therapy

The evidence was insufficient from one poor-quality trial to determine the effects of spinal manipulation compared with amitriptyline over the short term.[158] The spinal manipulation group showed more improvement compared with the amitriptyline group in daily headache intensity (adjusted difference −1.4, 95% CI −2.3 to −0.3), weekly headache frequency (adjusted difference −4.2, 95% CI −6.5 to −1.9), Short Form-36 Function score (adjusted difference 4.9, 95% CI 0.4 to 9.4), and over-the-counter medication use (difference −0.9, 95% CI −1.5 to −0.3) at 1 month. Attrition in the amitriptyline group was 27 percent, compared with 7 percent in the manipulation group.

Manual Therapies Compared With Biofeedback

No trial of physical modalities versus biofeedback met inclusion criteria.

Harms

No adverse events occurred in the trial comparing spinal manipulation to usual care.[157] The other poor-quality trial reported significantly fewer adverse events following spinal manipulation compared with amitriptyline (4.3% vs. 82.1%; RR 0.05, 95% CI 0.02 to 0.16) but the risk of withdrawal due to adverse events was not significantly different (1.4% vs. 8.9%; RR 0.16, 95% CI 0.02 to 1.33).[158] Patients in the manipulation group complained of neck stiffness which resolved in all cases and common side effects in the amitriptyline group included dry mouth, drowsiness, and weight gain.

Acupuncture for Chronic Tension Headache

Key Points

- There is insufficient evidence from two poor quality trials to determine the effects of Traditional Chinese needle acupuncture on short-term (2 trials), intermediate-term (1 trial) or long-term (1 trial) pain compared with sham acupuncture (SOE: insufficient).
- Laser acupuncture was associated with slight improvement in pain intensity (median difference −2, IQR 6.3, on a 0-10 VAS scale) and in the number of headache days per month (median difference −8, IQR 21.5) over the short term versus sham in one fair-quality trial (SOE: low).
- No trials comparing acupuncture to pharmacological therapy or to biofeedback were identified that met inclusion criteria.
- The fair-quality trial evaluating laser acupuncture reported that no adverse events occurred in either group (SOE: low).

Detailed Synthesis

Three small trials (n=30 to 50)[214-216] that evaluated acupuncture versus sham treatment for chronic tension headaches met inclusion criteria (Table 46 and Appendix D). Two trials

employed traditional Chinese needle acupuncture,[215,216] while one used low-energy laser acupuncture.[214] The number of acupoints ranged from six to ten across studies. The duration of treatment ranged from 5 to 10 weeks, with the total number of sessions ranging from eight to ten (20 to 30 minutes duration, 1 to 3 times per week). Sham treatment consisted of irrelevant acupuncture (superficial needle insertion in areas without acupuncture points) and sham acupuncture (blunt needle that simulates puncturing of the skin, laser power output set to zero).

Across trials, participants were primarily female (49% to 87%), mean ages ranged from 33 to 49 years, and headache frequency from 18 to 27 days per month. Two trials specifically excluded patients with other causes of chronic headache[214,215]; the third trial did not note if any of the patients had concomitant headaches.[216] One trial required patients to abstain from all other prophylactic therapies (with the exception of rescue analgesics),[216] and one trial excluded patients who had received any treatment for their headache in the 2 weeks prior to enrollment.[214] Concomitant (non-narcotic) medication was permitted in two trials,[215,216] the third stated that no patient took concomitant analgesics.[214] All trials assessed outcomes over the short term; one trial additionally provided intermediate- and long-term data.[216]

One trial was rated fair quality[214] and two poor quality[215,216] (Appendix E). In all three trials, random sequence generation and concealment of allocation were not clearly reported and the care providers were not blinded to treatment. Additional methodological concerns in the poor quality trials included unclear application of intention-to-treat methods, and failure to control for disproportionate baseline characteristics or to account for loss to followup in one trial each.

Table 46. Chronic tension headache: acupuncture

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Ebneshahidi, 2005[214] 3 months Duration of pain: NR *Fair*	A. Low-Energy Laser Acupuncture (n=25): 4 acupoints (two local and two distal), bilaterally (8 total): intensity 1.3J, output 100%, continuous mode, using vertical contact with pressure and a duration of 43 seconds. B. Sham Laser Acupuncture (n=25): Identical procedure to real electroacupuncture except power output set to 0 Treatment Protocol: 3 sessions per week for a total of 10 sessions (session length: NR)	A vs. B Age: 33 vs. 39 years Female: 80% vs. 80% Race: NR Number of headache days per month (0-28), median: 20 vs. 18 Pain intensity on VAS (0-10), median: 10 vs. 10 Duration of attacks, (hours), median: 10 vs. 8	A vs. B <u>3 months</u> Headache Days/Month, median change from baseline: −8 vs. 0, P<0.001 Headache Intensity (VAS), median change from baseline: −2 vs. 0, P<0.001 Duration of attacks (hours), median change from baseline: −4 vs. 0, P<0.001	NR

Author, Year, Followup,[a] Pain Duration, Study Quality	Intervention	Population	Function and Pain Outcomes	Other Outcomes
Karst, 2000[215] 1.5 months Duration of pain: NR *Poor*	A. Acupuncture (n=21) Traditional Chinese acupuncture; maximum of 15 needles, 10 acupoints B. Sham Acupuncture (n=18): blunt placebo needles and elastic foam were used to simulate puncturing and shield needle type. Treatment Protocol: 30-minute sessions twice weekly for 5 weeks (10 sessions total)	A vs. B Age: 50 vs. 47 years Female: 38% vs. 61% Race: NR Headache frequency: 27 vs. 27 days/month VAS (0-10): 6.2 vs. 6.3 Analgesic Intake/Month: 8.3 vs. 10.2	A vs. B <u>1.5 months</u> Frequency of headache attacks/month: 22.1 vs. 22.0; difference 0.1 (95% CI −6.6 to 6.8) Headache Severity, VAS: 4.0 vs. 3.9; difference 0.1 (95% CI −11.9 to 12.1)	A vs. B <u>1.5 months</u> Analgesic Intake/Month: 13.7 vs. 21.2; difference −7.5 (95% CI −22.2 to 7.2)
Tavola, 1992[216] (n=30) 1, 6, 12 months Duration of pain: 8 years *Poor*	A. Acupuncture (n=15): Traditional Chinese acupuncture; 6-10 acupoints chosen on an individual basis; insertion depth 10-20 mm; needles were left in place without the use of any manual or electrical stimulation B. Sham Acupuncture (n=15): same number of needles, inserted more superficially (depth 2-4 mm), in the same region used in real acupuncture group but in areas without acupuncture points Treatment Protocol: 20-minute sessions once per week for 8 weeks (8 sessions total)	A vs. B Age: 33 vs. 33 years Female: 87% vs. 87% Mean frequency of headache attacks per month: 18 vs. 17 Mean analgesic use: 12 vs. 12 units/month Mean HI (intensity X duration X frequency/30): 4.3 vs. 4.5 Mean duration of attacks (sum of the hours of headache in a month/number of attacks): 3.3 vs. 4.4	A vs. B <u>1 month</u> Responders, ≥33% improvement in HI: 86.7% vs. 60.0%; RR 1.44 (95% CI 0.91 to 2.28) Responders, ≥50% improvement in HI: 53.3% vs. 46.7%; RR 1.14 (95% CI 0.56 to 2.35) HI, mean[b]: 2.4 vs. 3.0; MD −0.60 (95% CI −6.12 to 4.92) Mean decrease in HI from baseline: 58.3% vs. 27.8% Mean decrease in headache attack frequency from baseline: 44.3% vs. 21.4% <u>6 months</u> HI, mean[b]: 2.2 vs. 3.1; MD −0.90 (95% CI −7.15 to 5.35), <u>12 months</u> Responders, ≥33% improvement in HI: 53.3% vs. 46.7%; RR 1.14 (95% CI 0.56 to 2.35) Responders, ≥50% improvement in HI: 40.0% vs. 26.7%; RR 1.50 (95% CI 0.53 to 4.26) HI, mean[b]: 3.2 (2.1) vs. 3.7 (2.2); MD −0.50 (95% CI −6.73 to 5.73)	A vs. B <u>1 month</u> Mean decrease in analgesic consumption from baseline: 57.7% vs. 21.7%

CI = confidence interval; HI = headache index; MD = mean difference; NR = not reported; RR = risk ratio; VAS = visual analog scale

[a] Unless otherwise noted, followup time is calculated from the end of the treatment period

[b] Means and standard error of the means (not shown) estimated from graphs.

Acupuncture Compared With Sham

None of the trials reported on function. All three trials reported pain outcomes, although the specific measures varied across the trials. The results were mixed depending on the type of acupuncture used. No significant differences were found between needle acupuncture and sham for any pain outcome evaluated during the short term in two small poor-quality trials,[215,216] or at intermediate and long-term followup in one of these trials[216] (Table 46). In the third small fair-quality trial,[214] laser acupuncture resulted in a significant reduction in the number of headache days per month (median −8, interquartile range [IQR] 21.5), in pain intensity on a 0 to 10 VAS scale (median −2, IQR 6.3), and in the duration of attacks (median −4 hours, IQR 7.5) over the short term compared with the sham group, which reported no improvement from baseline on any outcome at the 3-month followup (P<0.001 for all) (Figure 52).

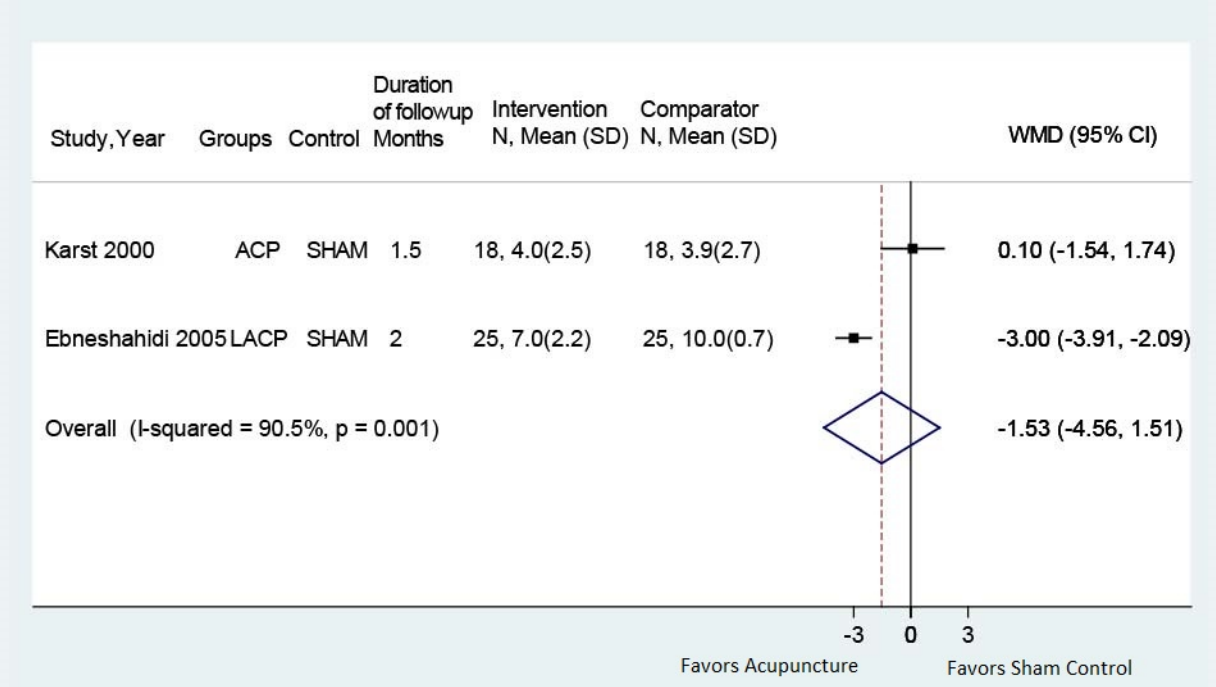
Acupuncture Compared With Pharmacological Therapy or Biofeedback

No trial of acupuncture versus pharmacological therapy and versus biofeedback met inclusion criteria.

Harms

Harms were generally not reported. The trial evaluating laser acupuncture reported that no adverse events occurred in either group.[214]

Figure 52. Acupuncture versus sham for chronic tension headache: effects on pain



ACP = standard needle acupuncture; CI = confidence interval; LACP = laser acupuncture; SD = standard deviation; WMD = weighted mean difference

Key Question 6: Differential Efficacy

RCTs that stratified on patient characteristics of interest, permitting evaluation of factors that might modify the effect of treatment, were considered for inclusion. Factors included age, sex, and presence of comorbidities (e.g., emotional or mood disorders). If a comparison is not listed below there was either no evidence identified that met the inclusion criteria or the included trials did not provide information on differential efficacy or harms. Studies likely had insufficient sample size to evaluate differential efficacy or harms, and evidence was considered insufficient.

Osteoarthritis of the Knee

Key Point

- There is insufficient evidence from one fair-quality trial (across 3 publications) that age, sex, race, BMI, baseline disability, pain, or depression status modify the effects of exercise in patients with OA of the knee. Sample sizes in the subgroup analyses from the FAST trial were likely inadequate to effectively test for modification.

Exercise Compared With Attention Control

One fair-quality trial (n=439) reported across three publications of the Fitness, Arthritis and Seniors Trial (FAST)[44,50,51] included in Key Question 3 compared muscle performance (i.e., resistance training) and aerobic exercise programs to an attention control and formally evaluated factors that may modify treatment in patients with OA of the knee. Details regarding these study populations are available in the Results section for Key Question 3 and in Appendix D. Two of the reports performed formal tests for interaction; none of the demographic or clinical variables evaluated were found to modify the effect of either type of exercise.[50,51] One trial explored whether age, sex, race, BMI, baseline disability, or baseline pain modified the effects of exercise on function based on ADL disability measures in a subgroup of patients who were free of ADL disability upon enrollment; however, no data were provided for evaluation.[50] A second publication looked at whether the effects of exercise on pain, disability, and depression were modified by baseline depression status, that is, high versus low depressive symptomology according to the Center for Epidemiologic Studies Depression scale over time (using an adjusted repeated measures analysis of variance). However, the authors do not provide results that directly examined modification by baseline depression without the time component.[51] The third FAST publication stratified on age, sex, race, and BMI and did not perform a formal statistical test for interaction.[44] Upon visual inspection, the point estimates across groups and strata are similar, suggesting that the effect of exercise on physical disability and knee pain was not modified by any patient characteristic evaluated.

Osteoarthritis of the Hip

Key Point

- There is insufficient evidence from one fair-quality trial that age, sex, baseline pain, and the presence of radiographic OA modify the effects of exercise in patients with OA of the hip. Study authors only reported on effects that include evaluation of these factors over time. Sample size was likely inadequate to effectively test for modification.

Exercise Compared With Usual Care

One fair-quality trial (n=203) included for Key Question 3 compared combination exercise therapy (strengthening, stretching, and endurance exercises) to usual care and stratified on age, sex, race, and BMI, but it did not formally test for interaction.[63] Details regarding this study population are available in the Results section for Key Question 3 and in Appendix D. Age, sex, education, self-reported knee OA, and baseline pain and Kellgren & Lawrence radiographic OA scores were defined *a priori* as subgroups of interest. Although older patients (age ≥65 years), women, patients with a lower NRS pain score at baseline, and patients with radiographic OA showed somewhat larger effects of exercise therapy on function and pain, data were not systematically reported and, based on the data provided, overlapping confidence intervals suggest that the effect of exercise was not modified by any of these variables.

Fibromyalgia

Key Point

- There was insufficient evidence from one poor-quality trial that baseline BMI (normal, overweight, obese) modifies the effects of multidisciplinary rehabilitation in patients with fibromyalgia. Study authors only report on effects that include evaluation of these factors over time. Sample size was likely inadequate to effectively test for modification.

Multidisciplinary Rehabilitation Compared With Usual Care

An additional publication (n=130)[227] of a poor-quality trial[226] included for Key Question 4 that compared multidisciplinary rehabilitation to usual care assessed potential modification of treatment based on baseline BMI (normal, overweight, obese). No significant interactions were found for the effect of BMI on exercise over time for any pain or function measure evaluated; however, the authors do not provide results that exclude effects of time. Details regarding this study population are available in the section on efficacy and in Appendix D.

Discussion

Key Findings and Strength of Evidence

The key findings of this review, including strength of evidence ratings, are summarized for each chronic pain condition in Tables 47-61 (interventions and comparators with no evidence for either function or pain outcomes are not shown); domains used to determine the overall strength of evidence are shown in Appendix G. All outcomes were considered direct. The strength of evidence was low or insufficient for many interventions and was limited by small numbers of trials for specific comparisons and for our specified time frames, particularly for long term. We focused on evaluating the persistence of effects for therapies beyond the course of treatment, using the following definitions for postintervention followup: short term (1 to <6 months), intermediate term (≥6 to <12 months) and long term (≥12 months). Evidence was particularly limited on effects on long-term outcomes.

The majority of trials compared interventions with usual care with very few trials employing pharmacological treatments or exercise as comparators. In general, effect sizes for most interventions were small, based on mean differences. There tended to be more evidence for the effects of interventions on pain than for function, and the effects on function were generally smaller or not clearly present.

No trials directly compared interventions with opioids and few trials reported effects of intervention on opioid use. Our previous reviews found opioids associated with small to moderate effects on pain during treatment (effects would not be expected to persist) with evidence almost exclusively from short-term (≤3 month) trials.[11,16,25,247] Information on adherence to interventions was not well-reported; poor adherence may have impacted some of our findings. Harms were poorly reported across interventions. No serious intervention-related adverse events requiring medical attention were identified; reported adverse events were generally minor (e.g., muscle soreness or increased pain with exercise, bruising with acupuncture) and time-limited (e.g., temporary worsening of pain).

Table 47. Chronic low back pain: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Exercise	slight +	none +	none +	slight ++	moderate +	moderate +
Psychological Therapies: CBT primarily	slight ++	slight ++	slight ++	slight ++	slight ++	slight ++
Physical Modalities: Short-Wave Diathermy	insufficient evidence	no evidence	no evidence	insufficient evidence	no evidence	no evidence
Physical Modalities: Ultrasound	insufficient evidence	no evidence	no evidence	none +	no evidence	no evidence
Physical Modalities: Low-Level Laser Therapy	slight +	none +	no evidence	moderate +	none +	no evidence
Manual Therapies: Spinal Manipulation	slight +	slight +	no evidence	none +	slight ++	no evidence
Manual Therapies: Massage	slight ++	none +	no evidence	slight ++	none +	no evidence
Manual Therapies: Traction	none +	no evidence	no evidence	none +	no evidence	no evidence
Mindfulness Practices: MBSR	none +	none +	none +	slight ++	slight +	none +
Mind-Body Practices: Yoga	slight ++	slight +	no evidence	moderate +	moderate ++	no evidence
Acupuncture	slight +	none +	none +	slight ++	none +	slight +
Multidisciplinary Rehabilitation	slight +	slight +	none +	slight ++	slight ++	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; MBSR = mindfulness-based stress reduction; none = no effect/no statistically significant effect; SOE = strength of evidence.

Table 48. Chronic low back pain: effects of nonpharmacological interventions compared with exercise

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Psychological Therapies: Operant therapy	no evidence	insufficient evidence	insufficient evidence	no evidence	insufficient evidence	insufficient evidence
Physical Modalities: Low-Level Laser Therapy	no evidence	none +	no evidence	no evidence	slight +	no evidence
Manual Therapies: Spinal Manipulation	none +	none +	no evidence	none +	slight +	no evidence
Manual Therapies: Massage	no evidence	none +	no evidence	no evidence	none +	no evidence
Mind-Body Practices: Yoga	none +	none +	no evidence	slight +	none +	no evidence
Mind-Body Practices: Qigong	none +	slight favoring exercise +	no evidence	slight favoring exercise +	none +	no evidence
Multidisciplinary Rehabilitation	slight ++	slight ++	none +	slight ++	slight ++	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; SOE = strength of evidence.

Table 49. Chronic neck pain: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Exercise	none +	no evidence	no evidence	none +	no evidence	no evidence
Psychological Therapies: PT-lead relaxation training	none +	none +	no evidence	none +	none +	no evidence
Physical Modalities: Low-Level Laser Therapy	moderate ++	no evidence	no evidence	moderate ++	no evidence	no evidence
Physical Modalities: Traction, Electromagnetic field	insufficient evidence	no evidence	no evidence	insufficient evidence	no evidence	no evidence
Manual Therapies: Massage	none +	none +	no evidence	no evidence	no evidence	no evidence

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Mind-Body Practices: Alexander Technique	slight +	slight +	no evidence	no evidence	no evidence	no evidence
Acupuncture	slight +	slight +	none +	none +	none +	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; PT = physical therapist; SOE = strength of evidence.

Table 50. Chronic neck pain: effects of nonpharmacological interventions compared with pharmacological treatments

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Exercise	insufficient evidence	insufficient evidence	no evidence	insufficient evidence	insufficient evidence	no evidence
Acupuncture	insufficient evidence	no evidence	no evidence	insufficient evidence	no evidence	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; SOE = strength of evidence.

Table 51. Chronic neck pain: effects of nonpharmacological interventions compared with exercise

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Psychological Therapies: PT-lead relaxation training	none +	none +	no evidence	none +	none +	no evidence
Manual Therapies: Massage	no evidence	no evidence	no evidence	no evidence	none +	no evidence
Mind-Body Practices: Body Awareness Therapy	none +	no evidence	no evidence	no evidence	no evidence	no evidence
Mind-Body Practices: Qigong	no evidence	insufficient evidence	insufficient evidence	no evidence	insufficient evidence	insufficient evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; PT = physical therapist; SOE = strength of evidence.

Table 52. Osteoarthritis of the knee: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Exercise	slight ++	slight +	slight +	slight ++	moderate +	none +
Psychological Therapies: Pain coping, CBT	none +	none +	none +	none +	none +	none +
Physical Modalities: Microwave Diathermy	insufficient evidence	no evidence	no evidence	insufficient evidence	no evidence	no evidence
Physical Modalities: Pulsed Short-Wave Diathermy	insufficient evidence	no evidence	insufficient evidence	insufficient evidence	no evidence	insufficient evidence
Physical Modalities: Ultrasound	slight +	none +	no evidence	slight +	none +	no evidence
Physical Modalities: TENS	no evidence	none +	no evidence	no evidence	none +	no evidence
Physical Modalities: Low-Level Laser Therapy	insufficient evidence	insufficient evidence	no evidence	insufficient evidence	insufficient evidence	no evidence
Physical Modalities: Electromagnetic Field	none +	no evidence	no evidence	none +	no evidence	no evidence
Physical Modalities: Superficial Heat	no evidence	no evidence	no evidence	insufficient evidence	no evidence	no evidence
Physical Modalities: Braces	no evidence	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence	no evidence
Manual Therapies: Joint Manipulation	no evidence	insufficient evidence	no evidence	no evidence	no evidence	no evidence
Manual Therapies: Massage	no evidence	insufficient evidence	no evidence	no evidence	insufficient evidence	no evidence
Mind-Body Practices: Tai Chi	insufficient evidence	insufficient evidence	no evidence	insufficient evidence	insufficient evidence	no evidence
Acupuncture	none +	none ++	no evidence	none +	none ++	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; none = no effect/no statistically significant effect; TENS = transcutaneous electrical nerve stimulation; SOE = strength of evidence

Table 53. Osteoarthritis of the knee: effects of nonpharmacological interventions compared with exercise

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Psychological Therapies: Pain coping	none +	none +	no evidence	none +	none +	no evidence
Manual Therapies: Joint Manipulation	no evidence	insufficient evidence	no evidence	no evidence	no evidence	no evidence
Acupuncture	insufficient evidence	no evidence	no evidence	no evidence	no evidence	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; SOE = strength of evidence

Table 54. Osteoarthritis of the hip: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Exercise	slight +	slight +	insufficient evidence	slight +	none +	insufficient evidence
Manual Therapies	no evidence	insufficient evidence	no evidence	no evidence	no evidence	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; SOE = strength of evidence

Table 55. Osteoarthritis of the hip: effects of nonpharmacological interventions compared with exercise

Intervention	**Function** *Short-Term* Effect Size SOE	**Function** *Intermediate-Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Manual Therapies	slight +	slight +	no evidence	slight +	insufficient evidence	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
SOE = strength of evidence

Table 56. Osteoarthritis of the hand: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Exercise	insufficient evidence	no evidence	no evidence	no evidence	no evidence	no evidence
Physical Modalities: Low-Level Laser Therapy	none +	no evidence	no evidence	none +	no evidence	no evidence
Physical Modalities: Heat Therapy	insufficient evidence	no evidence	no evidence	no evidence	no evidence	no evidence
Multidisciplinary Rehabilitation	none +	no evidence	no evidence	none +	no evidence	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
none = no effect/no statistically significant effect; SOE = strength of evidence

Table 57. Fibromyalgia: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Exercise	slight +	slight ++	none +	slight ++	none ++	none ++
Psychological Therapies: CBT	slight +	slight +	insufficient evidence	slight +	none +	insufficient evidence
Psychological Therapies: Biofeedback, Imagery	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence
Physical Modalities: Magnetic Pads	insufficient evidence	none +	no evidence	insufficient evidence	none +	no evidence
Manual Therapies: Massage (Myofascial Release)	no evidence	slight +	none +	insufficient evidence	insufficient evidence	slight +
Mindfulness Practices: MBSR	none ++	no evidence	no evidence	none ++	no evidence	no evidence
Mind-Body Practices: Qigong, Tai Chi	slight +	no evidence	no evidence	moderate +	no evidence	no evidence

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Acupuncture	slight ++	slight ++	no evidence	none +	none +	no evidence
Multidisciplinary Rehabilitation	slight +	slight +	slight +	none +	slight +	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; MBSR = mindfulness-based stress reduction; none = no effect/no statistically significant effect; SOE = strength of evidence

Table 58. Fibromyalgia: effects of psychological therapies compared with pharmacological treatments

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Exercise vs. paroxetine	no evidence	no evidence	no evidence	no evidence	insufficient evidence	no evidence
CBT vs. plus amitriptyline	insufficient evidence	no evidence	no evidence	insufficient evidence	no evidence	no evidence
Biofeedback vs. escitalopram	insufficient evidence	no evidence	no evidence	insufficient evidence	no evidence	no evidence
CBT vs. pregabalin; duloxetine	no evidence	slight +	no evidence	no evidence	none +	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; none = no effect/no statistically significant effect; SOE = strength of evidence

Table 59. Fibromyalgia: effects of nonpharmacological interventions compared with exercise

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Psychological Therapy: CBT, biofeedback, relaxation	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence
Multidisciplinary Rehabilitation	no evidence	no evidence	none +	no evidence	no evidence	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; none = no effect/no statistically significant effect; SOE = strength of evidence

Table 60. Chronic tension headache: effects of nonpharmacological interventions compared with usual care, placebo, sham, attention control, or waitlist

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Psychological Therapies: CBT plus Relaxation	insufficient evidence	insufficient evidence	no evidence	insufficient evidence	insufficient evidence	no evidence
Psychological Therapies: Relaxation only	no evidence	no evidence	no evidence	insufficient evidence	no evidence	no evidence
Physical Modalities: OTES	insufficient evidence	no evidence	no evidence	insufficient evidence	no evidence	no evidence
Manual Therapies: Spinal manipulation	slight +	no evidence	no evidence	moderate +	no evidence	no evidence
Acupuncture	no evidence	no evidence	no evidence	slight + (laser) insufficient evidence (needle)	insufficient evidence (needle)	insufficient evidence (needle)

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; OTES = occipital transcutaneous electrical stimulation; SOE = strength of evidence

Table 61. Chronic tension headache: effects of nonpharmacological interventions compared with pharmacological treatments

Intervention	Function *Short-Term* Effect Size SOE	Function *Intermediate-Term* Effect Size SOE	Function *Long-Term* Effect Size SOE	Pain *Short-Term* Effect Size SOE	Pain *Intermediate-Term* Effect Size SOE	Pain *Long-Term* Effect Size SOE
Psychological Therapies: CBT	insufficient evidence	insufficient evidence	no evidence	insufficient evidence	insufficient evidence	no evidence
Manual Therapies: Manipulation	no evidence	no evidence	no evidence	insufficient evidence	no evidence	no evidence

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
CBT = cognitive-behavioral therapy; SOE = strength of evidence

Low Back Pain. For chronic low back pain, compared with usual care, attention control, sham, or placebo, there was moderate evidence of slight improvement in function, at least in the short term, for massage, yoga, psychological therapies (cognitive-behavioral therapy [CBT]) (strength of evidence [SOE]: moderate) and low evidence for exercise, acupuncture, low-level laser therapy, spinal manipulation, multidisciplinary rehabilitation (SOE: low). With the exception of spinal manipulation, these interventions also showed slight improvement (exercise, acupuncture, massage, psychological therapies, multidisciplinary rehabilitation, SOE: low) or moderate

improvements (yoga, low-level laser therapy, SOE: low) in pain short term. The slight improvements in function compared with controls were sustained into the intermediate term for yoga, spinal manipulation, psychological therapies, and multidisciplinary rehabilitation, with low strength of evidence for all but the psychological therapies, for which SOE was moderate. No clear improvement in function was seen at intermediate term for exercise, acupuncture, massage or low-level laser therapy (SOE: low for all). Improvements in pain were seen in the intermediate term for exercise (slight effect SOE moderate) and yoga (moderate effect, SOE low) and mindfulness-based stress reduction (MBSR) (slight effect, SOE: low) as well as spinal manipulation, psychological therapies and multidisciplinary rehabilitation (slight effects, SOE: moderate). Long-term evidence was available for four intervention categories: psychological therapies, multidisciplinary rehabilitation, exercise, and acupuncture. The strongest evidence was for psychological therapies (CBT primarily), which were associated with slightly greater effects than usual care or attention control on both function and pain at short, intermediate, and long term (SOE: moderate for all time frames). Neither exercise nor acupuncture was associated with improved function long term, even though both demonstrated continued pain improvement (SOE: low for all). For multidisciplinary rehabilitation, effects on function from earlier time frames were not sustained in the long term versus usual care (SOE: low). High intensity multidisciplinary rehabilitation (≥20 hours/week or >80 hours total) was not clearly better than nonhigh intensity programs. Short-term effects on function and pain were somewhat larger with high intensity multidisciplinary rehabilitation than with nonhigh intensity interventions but the tests for interaction were not statistically significant. At intermediate term, estimates were similar for high intensity and nonhigh intensity programs.

In people with chronic low back pain, there were no clear differences in short-term function for comparisons of qigong, yoga, or spinal manipulation with exercise even though small improvements in pain were seen for yoga (SOE: low for all). Multidisciplinary rehabilitation was associated with small effects on function short term as well as pain (SOE: moderate). For Qigong, results for intermediate-term function and short-term pain slightly favored exercise (SOE: low for all). Again, multidisciplinary rehabilitation was associated with slight improvements in function and pain at intermediate term (SOE: moderate), but this was not sustained in the long term (SOE: low). Long-term data were only available for multidisciplinary rehabilitation.

Neck Pain. For chronic neck pain, in the short term, moderate effects on function and pain were seen for low-level laser therapy (SOE: moderate). In the short term and intermediate term, acupuncture and Alexander Technique were associated with slightly greater effect on function compared with usual care (both interventions), sham acupuncture or sham laser (SOE: low). The effect of acupuncture was not sustained long term (SOE: low) compared with sham acupuncture, sham laser, or usual care, and no improvement in pain was seen at any time frame (SOE: low). There were no clear improvements in function or pain across types of exercise (short term) or for psychological therapies or massage compared with usual care, sham procedures, or attention controls (SOE: low for all).

Knee Osteoarthritis. For knee osteoarthritis (OA), exercise, microwave diathermy and ultrasound were associated with functional improvement in the short term compared with usual care, attention control, or sham procedure; the effect size was small for exercise and ultrasound, and larger for diathermy (SOE: moderate for exercise, low for ultrasound, diathermy). While the

small effects of exercise on function persisted into the intermediate and long term (SOE: low for both), there were no clear benefits to ultrasound at intermediate term (SOE: low). Similarly, small short-term effects of ultrasound on pain did not persist to intermediate term (SOE: low) in contrast to moderate improvement in pain for exercise (SOE: low). Long term, the small improvement in function seen with exercise was sustained, but there was no clear effect on pain (SOE: low). There were no clear differences in function or pain associated with electromagnetic fields (short-term SOE: low), with psychological therapies for any time frame (SOE: low), or with acupuncture at short (SOE: moderate) or intermediate term (SOE: low) versus usual care, attention control, or sham procedure. There was no difference in function or pain between pain coping skills training and exercise at short term or intermediate term in one trial (SOE: low).

Hip and Hand Osteoarthritis. Evidence was sparse on interventions for hip and hand OA. Exercise was associated with slightly greater function than usual care at short and intermediate-term (SOE: low), but data were in sufficient to determine long-term effects. For pain, a small effect was seen only at short term; no differences were seen at the other time points (SOE: low for short term and intermediate term, insufficient for long term). Compared with exercise, a small effect on function was seen with manual therapy in the short and intermediate term, and small improvement in pain short term (SOE: low for all). For hand OA, no clear differences were seen for low-level laser therapy versus sham or for multidisciplinary rehabilitation versus waitlist control at short term for either function or pain (SOE: low).

Fibromyalgia. Short term, in patients with fibromyalgia, there was low-quality evidence that slight improvements on function were associated with exercise, CBT, and mind-body practices of tai chi and qigong (SOE: low for all) compared with wait list and attention control, and moderate-quality evidence for slight functional improvement acupuncture compared with sham acupuncture (SOE: moderate). Improvements in short-term pain were seen with exercise (SOE: moderate) and mind body practices (SOE: low), but not with acupuncture. No clear differences in function or pain outcomes were seen for MBSR (SOE: moderate) or multidisciplinary rehabilitation (SOE: low). Slightly greater effects on function continued into the intermediate term for acupuncture and CBT and massage (SOE: low), and were seen for myofascial release massage and multidisciplinary rehabilitation; there was no clear effect of magnetic mattress pads versus sham pad (SOE: low for all). Slight improvement in pain intermediate-term were seen for massage and multidisciplinary rehabilitation (SOE: low), but not for exercise (SOE: moderate), acupuncture, or magnetic mattress pads (SOE: low). Long term, small improvements in function continued for multidisciplinary rehabilitation but not for exercise or massage (SOE: low for all), and there was no clear impact on pain for exercise (SOE: moderate) or multidisciplinary rehabilitation (SOE: low). No clear differences were seen between multidisciplinary rehabilitation and exercise for the long term on function or pain (SOE: low). CBT was associated with a small benefit for function but not for pain compared with pregabalin at intermediate term (SOE: low).

Chronic Tension Headache. Only nine trials of nonpharmacological treatments for chronic tension headache met the inclusion criteria and all but one was considered poor quality, resulting in a rating of insufficient evidence for comparisons of psychological therapies with waitlist or attention control, electrical stimulation versus sham, and acupuncture versus sham. One fair-quality trial of laser acupuncture versus sham suggested moderate improvement in pain short

term (SOE: low), and another fair-quality trial of spinal manipulation versus usual care suggested a small effect on short-term function based on the Headache Impact Test (SOE: low). Approximately 25 percent of the patients in the trial had comorbid migraine headache.

Usual Care/Waitlist and Nonactive Comparators. For comparisons involving usual care/waitlist or nonactive comparators (placebo, sham, attention control), there were some differences depending on the specific comparator evaluated. For some interventions results different by control type. For example, in some analyses, acupuncture was associated with greater effects on pain in patients with chronic low back pain or OA when compared with usual care than when compared with sham acupuncture, suggesting that much of the benefit may be due to placebo or other nonspecific effect.

Harms. Harms were poorly reported across interventions. No serious intervention-related adverse events requiring medical attention were identified; reported adverse events were generally minor (e.g., muscle soreness with exercise, bruising with acupuncture) and time-limited (e.g., temporary worsening of pain).

Medication Use. Few trials compared opioid use pre- and post-intervention, and medication use in general was not well reported across trials.

Subgroups. One fair-quality trial in people with knee OA formally examined factors that might modify the effect of exercise on disability; the effect of exercise on activities of daily living disability did not appear to be modified by age, sex, baseline disability, knee pain score, body mass index, or race.[50] The few trials that reported subgroup analyses either did not provide sufficient data to assess modification by demographic or other factors or did not formally test for modification; trials were generally too small to effectively evaluate outcomes in subgroups.

Findings in Relationship to What Is Already Known

Many reviews have addressed the effects of interventions for chronic pain management during or immediately following treatments. We focused on evaluating the sustainability of effects for at least 1 month postintervention.

This review updates our previous review on low back pain[25] by incorporating new evidence on nonpharmacological treatments for chronic low back pain. Consistent with the prior review, we found exercise, yoga, various psychological therapies, acupuncture, spinal manipulation, and low-level laser therapy with small to moderate effects on function and/or pain. It differs from the prior review in focusing on durability of treatment effects 1 month or longer after completion of a course of treatment and basing estimates on meta-analyses when poolable data were available, and conducting stratified and sensitivity analyses to evaluate sources of heterogeneity and robustness of findings. For example, subanalyses of specific interventions within a given category of intervention (e.g., aerobic exercise within the general category of exercise suggests that despite the inherent heterogeneity within some of the categories, effect estimates results for specific interventions may be similar). Although we found some evidence that beneficial effects of some nonpharmacological therapies persist for up to 12 months following the end of a course of a treatment, data on longer-term (>1 year) outcomes were very sparse.

A recent Institute for Clinical and Economic Review (ICER) review[248] on chronic low back pain and neck pain used relevant portions of our previous review for chronic low back pain and

updated it with new publications so the findings are generally consistent with our review for this condition. For chronic neck pain, this report and the ICER report both suggest a small benefit for acupuncture. The ICER report focuses on evaluating comparative value for interventions and suggests that cognitive and mind-body therapies for treatment of chronic low back pain and chronic neck pain would be cost-effective, would meet value-based price benchmarks, and may result in only a small increase ($0.75) per member per month for a hypothetical payer plan covering 1 million members, compared with approximately $4.46 per member per month for pain medication.

Our findings indicate that a number of nonpharmacological treatments improve pain and/or function for specific chronic pain conditions included in this review. This is consistent with other reviews, including recent reviews on exercise[249] acupuncture,[250] and complementary health approaches[251] for chronic pain management across various conditions, an Agency for Healthcare Research and Quality (AHRQ) report on knee OA treatment,[252] and a review of chronic pain treatment guidelines on the use of manual and physical therapies.[253]

The protocol for a systematic review and network meta-analysis of interventions for fibromyalgia was identified;[254] no publication timeline for this review is currently available.

Applicability

The applicability of our findings may be impacted by a number of factors. Included trials provided limited information on symptom duration, clinical characteristics, comorbid conditions, and concomitant treatments, thus it is not clear to what extent these trials reflect the populations seen in clinical practice or how these impact our results. In addition, with the exception of fibromyalgia, information regarding diagnostic criteria for the pain condition of interest was limited. Information on the presence of overlapping chronic pain conditions or psychosocial factors was generally not provided in included trials, and the extent to which these characteristics were present in trial populations and their impact on our results is not clear. Across conditions, a majority of trial participants were female. The age of included populations generally reflected the ages impacted by the conditions. Evidence to how effectiveness varies by ages was limited. There was also heterogeneity in populations enrolled in the trials with regard to duration of chronic pain, severity of pain (most trials enrolled patients with at least moderate pain at baseline), as well as other factors (e.g., use of medications, medical and psychological comorbidities). Our findings are generally most applicable to people without such comorbidities who have moderate or severe intensity pain that has persisted for more than 12 months. The heterogeneity in populations across included trials likely is consistent with the heterogeneity seen in clinical practice, so our findings may be applicable to most primary care clinical settings.

Variability in interventions, comparators and cointerventions may impact our findings. For interventions, there was variability in the numbers of sessions, length of sessions, duration of treatment, methods of delivering the intervention and the experience and training of those providing the intervention. To address heterogeneity within intervention categories we abstracted details of techniques or methods used, (e.g. specific type of psychological intervention or Yoga) and attempted to stratify by them, however in most cases, data were insufficient to do so. In general, there were no clear differences in effects based on intervention factors or comparators; however analyses were limited by small numbers of trials. In clinical practice, most chronic pain patients likely use a combination of therapies and may continue to receive some types of therapies if benefit is perceived. It is unclear to what extent our findings represent the conditions

under which the various interventions are currently delivered. Evidence to identify optimal techniques and delivery of interventions is needed.

To facilitate interpretation of results across trials and interventions, we categorized the magnitude of effects for function and pain outcomes using the system described in our previous review.[25] Using this system, beneficial effects identified were generally in the small or moderate range. We recognize that effects that we classified as small (e.g., 5 to 10 points on a 0 to 100 scale for pain or function) may be below some proposed thresholds for minimum clinically important differences for some measures. However, our classification provides some consistent and objective benchmarks to assess magnitude of smaller effects across trials and interventions. Interpretation of clinically important differences in mean change for continuous variables is challenging. If data were provided we also evaluated the proportion of patients who experienced a clinically important improvement in pain or function. This provides valuable insight regarding clinically important improvement. For example, one trial[89] of MBSR versus usual care in low back pain reported a small improvement in function on a modified Roland Morris Disability questionnaire (1.87, 95% CI −3.14 to −0.60 on 0-23 scale); however, absolute difference between MBSR and usual care on the percentage of participants (20%) achieving a minimally clinically meaningful (≥30%) improvement from baseline (68.8% to 48.6%, risk ratio 1.56, 95% CI 1.14 to 2.14) suggests that the benefits may be more substantial.

Limitations of the Evidence Base

Evidence was sparse for most interventions. Data on long-term outcomes was particularly limited. There were also limited data on outcomes other than pain and function and on harms. Few trials directly compared an included intervention versus pharmacological therapy or the specified active comparator (exercise or biofeedback). Only 5 percent of included trials across conditions were considered to be of good quality; the majority were considered fair (59%). No trial of treatment for chronic tension headache was considered to be of good quality. For some interventions, it is possible to effectively blind participants and providers (e.g. CBT, multidisciplinary rehabilitations, exercise); thus, observed effects may be due in part to placebo, attention, or other nonspecific effects and results may have been susceptible to performance and other biases. Many included trials were small (< 70 participants) and only few or single trials were available for some interventions (e.g., some physical modalities). The combination of these factors led to a determination that evidence was insufficient. There was no or little includable evidence for a number of interventions, including electromuscular simulation, traction, superficial heat or cold, bracing, use of magnets, interferential therapy, transcutaneous electrical nerve stimulation, and manual therapies (other than for low back pain). For most conditions, evidence was also sparse for mindfulness and mind-body practices. Evidence on interventions for hip and hand OA and chronic tension headache was very limited.

Heterogeneity in clinical diagnosis and presentation was present for most of the conditions, with the exception of fibromyalgia. It is likely that included patients may have additional conditions and/or psychological comorbidities that were not described in the trials. Details provided by trials were insufficient to conduct meaningful subanalyses.

Some of the limitations described for the review process reflect limitations of the evidence base, including those related to heterogeneity within and across interventions and heterogeneity within a given condition. Details of concurrent interventions and components of usual care were generally not reported or poorly reported. Additionally, it is assumed that most patients with chronic pain likely continued medications and other therapies or practices during the trials. These

factors may have resulted in substantial mixing of effects of the intervention and cointerventions. These factors possibly attenuated observed effects.

Data on potential harms is sparse, although serious harms are not generally expected with the interventions included in this review. Serious treatment-related adverse events were not reported in any of the trials.

Implications for Clinical and Policy Decisionmaking

Our review provides some evidence that an array of nonpharmacological treatments provide small to moderate benefits function and pain that are durable for more than 1 month for the five common chronic pain conditions addressed in this review. Musculoskeletal pain, particularly of back and joint pain, is the most common single type of chronic pain. Age-adjusted rates of adults reporting pain in the last three months were highest for low back pain (28%), neck pain (15%), knee pain (19.5%) and severe headache or migraine (16%).[3,14]

The evidence synthesized in this review may help inform guidelines and health care policy (including reimbursement policy) related to use of noninvasive nonpharmacological treatments, and inform policy decisions regarding funding priorities for future research.

Recent guidelines[13] from the Centers for Disease Control and Prevention (CDC) in the United States and the Canadian Guideline for Opioid Use in Chronic Non-Cancer Pain[253] recommend nonopioid treatment as the preferred treatment for chronic pain. Further, guidelines from the American College of Physicians recommend nonpharmacological therapies over medications for chronic back pain.[16] Our findings support the feasibility of implementing these guideline recommendations by showing that there are some nonpharmacological treatments for chronic pain that have evidence of sustained effectiveness after the completion of therapy. Importantly, some interventions, such as exercise, CBT, multidisciplinary rehabilitation, mind-body interventions, and some complementary and integrative medicine therapies, such as acupuncture and spinal manipulation, also were associated with some sustained effects on function, although evidence beyond 12 months is sparse. There was no evidence suggesting serious harms from these interventions, although harms data were limited.

Our report reviewed evidence that may also help inform decisions regarding prioritization of nonpharmacological therapies by clinicians selecting therapy. Consistent with a biopsychosocial understanding of chronic pain,[3,7] evidence was somewhat more robust for “active” interventions that engage patients in movement and address psychological contributors to pain, particularly at longer-term followup, versus more “passive” treatments focused on symptom relief such as massage. Active interventions include exercise, multidisciplinary rehabilitation, psychological therapies (particularly CBT), and mind-body interventions. This provides some support for clinical strategies that focus on “active” interventions as primary therapies, with “passive” interventions used in a more adjunctive or supplementary role. Research is needed to compare “active” vs. “passive” strategies.

Our review also has policy implications related to access to treatment and reimbursement. Given heterogeneity in chronic pain, variability in patient preferences for treatments,[3,7] and differential responses to specific therapies in patients with a given chronic pain condition, policies that broaden access to a wider array of effective nonpharmacological treatments may have greater impact than those that focus on one or a few therapies. Several considerations could inform policy decisions regarding access to and coverage of nonpharmacological therapies. Policymakers could prioritize access to interventions with evidence of persistent effectiveness across different pain conditions, such as exercise, multidisciplinary rehabilitation, mind-body

interventions, and acupuncture. Because the level of supporting evidence varies from condition to condition, policymakers may need to consider the degree to which evidence may be reasonably extrapolated across conditions (e.g., effectiveness of psychological therapies for chronic low back pain may not necessarily be extrapolated to OA). Although the Affordable Care Act has improved access to complementary and integrative therapies, variability in reimbursement and authorization procedures remain a potential barrier. Although evidence supports the use of multidisciplinary rehabilitation over exercise therapy or usual care, primarily for low back pain, cost and availability remain important barriers particularly in rural areas. Our report suggests that less-intensive multidisciplinary rehabilitation may be similarly effective to high-intensity multidisciplinary rehabilitation, which could inform decisions about more efficient methods for delivering this intervention. Not all patients may require multidisciplinary rehabilitation.[255] Policy efforts that focus on use of multidisciplinary rehabilitation in individuals more likely to benefit (e.g., severe functional deficits, failure to improve on standard nonmultidisciplinary therapies, significant psychosocial contributors to pain) could also inform efforts to deliver this modality efficiently.

Limitations of the Systematic Review Process

There were limitations in the systematic review process. Our analysis was restricted to trials that reported outcomes after at least 1 month following the end of therapy (except when therapy lasted at least 6 months; in these cases, we included assessments made immediately post-treatment). We did not include trials of patients with chronic pain conditions other than those specified in the methods and excluded trials of patients with diffuse or mixed pain conditions. Some noninvasive nonpharamcological interventions (e.g., self-management education) were excluded, and we did not address invasive therapies. Trials that evaluated active comparators other than biofeedback (for headache) or exercise (all other conditions) or interventions as adjunctive treatment were excluded. Some meta-analyses were based on two or three trials; findings based on such meta-analyses must be interpreted with caution.

The interventions were grouped *a priori* to provide an organizational framework for the report. There is some overlap between categories and there a many other methods of grouping interventions. We performed separate or stratified analyses to the extent possible to evaluate specific techniques/methods within broader categories (e.g., we looked at different types of psychological therapies and mind-body practices). We also performed stratified analyses by comparator type where data were available. Sparse literature for many of the interventions precluded extensive examination specific types of intervention within a given category.

We excluded non-English-language articles; however, we did not identify large numbers of non-English-language articles in our review of bibliographies. We searched ClinicalTrials.gov and identified some potentially relevant studies, but none had results available. We did not search conference proceedings or other sources. We were unable to assess for publication bias using graphical or statistical methods to evaluate any potential impact of small samples, methodological limitations in trials, or heterogeneity in interventions, populations or outcomes. Based on hand searches of reference lists, searches of ClinicalTrials.gov, and suggestions from technical experts, we did not find evidence indicating the presence of unpublished literature sufficient to impact conclusions.

Research Recommendations

The gaps in the available evidence are many across the common conditions we included (Table 62). Four primary issues relate to (1) the need to understand the longer-term sustainability of intervention effects; (2) the need for standardization of interventions for future trials; (3) the standardization of research protocols for collection of and reporting of outcomes including harms; (4) the need for comparisons of interventions with pharmacological interventions. For many of these areas, future research would benefit from considering recommendations from organizations such as the Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials (IMMPACT)[256-261] and the Analgesic, Anesthetic, and Addiction Clinical Trials Translations, Innovations, Opportunities, and Networks (ACTTION)[262,263] and the research priorities outlined in the recent Federal Pain Research Strategy.[264]

To understand the sustainability of effects, methodologically rigorous traditional (explanatory) trials with longer followup are needed to better understand whether benefits are sustained over time under ideal conditions. In addition, well-designed pragmatic trial designs with long-term followup could facilitate understanding of how interventions are delivered and continued in real-world settings as well as effect sustainability. Methods for enhancing recruitment, adherence and retention need to be incorporated for all trials. Education of researchers examining nonpharmacological approaches to pain management on clinical trial design, execution, and analysis may also assist with improving the quality of the evidence base for many of the interventions.

Research to identify optimal techniques and their delivery would help define more standardized interventions to evaluate in future trials is needed. In addition, there is a need to understand what combinations of interventions may be most logical for a given condition and standardization of methods to study adjunct therapies. Pragmatic trials may help provide insight into these questions.

Standardization of research protocols for reporting and outcomes measures and use of a standard set of measures would facilitate comparison of results across trials. Outcome measures such as the Visual Analog Scale or Numeric Rating Scale may not fully capture the impact of pain or allow for accurate classification or evaluation of changes in chronic pain. Inclusion of recommendations for pain assessment[265] assessment that incorporate understanding of pathophysiological mechanisms and address multiple domains of pain, including temporal dimensions, sensory and affective qualities of pain and the location and bodily distribution of pain in trial planning and execution may facilitate more accurate classification and longitudinal tracking of response to interventions. Reporting the proportions of patients achieving a clinically meaningful improvement in pain, function, or quality of life as measures of "success" may provide additional clinical information to complement data on average changes in continuous measures of pain, function, and quality of life for which there is difficulty describing clinically important effects. Routine collection of common or known harms associated with interventions is needed in future trials.

There is heterogeneity with regard to research design, execution, and outcomes reporting in trials of interventions included in this review compared with well-funded trials of devices or pharmacological agents. Lack of funding to design methodologically sound studies with reasonable sample size of nonpharmacological interventions may have contributed to the general low quality of evidence.

Table 62. Summary of evidence gaps and research recommendations

Research Component	Evidence Gap	Future research recommendation
Study Design Methods and Reporting	Sparse evidence on the sustainability of effects; Limited information on adherence and need to maximize retention.	Traditional (explanatory) and pragmatic trials with long-term followup and use of methods to enhance recruitment, retention and adherence. Documentation of adherence. Consider recommendations from IMMPACT, ACTTION and Federal Pain Research Strategy.
Patient populations	Information on overlapping chronic pain conditions or psychosocial factors was generally not provided in included trials.	Documentation of coexisting conditions and factors in trials with sufficient sample-size to evaluate the differential impact of conditions and factors.
Interventions and comparators	Lack of information on optimal techniques, duration and frequency of treatment; Lack of evidence comparing interventions to pharmacological agents.	Research leading to standardization of techniques and their delivery to be used in future trials and understanding best combinations of interventions. Pragmatic trials may provide valuable information. Trails comparing interventions with pharmacological treatments.
Outcomes measures	Lack of consistency in types outcomes measures used for function and pain across trials makes it challenging to compare results across trials. Commonly used VAS or NRS for pain do not capture the impact of pain or allow for accurate classification or evaluation of changes in chronic pain. Common or know harms are not routinely collected.	Standardized protocols for types of outcomes to be assessed (including harms). Use measures that incorporate understanding of pathophysiological mechanisms and address multiple domains of pain. Report the proportions of patients achieving a clinically meaningful improvement for measures of pain and function as well as outcomes related to change in use of opioids, health care utilization and quality of life. Consider recommendations from IMMPACT, ACTTION and Federal Pain Research Strategy.

ACTTION = Analgesic, Anesthetic, and Addiction Clinical Trials Translations, Innovations, Opportunities, and Networks; IMMPACT = Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials; NRS = numeric rating scale; VAS = visual analog scale

Conclusions

Exercise, multidisciplinary rehabilitation, acupuncture, CBT, and mind-body practices were most consistently associated with durable slight to moderate improvements in function and pain for specific chronic pain conditions. Our findings provide some support for clinical strategies that focus on use of nonpharmacological therapies for specific chronic pain conditions. Additional comparative research on sustainability of effects beyond the immediate post-treatment period is needed, particularly for conditions other than low back pain.

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Acronyms and Abbreviations

Acronym/Abbreviation	Term
AC	Attention Control
ADL	Activities of daily living
AIMS	Arthritis Impact Measurement Scale
AQoL 6D	Assessment of Quality of Life version 6D
AUSCAN	Australia Canadian Osteoarthritis Hand Index
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
BMI	Body mass index
BPI	Brief Pain Inventory
BPI-SF	Brief Pain Inventory-Short Form
CBT	Cognitive-behavioral therapy
CDC HRQOL-4	Centers for Disease Control and Prevention's Health-Related Quality of Life Questionnaire
CES-D	Center for Epidemiologic Studies Depression Scale
CGI-I	Clinical Global Impressions of Improvement Scale
CGI-S	Clinical Global Impressions of Severity Scale
CI	Confidence interval
CSQ	Coping Strategies Questionnaire
DASS	Depression Anxiety Stress Scales
DPQ	Dallas Pain Questionnaire
DRI	Disability Rating Index
DFI	Dreiser Functional Index
EEG	Electroencephalography
EMG	Electromyography
EQ-5D	EuroQoL-5D
FABQ	Fear Avoidance Beliefs Questionnaire
FIHOA	Functional Index for Hand Osteoarthritis
FIQ	Fibromyalgia Impact Questionnaire
FMI	Freiburg Mindfulness Inventory
FRI	Functional Rating Index
FSI	Fatigue Symptom Inventory
GAR	Groningen Activity Restriction Scale
GCQ, GBB-24	Giessen Complaint Questionnaire
GDS	Geriatric Depression Scale
GPE	Global Perceived Effect Scale
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
GSI	Global Severity Index (Symptom Checklist-90-Revised)
HADS	The Hospital Anxiety and Depression Scale
HAM-A	Hamilton Anxiety Rating Scale (HAM-A)
HAM-D	Hamilton Depression Rating Scale (HAM-D)
HAQ	Health Assessment Questionnaire
HDI	Headache Disability Inventory
HHS	Harris Hip Score
HFAQ	Hannover Functional Ability
HIT-6	Headache Impact Test-6
HRQoL	Health-related quality of life
HSCL-25	Hopkin’s Symptom Checklist
HSS	Hospital for Special Surgery Knee Function
IPAQ	International Physical Activity Questionnaire
IPQ(-R)	Illness Perception Questionnaire(-Revised)
IQR	Interquartile range
ITT	Intention-to-treat
KPS	Knee Pain Scale
JLEQ	Japan Low Back Pain Evaluation Questionnaire
JOA	Japanese Orthopedic Association
LBP	Low back pain

Acronym/Abbreviation	Term
LBPOI	Low Back Pain Outcome Instrument
LBPRS	Low back pain rating scale
LLFDI	Late Life Function and Disability Instrument
MACTAR	McMaster Toronto Arthritis patient preference questionnaire
MASS	Mindful Attention Awareness Scale
MBSR	Mindfulness-based stress reduction
MCE	Motor control exercise
MCID	Minimal clinically important difference
MCS-12	Mental component score of the SF-12
MD	Mean difference
MIDAS	Migraine Disability Assessment questionnaire
MRDQ	Modified Roland-Morris Disability Questionnaire
MOS	Medical Outcome Study
MPI	Multidimensional Pain Inventory
MPQ(-SF)	McGill Pain Questionnaire(-Short Form)
NDI	Neck Disability Index
NHP	Nottingham Health Profile
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIH	National Institute of Health
NPAD	Neck Pain and Disability Index
NR	Not reported
NRS	Numeric rating scale
NS	Not statistically significant
NSAID	Nonsteroidal anti-inflammatory drug
NT	No treatment
OA	Osteoarthritis
OARSI-OMERACT	Osteoarthritis Research Society International – Outcome Measures in Rheumatology
ODI	Oswestry Disability Index
OKS	Oxford Knee Score
PDI	Pain Disability Index
PPS	Pain Perception Scale
PR	Partial response
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSEQ	Chronic Pain Self Efficacy Scale
PSFS	Patient-Specific Functional Scale
PSQI	Pittsburgh Sleep Quality Index
PSS	Perceived Stress Scale
PT	Physical therapy
QBPDS	Quebec Back Pain Disability Scale
QHS	Each night at bedtime
QOL	Quality of life
RAND-36 QoL	Quality of Life RAND-36
QoL VAS	Quality of Life Visual Analog Scale
RCT	Randomized controlled trial
RDQ	Roland-Morris Disability Questionnaire
RR	Relative risk
SD	Standard Deviation
SA	Sham acupuncture
SCL-90	Symptom Checklist 90
SF-12, SF-12 MCS/PCS	Short Form-12, Physical Component Score/Mental Component Score
SF-36, SF-36 MCS/PCS	Short Form-36, Physical Component Score/Mental Component Score
SF-MPQ	McGill Pain Questionnaire Pain Rating Index-Short-Form
SHCI	Subjective Health Complaint Inventory
SIP	Sickness Impact Profile
SKFS	Saudi version of the Knee Function Scale
SMD	Standardized mean difference
SOE	Strength of evidence

Acronym/Abbreviation	Term
SSDQ	Stanford Sleep Disorders Questionnaire
SSS	Swiss Spinal Stenosis Questionnaire
STAI	State-Trait Anxiety Inventory
TENS	Transcutaneous electrical nerve stimulation
UC	Usual Care
VAS	Visual analog scale
VF	Von Korff functional disability
VKPS	Von Korff pain scale
WHOQOL-BREF	World Health Organization Quality of Life-BREF instrument
WL	Waitlist
WMD	Weighted mean difference
WPAI	Work activity impairment subscale
WPSI	Wahler Physical Symptoms Inventory
ZPS	Zung Self-Rating Depression Scale

Appendix A. Search Strategies

Database: Ovid MEDLINE(R) without Revisions 1996 to May Week 2 2017

Search Strategy:

1 exp Low Back Pain/
2 exp Chronic Pain/
3 2 and (back or spine or spinal or radicular).ti,ab.
4 or/1-3
5 Neck Pain/ or neck.ti,ab.
6 exp Osteoarthritis/ or osteoarthritis.ti,ab.
7 Headache/ or headache.ti,ab.
8 Fibromyalgia/ or fibromyalgia.ti,ab.
9 exp Exercise Therapy/
10 exp Physical Therapy Modalities/
11 exp Braces/
12 exp Mind-Body Therapies/
13 exp Acupuncture Therapy/
14 exp Rehabilitation/
15 exp Psychotherapy/
16 exp Musculoskeletal Manipulations/
17 (noninvasive or non-invasive or nonpharmacologic* or non-pharmacologic*).ti,ab.
18 (exercise or physical therapy or cognitive or behavioral or feedback or relaxation or acceptance or commitment or traction or ultrasound or stimulation or laser or magnet* or inferential or electromuscular or diathermy or heat or cold or manipulation or manual or craniosacral or mindfulness or meditation or mind-body or yoga or pilates or Qigong or acupuncture or “functional restoration” or multidisciplin* or interdisciplin*).ti,ab.
19 rh.fs.
20 or/9-19
21 (or/5-8) and pain.mp.
22 20 and 21
23 limit 22 to (meta analysis or systematic reviews)
24 limit 23 to (english language and humans)
25 limit 22 to randomized controlled trial
26 limit 25 to (english language and humans)
27 4 and 20
28 limit 27 to randomized controlled trial
29 limit 28 to yr="2016 - 2017"
30 limit 29 to (english language and humans)
31 24 or 26 or 30

Database: EBM Reviews - Cochrane Central Register of Controlled Trials April 2017

1 exp Low Back Pain/
2 exp Chronic Pain/
3 2 and (back or spine or spinal or radicular).ti,ab.
4 or/1-3
5 Neck Pain/ or neck.ti,ab.
6 exp Osteoarthritis/ or osteoarthritis.ti,ab.

7 Headache/ or headache.ti,ab.
8 Fibromyalgia/ or fibromyalgia.ti,ab.
9 exp Exercise Therapy/
10 exp Physical Therapy Modalities/
11 exp Braces/
12 exp Mind-Body Therapies/
13 exp Acupuncture Therapy/
14 exp Rehabilitation/
15 exp Psychotherapy/
16 exp Musculoskeletal Manipulations/
17 (noninvasive or non-invasive or nonpharmacologic* or non-pharmacologic*).ti,ab.
18 (exercise or physical therapy or cognitive or behavioral or feedback or relaxation or acceptance or commitment or traction or ultrasound or stimulation or laser or magnet* or inferential or electromuscular or diathermy or heat or cold or manipulation or manual or craniosacral or mindfulness or meditation or mind-body or yoga or pilates or Qigong or acupuncture or functional restoration or multidisciplin* or interdisciplin*).ti,ab.
19 rh.fs.
20 or/9-19
21 (or/5-8) and pain.mp.
22 20 and 21
23 limit 22 to randomized controlled trial
24 4 and 20
25 limit 24 to randomized controlled trial
26 limit 25 to yr="2016 - 2017"
27 23 or 26
28 limit 27 to english language
29 limit 28 to medline records
30 28 not 29

Database: EBM Reviews - Cochrane Database of Systematic Reviews 2005 to December 21, 2016
1 chronic.ti,ab.
2 (back or spine or spinal or radicular or neck or osteoarthritis or fibromyalgia or headache).ti,ab.
3 (noninvasive or non-invasive or nonpharmacologic* or non-pharmacologic*).ti,ab.
4 (exercise or psychosocial or "cognitive behavioral therapy" or CBT or biofeedback or relaxation or "physical modal*" or traction or ultrasound or "transcutaneous electrical nerve stimulation" or TENS or laser or heat or cold or cryotherapy or magnet* or manual* or manipulation or massage or mindfulness or meditation or "mind-body" or "yoga to tai chi" or qigong or acupuncture or "functional restoration" or "occupational therapy" or multidisciplinary).ti,ab.
5 1 and 2
6 3 or 4
7 5 and 6

Appendix B. Included Studies

1. Abbasi M, Dehghani M, Keefe FJ, et al. Spouse-assisted training in pain coping skills and the outcome of multidisciplinary pain management for chronic low back pain treatment: a 1-year randomized controlled trial. Eur J Pain. 2012 Aug;16(7):1033-43. doi: 10.1002/j.1532-2149.2011.00097.x. PMID: 22337646.
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Appendix C. Excluded Studies

Exclusion Codes:

3 = Ineligible population
4 = Ineligible intervention
5 = Ineligible comparator
6 = Ineligible outcomes
7 = Ineligible study design for Key Question
8 = Not a study (letter, editorial, non-systematic review article, etc.)
9 = Inadequate duration of followup
10 = Systematic review not directly used, but studies checked for inclusion
11 = Not English language, but possibly relevant
12 = Not English language and not relevant

1. Aas RW, Tuntland H, Holte KA, et al. Workplace interventions for neck pain in workers. Cochrane Database of Systematic Reviews. 2011(4):CD008160. doi: http://dx.doi.org/10.1002/14651858.CD008160.pub2. PMID: 21491405. Exclusion: 10

2. Abasolo L, Carmona L, Hernandez-Garcia C, et al. Musculoskeletal work disability for clinicians: time course and effectiveness of a specialized intervention program by diagnosis. Arthritis & Rheumatism. 2007 Mar 15;57(2):335-42. doi: https://dx.doi.org/10.1002/art.22529. PMID: 17330282. Exclusion: 3

3. Abbott JH, Robertson MC, McKenzie JE, et al. Exercise therapy, manual therapy, or both, for osteoarthritis of the hip or knee: a factorial randomised controlled trial protocol. Trials. 2009 Feb 08;10:11. doi: 10.1186/1745-6215-10-11. PMID: 19200399. Exclusion: 8

4. Abdoli S, Rahzani K, Safaie M, et al. A randomized control trial: the effect of guided imagery with tape and perceived happy memory on chronic tension type headache. Scandinavian Journal of Caring Sciences. 2012 Jun;26(2):254-61. doi: http://dx.doi.org/10.1111/j.1471-6712.2011.00926.x. PMID: 21985338. Exclusion: 9

5. Abeles M, Solitar BM, Pillinger MH, et al. Update on fibromyalgia therapy. American Journal of Medicine. 2008 Jul;121(7):555-61. doi: http://dx.doi.org/10.1016/j.amjmed.2008.02.036. PMID: 18589048. Exclusion: 10

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9. Ahmed MS, Shakoor MA, Khan AA. Evaluation of the effects of shortwave diathermy in patients with chronic low back pain. Bangladesh Med Res Counc Bull. 2009;35(1):18-20. PMID: 19637541. Exclusion: 9

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12. Aker PD, Gross AR, Goldsmith CH, et al. Conservative management of mechanical neck pain: systematic overview and meta-analysis. BMJ. 1996 Nov 23;313(7068):1291-6. PMID: 8942688. Exclusion: 10

13. Akhmadeeva L, Valeeva D, Kharisova E, et al. A double blind randomized placebo controlled trial for non-invasive dynamic trans-cutaneous electrical nerves stimulation in management of tension type headaches: The first results. Cephalalgia. START: 2015 May 14 CONFERENCE END: 2015 May 17, 17th Congress of the International Headache Society, IHC 2015 Valencia Spain;35(6 SUPPL. 1):71. PMID: CN-01136421 NEW. Exclusion: 7

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15. Alastair Gibson J, Ahmed M. The effectiveness of flexible and rigid supports in patients with lumbar backache. Journal of Orthopaedic Medicine. 2002;24(3):86-9. Exclusion: 9

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Appendix D. Evidence Table

Table D-1. Data abstraction of randomized controlled trials
See Appendix B. Included Studies for references.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Abbassi 2012	Iran Number of centers: 2 Outpatient clinic	Married patients ages 18 to 70 with chronic LBP longer than 6 months Exclude: Patients with unexplained pain, pregnancy, did not speak Persian language, had active rheumatological disease, progressive neurological disease, serious cardiac or other internal medical condition, malignant, basic diseases, acute traumas, infections, or acute vascular catastrophes, major cognitive dysfunction, coexisting psychiatric morbidity as determined by a psychological screening interview and previous participation in a rehabilitation cognitive behavioral program	Randomized: 36 Treated: 32 Analyzed: 32 Attrition: 11% (4/36)
Abbott 2013	New Zealand 2 centers 1 general practitioner, 1 outpatient	Diagnosis of hip or knee OA fulfilling ACR criteria Exclude: Rheumatoid arthritis, previous knee or hip joint replacement surgery of affected joint, surgical procedure on lower limbs within 6 months, surgical procedure planned for lower limbs within 6 months, opioid analgesia or corticosteroid or analgesic injection intervention for hip or knee pain in past 30 days	Randomized:156 (87 with knee OA) Treated: 156 Analyzed: 147 Attrition: 6% (9/156)

Author, Year	Intervention, Comparator
Abbassi 2012	A: Multidisciplinary pain management program (n=12): 7 weekly 2 hour group sessions of training in pain coping and couple skills for the patient, led by psychologist and focusing on self-management. Components included education, self-management strategies, coping skills. Also education from orthopedic surgeon at second group session, medication management via private sessions with psychiatrist, and 1 group session with physiotherapist plus an individualized appointment with tailored exercises. B: Spouse-assisted multidisciplinary pain management program (n=10): 7 weekly 2 hour group sessions of training in pain coping and couple skills with spouses, otherwise similar to A. C: Standard medical care (n=11): Routine medical treatment only
Abbott 2013	A.Manual therapy (n=54) (30 knee OA/24 hip OA): 9 total sessions of 50 minutes, 7 sessions in the initial 9 weeks of the trial with 2 booster sessions at week 16. The sessions aimed to modify the quality and ROM of the target joint and associated soft tissue structures. Additional manual therapy interventions were prescribed individually as needed and all patients were prescribed a home program of joint range of motion exercises to be done three times per week. B.Exercise therapy (n=51) (29 knee OA/22 hip OA): 9 total sessions of 50 minutes, 7 sessions in the initial 9 weeks of the trial with 2 booster sessions at week 16. The sessions consisted of an aerobic warm-up, muscle strengthening, muscle stretching, and neuromuscular control exercises. Additional exercises were prescribed individually as needed and all subjects were prescribed a home exercise program to be done three times per week. C.Usual care (n=51) (28 knee OA/23 hip OA): Routine care from patients' own GP and other healthcare providers. Subjects participation in the use of the interventions outside of the trial was not influenced or restricted, but it was monitored. All subjects continued receiving usual care as above.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Abbassi 2012	Overall Age (mean): 45 years Female: 88% Race: NR*	Roland Disability Questionnaire (RDQ, 0-24) Pain (0-10 VAS) Depression Anxiety Stress Scale (DASS, 0 to 42, higher score indicates greater level of depression, anxiety or stress)	10.25 months
Abbott 2013	A vs B vs C (overall population) Age: 67 vs 67 vs 66 Females: 49% vs 52% vs 58% Years of OA diagnosis: 2.5 vs 2.6 vs 2.8 % hip OA: 44.4% vs 43.1% vs 45.1% % knee OA: 55.6% vs 56.9% vs 54.9% Both hip and knee OA: 22.2% vs 19.6% vs 25.5% Low risk of depression from depression screening test score: 50.9% vs 52.9% vs 51.0% WOMAC: 114.8 (56.3) vs 95.5 (57.3) vs 93.8 (52.8)	WOMAC (0-240, higher score=higher disability)	9.75 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Abbassi 2012	A vs. B vs. C, mean (SD) Baseline RDQ (0–24): 12.1 (5.7) vs. 11.2 (4.3) vs. 8.4 (3.3) Pain (0-10 VAS): 4.6 (2) vs. 5 (2.7) vs. 3.6 (1.7) 10.25 months RDQ (0–24): 8.8 (5.9) vs. 8.2 (5.4) vs. 10.4 (6.2), p=0.44 Pain (0–10 VAS): 3.7 (2.5) vs. 2.8 (2.7) vs. 4.3 (1.4), p=0.44
Abbott 2013	Knee OA A vs. C 9.75 months WOMAC change from baseline, mean change (95% CI): -31.5 (-52.7 to -10.3) vs 1.6 (-10.5 to 13.7) B vs. C 9.75 months WOMAC change from baseline, mean Δ (95% CI): -12.7 (-27.1 to 1.7) vs 1.6 (-10.5 to 13.7) Hip OA A vs. C 9.75 months WOMAC change from baseline, mean change (95% CI): -22.9 (-43.3 to -2.6) vs -7.9 (-30.9 vs 15.3) B vs. C 9.75 months WOMAC change from baseline, mean change (95% CI): -12.4 (-27.1 to 2.3) vs -7.9 (-30.9 vs 15.3)

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Abbassi 2012	NR
Abbott 2013	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Abbassi 2012	NR	NR
Abbott 2013	Knee OA A vs. B 9.75 months WOMAC change from baseline, mean change (95% CI): -31.5 (-52.7 to -10.3) vs -12.7 (-27.1 to 1.7) Hip OA A vs. B 9.75 months WOMAC change from baseline, mean change (95% CI): -22.9 (-43.3 to -2.6) vs -12.4 (-27.1 to 2.3)	A vs. B vs. C Inguinal hernia: 0% (0/54) vs 0% (0/51) vs 0% (0/51)

Author, Year	Funding Source	Quality	Comments
Abbassi 2012	Family Excellence Centre Grant	Poor	
Abbott 2013	Research contracts from the Health Research Council of New Zealand and the New Zealand Lottery Grants Board, grants from the Health Research Council, graduate student scholarship funding from Health Research Council, grant from the Lottery Grants Board and by the Centre for Physiotherapy Research	Fair	This study reported most outcomes across both OA types; only the WOMAC was stratified between hip and knee OA subjects (table III) and was therefore the only valid measure to report for our purposes Followup was labeled as 1 year. Based on study description, this was interpreted to include the treatment period (9 weeks). Combination therapy (n=50) was also included in study but not included in data abstraction because it was considered additive.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Ajimsha 2014	India Number of centers: 1 Outpatient	Nursing professional 20-40 years old; chronic musculoskeletal low back pain for ≥3 months Exclude: Osteoporosis Primary joint disease Metabolic bone disease Malignant bone disease Fracture Hyper mobility of the lumbar/sacral spine Cardiovascular or other medical disorder preventing strenuous exercise Radiculopathy Radiating pain Pregnancy Severe psychiatric disturbance Oral/systemic steroids Analgesics on >10 days per month for previous 6 months	Randomized: 80 Analyzed: 74 Attrition: 7.5% (6/80)
Al Rashoud 2014	Saudi Arabia, single-site, hospital	Inclusion Criteria: Patients with knee osteoarthritis (according to the American College of Rheumatology criteria)with an average pain intensity of ≥3 on a 10-cm visual analogue scale (VAS), ability to perform all movements included in the evaluation forms, ability to read or understand the patient information sheets, and ability to sign a consent form. For those patients with bilateral knee osteoarthritis, the most painful knee was assessed. Exclusion Criteria: Exclusion criteria included previous knee surgery, serious valgus or varus deformity, disease where laser treatment is contraindicated (cancer, uncontrolled diabetes mellitus, hypertension, etc.), and current use of medications that might interfere with LLLT treatment (e.g. corticosteroid injections).	Randomized: NR Treated: 49 Analyzed: 49 Attrition: NR

Author, Year	Intervention, Comparator
Ajimsha 2014	A. Myofascial release (n=38): Performed to 5 areas, total 40 minutes B. Sham myofascial release (n=36) Treatment given 3 times weekly for 8 weeks Both groups also received videotaped education on exercises
Al Rashoud 2014	A.Low Level Laser Therapy (n=26) Patients received laser treatment in a supine position, with the affected knee slightly flexed and supported by a rolled towel. The laser probe was placed sequentially and perpendicularly in full contact with the skin at five acupuncture points commonly used for treating knee osteoarthritis. Each point received a continuous beam of laser for 40 seconds. Additionally, all patients were advised to repeat straight leg raise exercises five times daily. Device: gallium aluminium arsenide laser device(Endolaser 476, Enraf Nonius, Rotterdam, The Netherlands) Diode: single 30-mW Wavelength: 830 nm Irradiation Area: 0.28 cm2 Dose: 1.2 J/acupoint, 6 J total per session for each patient No. of Treatments: NR (10)* B.Placebo Laser Group (n=23) Treatment parameters were identical except the device was inactive and only produced visible red light. *No. of Treatments estimated to be 10 but the exact number is not reported, although 5 sessions constituted their 'midpoint' followup.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Ajimsha 2014	Age: 36 vs. 34 years Female: 76% vs. 78% Duration of condition (months): 28.3±14.7 vs. 26.8±16.0	Primary outcomes: Pain: McGill Pain Questionnaire, rank order pain terms score 0-78 (higher number = more pain) Disability: Quebec Back Pain Disability Scale, 0-100 scale (higher number= more disability)	1 month
Al Rashoud 2014	A vs B Age: 52 vs. 56 Female: 62% vs. 65% Race: NR Mean Duration of Chronicity: 11 (3.1) Mean VAS (SD): 6.4 (1.9) vs. 5.9 (1.8) Median SKFS (IQR): 61.0 (44.0 to 71.0) vs. 60.0 (49.0 to 70.0)	Pain during movement score (VAS, range 0-10: higher scores indicate severity of pain) Saudi Knee Function Scale scores (SKFS, range 0-112: higher scores indicate severity of symptoms)	1.5 months, 6 months

Author, Year	**Results - Subquestion a** (vs. sham, no treatment, waitlist, attention control)
Ajimsha 2014	A vs. B, mean (SD) <u>Baseline</u> McGill Pain Questionnaire (0-78): 23.2 (8.7) vs. 23.0 (7.6), mean difference -1.00 (p=0.13) Quebec Back Disability Scale (0-100): 37.1 (11.8) vs. 35.3 (13.6), mean difference -0.97 (p=0.47) <u>1 month</u> McGill Pain Questionnaire (0-78): 13.1 (6.9) vs. 18.3 (7.5), mean difference -3.25 (p<0.005) Quebec Back Disability Scale (0-100): 28.7 (9.1) vs. 32.5 (10.4), mean difference -2.02 (p<0.005)
Al Rashoud 2014	A vs. B <u>1.5 months</u> Mean VAS Pain on Movement*: 3 vs. 4.2 Median SKFS (IQR): 31 (12 to 44) vs. 40 (29 to 54); median difference −10 (−23 to −4) p=0.054 <u>6 months</u> Mean VAS Pain on Movement*: 3.4 vs. 5.2 Median SKFS (IQR): 31 (19 to 43) vs. 51 (33 to 55); median difference −21.0 (95%CI −34.0 to −7.0) p=0.006 *Pain values were abstracted from a graph and no SD was given.

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Ajimsha 2014	NR
Al Rashoud 2014	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Ajimsha 2014	NR	A vs. B Withdrawals: 2 vs. 4 Withdrawals due to AE: NR Serious AEs: 0 vs. 0 Nonserious AEs: Increase of pain in first week: 26% (10/38) vs. 2.8% (1/36)
Al Rashoud 2014	NR	No adverse effects were observed in this study.

Author, Year	Funding Source	Quality	Comments
Ajimsha 2014	Mahatma Gandhi University	Fair	
Al Rashoud 2014	Scholarship granted by the General Department of Medical Services of Ministry of Interior, Security Forces Hospital, Riyadh, Saudi Arabia.	Fair	*No. of Treatments estimated to be 10 but the exact number is not reported, although 5 sessions constituted their 'midpoint' followup.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Alda 2011	Spain 3 primary healthcare centres in Zaragoza, Spain	Inclusion: FM diagnosis based on ACR 1990 criteria, age 18-65, able to understand and read Spanish, no pharmacological treatment currently or willing to discontinue it for two weeks before start of study Exclusion: psychological treatment in past 2 years, severe Axis I psychiatric disorder, severe Axis II psychiatric disorder, other medical disorder that would prevent subject from following treatment protocol, pregnant or nursing	Randomized: 169 Analyzed: 141 Treated: A vs B vs C: 100% vs 100% vs 98% Attrition: 17% (28/169)
Alfano 2001	United States 1 center Outpatient	Aged 18 to 65 with a diagnosis of FM fulfilling 1990 ACR criteria Exclude: Presence of other systemic rheumatologic condition, pacemaker, presence of metal fragments or implants, pending litigation, receipt of Worker's Compensation benefits, pregnancy	Randomized: 117 Treated: 109 (23/117) Analyzed: 94 Attrition: 20%

Author, Year	Intervention, Comparator
Alda 2011	A.CBT (n=49): 10-12 week program consisting of 10 weekly 90-minute group sessions. Cognitive restructuring and training in cognitive and behavioral coping strategies. Administered by "trained therapists." Of 57 randomized, 1 received 1 session, 2 received 6 sessions, 6 received 7 sessions, 5 received 8 sessions, 43 received 9 sessions, 84% (48/57) received 80% of sessions. B.Recommended pharmacological treatment (n=46): Treatment with pregabalin (300-600 mg/day); in addition, duloxetine (60-120 mg/day) was administered to patients with major depressive disorder. A psychiatrist administered treatment and conducted followup with patients at baseline and each month after baseline during the 6-month study. Adherence to medication was NR, although withdrawals due to medication adverse effects was reported. C.Treatment as usual (n=46): standard care offered by general practitioners at subjects' health centres. The doctors received a guide for the treatment of FM in primary care that recommended the same treatment as in B.
Alfano 2001	A.Magnetic field with uniform polarity (n=30): A magnetic mattress composed of a grid of ceramic magnets with the dimensions 2.5x5.1x1.0 cm produced a magnetic field of uniform south (negative) polarity ranging in a magnetic flux of 0.6 to 0.3 mT. Subjects slept on the pad for 6 months and it was placed between the subjects' mattress and box spring B.Magnetic field with varied polarity (n=26): Disc shaped ceramic magnets, 1.8 cm in diameter and 0.3 cm thick, were spaced 12.5 cm apart on the width and 5 cm apart on the length of a pad. Magnets were oriented so that the same pole faced the body and the magnetic flux of the field varied with distance above the pad, ranging from 0.03 to 0.28 mT above the pad. In the space between the magnetics, the field varied in polarity. Subjects slept on the pad for 6 months and the pad was placed above the mattress. C.Sham pad of magnetic field with uniform polarity (n=24 analyzed in the combined sham pad groups): Pad was identical in appearance to the pad used in group A but magnets were demagnetized by heating to high temperatures. Subjects slept on the pad for 6 months and it was placed between the subjects' mattress and box spring. D.Sham pad of magnetic field with varied polarity (n=24 analyzed in the two combined sham pad groups): Pad was identical in appearance to the pad used in group B but magnets were demagnetized by heating to high temperatures. Subjects slept on the pad for 6 months and it was placed between the subjects' mattress and box spring E.Usual care (n=14): Subjects were instructed to maintain current FM treatment regimens that were reported at baseline All subjects: Instructed to continue current FM treatment regimens but refrain from initiating additional therapies during the study*.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Alda 2011	A vs B vs C Age: 46 vs 47 vs 47 Females: 95% vs 93% vs 96% Years since diagnosis: 12.9 (7.1) vs 11.2 (3.9) vs 11.7 (4.0) FIQ: 65.9 (10.9) vs 66.4 (9.9) vs 64.5 (10.5) Pain VAS: 64.2 (10.8) vs 68.1 (9.8) vs 64.7 (10.4) HAM-D: 14.5 (3.9) vs 14.9 (4.0) vs 14.1 (4.6) HARS: 10.8 (4.3) vs 11.2 (3.8) vs 9.5 (3.0) Comorbid major depressive disorder: 47% vs 46% vs 55% Currently in litigation: 30% vs 21% vs 29%	FIQ (0-100, higher scores= higher impairment) Pain VAS (0-100, higher scores=greater pain) Hamilton Rating Scale for Depression (HAM-D) (17-item version, 0-50, higher scores=higher depression) Hamilton Anxiety Rating Scale (HARS) (0-56, higher scores=greater anxiety)	6 months
Alfano 2001	A vs B vs C+D vs E Age: 44 vs 47 vs 46 vs 45 Female: 92% vs 87% vs 96% vs 100% FIQ: 51.6 (13.2) vs 55.5 (12.1) vs 51.5 (14.1) vs 53.9 (11.8) FIQ score ranges: 21-40: 24% vs 13% vs 22% vs 18% 41-60: 43% vs 57% vs 56% vs 47% 61-80: 32% vs 30% vs 22% vs 35% Pain intensity NRS: 7.1 (2.3) vs 7.0 (2.4) vs 6.7 (2.3) vs 7.0 (2.3)	FIQ (0-80, higher score=higher impact); pain intensity NRS (0-10, higher score=higher pain)	Immediately post intervention (treatment of 6 months)

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Alda 2011	A vs C 6 months, ITT analysis using LOCF method: FIQ: 48.8 (9.1) vs 53.3 (7.5), p <0.05; MD -4.5 (95% CI -7.91 to -1.09), p=0.01 Pain VAS: 40.7 (10.9) vs 44.3 (8.6), p >0.05; MD -3.6 (95% CI -7.617 to 0.417), p=0.08 HAM-D: 7.9 (2.5) vs 8.6 (2.5), p < 0.05; MD -0.7 (95% CI -1.719 to 0.319), p=0.18 HARS: 7.3 (3.0) vs 7.6 (2.1), p <0.05; MD -0.3 (95% CI -1.361 to 0.761), p=0.58
Alfano 2001	A vs C+D† FIQ: 38.3 (18.3) vs 47.9 (19.6), (MD -9.6, 95% CI -20.0 to 0.8) p=0.069 Pain intensity NRS: 4.8 (2.4) vs 6.2 (2.8), (MD -1.4, 95% CI -2.8 to 0.05) p=0.058 B vs C+D† FIQ: 47.4 (17.9) vs 47.9 (19.6), (MD -0.5, 95% CI -11.2 to 10.2) p=0.93 Pain intensity NRS: 6.3 (2.5) vs 6.2 (2.8), (MD 0.1, 95% CI -1.4 to 1.6) p=0.89 A vs E FIQ: 38.3 (18.3) vs 48.4 (17.7), (MD -10.1, 95% CI -21.9 to 1.7) p=0.09 Pain intensity NRS: 4.8 (2.4) vs 6.6 (2.7), (MD -1.8, 95% CI -3.4 to -0.2) p=0.03 B vs E FIQ: 47.4 (17.9) vs 48.4 (17.7), (MD -1.0, 95% CI -13.0 to 11.0) p=0.87 Pain intensity NRS: 6.3 (2.5) vs 6.6 (2.7), (MD -0.3, 95% CI -2.0 to 1.4) p=0.73 A+B (pooled) vs C+D† FIQ: 42.9 (18.5) vs 47.9 (19.6), (MD -5.0, 95% CI-14.1 to 4.1) p=0.28 Pain intensity NRS: 5.6 (2.5) vs 6.2 (2.8), (MD -0.6, 95% CI-1.9 to 0.7) p=0.35 A+B (pooled) vs E FIQ: 42.9 (18.5) vs 48.4 (17.7), (MD -5.5, 95% CI -14.4 to 3.4) p=0.22 Pain intensity NRS: 5.6 (2.5) vs 6.6 (2.7), (MD -1.0, 95% CI-2.2 to 0.2) p=0.11

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Alda 2011	A vs B 6 months: FIQ: 48.8 (9.1) vs 52.8 (9.2), p <0.05; MD -4.0 (95% CI -7.730 to -0.270), p=0.04 Pain VAS: 40.7 (10.9) vs40.5 (9.6), p>0.05; MD 0.2 (95% CI -3.996 to 4.396), p=0.92 HAM-D: 7.9 (2.5) vs 8.2 (2.0), p>0.05; MD -0.3 (95% CI -1.226 to 0.626), p=0.52 HARS: 7.3 (3.0) vs 7.4 (2.6), p > 0.05; MD -0.1 (95% CI -1.247 to 1.047), p=0.86
Alfano 2001	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Alda 2011		A vs B vs C Adverse Events NR Withdrawals due to Adverse Events: 0 vs 5% vs 4% Total withdrawals: 9% vs 11% vs 13%
Alfano 2001		There were no differences in adverse events between functional and sham pad groups. Type of adverse events was not reported and none of events were stated to relate to magnetic treatments

Author, Year	Funding Source	Quality	Comments
Alda 2011	Carlos III Health Institute of the Spanish Ministry of Health and Consumption	Fair	
Alfano 2001	Grant (5 U24 DE 11924) from the National Center for Complementary and Alternative Medicine, funds from the National Institutes of Health, and a gift from a large private Canadian charitable foundation	Fair (all)	*Primary care physicians of all subjects were asked to limit treatment of flareups to modalities such as heat or cold when possible †Demographics and results for the two sham pad groups were combined and reported together Report comparisons of pads separately and pooled (NOTE). Results were pooled given that there were not statistically significant differences between the two groups. MDs and p values calculated by AAI. N's used for calculations were as follows: Pad A (A): n=30 Pad B (B): n=26 Sham (C+D): n=24 Usual care (E): n=14 Pooled A+B: n=56

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Altan 2005	Turkey Setting NR	Localized pain and taut bands in the neck for a ≥ 3 months, bilateral and significantly more tenderness in the 3 cervical trigger points (upper trapezius, supraspinatus, and suboccipital muscles) compared to the control point (a nontender point over deltoid muscle). Exclude: Fibromyalgia diagnosis, cervical arthrosis, disc hernia, cervical vertebral fracture, radiculopathy, or myelopathy, other major pathology	Randomized: 53 Treated: NR Analyzed:: 48 Attrition: 12% (6/51)
Altan 2009	Turkey 1 center Outpatient	Diagnosis of FM according to ACR criteria Exclude: Accompanying rheumatoid disease, unstable hypertension, severe cardiopulmonary problems, psychiatric disorder affecting participant compliance	Randomized: 50 Treated: 49 Analyzed: 49 Attrition: 2% (1/50)
Amris 2014	Denmark 1 Outpatient rheumatology clinic	Inclusion: age 18+, chronic widespread pain/fibromyalgia diagnosed according to 1990 ACR criteria (i.e., reporting of pain axially and in a minimum of 3 body quadrants), fluent in Danish Exclusions: psychiatric disorder, uncontrolled rheumatic or medical disease capable of causing chronic widespread pain	Randomized: 191 Analyzed: 170 Attrition: 12% (21/170)

Author, Year	Intervention, Comparator
Altan 2005	A.GaAs laser treatment (n=26/23) over the 3 trigger points bilaterally and 1 point in the taut bands in trapezius muscle bilaterally for 2 min over each point once a day for 2 weeks. Laser parameters: wavelength of 904 nm, frequency range of 5–7000 Hz, and maximum power of 27 W, 50 W, or 27x4 W B.Sham laser treatment (n=27/25) using the same instrument in the same way over the same points as in group 1 but not turning it on. All laser applications were performed by the same physiotherapist. All patients in both groups were instructed to perform daily isometric exercises and stretching just short of pain for 2 weeks at home No analgesic during the treatment and control periods.
Altan 2009	A.Pilates (n=25): 1 hour Pilates program administered 3 times per week for 12 weeks. Program followed basic principles of Pilates method consisting of postural education, search for neutral position, sitting exercise, antalgic exercises, stretching exercises, proprioceptivity improvement exercises, and breathing education B.Attention control (n=24): Instruction in home exercise relaxation/stretching program of 1 hour sessions 3 times per week for 12 weeks. Exercise program consisted of relaxation techniques, dynamic and active stretching, and passive stretching All patients: Education session about available diagnosis and treatment of FM
Amris 2014	A.Multidisciplinary treatment (n=84): 2-week program conducted by multidisciplinary team of rheumatologist, psychologist, nurse, and occupational and physical therapists. Scheduled program each day, with daily time schedule between 3 and 5 hours; in total, 35 hours. Treatment aimed to improve functional ability and pain coping. Program included education, sleep hygiene, group discussions, physical therapy including graded activity and activity pacing, adaptations and modifications to increase participation in activities of daily living. 53% of subjects missed no sessions, and 88% attended 5 or more days. B.Waiting list control group (n=86): No treatment during first phase of study (6 months), then offered A at the end of the waiting list plus an additional 16-week course of either individualized physiotherapy or occupational therapy in the second study phase

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Altan 2005	A vs B Age: 43 vs 43 years Female: 87% vs 48% Pain duration: 4.7 vs 4.4 years Pain (0-10): 6.85 (0.35) vs 6.24 (0.32) Pain (5-point scale): 2.35 (0.16) vs 2.20 (0.14) Tenderness (0-18 points): 6.78 (0.57) vs 6.68 (0.71)	Pain severity (VAS 0-10, higher score worse pain) Pain severity (VAS 0-5, 0=no pain, 1 = mild, 2=moderate, 3= severe, or 4=unbearable)	3 months
Altan 2009	A vs B Age: 48 vs 50 Female: 100% vs 100% FIQ: 80.8 (17.2) vs 80.1 (18.7) Pain VAS: 6.1 (1.7) vs 6.3 (1.8) NHP: 297.1 (124.2) vs 280.3 (86.6)	FIQ (0-100, higher score=higher disability); pain VAS (0-10, higher score=higher pain); Nottingham Health Profile (NHP) (range NR)	3 months
Amris 2014	A vs B Age: 44 vs 44 Female: 100% vs 100% Pain duration, years, median: 11 vs 10 Years since FM diagnosis, median: 1 vs 1 Fibromyalgia Impact Questionnaire: 64.0 (15.8) vs 65.7 (13.0) FIQ Pain VAS: 7.1 (2.0) vs 7.4 (1.7) Generalized Anxiety Disorder-10, Median (quartiles): 17.5 (13-26) vs 17.0 (13-23) Major Depression Inventory, Median (quartiles): 18.0 (13-27) vs 21.0 (15-27) SF-36 Physical Composite Score: 27.1 (6.9) vs 27.2 (7.0) SF-36 Mental Composite Score: 39.4 (12.2) vs 37.8 (9.8) SF-36 Physical Functioning scale, Median (quartiles):: 40.0 (25-55) vs 40.0 (25-50)	Fibromyalgia Impact Questionnaire, (0-100, higher scores = greater impact of FM) FIQ-Pain VAS (0-10, higher scores=greater pain) Generalized Anxiety Disorder-10 (scale NR, higher scores=greater anxiety) Major Depression Inventory (scale NR, higher scores = greater depression) SF-36 Physical Composite Score (scale NR, higher scores = better function) SF-36 PCS Responder: ≥4 point improvement SF-36 Mental Composite Score (scale NR, higher scores = better function) SF-36 MCS Responder: ≥6 point improvement SF-36 Physical Functioning scale (scale NR, higher scores = better function)	5.5 months

Author, Year	**Results - Subquestion a** (vs. sham, no treatment, waitlist, attention control)
Altan 2005	A vs B <u>3 months:</u> Pain (0-10): 3.17 (0.58) vs 3.80 (0.51), MD -0.63 (95% CI -0.95 to -0.31) p=0.0002 Pain (0-5): 1.09 (0.22) vs 1.16 (0.20), MD -0.07 (95% CI -0.19 to .05), p=0.254
Altan 2009	A vs B <u>3 months</u> FIQ: 69.3 (24.7) vs 77.6 (22.2), (MD -8.3, 95% CI -21.8 to 5.2) p=0.222 Pain VAS: 5.2 (2.5) vs 6.5 (2.1), (MD -1.3, 95% CI -2.6 to 0.03) p=0.055 NHP: 224.2 (129.1) vs 246.3 (128.1), (MD -22.1, 95% CI -96.0 to 51.8), p=0.551
Amris 2014	A vs B 5.5 months *Change from baseline (95% CI); mean difference between A and B (95% Confidence Interval)* FIQ total: change -1.28 (-3.90, 1.33) vs. -1.37 (-4.01, 1.28); between group mean difference 0.08 (-3.64 to 3.80), p=0.96 FIQ pain VAS: change 0.07 (-0.31, 0.44) vs. -0.14 (-0.52, 0.27); between group mean difference 0.21 (-0.32 to 0.74), p = 0.44 Generalized Anxiety Disorder-10: change -0.78 (-2.01, 0.46) vs. -0.54 (-1.80, 0.72); between group mean difference -0.24 (-2.00 to 1.53), p=0.79 Major Depression Inventory: change -1.73 (-3.19, -0.27) vs. -0.47 (-1.96, 1.01) between group mean difference -1.26 (-3.34 to 0.82), p = 0.23 SF-36 Physical Composite Score: change 1.35 (0.27, 2.43) vs. 0.78 (-0.30, 1.86); between group mean difference 0.57 (-0.95 to 2.10), p =0.46 SF-36 Mental Composite Score: change 2.29 (0.41, 4.18) vs. 1.15 (-0.73, 3.03); between group mean difference 1.14 (-1.52 to 3.81), p=0.40 SF-36 Physical Functioning scale: change 1.10 (-1.34, 3.55) vs. 1.58 (-0.87, 4.03); between group mean difference-0.48 (-3.94 to 2.99), p=0.79 *Responders* SF-36 MCS: 27% (26/96) vs. 27% (26/95), p=0.95; RR 0.99 (95% CI 0.62 to 1.6) p=0.96 SF-36 PCS: 27% (26/96) vs. 23% (22/95), p=0.41; RR 1.16 (95% CI 0.72 to 1.91) p=0.53

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Altan 2005	
Altan 2009	
Amris 2014	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Altan 2005		NR
Altan 2009		None
Amris 2014		A vs B Withdrawals 13% (12/96) vs 9/95 (10%) Adverse events: NR

Author, Year	Funding Source	Quality	Comments
Altan 2005	NR	Fair	
Altan 2009	NR	Fair	Outcomes not reported: number of tender points, algometric score, and chair stand test MDs and p values calculated by AAI using n=25 for Pilates group and n=24 for the control group NHP had differences between groups at baseline, potentially significant enough for further analysis
Amris 2014	The Oak Foundation Schioldanns Fond Danish Rheumatism Association	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Andersen 2008	Denmark 12 different located units of Danish public administration authority	Office workers (some with and some without neck pain - we only include those with neck pain) Exclude: health risks (hypertension, disc prolapse, severe spinal disorders, history of trauma, pregnancy), too few volunteers in a specific unit	Randomized: NR* Treated: 182 Analyzed: NR Attrition: NR *Total patients randomized (n=549) included patients with and without neck pain. Randomization of clusters formed from workers on the same work floor.
Ang 2010	USA Subjects were referred from community rheumatology offices	Inclusion: FM diagnosis based on ACR 1990 criteria, FIQ pain score >3, FIQ physical impairment score ≥2, taking stable doses of pain-related medications for at least 4 weeks, female. Exclusions: peripheral neuropathy, diabetes, demyelinating disorders, inflammatory rheumatic diseases	Randomized: 32 Analyzed: 28 Attrition: 14% (4/28)

Author, Year	Intervention, Comparator
Andersen 2008	A.Specific resistance training (n=61): dynamic strengthening exercises for shoulder girdle and static exercises for neck muscles with progressive resistance B.All-round physical exercise (n=59): increase activity as part of lifestyle such as riding bike to work; workplace activity such as steppers near copy machine, punch bags in hall, group session of Nordic walking and programs for strength and aerobic fitness C.Reference intervention (n=62): form groups to improve health and working conditions through workplace ergonomics, stress management, organization of work, cafeteria food quality Intervention for 1 year; all groups were allowed 1 hour per week during working time for activities, and each group received equal amount of attention
Ang 2010	A.CBT (n=15): Usual care plus 6 weekly 30-40 minute sessions of CBT delivered by telephone by a psychology graduate student. The therapist followed a manualized treatment protocol and subjects received a companion workbook. Components of CBT included activity pacing, pleasant activity scheduling, relaxation, automatic thoughts and pain, cognitive restructuring, and stress management. B.Usual care (n=13): customary care from subject's treating physician All subjects were asked to stay on the same pain-related medication regimen, including dosing, throughout the study period.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Andersen 2008	A + B + C Age: 45 years Female: 78% Baseline information given for the groups combined A vs B vs C Pain intensity: 5.0 (0.2) vs 5.0 (0.2) vs 4.7 (0.2) A and B baseline pain intensity given in text, C baseline pain intensity estimated from Figure 4A Duration of pain (number of days in last 3 months): 45 (2.9) vs 47 (2.9) vs 43 (2.8)	Neck pain intensity during last 3 months (scale 0-9, higher score=worse pain) Days of pain (number of days having neck trouble in last 3 months),	6 and 12 months
Ang 2010	A vs B Age, years: 51 vs 47 Female: 100% vs 100% White: 81% vs 80% Duration of FM, years: 11.8 (4.6) vs 12.3 (7.9) FIQ total: 62.2 (15) vs 67.8 (12) FIQ PI: 5.6 (1.8) vs 5.4 (1.7) FIQ Pain: 7.6 (1.8) vs 7.8 (1.4) PHQ-8: 10 (5.4) vs 13 (4.5) Taking opioids: 52% vs 40%	FIQ total (0-100, higher scores= higher impact of FM; MCID 14%) FIQ PI (0-10, higher score=higher impact of FM) FIQ Pain (Pain VAS): (0-10, higher score=higher pain) PHQ-8 (0-24, higher scores=greater depression)	1.5 months

Author, Year	**Results - Subquestion a** (vs. sham, no treatment, waitlist, attention control)
Andersen 2008	A vs C <u>6-month</u> Pain severity (0-9): 3.4 (0.2) vs 4.2 (0.2), MD -0.80 (-0.87 to -0.73), p<0.001 <u>12-month</u> Pain severity: 3.8 (0.2) vs 4.6 (0.2), MD -0.80 (-0.87 to -0.73), p<0.001 Days of pain: 25 (3.3) vs 30 (3.1) p>0.05 B vs C <u>6-month</u> Pain severity: 3.6 (0.2) vs 4.2 (0.2), MD -0.60 (-0.67 to -0.53), p<0.001 <u>12-month</u> Pain severity: 3.6 (0.2) vs 4.6 (0.2), MD -1.0 (-1.07 to -0.93), p<0.001 Days of pain: 26 (3.2) vs 30 (3.1) p>0.05 Pain intensity 6-month C value and 12-month A, B, C values estimated from Figure 4A
Ang 2010	A vs B 1.5 months, *proportion of patients with clinically meaningful improvement from baseline* : FIQ total: 33% (5*/15) vs. 15%, (2*/13), p=0.3; RR 2.2 (95% CI 0.5, 9.3) *n's back-calculated based on % given and group N *mean change from baseline* : FIQ PI: -0.6 (2.3) vs. 0.5 (1.2), adjusted p=0.13; overall effect size = 0.5 (moderate) FIQ Pain: -0.6 (1.6) vs. -0.3 (1.7), adjusted p=0.6; overall effect size = 0.2 (small) PHQ-8: -0.9 (5.2) vs. 0.0 (4.1), adjusted p=0.8; overall effect size = 0.6

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Andersen 2008	
Ang 2010	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Andersen 2008		NR
Ang 2010		A vs B Withdrawals: 12% vs 13% Adverse events: NR

Author, Year	Funding Source	Quality	Comments
Andersen 2008	Ministry of Culture Committee on Sports Research N200310016 and the National Board of Health under the Ministry of the Interior and Health	Poor	
Ang 2010	NR	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Aslan Telci 2012	Turkey Setting NR	Cervical arthritis with pain for at least 6 months Exclude: Pain or numbness radiating to the arms; impingement; thoracic outlet syndrome; prior cervical surgery; conservative treatment within the last 6 months; proven specific pathology such as a malignancy, fracture or systemic rheumatoid disorder; impingement; thoracic outlet syndrome	Randomized: 60 Treated: NR Analyzed: NR Attrition: NR

Author, Year	Intervention, Comparator
Aslan Telci 2012	A.Home exercises (n=20) consisting of active range of motion, stretching, isometric and dynamic strengthening and endurance exercises, relaxation with breathing exercises, and proprioception. They attended clinic followup once a week for a total of 3 weeks and were asked to continue their exercise program for at least another month (1.5 months in total). B.Nonsteroidal anti-inflammatory drugs and muscle relaxants for 15 days (n=20). All patients received verbal advice regarding pain control, posture, and ergonomics.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Aslan Telci 2012	A vs B vs C Age: 48 vs 52 years Female: 85% vs 75% Pain: 6.67 (1.87) vs 6.41 (2.20) NDI: 14.00 (6.22) vs 10.70 (5.87) Nottingham: 179.7 (116.4) vs 248.4 (121.5) Beck: 10.45 (6.86) vs 10.35 (7.31) Pain duration: 12 vs 12 months BMI: 25 vs 27 Employed: 50% vs 40% Education year: 12 vs 11	Pain severity (VAS scale 0-10, higher score worse pain) NDI: (VAS scale 0-50, higher score greater disability) Nottingham Health Profile (scale 0-100, lower score greater disability) Beck Depression Inventory (scale 0-63, higher score, more severe the depression)	3 and 6 months

Author, Year	**Results - Subquestion a** (vs. sham, no treatment, waitlist, attention control)
Aslan Telci 2012	

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Aslan Telci 2012	A vs B <u>3 month</u> Pain (0-10): 4.08 (2.21) vs 5.08 (1.89), MD -1.0 (95% CI -2.32 to 0.32), p=0.132 NDI (0-50): 9.35 (4.75) vs 11.51 (6.49), MD -2.16 (95% CI -5.80 to 1.48), p=0.237 NHP (0-100): 89.21 (93.22) vs 229.97 (132.29), MD -140.76 (95% CI -214.0 to -67.5), p=0.0004 BDI (0-63): 6.75 (4.94) vs 10.70 (8.46), MD -3.95 (95% CI -8.38 to 0.48), p=0.079 <u>6 month</u> Pain:4.52 (2.52) vs 5.31 (2.05), MD -0.79 (95% CI -2.26 to 0.68), p=0.284 NDI: 11.85 (5.60) vs 13.65 (6.59), MD -1.8 (95% CI -5.71 to 2.11), p=0.358 NHP: 122.3 (89.8) vs 257.6 (136.0), MD -135.3 (95% CI -209.1 to -61.5), p=0.007 BDI: 8.30 (5.69) vs 11.75 (8.74), MD -3.75 (95%CI -8.47 to 0.97), p=0.116

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Aslan Telci 2012		NR

Author, Year	Funding Source	Quality	Comments
Aslan Telci 2012	NR	Poor	Nottingham scores do not fall within the range of possible scores (0-100)

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Assefi 2005	United States, setting not reported	Inclusion Criteria: English speaking adults >18 diagnosed with Fibromyalgia with baseline global pain score of 4 or greater on a VAS (0-10). Kept fibromyalgia related treatments/therapies constant throughout study. Exclusion Criteria: Patients who reported other pain-related medical conditions or potential contraindications to acupuncture, were pregnant or breastfeeding, used narcotics that could blunt the effects of acupuncture, were involved in litigation related to fibromyalgia or had previously received acupuncture.	Randomized: 100 Treated: 96 Analyzed: 86 Attrition: 14% (14/100)

Author, Year	Intervention, Comparator
Assefi 2005	A.Acupuncture (n=23) Patients randomized to intervention group received directed acupuncture in accordance with Traditional Chinese Medicine. No. of Sessions: 24 (2/week for 12 weeks) Needle Depth: Standard depth(?) Length of Insertion: 30 min/acupoint Needles: Disposable Chinese, Japanese or Korean needles, (34 to 40 gauge) according to practitioner preference. Sham Acupuncture (groups B, C, D): Participants were randomized to three different possible sham acupuncture treatments, each of which followed the same treatment protocol as the intervention group. B.Needling for Unrelated Condition (n=22) One controlled for acupoint specificity and involved acupuncture typically used to treat irregular menses (rather than fibromyalgia points), in accordance with Traditional Chinese Medicine. C.Sham Needling (n=22) Another sham intervention used body locations not recognized as true acupoints or meridians for needling (sham needling). D.Simulated Acupuncture (n=19) The third sham treatment controlled for needle insertion, and involved noninsertive simulated acupuncture at the same acupoints used in the directed acupuncture.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Assefi 2005	A vs. B vs. C vs. D Age (SD): 46 vs. 46 vs. 49 vs. 48 years Female: 88% vs. 96% vs. 100% vs. 96% Race: 96% vs. 88% vs. 96% vs. 92% white Mean (SD) duration of pain, years: 12 (18) vs. 9 (7) vs. 9 (7) vs. 10 (16) Pain Intensity (VAS, 0-10): 7.0 (2) vs. 6.9 (2) vs. 6.8 (2) vs. 7.3 (2) Fatigue Intensity (VAS, 0-10): 7.5 (2) vs. 8.1 (1) vs. 7.3 (2) vs 7.9 (2) Sleep Quality (VAS, 0-10): 4.0 (2) vs. 2.8 (2) vs. 3.7 (2) vs. 2.6 (2) Overall Well-Being (VAS, 0-10): 4.2 (2) vs. 4.7 (2) vs 3.9 (2) vs. 3.7 (2) SF-36 Mean Summary Scores Physical Component: 28 (8) vs. 31 (9) vs. 31 (8) vs. 32 (9) Mental Component: 42 (11) vs. 41 (12) vs. 42 (8) vs. 42 (9) *Prior preventive therapy separated out by therapy type, these values represent minimum percentage reported who sought prior therapies.	Pain Intensity (VAS, 0-10: higher scores indicate severity of pain) Intensity of Fatigue (VAS, 0-10: higher scores indicate severity of pain) Sleep Quality (VAS, 0-10: higher scores indicate better sleep) Overall Well-Being (VAS, 0-10: higher scores indicate better quality of life) SF-36 Physical Component (SF-36 PCS; physical health scores summed and negatively weighted by mental health scores, higher scores indicate more optimal health) SF-36 Mental Component (SF-36 MCS; mental health scores summed negatively weighted by physical health scores, higher scores indicate more optimal health)	3 and 6 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Assefi 2005	A. vs B vs. C vs. D. 3 months: Pain Intensity (VAS)*: 6.0 vs. 5.4 vs. 5.4 vs. 4.5; p> 0.2 Intensity of Fatigue (VAS)*: 6.0 vs. 6.0 vs. 4.8 vs. 4.3; p=0.19 Sleep Quality (VAS)*: 4.3 vs. 4.1 vs. 5.2 vs. 5.5; p=0.18 Overall Well-Being (VAS)*: 4.9 vs. 4.9 vs. 5.0 vs. 6.3; SF-36 Physical Component Summary Score*: 31 vs. 39 vs. 31.5 vs. 40 SF-36 Mental Component Summary Score*: 46 vs. 46.5 vs. 48.5 vs. 47 6 months: Pain Intensity (VAS)*: 5.7 vs. 6.0 vs. 5.2 vs. 5.2 Intensity of Fatigue (VAS)*: 6.4 vs. 6.9 vs. 5.7 vs. 4.4 Sleep Quality (VAS)*: 4.3 vs. 3.4 vs. 5.4 vs. 5.5 Overall Well-Being (VAS)*: 4.6 vs. 4.6 vs. 5.7 vs. 5.7 SF-36 Physical Component Summary Score*: 31 vs. 36 vs. 31. vs. 39 SF-36 Mental Component Summary Score*: 43 vs. 45 vs. 50 vs. 46.5 *outcome values were estimated from graphs. The following MD's were taken from a multivariate regression model that adjusted for time across all weeks of the study and pooled all the sham intervention data: Pain Intensity (VAS): MD 0.5 cm (95% CI, -0.3 to 1.2 cm); P>0.2 Intensity of Fatigue (VAS): MD 0.5 cm (95% CI, -0.2 to 1.2cm); P=0.19 Sleep Quality (VAS): MD -0.5 cm (95% CI, -1.3 to 0.2 cm); P=0.18 Overall Well-Being (VAS): MD -0.3 (95%CI, -1.0 to 0.3 cm); P>0.2 SF-36 Physical Component Summary Score: MD -0.4 (95%CI, -2.3 to 1.5); P>0.2 SF-36 Mental Component Summary Score: MD -1.5 (95%CI, -4.0 to 1.0); P>0.2

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Assefi 2005	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Assefi 2005	NR	89 participants reported AEs. 37% (35/96) reported discomfort at needle insertion sites, 30% (29/96) reported bruising, 3% (3/96) reported nausea and 0.3%(1/96) felt faint at some point during the study. Patients assigned to simulated acupuncture (29%, 5/19) had significantly less discomfort than those in directed acupuncture (61%, 14/23), acupuncture for unrelated condition (70%, 15/22) or sham needling (64% 14/22); P = 0.02

Author, Year	Funding Source	Quality	Comments
Assefi 2005	This project was funded by Research Grant RO1AT00003 from the National Center for Complementary and Alternative Medicine.	Good	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Banth 2015	Iran Number of centers: unclear Clinic and Outpatient	Patients age 30–45 years, history of nonspecific medical history of NSCLBP, persisting pain for persisting for ≥6 months, female, educated at least up to high school Exclude: History of spine surgery, combination with other chronic disease, psychotherapy in the last 2 years, unavailability in 3 months	Randomized: 88 Treated: 88 Analyzed: 48 Attrition: 54% (40/88)
Baptista 2012	Brazil Outpatient rheumatology clinics	Inclusion: FM diagnosis based on ACR 1990 criteria, female, age between 18 and 65 years, not having altered treatment in past 4 weeks Exclusion: other rheumatic diseases, painful joint diseases, uncontrolled cardiopulmonary diseases, diseases of the lower limbs, uncontrolled diabetes	Randomized: 80 Analyzed: 75 Attrition: 6% (5/80)

Author, Year	Intervention, Comparator
Banth 2015	A. Mindfulness-based stress reduction, 8 1.5 hour group sessions over 8 weeks, with 30-45 minute daily home sessions B. Usual care 48 of 88 patients were analyzed, n for each group not reported
Baptista 2012	A. Dance (n=38): One hour belly dance classes twice a week for 16 weeks B. Waiting list control (n=37), with dance offered at end of the study

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Banth 2015	A vs. B (NR) Age: 40 years Female: 100% Race: NR Duration of symptoms: 6 months Very low physical quality of life: 9.8% Low physical quality of life: 54.8% Moderate physical quality of life: 36.4%	McGill Pain questionnaire total score (0 to 45) Quality of life (SF-12) (eight health constructs Physical functioning; role physical; bodily pain; general health; vitality; social functioning; role emotional; and mental health with scores from 0-100)	1 month
Baptista 2012	A vs B: Age: 50 vs 49 Female: 100% vs 100% Race NR FIQ: 5.9 vs 6.3 6-minute walk test: 372.8 vs 332.0, p=0.015 Pain VAS: 7.7 vs 7.5 SF-36 Pain: 29.6 vs 25.7 BDI: 23.9 vs 21.2 STAI part 1: 50.5 vs 52.8 STAI part 2: 51.1 vs 53.0, p=0.06 SF-36 Function: 44.9 vs 32.6, p<0.001 SF-36 Limitation due to physical aspects: 24.7 vs 8.8, p<0.001 SF-36 Mental Health: 46.0 vs 43.4	FIQ (0-10, higher scores=worse function and symptom severity) 6 minute walk test (meters traveled on 20-meter course) (higher scores =less impairment) Pain VAS (0-10, higher scores=greater pain) Beck Depression Inventory (0-21, higher scores=greater depression) State-Trait Anxiety Inventory (scale NR, higher scores=greater anxiety) SF-36 (0-100, higher scores = better quality of life)	4 months

Author, Year	**Results - Subquestion a** (vs. sham, no treatment, waitlist, attention control)
Banth 2015	A vs. B, (mean, SD) <u>Baseline</u> McGill Pain questionnaire (0-45) 26.08 (5.4) vs. 26.71 (4.4) SF-12 Mental component (0-100) 23.44 (4.0) vs. 22.38 (3.8) SF-12 Physical component (0-100) 20.83 (4.6) vs. 19.96 (3.5) <u>1 month</u> McGill Pain questionnaire 13.58 (3.8) vs. 23.60 (4.1) SF-12 Mental component 31.54 (4.3) vs. 24.29 (5.2) SF-12 Physical component 28.08 (4.2) vs. 21.08 (3.3)
Baptista 2012	A vs B <u>4 months:</u> FIQ: 4.3 (1.8) vs 5.9 (1.9); MD -1.6 (95% CI -2.45 to -0.75), p=0.0004 Pain VAS: 4.7 (2.6) vs 7.3 (1.7); MD -2.6 (95% CI -3.61 to -1.59), p <0.0001 BDI: 23.1 (15.3) vs 23.5 (13.7); MD -0.40 (95% CI -7.09 to 6.29), p=0.91 STAI part 1: 49.4 (10.0) vs 51.8 (9.4); MD -2.40 (95% CI -6.87 to 2.07), p=0.29 STAI part 2: 49.8 (9.1) vs 54.1 (10.1); MD -4.3 (95% CI -8.72 to 0.12), p =0.06 SF-36 function: 56.3 (19.9) vs 39.1 (22.0); MD 17.2 (95% CI 7.55 to 26.85), p = 0.0007 SF-36 Limitation due to physical aspects: 36.5 (32.4) vs 13.8 (26.5); MD 22.7 (95% CI 9.06 to 36.34), p=0.001 SF-36 Pain: 46.0 (19.2) vs 29.1 (21.1); MD 16.9 (95% CI 7.62 to 26.18), p = 0.0005 SF-36 Mental Health: 52.3 (20.8) vs 46.2 (22.6); MD 6.1 (95% CI -3.89 to 16.09), p =0.23

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Banth 2015	NR
Baptista 2012	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Banth 2015	NR	NR
Baptista 2012		NR

Author, Year	Funding Source	Quality	Comments
Banth 2015	None	Poor	Pre-post quasi time series intervention study
Baptista 2012	CAPES scholarship	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Basford 1999	US Number of centers: 1 Outpatient rehabilitation clinic	Healthy adults ages 18-70 years with nonradiating low back pain more than 30 days. Exclude: patients with litigation or workman's compensation issues pending and/or received corticosteroids within last 30 days.	Randomized: 59 Treated: 59 Analyzed: 56 Attrition: 5% (3/59)
Battisti 2004	Italy, outpatient	Inclusion Criteria: NR Exclusion Criteria: NR	Randomized: 90 Treated: 90 Analyzed: 90 Attrition: 0% (0/90)

Author, Year	Intervention, Comparator
Basford 1999	A.Nd:YAG laser (n=27): 542mW/cm^2 for 90 seconds at two sites simultaneously at four equally spaced levels (a total of 8 points) along the L2 to S3 Para spinal tissues; 3 times a week for 4 weeks. B.Sham treatment (n=29): Same as above but irradiated with inactive probes.
Battisti 2004	A.Therapeutic Application of Musically Modulated Electromagnetic Field (TAMMEF) (n=30) Application of low frequency electromagnetic fields through two amplifiers (A and B) feeding two electromagnets. The anatomical region treated is placed between opposing faces of the electromagnets (3x4 cm). The current from amplifier B feeds a loud speaker that plays music. The music modifies parameters (frequency, intensity, waveform) of the electromagnetic field in time, randomly varying within respective ranges. No. of Sessions: 15 daily sessions Length of Sessions: 30 minutes each B.Extremely Low Frequency (ELF) (n=30) Similar treatment as Intervention A except the electromagnetic field is stabilized at a frequency of 100Hz in a sinusoidal waveform. No. of Sessions: 15 daily sessions Length of Sessions: 30 minutes each C.Simulated (Sham) Frequency Field (n=30) Functionally similar operation to the other groups except a simulated (noneffective) field is used, but the patients remain blinded to its effectiveness. No. of Sessions: 15 daily sessions Length of Sessions: 30 minutes each

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Basford 1999	A vs. B Age: 48 vs.48 years Female: 40% vs. 55% Nature of pain (% described as burning or aching: 87% vs. 72% Symptom duration (months): 4.5 vs. 6.5 Previous physical therapy, injection or chiropractic treatment: 57 vs. 69 Analgesic use (number per day): 4.6 vs. 4.4 Lumbar spine X-rays showing changes compatible with mild to moderate degenerate spine disease (%): 70 vs. 86	Oswestry score (Oswestry Disability Questionnaire, total scored/ 50 x 100= %) Patient perception of benefit Lumbar mobility (Schober test, marking points 5cm above and 5cm below the L5-Sl junction standing in a neutral position and measuring the excursion of points when bending forward to their maximal extent) Pain (Visual analog scales (0 mm, no pain;100 mm, incredibly severe pain)	Short term 1 month
Battisti 2004	A+B Age: 58.9 (7.4) Female: 70% Race: NR Mean Duration of Chronicity: 11 (3.1) A vs. B Mean Lequesne Pain Score*: 6.88 vs. 6.28 vs. 6.15 Mean Lequesne Function Score*: 3.65 vs. 4.28 vs. 3.48 *The study separated outcome values out into slight, moderate and severe disease patient groups for each treatment arm. These values are combined values for each intervention groups estimated from graphs in the study. SD was not reported.	Primary: Lequesne Algo-Functional Index for Knee Osteoarthritis Lequesne Pain (range 0-10: higher scores indicate severity of pain) Lequesne Function (range 0-10: higher scores indicate better function)	immediate post-treatment, 1 month

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Basford 1999	A vs B, mean Baseline Oswestry Disability Index: 21 vs. 25, mean difference -3.5 (95% CI -7.8 to 0.8) Maximal pain in last 24 hours (0-100 VAS): 35.2 vs. 37.4, mean difference -2.5 (95% CI -14.9 to 10.0) 2-month outcomes Oswestry Disability Index (0-100): 14.7 vs. 22.9, difference -8.2 (95% CI -13.6 to -2.8) Maximal pain in last 24 hours (0-100 VAS): 19.1 vs. 35.1, difference -16.0 (95% CI -28.3 to -3.7)
Battisti 2004	A vs. C 1 month Mean Lequesne Pain Score*: 1.4 vs. 6.85 Mean Lequesne Functionality*: 6.5 vs. 3.83 B vs. C 1 month Mean Lequesne Pain Score*: 1.4 vs. 6.85 Mean Lequesne Functionality*: 7.1 vs. 3.83 *The study separated outcome values out into slight, moderate and severe disease patient groups for each treatment arm. These values are combined values for each intervention groups estimated from graphs in the study. SD was not reported.

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Basford 1999	NR
Battisti 2004	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Basford 1999	NR	None
Battisti 2004	NR	NR

Author, Year	Funding Source	Quality	Comments
Basford 1999	Mayo Clinic and Foundation	Fair	
Battisti 2004	This study was supported in part by a contribution from the “Fondazione del Monte dei Paschi di Siena”, Siena, Italy.	Poor	*The study separated values out into slight, moderate and severe disease patients for each treatment arm. These values are combined values for each intervention groups estimated from graphs in the study. SD was not reported.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Bendix 1995 1997 1998 **Note: Project B in Bendix 1998**	Denmark Number of centers: Unclear Inpatient	Patients age 18 to 59 with chronic LBP for at least 6 months and threatened job situation Exclude: Patients with current disc herniation, surgically remediable back lesions, inflammatory disease, pregnancy, cancer, clinically relevant fractures, and social pension	Randomized: 132 Treated: 106 Analyzed:106 Attrition: 11% (14/132) at 3.25 months, 22% at 12 months

Author, Year	Intervention, Comparator
Bendix 1995 1997 1998 **Note: Project B in Bendix 1998**	A: Multidisciplinary treatment (n=46): Muscle, psychological, and ADL testing, followed by exercise (fitness, endurance, coordination, stretching, progressive weight training), occupational therapy (focused on work situations and work intensification), psychological treatment (behavioral approach, daily relaxation, weekly individualized counseling), education, job analysis course, recreational activities. 7.5 hours/day daily for 3 weeks (39 hours/per week), then one 6 hour session once weekly for 3 weeks, including psychological, physical, and ergonomic training. B: Combined psycho-physical program (n=43): Psychological pain management, active physical training: "warm-up" exercises, progressive weight training, 2 hour sessions twice weekly for 6 weeks (total 24 hours) C: Exercise (n=43): Aerobics, progressive weight training, and traditional Swedish "back to school "principles, 2 hour sessions twice weekly for 6 weeks (total 24 hours)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Bendix 1995 1997 1998 **Note: Project B in Bendix 1998**	A vs. B vs. C Age (mean): 40 vs. 44 vs. 42 Female: 75% vs. 77% vs. 74% Race: NR Medication: 75% vs. 66% vs. 74% Back surgery: 15% vs. 17% vs. 32% Back pain (0-10): 5.3 vs. 5.9 vs. 5.4	Low Back Pain Rating Scale (0-30, higher score indicates more disability) Pain (0-10 NRS) Overall assessment (1=much better to 5=much worse) Prescription medication use (0=no medications to 10=morphine >4 days/week) Increase in proportion able to work	3.25, 12, 24, and 60 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Bendix 1995 1997 1998 **Note: Project B in Bendix 1998**	NR

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Bendix 1995 1997 1998 **Note: Project B in Bendix 1998**	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Bendix 1995 1997 1998 **Note: Project B in Bendix 1998**	A vs. B vs. C, median (IQR) <u>Baseline (IQR not reported)</u> Low Back Pain Rating Scale (0-30): 15.5 vs. 15.3 vs. 14.4 Back pain (0-10 NRS): 5.3 vs. 5.9 vs. 5.4 Leg pain (0-10 NRS): 2.9 vs. 3.7 vs. 3.7 Days of sick leave in last 3 years: 296 vs. 440 vs. 300 <u>3.25 months</u> Low Back Pain Rating Scale (0-30): 8.5 (5-15) vs. 16.1 (11-19) vs. 13.5 (10-17), p=0.002 Back pain (0-10 NRS): 2.7 (1.4-4.3) vs. 5.6 (3.8-7.6) vs. 4.4 (2.4-6.2), p<0.001 Leg pain (0-10 NRS): 0.4 (0-2.3) vs. 3.1 (0.5-5.9) vs. 2.6 (0.1-4.6), p=0.01 Days of sick leave: 25 (0-103) vs.122 (60-122) vs. 13 (0-122), p=0.005 Health care system contacts: 0.5 (0-2.4) vs. 2.8 (0.4-4.6) vs. 1.3 (0.1-3.1), p=0.05 <u>12 months</u> Low Back Pain Rating Scale (0-30): 8.9 (5-13) vs. 16.4 (14-19) vs. 13.7 (9-17), p<0.001 Back pain (0-10 NRS): 3.3 (2.1-5.6) vs. 6.5 (4.8-7.7) vs. 5.3 (3.3-7.6), p=0.005 Leg pain (0-10 NRS): 2.1 (0.2-4.13) vs. 4.8 (2.3-7.3) vs. 2.8 (1.4-7.0), p=0.008 Days of sick leave: 52 (0-127) vs. 295 (0-390) vs. 100 (0-390), p=0.002 Health care system contacts: 4.5 (0.3-12.3) vs. 12.0 (0.8-23.3) vs. 11.8 (4.0-25.0), p=0.002 <u>24 months</u> Low Back Pain Rating Scale (0-30): 10 (6-14) vs. 17 (9-21) vs. 14 (9-17), p=0.003 Back pain (0-10 NRS): 3 (2-6) vs. 6 (4-8) vs. 5 (3-7), p=0.08 Leg pain (0-10 NRS): 2 (0-5) vs. 5 (1-6) vs. 4 (2-6), p=0.08 Days of sick leave: 2.5 (0-29) vs. 37 (0-552) vs. 11 (0-80), p=0.06 Health care system contacts: 5 (0-19) vs. 21 (3-34) vs. 14 (7-27), p=0.03 Overall assessment (1-5): 2 (1-3) vs. 3 (2-3) vs. 3 (2-4), p=0.005 <u>60 months (IQR not reported)</u> Low Back Pain Rating Scale (0-30): 8 vs. 16 vs. 14, p=0.02 Back pain (0-10 NRS): 4 vs. 6 vs. 5, p=0.3 Leg pain (0-10 NRS): 3 vs. 4 vs. 4, p=0.07 Prescription medications (0-10): 0 vs. 4 vs. 4, p=0.009 Overall assessment (1-5): 2 vs. 3 vs. 3, p=0.004 Increase in proportion able to work: 30% vs. 23% vs. 0%, p=0.001 Days of sick leave: 13 vs. 11 vs. 88, p=0.2 Health care system contacts: 15 vs. 10 vs. 24, p=0.2 Back surgery: 5% vs. 10% vs. 10%, p=0.7	NR

Author, Year	Funding Source	Quality	Comments
Bendix 1995 1997 1998 **Note: Project B in Bendix 1998**	Danish Rheumatism Association, Nycomed-DAK, AP Moller and Wife's Foundation, Pensam, the Danish Insurance Association, Meyer's Foundation, Minister Ema Hamilton's Foundation, Director Ib Henriksen's Foundation, the Research Foundation of Copenhagen University, Hafnia Foundation, Peter Ryholt's Foundation, Ingrid Munkholm's Foundation, Danish Society for Manual Medicine, Lily Benthine Lund's Foundation	Fair	Multidisciplinary treatment patients only had 3 weeks of treatment, the other groups had 6 weeks though.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Bendix 1996 1998 **Note: Project A in Bendix 1998**	Denmark Number of centers: 1 Outpatient	Patients 18 to 59 years old with disabling LBP >6 months and threatened job situation Exclude: Patients with current disk herniation inflammatory disease of the back, pregnancy, cancer, osteoporosis with or without fractures and people receiving social pensions	Randomized: 106 Treated: 104 Analyzed: 94 Attrition: 11% (94/106) at 3.26 months, 9.4% (10/106) at 24 months

Author, Year	Intervention, Comparator
Bendix 1996 1998 **Note: Project A in Bendix 1998**	A: Multidisciplinary treatment (n=55): Muscle, psychological, and ADL testing, followed by exercise (fitness, endurance, coordination, stretching, progressive weight training), occupational therapy (focused on work situations and work intensification), psychological treatment (behavioral approach, daily relaxation, weekly individualized counseling), education, job analysis course, recreational activities. 7.5 hours/day daily for 3 weeks (39 hours/per week), then one 6 hour session once weekly for 3 weeks, including psychological, physical, and ergonomic training. B. Control (n=51): Standard medical care

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Bendix 1996 1998 **Note: Project A in Bendix 1998**	A vs. B Age (median): 41 vs.40 years Female: 71% vs. 69% Race: NR Back pain (0-10): 6.1 vs. 6.1 Medication for LBP: 80% vs. 73% Previous back surgery: 16% vs. 18%	Low Back Pain Rating Scale (0-30, higher score indicates more disability) Pain (0-10 NRS) Days of sick leave Health care system contacts Overall assessment (1=much better to 5=much worse) Prescription medication use (0=no medications to 10=morphine >4 days/week) Increase in proportion able to work	3.25, 24, and 60 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Bendix 1996 1998 **Note: Project A in Bendix 1998**	A vs. B , median (IQR) <u>Baseline (IQR not reported)</u> Low Back Pain Rating Scale (0-30): 16.9 vs. 15.9 Back pain (0-10 NRS): 6.1 vs. 6.1 Leg pain (0-10 NRS): 4.1 vs. 4.6 Days of sick leave in 3 years: 340 vs. 370 <u>3.25 months</u> Low Back Pain Rating Scale (0-30): 12.1 (7.2-16.8) vs. 16.8 (13.1-20.1), p<0.001 Back pain (0-10 NRS): 5.7 (2.3-7.8) vs. 6.9 (4.8-7.8), p=0.05 Leg pain (0-10 NRS): 3.5 (0.3-7.0) vs. 5.4 (3.0-7.3), p=0.17 Days of sick leave: 10 (0-122) vs. 122 (24.5-122), p=0.02 Contacts to health-care system: 1.6 (0.4-3.9) vs. 5.3 (1.8-11.5), p<0.001 <u>24 months</u> Low Back Pain Rating Scale (0-30): 16 (8-19) vs. 15 (11-18), p=0.9 Back pain (0-10 NRS): 6 (3-8) vs. 6.5 (4-7), p=0.5 Leg pain (0-10 NRS): 4.5 (1-7) vs. 4 (1-7), p=0.9 Days of sick leave: 15 (0-123) vs. 123 (71-375), p<0.001 Health care system contacts: 12 (4-25) vs. 26 (16-58), p<0.001 Overall assessment (1-5): 3 (2-3) vs. 3 (2-4), p=0.3 <u>60 months</u> Low Back Pain Rating Scale (0-30): 12 vs. 16, p=0.2 Back pain (0-10 NRS): 5 vs. 5, p=1.0 Leg pain (0-10 NRS): 4 vs. 5, p=0.6 Prescription medications (0-10): 3 vs. 4, p=0.7 Overall assessment (1-5): 2 vs. 3, p=0.1 Increase in proportion able to work: 11% vs. 34%, p=0.05 Days of sick leave: 10 vs. 50, p=0.4 Health care system contacts: 16 vs. 48, p=0.1 Back surgery: 7% vs. 12%, p=0.4

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Bendix 1996 1998 **Note: Project A in Bendix 1998**	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Bendix 1996 1998 **Note: Project A in Bendix 1998**	NR	NR

Author, Year	Funding Source	Quality	Comments
Bendix 1996 1998 **Note: Project A in Bendix 1998**	Danish Rheumatism Association, Nycomed-DAK, AP Moller og Hustrus Fond, Pensam, Assurandorsocietetet, Meyer's Foundation, Minister Erna Hamilton's Foundation, Direkt0r lb Henriksen's Foundation, The Research Foundation of the Copenhagen University, Hafnia Foundation, Peter Ryholt's Foundation, Ingrid Munkholm's Foundation, Danish Society for Manual Medicine, Lily Benthine Lund's Foundation	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Bendix 2000	Denmark Number of centers: 1 Outpatient back center	Patients with chronic LBP referred to a back center with threatened job situation due to LBP Exclude: Patients with herniated nucleus pulposus, surgically treatable instability with or without spondylolisthesis, inflammatory back disease, osteoporosis, cancer, or any medical or psychiatric condition preventing intensive physical training in classes, and patients who received a disability pension	Randomized: 138 Treated: 106 Analyzed: 99 Attrition: 22% (99/138)
Bennell 2005	Australia, 1 community setting	Inclusion: age >50 years, knee pain on most days of the past month, osteophytes on xray, and pain or difficulty in rising from sitting or climbing stairs. Exclusion: physiotherapy or knee surgery (in the previous 12 months), lower limb arthroplasty, Synvisc or intra-articularsteroid injections (in the previous six months), a systemic arthritic condition, a severe medical condition, poor skin condition, known allergic reaction to tape, or a body mass index of more than 36	Randomized: 140 Treated: 124 Analyzed: 119 Attrition: 15% (21/140)

Author, Year	Intervention, Comparator
Bendix 2000	A: Functional Restoration (n=59): Physical training (supervised aerobic class for 1 hour, strengthening for 1 hour), occupational therapy (1.5 hours, including lifting, push and pull exercises, sitting and standing work positions, biofeedback), psychologic therapy (1.5 hours, including cognitive-behavioral therapy, relaxation and visualization), stretching, education/back school, recreational activities. 7.5 hours/day for 3 weeks, then 7.5 hour sessions 2 and 3 weeks after the intensive program, and at 2 months B: Outpatient physical training (n=68): 1.5 hour sessions, 3 times a week for 8 weeks (aerobic and strengthening exercises)
Bennell 2005	A.Physiotherapy (n=73) Knee taping; exercises to retrain the quadriceps, hip, and back muscles; balance exercises; thoracic spine mobilization; and soft tissue massage. All treatments were individual sessions lasting 30 to 45 minutes once weekly for four weeks, then fortnightly for eight weeks. Home exercises were to be done three times daily. Participants were provided with standardized home exercise. B.Control (n=67) Placebo: sham ultrasound and topical non-therapeutic gel. 30 to 45 minutes once weekly for four weeks, then fortnightly for eight weeks. Participants were compliant during the intervention period, with 95% of treatment sessions attended. During the intervention and follow up periods, 72% and 50% of home exercise sessions were completed, respectively.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Bendix 2000	A vs. B Age (median): 40 vs. 43 years Female: 66% vs.65% Race: NR	Back pain (0–10) Leg pain (0-10) Low Back Pain Rating Scale (0-30) Sick leave (days) Health care contacts (#) Overall assessment (1-5, 1=much better and 5=much worse)	10 months
Bennell 2005	A vs B Age: 67 vs 70 years Female: 68% vs 66% BMI: 29 vs 29 Duration of Symptoms: 9.6 vs 8.7 years WOMAC, Physical Function (mean, 95% CI): 27.6 (25.2, 29.9) vs 28.4 (26.0, 30.7) WOMAC, Pain (mean, 95% CI): 8.2 (7.5, 8.9) vs. 8.0 (7.3, 8.6) VAS Pain on movement (mean, 95% CI): 5.3 (4.8, 5.7) vs. 5.2 (4.8, 5.6) KPS, Severity (mean, 95% CI): 16.6 (15.5, 17.7) vs. 16.4 (15.5, 17.3) KPS, Frequency (mean, 95% CI): 23.5 (22.5, 24.5) vs. 22.8 (21.8, 23.7) SF-36, Physical Function (mean, 95% CI): 40.8 (36.0, 45.6) vs. 40.8 (36.6, 45.0) SF-36, Bodily Pain (mean, 95% CI): 53.7 (48.5, 58.9) vs. 57.0 (52.8, 61.1) SF-36, Role Physical (mean, 95% CI): 33.7 (24.6, 42.8) vs. 34.7 (24.8, 44.6) AQoL (mean, 95% CI): 0.45 (0.41, 0.49) vs. 0.46 (0.42, 0.51)	Responders: global change in pain (proportion of patients with a score of 4 or 5 on a 5 point Likert scale); Responders: proportion of patients with a clinically significant change of ≥1.75 on VAS; WOMAC physical function scores (scale 0-68; higher score=worse function); WOMAC pain scores (scale 0-20; higher score=more severe pain); Pain on movement over the past week (VAS, 0-10; higher score=greater pain); Knee Pain Scale (KPS), Severity subscale (scale 0-36, higher scores=more severe pain); Knee Pain Scale (KPS), Frequency subscale (scale 0-30, higher scores=more frequent pain); Short Form 36 general health questionnaire (SF-36), Physical Function, Physical Role, and Bodily Pain subscales (scales 0-100, higher scores=better quality of life); Assessment of quality of life (AQoL) index (scale -0.04 to 1.0, higher scores=greater quality of life)	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Bendix 2000	NR
Bennell 2005	A vs B (mean, 95% CI) <u>3 months (ITT analysis)</u> Responders, global improvement in pain: 59% vs. 50%, p=0.31 Responders, VAS pain: 58% vs. 42%, p=0.07 WOMAC, Physical Function: 20.0 (17.4, 22.6) vs 21.7 (19.0, 24.4); MD in change scores between groups: -0.9 (-4.4, 2.7) WOMAC, Pain: 5.8 (5.1, 6.5) vs 6.0 (5.2, 6.8); MD in change scores between groups: -0.4 (-1.5 to 0.7) VAS pain on movement: 3.2 (2.8, 3.6) vs 3.5 (3.0, 4.1); MD in change scores between groups: -0.5 (-1.2 to 0.3) KPS, Severity: 13.5 (12.5, 14.5) vs. 14.3 (13.4, 15.3); MD in change scores between groups: -1.0 (-2.5, 0.6) KPS, Frequency: 19.4 (18.1, 20.7) vs. 20.3 (18.9, 21.7); MD in change scores between groups: -1.7 (-3.5, 0.1) SF-36, Physical Function: 50.5 (45.7, 55.4) vs 46.2 (40.7, 51.8); MD in change scores between groups: 4.3 (-1.8, 10.4) SF-36, Bodily Pain: 60.4 (55.0, 65.7) vs 61.8 (56.3, 67.4); MD in change scores between groups: 1.8 (-6.7, 10.3) SF-36, Role Physical: 47.0 (38.4, 55.6) vs 46.5 (36.7, 56.3); MD in change scores between groups: 1.6 (-11.1, 14.3) AQoL: 0.52 (0.48, 0.56) vs 0.48 (0.43, 0.52); MD in change scores between groups: 0.05 (0.01, 0.10)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Bendix 2000	NR
Bennell 2005	NA

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Bendix 2000	A vs. B, median (IQR) Baseline not reported 10 months Back pain (0–10): 5.1 (2–7) vs. 5.7 (3–7.3), p=0.33 Leg pain (0-10): 2.8 (0-7) vs. 3.5 (1-6.3), p=0.43 Low Back Pain Rating Scale, ADL assessment (0–30): 12 (6–21) vs. 13 (9–19), p=0.41 Overall assessment (1–5): 1.7 (1–3) vs. 2.7 (2–3.3), p=0.03 Sick leave (days): 5.5 (0-113) vs. 2.5 (0-301), p=1.00 Health care contacts (#): 2.5 (0-10) vs. 4 (0-12.3), p=0.28 Work capable: 75% (36/48) vs. 69% (35/51), p=0.64	NR
Bennell 2005	NA	A vs B Withdrawals: 23% (17/73) vs 6% (4/67); RR 6.0 (95% CI 1.4, 25.5) Group A: Minor skin irritation (48%), increased pain with exercises (22%), pain with massage (1%) Group B: Increased pain (2%), itchiness and pain with application of gel (2%) (All were minor and short-lived)

Author, Year	Funding Source	Quality	Comments
Bendix 2000	Danish Rheumatism Association, the Gerda and Aage Hensch Foundation, the Director Ib Henriksen's Fund, the Insurance Company for Industrial Injuries, the Lilly Benthine Lunds Fund, the DANICA Pension, the Municipal Pension Insurance Company Ltd., and the Danish Society for Manual Medicine	Fair	
Bennell 2005	National Health and Medical Research Council (grant No 114277)	Fair	The primary outcomes were reanalyzed using only the data from those who completed the trial. At 24 weeks, a greater proportion of physiotherapy participants (77%) reported global improvement (from baseline) compared with placebo participants (49%) (p = 0.005) at this time. More physiotherapy participants (66%) reported a clinically relevant reduction in pain on VAS than did placebo participants (48%) (p = 0.027). Also report drug use (but not opioids specifically): drug use was similar between the physiotherapy and placebo groups over the treatment period (analgesics, 23%v21%; non-steroidal anti-inflammatory drugs, 22%v24%; glucosamine, 3%v6%).

Author, Year	Country Number of centers and setting	Inclusion/Exclusion Criteria	Number randomized, analyzed Attrition
Bennell 2016	Australia Multiple centers, number NR Type of center NR	Inclusion: ≥50 yars old, diagnosis of knee OA fulfilling ACR criteria, knee pain ≥3 months, average pain during previous week ≥40 on 100 mm VAS scale, at least moderate difficulty with daily activities (WOMAC physical function subscale ≥25). Exclusion: systematic arthritic conditions such as rheumatoid arthritis, medical condition precluding safe exercise, self-reported history of serioius mental illness, self-reported diganosis of current clinical depression, neurological condition, multiple sclerosis or stroke, knee surgery or total joint replacement within past 6 months, current or previous use within 3 months of oral or intra-articular corticosteroid use, physiotherapy, chiropractic or acupuncture treatment or exercises specifically for the knee in past 6 months, walking exercise for >30 minutes continuously daily, >2 times per week of structured and/or supervised exercise program, participating in or previous participation in a formal PCST program, inability to walk unaided, inability to comply with the study protocol	Randomized: 149 Analyzed: 122 Attrition: 18% (27/149)

Author, Year	Intervention, Comparator
Bennell 2016	A. Pain coping skills training (n=74): 10 sessions of 45 minutes over 12 weeks. Sessions consisted of pain education as well as training in cognitive and behavioral pain coping skills and application. Participants were instructed to practice skills daily during 12 week intervention and as needed during follow-up period. B. Exercise (n=75): 10 sessions of 25 minutes over 12 weeks. Sessions consisted of 6 strenthening exercises. Participants were instructed to perform exercises 4 times a week during 12 week intervention and 3 times a week during the follow-up period.

Author, Year	Study participants	Outcome measures	Duration of followup
Bennell 2016	A vs B Age, years: 63 vs 63 Female: 61% vs 59% Duration of symptoms, years, median (IQR): 6 (4-10) vs 6 (3-10) Radiographic disease severity, %: Grade 2: 45% vs 40% Grade 3: 28% vs 25% Grade 4: 27% vs 35% Opioid use, %: 4% vs 1% Employment status, %: Currently employed: 50% vs 52% Unable to work due to health: 4% vs 12% Retired: 39% vs 31% Not employed: 7% vs 4% Comorbidities: Heart disease/hypertension: 38% vs 41% Osteoporosis/osteopenia: 14% vs 11% Depression: 10% vs 8% Stomach ulcer/pains: 11% vs 13% Cancer: 12% vs 4% WOMAC physical function: 35.0 (7.4) vs 34.3 (7.2) WOMAC pain: 8.7 (2.8) vs 8.6 (2.7) Pain overall VAS: 58.7 (12.6) vs 59.1 (12.4) Pain with walking VAS: 61.3 (17.3) vs 60.9 (17.1) DASS21 depression scale: 6.4 (8.5) vs 5.7 (7.1) DASS21 anxiety scale: 6.5 (6.5) vs 5.4 (6.5) AQoL-6D: 0.71 (0.16) vs 0.71 (0.14)	WOMAC physical function (0-68, higher score=lower function); WOMAC pain (0-20, higher score=higher pain); pain overall VAS (0-100, higher score=higher pain); pain on walking VAS (0-100, higher score=higher pain); DASS21 depression scale (0-42, higher score=higher depression); DASS21 anxiety scale (0-42, higher score=higher anxiety); patient overall global change (1-7, higher score=higher improvement); patient function global change (1-7, higher score=higher improvement); patient pain global change (1-7, higher score=higher improvement)	5 and 9 months

Author, Year	Results - Subquestion a (vs. Sham, no treatment, waitlist, attention control)
Bennell 2016	

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Bennell 2016	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse events including withdrawls
Bennell 2016	A vs B <u>5 months</u> WOMAC physical function*: 23.4 (12.2) vs 21.4 (12.0), MD 2.0 (95% CI -2.4 to 6.4), p=0.37 WOMAC physical function change from baseline: 10.7 (1.7) vs 12.5 (1.6), MD -2.1 (95% CI -6.4 to 2.1), p NS WOMAC pain*: 6.2 (3.0) vs 6.3 (3.3), MD -0.1 (95% CI -1.2 to 1.0), p=0.86 WOMAC pain change from baseline: 2.3 (0.5) vs 2.4 (0.4), MD -0.1 (95% CI -1.3 to 1.1), p NS Pain overall VAS*: 35.7 (23.9) vs 36.0 (24.6), MD -0.3 (95% CI -9.0 to 8.4), p=0.95 Pain overall VAS change from baseline: 22.3 (3.2) vs 21.7 (3.3), MD 1.0 (95% CI -7.0 to 9.0), p NS Pain with walking VAS*: 39.1 (25.2) vs 42.3 (26.0), MD -3.2 (95% CI -12.4 to 6.0), p=0.49 Pain with walking VAS change from baseline: 23.5 (3.4) vs 17.4 (3.7), MD 6.1 (95% CI -3.2 to 15.3), p NS DASS21 depression scale*: 4.3 (7.0) vs 5.5 (8.4), MD -1.2 (95% CI -4.0 to 1.6), p=0.40 DASS21 depression scale change from baseline: -0.1 (1.1) vs -1.0 (1.2), MD 0.5 (95% CI -2.8 to 3.8), p NS DASS21 anxiety scale*: 4.0 (4.3) vs 4.9 (6.9), MD -0.6 (95% CI -3.0 to 1.2), p=0.39 DASS21 anxiety scale change from baseline: 1.8 (1.0) vs -0.6 (0.9), MD 2.0 (95% CI -0.4 to 4.3), p NS AQoL-6D*: 0.79 (0.16) vs 0.76 (0.15), MD 0.03 (95% CI -0.02 tp 0.09) p=0.29 AQoL-6D change from baseline: -0.1 (0.0) vs 0.0 (0.0), MD 0.0 (95% CI -0.1 to 0.0), p NS <u>9 months</u> WOMAC physical function*: 21.3 (9.8) vs 18.1 (11.2), MD 3.2 (95% CI -0.6 to 7.0), p=0.10 WOMAC physical function change from baseline: 13.1 (1.5) vs 15.3 (1.6), MD -2.7 (95% CI -6.9 to 1.5), p NS WOMAC pain*: 5.8 (3.0) vs 5.4 (3.4), MD 0.4 (95% CI -0.8 to 1.6), p=0.49 WOMAC pain change from baseline: 3.0 (0.5) vs 3.3 (0.5), MD -0.3 (95% CI -1.6 to 1.1), p NS Pain overall VAS*: 34.8 (21.2) vs 34.5 (23.8), MD 0.3 (95% CI -7.8 to 8.4), p=0.94 Pain overall VAS change from baseline: 23.9 (2.9) vs 24.1 (3.2), MD 0.2 (95% CI -8.2 to 8.5), p NS Pain with walking VAS*: 37.3 (23.3) vs 37.5 (26.2), MD -0.2 (95% CI -9.1 to 8.7), p=0.96 Pain with walking VAS change from baseline: 24.2 (2.8) vs 22.2 (3.7), MD 1.8 (95% CI -6.3 to 9.9), p NS DASS21 depression scale*: 3.5 (4.3) vs 4.9 (7.5), MD -1.4 (95% CI -3.6 to 0.8), p=0.21 DASS21 depression scale change from baseline: 2.3 (0.9) vs -0.4 (0.9), MD 2.2 (95% CI 0.2 to 4.3), p<0.05 DASS21 anxiety scale*: 3.0 (3.4) vs 4.6 (6.0), MD -1.6 (95% CI -3.4 to 0.2), p=0.07 DASS21 anxiety scale change from baseline: 2.7 (0.7) vs 0.0 (1.1), MD 2.0 (95% CI -0.3 to 4.4), p NS AQoL-6D*: 0.81 (0.12) vs 0.78 (0.16), MD 0.03 (95% CI -0.02 to 0.08), p=0.24 AQoL-6D change from baseline: -0.1 (0.0) vs 0.0 (0.0), MD 0.0 (95% CI -0.1 to 0.0), p NS Percent of patients using opioids: 10% (7/72) vs 13% (9/71), RR 0.77 (95% CI 0.3 to 1.9), p=0.58	A vs B** <u>During treatment</u> Increased knee pain: 3% (2/72) vs 31% (22/71), RR 0.09 (95% CI 0.02 to 0.37), p<0.001 Pain in other regions: 4% (3/72) vs 15% (11/71), RR 0.27 (95% CI 0.08 to 0.92), p=0.02 Swelling/inflammation: 3% (2/72) vs 3% (2/71), RR 0.99 (95% CI 0.14 to 6.8), p=0.99 Increased stiffness: 0% (0/72) vs 3% (2/71), RR IC Knee instability: 0% (0/72) vs 1% (1/71), RR IC <u>During follow-up</u> Increased knee pain: 7% (4/60) vs 10% (6/61), RR 0.68 (95% CI 0.20 to 2.28), p=0.53 Pain other region: 0% (0/60) vs 11& (7/61), RR IC Swelling/inflammation: 0% (0/60) vs 3% (2/61), RR IC Increased stiffness: 0% (0/60) vs 0% (0/61), RR IC

Author, Year	Funding source	Quality	Comments
Bennell 2016	Australian Health Management, National Health and Medical Research Council (631717)	Fair	*MDs, CIs, and p values calculated by Spectrum **RRs, CIs, and p values calculated by Spectrum DASS-21: Depression Anxiety Stress Scales

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Berman 1999	USA, University of Maryland	Inclusion criteria: 50+ years old , diagnosis of knee OA by ACR criteria, at least moderate pain 6+ months, taking analgesics or NSAIDs of 1+ month, Kellgren-Lawrence grade 2+ OA by xray, Exclusion criteria: intra-articular steroid injection within 4 weeks, severe or uncontrolled concomitant illness, history of bleeding diathesis or use of anticoagulant	Randomized: 73 Treated: 73 Analyzed: 73 (ITT, last carrie forward) Attrition at 1 month: 5% (4/73 Attrition at 2 months: 11% (8/ Attrition at 3 months: 21% (15/73) (see comments)
Berman 2004	United States Multi-site two outpatient clinics at an academic teaching hospital and one clinical trials facility	Inclusion: age 50 years or older, diagnosis of osteoarthritis of the knee, radiographic evidence of at least 1 osteophyte at the tibiofemoral joint (Kellgren-Lawrence grade ≥2), moderate or greater clinically significant knee pain on most days during past month Exclusion: presence of serious medical conditions that precluded participation in study, bleeding disorders that might contraindicate acupuncture, intra-articular corticosteroid or hyaluronate injections (as well as any knee surgeries or concomitant use of topical capsaicin cream) during past 6 months, previous experience with acupuncture, or any planned events (including total knee replacement) that would interfere with participation in the study during the following 26 weeks.	Randomized: 381 Analyzed: 283 Attrition: 23.8% (102/381)
Beurskens 1997	Netherlands Number of centers: 1	Patients with at least 6 weeks of nonspecific LBP, no traction treatment Exclude: Patients whose conditions improved in the previous 2 weeks	Randomized: 151 Treated: 150 Analyzed:150 Attrition: <.0006% (1/151) IT done

Author, Year	Intervention, Comparator
Berman 1999	A.Acupuncture (n=37): based on the Traditional Chinese Medicine theory for treating *Bi* syndrome; needles (0.22 mm, 34 gauge) inserted to a depth of 0.4-0.6 inches at 5 local points and 4 distal points until elicitation of de qi; two electrodes were attached to needles at local points, electrical stimulation with 2.5 to 4 Hz, pulses of 1.0 ms duration was used for 20 minutes; patients asked to remain on their baseline analgesic/anti-inflammatory regimens and not to begin any new physiotherapy or exercise programs B.Usual care (n=36): asked to remain on their current level of oral therapy throughout the trial Both groups received 20 minute treatments, 2/week for 8 weeks
Berman 2004	A. Acupuncture (n=186): Gradually tapering treatment schedule - 8 weeks of 2 treatments per week, followed by 2 weeks of 1 treatment per week, 4 weeks of 1 treatment every other week, and 12 weeks of 1 treatment per month. Total of 26 weeks, 25 possible sessions. Additionally, acupuncturists applied electrical stimulation at knee points Xiyan at low frequency (8 Hz and square biphasic pulses (0.5 ms puls width) for 20 minutes. Screens at the waist were used in both groups to facilitate blinding and prevent observation of the procedures at the knee. Acupoints: 5 local and 4 distal points. if both knees were affected, 9 needles were inserted in each leg Needles: 32-gauge (0.25mm) Insertion depth: 0.3 to 1.0 inch B. Sham acupuncture (n=183): Overall schedule identical to group 1. Modified combined insertion and noninsertion procedure. inserted 3 needles into sham points in the abdominal area, 3cm lateral and above the umbilicus and then applied 2 pieces of adhesive tape next to needles. in addition they tapped a mock plastic needle guiding tube on the surface of the 9 'true' acupoints in the leg to produce some discernible sensation then immediately applied a needle with adhesive tape to the dermal surface without insertion. 20 minutes for each point. Additionally, a mock electric stimulation was attached to sham needles at the knee. Screens at the waist were used in both groups to facilitate blinding and prevent observation of the procedures at the knee. Acupoints: 5 local and 4 distal points. if both knees were affected, 9 needles were inserted in each leg
Beurskens 1997	A.Continuous traction (n=77): Traction with Eltrac, DIMEC Delft Instrument, minimum force of 35% and maximum of 50% of body weight, 12 sessions in 5 weeks, 20 minutes per session B.Sham traction (n=74): Similar treatment but 20% body weight

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Berman 1999	A vs B Age: 66 vs. 66 Female: 47% vs. 72% Caucasian: 92% vs. 74% BMI: 32 vs. 32 Duration of symptoms: 7.5 vs. 6.9 years WOMAC Total: 48.4 (16.1) vs. 51.4 (12.3) WOMAC Disability: 34.3 (12.1) vs. 34.4 (9.2) WOMAC Pain: 9.6 (3.3) vs. 9.9 (2.8) Lequesne Index: 11.7 (3.5) vs. 12.3 (3.5)	WOMAC index (scales unclear; higher scores=worse disability) Lequesne scale (0-24, higher scores=worse disability)	1 month
Berman 2004	A vs B Age, years: 65.2(8.4) vs 66.2(8.7) Female: 63.2% vs 61.8% non-Hispanic white: 70% vs. 70.7% 2 Target Knees: 25.0% vs. 28.9% Length of diagnosis of osteoarthritis <5 years (%): 53.8% VS. 53% 6-10 years (%): 19.9% vs. 18.0% > 10 years (%): 25.8% vs. 29.0% % using opioids: 5.5% vs. 5.0% % using simple analgesics: 10.2% WOMAC Function: 31.31(12.06) vs. 31.29 (12.00) WOMAC Pain: 8.92 (3.42) vs. 8.90 (3.39) SF-36 Physical Health Score: 48.69 (20.44) vs. 49.65 (19.92) Patient Global Assessment: 2.95 (0.97) vs. 3.08 (0.88)		
Beurskens 1997	A vs. B Age (mean): 39 vs. 42 years Female: 44% vs. 43% Race: NR Chronic pain >6 months: 52% vs. 54% Previous LBP: 86% vs. 77% General Heath Questionnaire 0-36 (mean): 8.3 vs. 8.6 Severity, First main complaint 100mm VAS (mean): 75 vs. 73 Severity, Second main complaint 100mm VAS (mean): 74 vs. 70 Pain score during measurement, 100mm VAS (mean): 61 vs. 55 Pain score last week, 100mm VAS (mean): 62 vs. 62 ADL disability VAS (mean): 67 vs. 70 RDQ (mean): 12 vs. 12	Global perceived effect: ratings on a 7 point scale, dichotomized in "improved" (completely recovered and much improved vs. "not improved (slightly improved a, not changed, slightly worsened, and vastly worsened) First main complaint: 100 mm VAS (best score 0, worse score 100) Second main complaint: 100 mm VAS (best score 0, worse score 24) Roland Disability: 24 item questionnaire (best score 0, worst score 10) Pain at the moment: 100 mm VAS (best score 0, worse score 100) Pain last week: 100 mm VAS (best score 0, worse score 100) Severity of LBP: scored on an 11 point scale (best score 0, worst score 10) Range of motion: degrees (mean) Activities of Daily Living (ADL) disability: 100 mm VAS (best score 0, worse score 100) Work absence: days (mean) Medical consumption: number and %	1.75 and 5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Berman 1999	A vs. B <u>1 month</u> WOMAC Total: 31.58 (18.27) vs. 50.43 (14.1), p<0.001; MD -18.9 (95% CI -26.5, -11.2) WOMAC Disability: 23.17 (13.92) vs. 36.78 (10.71); p<0.001; MD -13.6 (95% CI -19.4, -7.8) WOMAC Pain: 5.56 (3.44) vs. 9.51 (3.01), p<0.001; MD -4.0 (95% CI -5.5, -2.4) Lequesne Index: 9.34 (4.09) vs. 12.41 (3.47), p<0.001; MD -3.1 (95% CI -4.8, -1.3)
Berman 2004	A vs. B 6 months (n=142 vs n=141) Δ from baseline, WOMAC Function: -12.42(1.12) vs. -9.88 (0.93), p<0.01 Δ from baseline, WOMAC Pain: -3.79(0.33) vs. -2.92(0.30), p<0.01 Δ from baseline, SF-36 Physical Health Score: 10.7 (1.6) vs. 8.2 (1.5), p=0.21 Δ from baseline, Patient Global Assessment: 0.45 (0.08) vs. 0.19 (0.09), p=0.02
Beurskens 1997	A vs. B, mean <u>Baseline</u> Pain at the moment (0-100 VAS): 61 vs. 55 Pain in last week (0-100 VAS): 62 vs. 62 Severity of LBP (0-10): 4.9 vs. 4.9 ADL disability (0-100 VAS): 67 vs. 70 <u>7 weeks</u> Global perceived effect "improved": 50% vs. 48%, difference 2% (95% CI -14% to 18%) RDQ: 4.4 vs. 4.3, difference 0.1 (95% CI -1.8 to 1.9) Pain at the moment (0-100 VAS): 28.5 vs. 22.8, difference 5.7 (95% CI -4.6 to 15.9) Pain last week (0-100 VAS): 24.2 vs. 23.9, difference 0.3 (95% CI -9.9 to 10.5) Severity of LBP (0-10): 2.3 vs. 2.2, difference 0.1 (95% CI -0.6 to 0.9) ADL disability (0 to 100 VAS): 27.1 vs. 29.4, difference -2.4 (95% CI -13.6 to 8.9) Work absence (days): 23.5 vs. 27.8, difference -4.3 (95% CI -14.7 to 6.1) Medical consumption: 34% vs. 25%, difference 9% (95% CI -6% to 24%) <u>21 weeks</u> Global perceived effect: 47% vs. 44%, difference 3% (95% CI -13 to 19 %) RDQ: 4.7 vs. 4.0, difference 0.7 (95% CI -1.1 to 2.6) Pain at the moment: 23.8 vs. 20.1, difference 3.7 (95% CI-8.4 to 15.8) Pain last week: 25.0 vs. 25.5, difference -0.5 (95% CI -11.5 to 10.6) Severity of LBP: NR ADL disability: 25.7 vs. 25.8, difference 0.1 (95% CI -11.5.0 to 11.2) Work absence (days): 35.7 vs. 43.7, difference -8.0 (95% CI -27 to 11) Medical consumption: 45% vs. 42%, difference 3% (95% CI -13% to 19%); p=0.71

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Berman 1999	
Berman 2004	
Beurskens 1997	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Berman 1999		No patients reported side-effects from the acupuncture sessions
Berman 2004		A vs. B (n=142 vs. 141) Adverse Events, n: Heart disease - 1 vs 0 Cancer - 2 vs 0 Non-study-related injuries - 3 vs 1 Exacerbation of knee pain - 0 vs 1 non-arthritis-related surgery - 6 vs 3 Stroke - 1 vs 0 Pneumonia - 1 vs 0 Total, n (%) - 14 (7.4%) vs 5 (2.6%) Withdrawals: 33 vs 25
Beurskens 1997	NR	NR

Author, Year	Funding Source	Quality	Comments
Berman 1999	Maurice Laing Foundation, NIH - National Center of Complementary and Alternative Medicine, and National Institutes of Arthritis/Musculoskeletal/Skin Diseases (Grant no 1 R21-RR09327- 01)	Fair	A comparison of the 58 study participants (completers) to those who did not complete the full 12 week protocol showed that those who dropped out had a higher mean score on the WOMAC (p=0.05), had experienced OA longer (p=0.04), and were younger (p=0.05) than those who completed the protocol.
Berman 2004	"The National Center for Complementary and Alternative Medicine and the National Institute of Arthritis and Musculoskeletal and Skin Diseases provided funding for this study. The agencies had no role in the collection, analysis, or interpretation of the data or in the decision to submit the manuscript for	Fair	*Study also featured a third education group that was not abstracted.
Beurskens 1997	NR	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Birch 1998	USA Setting: Hospital-based pain management center and neurology clinic	Chronic myofascial neck pain > 6 months; painful area sensitive to moderate touch; unsuccessful response to physical therapy, medication, and a soft collar; age between 18 and 65 years; willingness to participate in study. Excluded: Disc herniation, cervical osteoarthritis, infection, malignancy, collapsed vertebra, thoracic outlet syndrome, temporomandibular joint dysfunction, collagen vascular disease, brachial plexopathy, schizophrenia, delusional disorder, psychotic disorder, dissociative disorder, bipolar disorder, or ongoing litigation concerning their neck pain.	Randomized: 46 Treated: 46 Analyzed:: 36 Attrition:22% (10/46)

Author, Year	Intervention, Comparator
Birch 1998	A.Relevant acupuncture (n=11) in 2 stages: Stage 1, bilateral needles on hands and feet at SI3, BL62, GB41, and TW5. Needles in hand and foot connected by copper wire through alligator clips with a silicone diode in one clip, and left in place for 10 minutes. Stage 2, needling on 6 acupuncture points in the neck, shoulder, and upper back at left and right GB20, left and right GB21, left and right GB12, left and right BL10, left and right BL11, and GV14. Infrared lamp applied over the needled area for 10 minutes. B.Irrelevant acupuncture (n=13) in 2 stages: Stage 1, bilateral needles on hands and feet at LI5, GB42, TW8, and ST41. Needles connected by cords that looked like the cords used in group A, but connections were severed. Needles and cords left in place for 10 minutes. Stage 2, needling in shoulder and upper back on 6 acupuncture points, left and right BL16, left and right SI9, and left and right LI15. Light was shone over area needled, but no heat was felt. Needles and light left in place for 10 minutes. C.Medication only (n=12), nonsteroidal anti-inflammatory drug, Trilisate 30 minute treatment twice per week for 4 weeks, then once per week for 4 weeks, total 14 treatments

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Birch 1998	A vs B vs C Age: 41 vs 38 vs 39 years Female: 86% vs 77% vs 86% Pain duration: 82 vs 92 vs 91 months Married: 36% vs 23% vs 50% Employed: 86% vs 69% vs 77% Completed high school: 100% vs 100% vs 100% Pain intensity (0-10) 4.8 vs 4.7 vs 4.9 SF-MPQ*: 16.1 vs 16.2 vs 16.8 (*estimated from Fig 1; no sd provided)	Comprehensive Pain Evaluation Questionnaire (CPEQ) McGill Pain Questionnaire (MPQ) (scale: 0-33 sensory, 0-12 affective, 0-5 present pain intensity; higher score = greater pain) Pain intensity rating hourly (scale, 0=no pain, 1-2= mild, tolerable, low pain; 3-4=moderate pain, can be ignored at times; 5-6=intense, distressing, just able to continue activities; 7-8=very intense, difficulty concentrating, interferes with activity; 9-10=excruciating, incapacitating, worst pain possible) Short-Form 36 (SF-36) (scale 0-100, higher score=better QoL) Symptom Checklist 90 (SCL-90-R) (9 subscales; somatization, obsessionality, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoia, and psychoticism; higher scores=greater psychiatric distress)	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Birch 1998	A vs B <u>3 month outcomes</u> SF-MPQ* (0-33): 9.0 vs 15.1 (*estimated from Fig 1; no sd provided)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Birch 1998	A vs C <u>3 month outcomes</u> SF-MPQ* (0-33): 9.0 vs 18.0 (*estimated from Fig 1; no sd provided)

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Birch 1998		NR

Author, Year	Funding Source	Quality	Comments
Birch 1998	NR	Poor	SF-36: values NR, p=ns and Medication (Trilisate) use: values NR, A<B, p<0.05; however, whether these refer to immediate posttreatment or at the 3 month followup is not clear.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Blanchard 1990	United States, number of sites/setting not reported	Inclusion Criteria: Patients with tension-type headache; patients required to report HA activity for an average of 4days/week over 4 week baseline Exclusion Criteria: Migraine or combined migraine and tension headache, other forms of headache.	Randomized: 77 Treated: 77 Analyzed: 66 Attrition: 14.2% (11/77)

Author, Year	Intervention, Comparator
Blanchard 1990	A.Progressive muscle relaxation (PMR) alone (n=19) Tension-release cycles for 16 muscle groups to enable participants to relax and cope with daily stresses. No. of Sessions: Ten sessions (2/week for 3 weeks followed by 1/week for 3 weeks and one final session at week 8) Length of Sessions: 30-70 min each B.PMR plus cognitive therapy (PMR + Cog) (n=16) In addition to relaxation regimen undergone by group a, patients were trained in cognitive stress coping techniques* No. of Sessions: 11 sessions (2 or 1 sessions per week over 8 weeks) Length of Sessions: 45-90 min each C.Pseudomeditation (attention control) (n=16) Patients were engaged in body awareness training and mental control. No. of Sessions: 11 sessions over 8 weeks, Length of Sessions: 40-45 min each. D.Monitoring (waitlist control) (n=15) Monitoring via phone, clinical visits and patient diaries.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Blanchard 1990	A vs. B vs. C vs. D Age: 43 vs 38 vs 39 vs 37 years Sex: 58% vs. 56% vs. 45% vs 66% female Race: NR Mean duration of chronicity: 13.9 vs 13.0 vs. 15.3 vs 14.3 years Mean frequency of headache, days (SD): NR Patients who had prior preventative treatments: 100% were seeking nondrug treatments Patients who overused medications: NR Mean number of analgesic medications used at baseline (SD): NR Headache Index Scores (SD): 5.63 (3.26) vs. 5.82(4.08) vs. 5.23 (3.48) vs. 5.05 (3.44) Medication Index Scores (SD): 16.9 (17.8) vs. 39.8(57.8) vs. 12.1 (11.0) vs. 24.0 (25.5)	Proportion of Patients with ≥50% improvement in Headache Index scores; Headache Index (average daily headache activity [i.e., score range from 0, no headache, to 5 intense, incapacitation headache]; index score range: 0-20; 28 weekly headache ratings / 7); Medication index (average daily headache medication consumption: medication potency x daily dose level)	1 month

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Blanchard 1990	A vs. C 1 month Proportion of patients with ≥50% improvement in Headache Index scores: 31.6% (6/19) vs. 43.7% (7/16); RR 0.72 (95% CI 0.65 to 1.69), p=0.848 Headache Index Scores (SD): 3.82 (2.59) vs. 4.63 (4.3); MD -0.81 (95%CI -3.21 to 1.59), p=0.49 Medication Index Scores (SD): 9.8 (10.4) vs. 8.3; MD 1.5 (95%CI -6.76 to 9.76), p=0.71 A vs. D 1 month Proportion of patients with ≥50% improvement in Headache Index scores: 31.6% (6/19) vs. 20% (3/15); RR 1.58 (95%CI 0.75 to 2.11), p=0.388 Headache Index Scores (SD): 3.82 (2.59) vs. 4.45 (3.38); MD -0.63 (95%CI -2.71 to 1.45), p=0.54 Medication Index Scores (SD): 9.8 (10.4) vs. 22.5 (25.1); MD -12.7 (95% CI -25.6 to 0.21), p=0.05 B vs. C 1 month Proportion of patients with ≥50% improvement in Headache Index scores: 62.5% (10/16) vs. 43.7%(7/16); RR 1.43 (95%CI 0.81 to 1.97), p=0.309 Headache Index Scores (SD): 3.20 (3.70) vs. 4.63 (4.3); MD -1.43 (95% CI -4.33 to 1.47), p=0.321 Medication Index Scores (SD): 20.7(33.9) vs. 8.3 (13.6); MD 12.4 (95% CI -6.82 to 31.62), p=0.197 B vs. D 1 month Proportion of patients with ≥50% improvement in Headache Index scores: 62.5% (10/16) vs. 20% (3/15); RR 3.13(95%CI 0.91 to 2.45) p=0.109 Headache Index Scores (SD): 3.20 (3.70) vs. 4.45 (3.38); MD -1.25 (95% CI -3.86 to 1.36), p=0.335 Medication Index Scores (SD): 20.7(33.9) vs. 22.5 (25.1); MD -1.80 (95% CI -23.83 to 20.23), p=0.869

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Blanchard 1990	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Blanchard 1990	NR	NR

Author, Year	Funding Source	Quality	Comments
Blanchard 1990	National Institute of Neurological and Communicative Disorders and Stroke Grants NS-15235 and NS-23440, National Institute of Mental Health Grant MH-41341	Poor	Headache Index reduction >50% were scheduled for 3, 6 and 12 month followup. 3 month data was obtained for 26 patients. This study included four comparator groups but we have excluded one (PMR+cognitive therapy) because it does not match our protocol (e.g., incremental value of adding interventions). The dropouts (n=11) on average tended to be younger, to have had headaches for a shorter duration, and to have less severe headaches than completers, all factors associated with better outcome.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Blodt, 2015	Germany Number of centers: 1 Rehabilitation clinic	Patients age 20 to 65 years, LBP for at least 3 months but not longer than 5 years, more prominent than pain in other spine areas, average pain intensity in the previous 7 days ≥ 40 mm measured on a VAS (0–100 mm). Exclude: Patients with LBP due to accident or malignant disease, inflammatory arthropathy, history of spine surgery, prolapsed vertebral disc or spondylolisthesis with radicular symptoms, planned start of physiotherapy and other therapies (e.g., acupuncture, massage, spinal manipulation, neuroflexotherapy, feldenkrais) against LBP, activities including swimming, yoga, Pilates, tai chi, kung fu, tai bo, gymnastics, regular (> once a week) intake of analgesics, pregnancy or planned pregnancy within the treatment period, severe acute or chronic disorders (physical or mental), or alcohol abuse, current participation in any qigong/or exercise therapy or within 12 months, participation in another trial during the last 6 months, or a history of participation in any qigong/or exercise therapy/low back pain study.	Randomized: 128 Treated: 127 Analyzed: 127 Attrition:10% (13/128)

Author, Year	Intervention, Comparator
Blodt, 2015	A.Qigong (n=64): 12 once weekly 90 minute sessions over 3 months with 14 basic level movement exercises for the spine and legs and 7 intermediate exercises to change "qi" B.Exercise (n=63): 12 sessions over 3 months, weekly 60 minute exercise therapy with warm-up using a dynamic gym ball and strengthening exercises, then stretching exercises and relaxation E28

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Blodt, 2015	A vs. B Age (mean): 46 vs. 48 years Female: 91% vs. 70% Race: NR Duration of low back pain: 3 vs. 3 years Medication intake: 38% vs. 44% Average low back pain (VAS; mean): 55.6 vs. 52.1 Low back pain/disability (RMD; mean): 6.2 vs. 5.7 Physical health (SF-36, mean): 41.8 vs. 42.6 Mental health (SF-36, mean): 46.3 vs. 49.2 Quality of sleep (mean): 4.7 vs. 4.7 Sleep satisfaction (mean): 4.9 vs. 5.1 Self-efficacy, Schützler & Witt (mean): 19.4 vs. 19.3	Pain (VAS 0–100 VAS) Roland Morris Disability (RMD) Questionnaire (0-24) SF-36 Bodily pain (0-100) SF-36 Physical component (0-100) SF-36 Mental component score (0-100) Quality of sleep (0=very good to 10=very bad) Sleep satisfaction (0=very satisfied to 10=not at all satisfied) Self-efficacy, Schützler & Witt (Higher values indicate better status)	3 and 9 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Blodt, 2015	NR

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Blodt, 2015	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Blodt, 2015	A vs. B, mean (SD) <u>Baseline</u> Average low back pain (0-100 VAS): 55.6 (14.2) vs. 52.1 (10.5) RDQ: 6.2 (3.4) vs. 5.7 (3.4) Quality of sleep (0-10): 4.7 (2.7) vs. 4.7 (2.4) Sleep satisfaction (0-10): 4.9 (2.9) vs. 5.1 (2.5) SF-36 Physical component score: 41.8 (8.5) vs. 42.6 (7.5) SF-36 Mental component score: 46.3 (10.8) vs. 49.2 (10.1) <u>3 months</u> Average low back pain (0-100 VAS): 35.1 (95% CI 30.0 to 40.3) vs. 27.4 (95% CI 22.8 to 32.1); difference 7.7 (95% CI 0.7 to 14.7) RDQ: 4.1 (95% CI 3.3 to 4.8) vs. 3.1 (95% CI 2.4 to 3.8), difference 0.9 (95% CI –0.1 to 2.0) Quality of sleep (0-10): 4.6 (95% CI 3.9 to 5.2) vs. 4.5 (95% CI 3.9 to 5.2); difference 0.0 (95% CI–0.9 to 1.0) Sleep satisfaction (0-10): 5.0 (95% CI 4.4 to 5.7) vs. 4.8 (95% CI 4.2 to 5.4); difference 0.3 (95% CI –0.6 to 1.1) SF-36 Bodily pain: 43.0 (95% CI 41.2 to 44.8) vs. 44.6 (95% CI 42.6 to 46.5); difference 1.5 (95% CI -1.2 to 4.2) SF-36 Physical component score: 45.8 (95% CI 43.9 to 47.7) vs. 46.6 (95% CI 44.7 to 48.4); difference -0.8 (95% CI –3.4 to 1.9) SF-36 Mental component score: 45.4 (95% CI 42.7; 48.1) vs. 46.6 (95% CI 44.3; 49.0); difference 11.2 (95% CI –4.9 to 2.4) <u>9 months</u> Average low back pain (0-100 VAS): 35.9 (95% CI 29.8 to 42.1) vs. 28.8 (95% CI 23.5 to 34.1); difference 7.1 (95% CI –1.0 to 15.2) RDQ: 4.3 (95% CI 3.4 to 5.2) vs. 3.1 (95% CI 2.5 to 3.8); difference 1.2 (95% CI 0.1 to 2.3) Quality of sleep: 4.5 (95% CI 4.0 to 5.1) vs. 4.7 (95% CI 4.1 to 54.3); difference -0.2 (95% CI -1.0 to 0.7) Sleep satisfaction: 5.1 (95% CI 4.5 to 5.7) vs. 5.1 (95% CI 4.5 to 5.7); difference -0.1 (95% CI –0.9 to 0.8) SF-36 Bodily pain: 41.4 (95% CI 39.1 to 43.7) vs. 43.4 (95% CI 40.9 to 45.9); difference -2.0 (95% CI 5.4 to 1.4) SF-36 Physical component score: 44.8 (95% CI 42.5 to 47.0) vs. 46.5 (95% CI 44.4 to 48.7); difference -1.8 (95% CI -4.9 to 1.3) SF-36 Mental component score: 45.0 (95% CI 41.9 to 48.2) vs. 45.5 (95% CI 42.9 to 48.1); difference -0.5 (95% CI -4.6 to 3.6)	A vs. B Adverse events: 7% (10/127) vs. 7% (10/127)

Author, Year	Funding Source	Quality	Comments
Blodt, 2015	Karl and Veronica Carstens Foundation	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Boline 1995	USA, single site, outpatient clinic	Inclusion Criteria: Patients aged 18-70 with a headache duration of at least 3 months and with at least one episode per week. CTTH Diagnosis was determined by the examining team according to IHS criteria. Patients with overlap in CM were included if examiners determined headache problem was predominantly tension-type. Exclusion Criteria: Exclusion for pregnancy, active treatment for headaches within past three months, contraindications to amitriptyline therapy (e.g. cardiac arrhythmias and glaucoma) or spinal manipulative therapy (e.g. metastases, fractures, inflammatory disease), as determined by history, physical and radiological examination.	Randomized: 150 Treated: 126 Analyzed: 70 vs. 56 Attrition: 16.0% (24/150)
Bono 2015	Italy, number of sites/setting not reported	Inclusion Criteria: >18 years old, at least two years of CTTH (by ICCHD classification), at least four attacks/week, failure on at least three well-conducted preventative drug treatments. Exclusion Criteria: Use of preventative treatment in the last two months, previous TES treatment, severe anxiety or mood depression, severe sleep disturbances, and associated disabling neurologic or other psychiatric disorders.	Randomized: 83 Treated: 83 Analyzed: 83 Attrition: NR

Author, Year	Intervention, Comparator
Boline 1995	A.Spinal Manipulative Therapy (n=70) Participants received short-lever, low-amplitude, high-velocity thrust techniques. Doctor determined by manual palpation, the cervical, thoracic or lumbar spinal segments to be manipulated. Moist heat and light massage preceded manipulation. No. of Sessions: Twelve sessions (2/week for 6 weeks) Length of Sessions: 20 minutes each B.Amitriptyline (n=56) Dose titration of amitriptyline for 6 weeks. Nighttime, daily doses began at 10mg/day for first week, then increased to 20mg/day in the second, followed by 30mg/day in the third week and after. Dose reduction for adverse effects if medicine was not tolerated. Patients instructed to continue use of OTC medications as-needed.
Bono 2015	A.Occipital Transcutaneous electrical stimulation (OTES) (n=54) Electrostimulator generated biphasic impulses via 50mm X 90mm self-adhesive electrodes placed on occipital region Pulse Width: 250 µs Frequency: 40 Hz Intensity: 20 mA No. of Sessions: 3/day for two consecutive weeks (total of 42 sessions) Length of Sessions: 30 min B.Sham OTES (n=29) Same device/procedure, but no current was delivered.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Boline 1995	A vs. B Age: 40.9 vs 42.7 Female: 54.3 vs. 69.6 Race: NR Mean duration of chronicity: 13.4 vs 13.6 years Daily Headache Intensity: 5.6(2.7) vs. 5.0(3.3) Weekly headache frequency: 12.4(7.4) vs. 10.8(7.5) OTC Medication Usage: 1.7 (1.7) vs. 2.1(2.3) SF-36 Function Health Status Global Score (% points): 67.2(14) vs. 71.3(13)	Δ from baseline, Headache Intensity (range 0-20: total ratings per period / number of days per period) Δ from baseline, Headache Frequency (range 0-28: total of all headache ratings 2 or above) Δ from baseline, OTC medication usage (no. of tablets/day) SF-36 Functional Health Status Global Score (summation of all SF-36 dimensions)	1 month
Bono 2015	A vs. B Age: 42 vs 40 years Female: 81% vs 66% Race: NR Mean duration of chronicity: NR Mean frequency of headache, days (SD): 29.0 Patients who had prior preventative treatments: NR MIDAS: 63 (26) vs 50 (14); MD 13 (95% CI 2.65 to 23.35) p=0.014 VAS: 8 (1) vs 8 (2); MD 0 (95%CI -0.65 to 0.65) p=1.00 Beck Depression Inventory-II (BDI-II) Score (SD): 8 (3)vs 8 (3) p=0.32; MD 0 (95%CI -1.37 to 1.37) p=1.00 Hamilton Anxiety Rating Scale (HARS) Score (SD): 7 (3) vs 7(3) p=0.70; MD 0 (95%CI -1.37 to 1.37) p=1.00 Proportion of patients who overused medications, n (%): 23 (43%) vs 15 (52%)	Migraine Disability Assessment (MIDAS, 0-21+ e.g. little or no disability to severe disability); Visual Analogue Scale (VAS, 0-10: higher scores indicate severity of pain); Beck Depression Inventory-II (BDI-II; total:0-63, higher scores indicate severity of depressive symptoms); Hamilton Anxiety Rating Scale (HAM-A, 14 ratings of 0-5, higher scores indicate severity of depressive symptoms); Δ in monthly acute medications use	1 month, 2 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Boline 1995	NR
Bono 2015	<u>A vs. B</u> <u>1month</u> Patients who achieved ≥50% reduction in headache days (at 30 days %): 85%(46/54) vs. 7%(2/29) p<0.001; RR 12.35 (95%CI 3.22 to 47.26) p=0.0000 <u>2months</u> MIDAS(0-21+): 16(11) vs 51 (24); MD -35.00 (95%CI -42.64 to -27.36) p=0.0001 VAS(0-10): 3(2) vs 8(1); MD -5.0 (95%CI -5.79 to -4.21) p=0.0001 Beck Depression Inventory-II (BDI-II) Score (SD): 7(3) vs 8 (2); MD -1.00 (95%CI -2.24 to 0.24) p=0.111 Hamilton Anxiety Rating Scale (HAM-A) Score (SD): 6 (2) vs 7(2); MD -1.00(95%CI -1.92 to -0.08) p=0.0328 Proportion of patients who overused medications, n (%): 4/54 (7%) vs 14/29 (48%); RR 0.15 (95%CI 0.06 to 0.42) p=0.0000

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Boline 1995	A vs B 1 month Daily Headache Intensity*: 3.8 vs. 5.2; MD 1.4 (95%CI 0.3, 2.3) p=0.003 Weekly headache frequency*: 7.6 vs 11.8; MD 4.2 (95%CI 1.9, 6.5) p=0.0004 OTC Medication Usage*: 1.3 vs 2.2; MD 0.9 (95%CI 0.3, 1.5) p=0.005 SF-36 Function Health Status Global Score (% points)*: 78.8 vs 73.9; MD 4.9 (95%CI 0.4, 9.4) p=0.005 *adjusted means after control for differences in baseline values
Bono 2015	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Boline 1995	NR	A vs B 4.3% (3/70) experienced neck stiffness that disappeared after 2 weeks of treatment vs. 82.1%(46/56) experienced adverse events including dry mouth, drowsiness, or weight gain. 1/70 withdrew due to increased neck pain vs 5/56 withdrew due to adverse effects, significant difference not detected.
Bono 2015	NR	"Neither adverse events nor side effects occurred in the real or sham group."

Author, Year	Funding Source	Quality	Comments
Boline 1995	Funding provided by Foundation for Chiropractic Education and Research Grant #90-03-01	Poor	Best case analysis: all 5 drop-out is SMT group improved in the 4 major outcomes corresponding to the mean improvement of the patients who completed the study in that group and all 19 in the control did not improve from baseline. The significant difference between the groups increased slightly in favor of the spinal manipulation group in all four major outcome measures tested and remained highly significant ($p < .001$). Worst case analysis: all 5 drop-out is SMT group did not improve from baseline in the 4 major outcomes and all 19 in the control group had an improvement in the four major outcome measures corresponding to the mean improvement of the patients who completed the study in that group. This analysis did not change the significant difference between groups, favoring the spinal manipulation group, of any of the four major outcome measures tested at four weeks posttreatment. For headache intensity, headache frequency, and over-the-counter medication the p-value remained at or below .001 and for global SF-36 score the p value changed to .025.
Bono 2015	"This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors."	Poor	*Some outcomes were not separated out for CTTH and are reported for allodynic vs non-allodynic patients: Δ in the number of headache-free days/month: NR* Δ in total headache days per month: NR* Mean reduction of headache days per month: NR* 2 wks post treatment: Patients who achieved ≥50% reduction in headache days (at 30 days %): 85%(46/54) vs. 7%(2/29) $p<0.001$; RR 12.35 (95%CI 3.22 to 47.26) $p=0.0000$

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Brinkhaus 2006a	Germany Number of centers: 30 Outpatient	Clinical diagnosis of chronic LBP ≥6 months Age 49-75 years Average pain intensity of ≥40 on 100-mm VAS on previous 7 days Only oral non-steroidal anti-inflammatory drugs for pain treatment in the 4 weeks before treatment Exclude: Protrusion or prolapse of ≥1 intervertebral discs with concurrent neurological symptoms Radicular pain Prior vertebral column surgery Infectious spondylopathy LBP caused by inflammatory, malignant, or autoimmune disease Congenital deformation of the spine, except for slight lordosis or scoliosis Compression fracture caused by osteoporosis Spinal stenosis Spondylolysis or spondylolisthesis Patients with Chinese medicine diagnoses warranting treatment with moxibustion Acupuncture treatment during the past 12 months	Randomized: 210 Treated: 140 Analyzed: 210 Attrition: 0% (0/210)

Author, Year	Intervention, Comparator
Brinkhaus 2006a	A.Needle acupuncture (n=140): 12 acupuncture sessions, 30 minutes each, over 8 weeks (usually 2 sessions/week for 4 weeks then 1 session/week for remaining 4 weeks). Acupuncture physicians had ≥140 hours of acupuncture training and ≥3 years of experience. Semistandardized acupuncture treatment using sterile, disposable, 1-time needles. Needle length and diameter were not defined. All patients were treated with local and distant points including (bilaterally) ≥4 local points and ≥2 distant points from a set selection. Patients that were experiencing local or pseudoradicular sensation, ≥2 local points were acupunctured. Other acupuncture points (including ear and trigger points) could be chosen individually. Physicians were instructed to achieve de qi if possible, and needles were to be stimulated manually at least once during each session. B.Sham (minimal) acupuncture (n=70): 12 sessions, 30 minutes each, over 8 weeks (the same as for the acupuncture group). Acupuncturists received a videotape, oral instruction and brochure detailing minimal acupuncture. ≥6 of 10 predefined nonacupuncture points were needled bilaterally using superficial insertion with fine needles 20-40mm in length. Points were not in area of the back where patients were experiencing pain, and de qi and manual stimulation were avoided. All: Oral non-steroidal anti-inflammatory drugs were allowed for treatment of chronic LBP if needed; use of corticosteroids or pain-relieving drugs that act through the central nervous system was prohibited.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Brinkhaus 2006a	A vs. B Age: 59 vs. 58 Female: 64% vs. 75% Race: NR Duration of LBP, years: 14.7 vs. 13.6 Number of days with pain during past month: 24.6 vs. 26.2 Number of days with limited function during past 6 months: 88.0 vs. 103.3 Baseline PDI score: 28.9 vs. 31.5 Baseline HFAQ (FFbH-R) score: 57.1 vs. 57.2 Baseline VAS score for LBP intensity: 63.2 vs. 66.6 Baseline SF-36 physical health score: 32.8 vs. 31.8 Baseline SF-36 mental health score: 48.5 vs. 48.0 Baseline SF-36 subscale pain score: 35.2 vs. 32.5 Baseline SES affective pain score: 50.2 vs. 50.9 Baseline SES sensory pain score: 49.7 vs. 49.1 Baseline ADS score: 53.0 vs. 53.0 Prior acupuncture treatment: 32% vs. 36% Physiotherapy in the past 6 months: 26% vs. 29% Use of analgesics in the past 6 months: 40$ vs. 37%	Funktionsfragebogen Hannover-Rücken (FFbH-R) (0-100, higher scores indicate better function) Pain Disability Index (0-70, higher scores indicate greater disability) Number of days with limited function LBP intensity (0-100 VAS) Days with pain SF-36 physical component (0-100) SF-36 mental component SF-36 pain subscale Allgemeine Depressionsskala depression scale (reported as t-standard)	4 months, 10 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Brinkhaus 2006a	A vs. B, mean (SD) <u>Baseline</u> Funktionsfragebogen Hannover-Rücken (FFbH-R) (0-100): 57.1 (18.6) vs. 57.2 (17.3) Pain Disability Index (0-70): 28.9 (11.1) vs. 31.5 (11.1) Number of days with limited function in past 6 months: 88.0 (58.0) vs. 103.3 (64.4) LBP intensity (0-100 VAS): 63.2 (13.2) vs. 66.6 (15.7) SF-36 physical component (0-100): 32.8 (8.2) vs. 31.8 (8.3) SF-36 mental component (0-100): 48.5 (10.7) vs. 48.0 (11.1) SF-36 pain subscale (0-100): 35.2 (14.8) vs. 32.5 (13.1) Allgemeine Depressionsskala (ADS) (t standard): 53.0 (7.7) vs. 53.0 (7.3) <u>4 months</u> FFbH-R (0-100): 66.0 (20.1) vs. 64.1 (22.9), difference 1.9 (95% CI -4.2 to 8.0) Pain Disability Index (0-70): 19.3 (13.9) vs. 21.4 (15.6), difference -2.1 (95% CI -6.3 to 2.1) Number of days with limited function in past 6 months: 40.9 (42.3) vs. 59.5 (53.7), difference -18.6 (95% CI -33.3 to -3.9) LBP intensity (0-100 VAS): 38.4 (29.8) vs. 42.1 (30.3), difference -3.8 (95% CI -12.4 to 4.9) SF-36 physical component (0-100): 39.3 (9.9) vs. 37.6 (11.3), difference 1.7 (95% CI -1.3 to 4.7) SF-36 mental component (0-100): 49.9 (10.0) vs. 46.8 (12.9), difference 3.1 (95% CI -0.5 to 6.6) SF-36 pain subscale (0-100): 53.6 (22.9) vs. 49.6 (23.6), difference 3.9 (95% CI -2.7 to 10.7) ADS (t standard): 49.7 (8.6) vs. 50.3 (10.7), difference -0.6 (95% CI -2.5 to 3.7) <u>10 months</u> FFbH-R (0-100): 66.0 (20.4) vs. 63.1 (21.6), difference 2.9 (95% CI -3.2 to 9.0) Pain Disability Index (0-70): 19.0 (13.4) vs. 23.0 (15.0), difference -4.0 (95% CI -8.1 to 0.1) Number of days with limited function in past 6 months: 42.4 (56.3) vs. 52.9 (57.1), difference -10.5 (95% CI -27.0 to 6.1) LBP intensity (VAS 0-100): 39.2 (29.2) vs. 44.9 (30.4), difference -5.7 (95% CI -14.4 to 3.0) SF-36 physical component (0-100): 38.9 (10.0) vs. 36.1 (10.3), difference 2.8 (95% CI -0.2 to 5.7) SF-36 mental component (0-100): 50.5 (10.4) vs. 47.2 (11.9), difference 3.3 (95% CI 0.1 to 6.5) SF-36 pain subscale (0-100): 52.4 (23.2) vs. 44.0 (22.9), difference 8.5 (95% CI 1.7 to 15.2) ADS (t standard): 48.2 (9.1) vs. 50.7 (9.7), difference -2.5 (95% CI -5.3 to 0.4)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Brinkhaus 2006a	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Brinkhaus 2006a	NR	A vs. B Withdrawals: 7% (10/147) vs. 9% (7/75) Withdrawals due to AEs: NR Serious AEs: 9% (13/140) vs. 6% (4/70), RR 1.63 (95% CI 0.55 to 4.8) Nonserious AEs: 11% (15/140) vs. 17% (12/70), RR 0.63 (95% CI 0.31 to 1.26)

Author, Year	Funding Source	Quality	Comments
Brinkhaus 2006a	Supported by the following German social health insurance funds: Techniker Krankenkasse, BKK Aktiv, Betriebskrankenkasse der Allianz Gesellschaften, Bertelsmann BKK, Bosch BKK, BKK BMW, DaimlerChrysler BKK, BKK Deutsche Bank, Ford Betriebskrankenkasse, BKK Hoechst, HypoVereinsbank Betriebskrankenkasse, Siemens-Betriebskrankenkasse, Handelskrankenkasse, Innungskrankenkasse Hamburg, Deutsche Angestellten-Krankenkasse, Barmer Ersatzkasse, Kaufmännische Krankenkasse, Hamburg-Münchener Krankenkasse, Hanseatische Krankenkasse, Gmünder Ersatzkasse, HZK Krankenkasse für Bau- und Holzberufe, Brühler Ersatzkasse, Krankenkasse Eintracht Heusenstamm and Buchdrucker Krankenkasse.	Good	A vs. B only for outcomes at 6 & 12 months, so didn't list results for Group C - C. Waiting list (n=74): No acupuncture treatment for 8 weeks after randomization, after which they received 12 sessions of acupuncture treatment as described for group A. - in text results section ("efficacy"), patients in the waiting list group (group C) showed improvements after receiving acupuncture between weeks 9 & 16; these improvements were similar to those seen in patients in the acupuncture group (group A).

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Brismee 2007	United States, "general community"	Inclusion Criteria: Subjects aged 50 years or older with knee pain. Selection of subjects was based on the Classification Criteria of the American Rheumatism Association for Osteoarthritis of the Knee. Exclusion Criteria: Exclusion if they could not read or write English, could not ambulate at least 25 feet (7.6 m), had a medical condition involving knee trauma or intra-articular knee injection within one month, exercise-induced or uncontrolled angina within three months, severe dyspnoea at rest, terminal illness, uncontrolled hypertension, acute or chronic renal failure, bilateral total knee arthroplasties, or a Mini- Mental State Exam score of 23 or lower.	Randomized: 41 Treated: 40 Analyzed: 31 Attrition: 24.3% (10/41)
Bronfort 2011	US, Minnesota Number of centers: 1 Outpatient and clinic	Patients 18 to 65 years of age, who had a primary complaint of mechanical LBP of at least 6-week duration with or without radiating pain to the lower extremity Exclude: Patients with previous lumbar spine fusion surgery, progressive neurological deficits, aortic or peripheral vascular disease, pain scores of less than 3 (0–10 scale), pending or current litigation, or ongoing treatment for back pain by other health care providers.	Randomized: 301 Treated: 245 Analyzed: 245 Attrition: 19% (57/301)

Author, Year	Intervention, Comparator
Brismee 2007	A.Tai Chi (n=18) Subjects in the tai chi group attended group tai chi classes for six weeks followed by six weeks of home video tai chi practice. No. of Treatments: 3/week for 12 weeks (36 total) Length of Treatments: 40 min/session B.Attention Control (n=13) Subjects in the attention control group attended group lectures and discussions covering health-related topics. They did not take part in any further activity past 6 week group period. No. of Treatments: 3/week for 6 weeks (18 total) Length of Treatments: 40 min/session
Bronfort 2011	A. Chiropractic spinal manipulation therapy, SMT (n=100): 1 to 2 times per week over 12 weeks, 15 to 30 minute short-lever, low-amplitude, high-velocity SMT to low back B: Supervised exercise therapy, SET (n=100): trunk strengthening exercises with 3 sets of trunk extensions and leg extensions, trunk lifted to 5 to 10 degrees past horizontal for a total range of motion of 80 to 90 degrees; approximately 20 1 hour sessions over 12 weeks C. Home exercise and advice, HEA (n=101): Instruction in two 1 hour sessions on self care measures; ice and heat, stretching and strengthening exercises, a book and laminated cards describing exercises to do daily

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Brismee 2007	A vs B Age: 71 vs. 69 Female: 86.4% vs. 78.9% Race: NR Mean Duration of Chronicity: NR Overall (WOMAC): 64.58(17.44) vs. 59.63(15.22) Physical Function (WOMAC): 42.74(12.07) vs. 37.63(10.61) Stiffness (WOMAC): 5.57(1.17) vs. 5.11(1.37) Pain (WOMAC): 16.48(5.33) vs. 16.9(4.23) Pain (VAS): 4.67(2.59) vs. 4.16(1.79)	Western Ontario and McMaster Osteoarthritis Index Overall (WOMAC, range 26-130: higher scores represent more pain, stiffness and disability) Physical Function (WOMAC, range 17-85) Stiffness (WOMAC, range 2-10) Pain (WOMAC, range 7-35) Pain (VAS)	1.5 months
Bronfort 2011	A vs. B vs. C Mean age: 45.2 vs. 44.5 vs. 45.6 years Female sex: 67% vs. 57% vs. 58% Race: NR Pain all or most of the time: 55% vs. 51%vs. 60% Duration of back pain: 5.0 vs. 4.8 vs. 5.0 years Mean pain severity score (0-10): 5.4 vs. 5.1 vs. 5.2 Modified RDQ (0-23): 8.7 vs. 8.4 vs. 8.7 SF- 36 PCS: 43 vs. 44 vs. 43 SF- 36 MCS: 55 vs. 54 vs. 54 Depression score Scale) (0=no depression, 16=mild, 60=maximum): 6.7 vs. 7.9 vs. 8.1	Pain (0-10 NRS) Modified Roland Morris Disability Questionnaire (0=no disability, 23=maximum disability) SF- 36-Item Short Form Health Survey Physical component (norm-based mean=50) SF- 36-Item Short Form Health Survey Mental component (norm-based mean=50) Over-the-counter pain medication in past week (days)	4 and 9 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Brismee 2007	A vs. B 1.5 months Overall (WOMAC): 60.28 (23.8) vs. 57.73 (19.58); MD 2.55 (95%CI -13.94 to 19.04) p=0.754 Physical Function (WOMAC): 38.61 (15.62) vs. 37.58 (13.12); MD 1.03 (95% -9.87 to 11.93) p=0.848 Stiffness (WOMAC): 5.28 (1.53) vs. 4.54 (1.51); MD 0.74 (95%CI -0.39 to 1.87) p=0.192 Pain (WOMAC): 16.39 (6.96) vs. 16 (4.88); MD 0.39 (95%CI -4.21 to 4.99) p=0.390 Pain (VAS): 3.46 (2.45) vs. 3.19 (1.97); MD 0.27 (95%CI -1.42 to 1.96) p=0.746
Bronfort 2011	NR

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Brismee 2007	NR
Bronfort 2011	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Brismee 2007	NR	"Sporadic complaints of minor muscle soreness and foot and knee pain were made mainly during the first few days of the intervention. No other adverse effect associated with the practice of tai chi was reported by the participants."
Bronfort 2011	A vs. B. vs. C, mean (SD) <u>Baseline</u> Pain (0-10 NRS): 5.4 (1.5) vs. 5.1 (1.3) vs. 5.2 (1.5) Modified RDQ (0-23): 8.7 (4.3) vs. 8.4 (4.5) vs. 8.7 (4.8) SF-36 PCS (norm-based mean=50): 42.8 (7.4) vs. 43.7 (7.4) vs. 42.8 (7.9) SF-36 MCS (norm-based mean=50): 55.1 (7.8) vs. 53.7 (8.4) vs. 53.6 (8.7) OTC pain medication use in past week (days): 1.8 (2.0) vs. 1.9 (2.1) vs. 2.1 (2.3) <u>4 months</u> Pain (0-10 NRS): 3.3 (2.4) vs. 2.9 (2.1) vs. 3.1 (2.1), adjusted difference 0.3 (95% CI -0.5 to 1.0) for A vs. B and 0.1 (95% CI -0.6 to 0.9) for A vs. C Modified RDQ (0-23): 4.9 (5.2) vs. 4.0 (4.9) vs. 4.2 (4.2), adjusted difference 0.5 (95% CI -1.0 to 2.1) for A vs. B and 0.7 (95% CI -0.9 to 2.3) for A vs. C SF-36 PCS (norm-based mean=50): 48.6 (8.4) vs. 50.6 (7.9) vs. 49.1 (6.9), adjusted difference -1.8 (95% CI -4.4 to 0.9) for A vs. B and -0.3 (95% CI -3.0 to 2.4) for A vs. C SF-36 MCS (norm-based mean=50): 55.9 (7.2) vs. 54.8 (8.0) vs. 55.1 (7.8), adjusted difference 0.4 (95% CI -2.0 to 2.9) for A vs. B and -0.5 (95% CI -3.0 to 2.1) for A vs. C OTC pain medication use in past week (days): 1.6 (2.4) vs. 1.4 (2.1) vs. 1.5 (2.2), adjusted difference 0.4 (95% CI -0.4 to 1.1) for A vs. B and 0.4 (95% CI -0.3 to 1.2) for A vs. C <u>9 months</u> Pain (0-10 NRS): 3.3 (2.1) vs. 2.8 (2.3) vs. 2.8 (2.2), adjusted difference 0.3 (95% CI -0.5 to 1.1) for A vs. B and 0.3 (95% CI -0.6 to 1.1) for A vs. C Modified RDQ (0-23): 5.1 (4.9) vs. 3.8 (4.7) vs. 4.1 (4.7), adjusted difference 0.4 (95% CI -1.2 to 2.0) for A vs. B and -0.1 (95% CI -0.7 to 0.5) for A vs. C SF-36 PCS (norm-based mean=50): 48.4 (8.0) vs. 50.4 (7.2) vs. 49.6 (7.0), adjusted difference -1.7 (95% CI -4.2 to 0.8) for A vs. B and -1.0 (95% CI -3.5 to 1.5) for A vs. C SF-36 MCS (norm-based mean=50): 55.2 (7.5) vs. 53.9 (8.6) vs. 56.0 (6.6), adjusted difference 2.4 (95% CI -0.2 to 5.0) for A vs. B and -2.2 (95% CI -4.9 to 0.5) for A vs. C OTC pain medication use in past week (days): 1.8 (2.3) vs. 1.8 (2.4) vs. 1.6 (2.3), adjusted difference 0.1 (95% CI -0.8 to 0.9) for A vs. B and 0.4 (95% CI -0.4 to 1.3) for A vs. C Differences baseline outcome values; also adjusted for gender and night pain when interactions were not present	A vs. B vs. C Nonserious adverse events: 1% (1/100) vs. 1% (1/100) vs. 4% (4/101) All adverse events were considered non-serious.

Author, Year	Funding Source	Quality	Comments
Brismee 2007		Poor	
Bronfort 2011	NR	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Brosseau 2005	Canada Number of centers unclear Rheumatology treatment facilities	Diagnosis of hand OA fulfilling ACR criteria, symptoms for at least 3 months, aged 45 to 80 years old, pain VAS score of 4 or greater, x-ray evidence of joint space narrowing in the hands, available for the study treatment schedule Exclude: Orthopedic or rheumatologic comorbidities, evidence of chondrocalcinosis, prior surgery for finger joints, acute disease, uncontrolled diabetes mellitus, untreated hypertension, neurological deficits or other mental disorders, anticipated change in type or dosage or prescribed initial analgesic medication during study, current rehabilitation treatment or other pain-related treatment (aside from medication), previous experience with low-level laser therapy, corticosteroid injection of finger joints within previous 12 months, pregnancy, photosensitivity, cancer, plans to move within 6 months	Randomized: 88 Treated: 88 Analyzed: 86 Attrition: 5% (4/88)
Brouwer 2006	The Netherlands, multi-center	Inclusion Criteria: The inclusion criteria were symptomatic unicompartmental knee OA and a malalignment in patients aged 18 years and over. We diagnosed the OA as unicompartmental when the symptoms (pain and tenderness of the joint margins) were located over the medial or the lateral tibiofemoral compartment of the knee in combination with osteoarthritic signs according to the Ahlback score (Ahlback>0) in the same medial or lateral tibiofemoral compartment of the knee as well as in combination with varus alignment (in combination with medial compartment OA) or valgus alignment (in com-bination with lateral compartment OA), respective Exclusion Criteria: Patients with concurrent symptomatic OA of medial and lateral compartments, symptomatic patellofemoral OA(scored on the lateral radiograph of the knee), no malalignment, rheumatoid arthritis, previous high tibial osteotomy, symptomatic hip or ankle pathology, and an insufficient command of the Dutch language were excluded.	Randomized: 118 Treated: (89) 49+40 Analyzed: 89 Attrition: 25% (29/118)

Author, Year	Intervention, Comparator
Brosseau 2005	A.Low-level laser therapy (n=42): 3 sessions lasting 20 minutes per week for 6 weeks In each session, a Gallium Aluminum Arsenide low level laser was used on radial, median, and ulnar nerves on the most affected hand; each nerve had 3 points irradiated for 1 second each for a total of 15 points. In addition, each painful joint on the most affected hand was irradiated at 4 points for 1 second each. B.Sham low-level laser therapy (n=46): same procedure as the active treatment but a sham laser probe was used. All patients: Attended three sham low-level laser therapy sessions prior to the treatment period
Brouwer 2006	. Brace (n=60) Patients were fitted with a commercially available knee brace that allowed medial unloading or lateral unloading and also received usual care. Device: Oasys brace, Innovation Sports, Irvine, CA, USA . Usual Care (n=57) Usual care was identical in both groups and consisted of patient education (ad-aptation of activities and/or weight loss), and (if needed) physical therapy and analgesic

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Brosseau 2005	A vs B Age: 64 vs 65 Female: 74% vs 83% % taking medications: 60% vs 61% Diagnosis of OA, years: 7.5 (8.0) vs 8.5 (8.6) Pain intensity VAS: 56.9 (18.4) vs 49.4 (22.4) AUSCAN function: 2.2 (0.9) vs 2.1 (0.7) AUSCAN pain: 2.4 (0.6) vs 2.1 (0.7)	AUSCAN function (0-4, higher score=higher dysfunction); AUSCAN pain intensity (0-4, higher score=higher dysfunction); pain VAS (0-100, higher score=higher pain); patient global assessment	1.5 and 4.5 months
Brouwer 2006	A vs B Age*: 59.2 Female: 48% vs. 51% Race: NR Mean Duration of Chronicity: 6.7vs. 4.9 years Mean Pain Severity (VAS): 6.6 (2.4) vs. 5.5 (2.0) Mean Knee Function (HSS): 64.9 (12.0) vs. 69.0 (9.5) Quality of Life (EQ-5D): 0.50 (0.30) vs. 0.56 (0.26) *Age only reported for total population	Pain Severity (VAS, range 0-10) Hospital for special surgery score (HSS, range 0-100) Quality of Life (EQ-5D, 0-1)	6 months, immediate post-treatment (12 months)

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Brosseau 2005	A vs B <u>4.5 months</u> AUSCAN function: 1.9 (0.9) vs 1.7 (0.8), (MD 0.2, 95% CI -0.2 to 0.6) p=0.28 AUSCAN pain: 1.9 (0.9) vs 1.8 (0.8), (MD 0.1, 95% CI -0.3 to 0.5) p=0.59 Pain VAS: NR Patient global assessment: Fully improved: 0% vs 3% Partially improved: 40% vs 33.3% No improvement: 60% vs 52%
Brouwer 2006	<u>A vs. B</u> <u>6 months</u> Pain Severity (VAS): MD -0.58 (95%CI -1.48 to 0.32) Knee Function (HSS): MD 3.2 (95%CI -0.58 to 6.98) p<0.1 Quality of Life (EQ-5D): MD 0.01 (95%CI -0.08 to 0.10) <u>12 months (post-treatment)</u> Pain Severity (VAS): MD -0.81 (95%CI -1.76 to 0.14) p <0.1 Knee Function (HSS): MD 3.0 (95%CI -1.05 to 7.05) Quality of Life (EQ-5D): MD 0.01 (95%CI -0.08 to 0.10)

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Brosseau 2005	
Brouwer 2006	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Brosseau 2005		A vs B Erythema: 2% (1/42) vs 0% (0/46) Start of period after menopause: 2% (1/42) vs 0% (0/46)
Brouwer 2006		

Author, Year	Funding Source	Quality	Comments
Brosseau 2005	Grants from the Ontario Arthritis Society (CANADA) (grant number TAS 302), Ontario Ministry of Health and Long-Term Care (grant number HRPD-05225), University Research Chair, and Ministry of Human Resources	Good	MDs and p values calculated by using n=41 for intervention group and n=45 for control group
Brouwer 2006		Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Buckelew 1998	United States 2 centers Hospital and outpatient	Yunus' criteria for diagnosis of FM Exclude: Organic brain syndrome, psychotic disorder, unstable or uncontrolled medical conditions, major communicative disorder, rheumatoid arthritis, wide-spread osteoarthritis, subjective pain < 4 on 0-10 VAS, regular aerobic exercise, biofeedback training within previous year	Randomized: 119 Treated: 119 Analyzed: 101 Attrition: 15% (18/119)

Author, Year	Intervention, Comparator
Buckelew 1998	A.Biofeedback (n=25): 1 session for 1.5-3 hours per week for 6 weeks and instructions to train 2 additional times independently per week. Subjects were taught cognitive and muscular relaxation strategies. B.Exercise (n=26): 1 session for 1.5-3 hours per week for 6 weeks and instructions to train 2 additional times independently per week. Sessions consisted of active range of motion exercises, strengthening exercises, low to moderate intensity aerobic exercise, proper posture and body mechanic instruction, and instructions on the use of heat, cold, and massage C.Attention control (n=27): 1 session for 1.5-3 hours per week for 6 weeks and instructions to train 2 additional times independently per week. Subjects received educational information on diagnosis and treatment of FM and general health topics information

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Buckelew 1998	A vs B vs C Age: 44 vs 46 vs 44 Female: 97% vs 93% vs 90% Duration of symptoms (years): 11.6 (10.0) vs 11.6 (8.9) vs 10.0 (9.0) Duration of diagnosis (years): 2.5 (2.9) vs 3.0 (3.4) vs 2.5 (2.4) AIMS physical activity subscale: 6.0 vs 4.0 vs 6.0 Pain behavior observation measure: 5.0 vs 4.0 vs 3.4 Pain VAS: 5.8 vs 6.3 vs 5.9 SCL-90-R Global Severity Index: 69.0 vs 72.5 vs 63.5 CES-D: 16.0 vs 15.0 vs 12.5 Sleep scale: 7.0 vs 8.0 vs 5.5	AIMS physical activity subscale (0-10, higher score=lower activity); pain behavior observation method (number of behaviors concomitant to pain counted in a ten minute span, higher number=higher number of pain-related behaviors observed); pain VAS (0-10, higher score=higher pain); SCL-90-R Global Severity Index (0-360, higher score=more severe psychological symptoms); CES-D (0-60, higher score=more severe symptoms of depression); sleep scale (0-12, higher score=worse sleep)	3, 12, and 24 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Buckelew 1998	A vs C <u>3 months</u> AIMS physical activity subscale, median (median Δ from baseline): 6.0 (0) vs 6.0 (0) Pain behavior observation measure, median (median Δ from baseline): 2.5 (-1) vs 3.0 (0) Pain VAS, median (median Δ from baseline): 5.2 (-0.2) vs 5.8 (-0.5) SCL-90-R Global Severity Index, median (median Δ from baseline): 65.0 (-2) vs 65.0 (0) CES-D, median (median Δ from baseline): 10.0 (-2) vs 13.0 (3) Sleep scale, median (median Δ from baseline): 7.0 (0) vs 5.0 (0) <u>24 months</u> AIMS physical activity subscale, median (median Δ from baseline): 6.0 (0) vs 6.0 (0) Pain behavior observation measure, median (median Δ from baseline): 2.5 (-0.5) vs 3.0 (1) Pain VAS, median (median Δ from baseline): 5.2 (-1.1) vs 5.4 (-0.6) SCL-90-R Global Severity Index, median (median Δ from baseline): 64.0 (-1) vs 67.0 (-1) CES-D, median (median Δ from baseline): 10.0 (-2) vs 12.0 (-2) Sleep scale, median (median Δ from baseline): 6.0 (-2) vs 6.0 (0) B vs C <u>3 months</u> AIMS physical activity subscale, median (median Δ from baseline): 4.0 (0) vs 6.0 (0) Pain VAS, median (median Δ from baseline): 5.4 (-0.8) vs 5.8 (-0.5) SCL-90-R Global Severity Index, median (median Δ from baseline): 65.5 (-3) vs 65.0 (0) CES-D, median (median Δ from baseline): 13.5 (-2.5) vs 13.0 (3) Sleep scale, median (median Δ from baseline): 8.0 (0) vs 5.0 (0) <u>24 months</u> AIMS physical activity subscale, median (median Δ from baseline): 4.0 (0) vs 6.0 (0) Pain VAS, median (median Δ from baseline): 5.5 (-1.2) vs 5.4 (-0.6) SCL-90-R Global Severity Index, median (median Δ from baseline): 65.5 (-2.5) vs 67.0 (-1) CES-D, median (median Δ from baseline): 11.5 (-3.5) vs 12.0 (-2) Sleep scale, median (median Δ from baseline): 7.5 (0) vs 6.0 (0)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Buckelew 1998	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Buckelew 1998	A vs B <u>3 months</u> AIMS physical activity subscale, median (median Δ from baseline): 6.0 (0) vs 4.0 (0) Pain behavior observation measure, median (median Δ from baseline): 2.5 (-1) vs 2.0 (-1) Pain VAS, median (median Δ from baseline): 5.2 (-0.2) vs 5.4 (-0.8) SCL-90-R Global Severity Index, median (median Δ from baseline): 65.0 (-2) vs 65.5 (-3) CES-D, median (median Δ from baseline): 10.0 (-2) vs 13.5 (-2.5) Sleep scale, median (median Δ from baseline): 7.0 (0) vs 8.0 (0) <u>24 months</u> AIMS physical activity subscale, median (median Δ from baseline): 6.0 (0) vs 4.0 (0) Pain behavior observation measure, median (median Δ from baseline): 2.5 (-0.5) vs 4.0 (0) Pain VAS, median (median Δ from baseline): 5.2 (-1.1) vs 5.5 (-1.2) SCL-90-R Global Severity Index, median (median Δ from baseline): 64.0 (-1) vs 65.5 (-2.5) CES-D, median (median Δ from baseline): 10.0 (-2) vs 11.5 (-3.5) Sleep scale, median (median Δ from baseline): 6.0 (-2) vs 7.5 (0)	NR

Author, Year	Funding Source	Quality	Comments
Buckelew 1998	Grants from NIAMS (DHHS 1-RZ9-AR39481) and the National Institute on Disability and Rehabilitation Research (H133B80075).	Poor (all)	Only significant between group differences occurred in the physical activity measure between exercise and combination groups in comparison to the attention control. The following information was given, " Post hoc comparisons revealed that the exercise and combination groups had scores reflecting improved physical activity levels relative to the attention control group at posttreatment and at most of the followup periods." Specific followup periods were not specified. Table 5 may give more information Outcomes not reported: Physicians rating of disease severity, self efficacy measures, Tender Point Index, myalgic score Biofeedback and exercise (n=30) group was also included in the study but not included in data abstraction because it was considered additive

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Cakir 2014	Turkey, multi-site, outpatient	Inclusion Criteria: Patients with pain for at least at 6 months least, diagnosed with knee OA according to American College of Rheumatology guidelines, confirmed with radiologically in Kellgren-Lawrence grades of 2 or 3, aged 40-80 years old were eligible. Exclusion Criteria: Patients were excluded if they had an experience of any physical therapy agent, intra-articular corticosteroid therapy or chondroprotective agents during the 30 days prior to the study or viscosupplementation treatment within 6 months prior to the study, if they had a diagnosis of joint infection, neoplasm, diabetes mellitus, paresis, osteonecrosis, recent trauma, ascertained/suspected pregnancy or lactating and poor general health status. Other exclusion criteria were any history of contraindication of heat therapy or previous major surgery.	Randomized: 60 Treated: 60 Analyzed: 58 Attrition: 3.3% (2/60)
Carlsson 2001	Sweden Number of centers: 1 Outpatient pain clinic in university hospital setting	Lumbar or lumbosacral low back pain for a duration of 6 months or longer No radiation of pain below the knee level Normal neurologic examination findings of lumbosacral nerve function, including deep tendon reflexes, plantar response, voluntary muscle activation, straight leg raising, and sensory function. Exclude: Major trauma or systemic disease Ongoing pregnancy History of acupuncture treatment	Randomized: 51 Treated: 34 Analyzed: 50 Attrition: 2% (1/51) *Note on study design and analysis:* Patients with a global assessment of "worse" or "unchanged" at the 1 month or 3 month followups were excluded and labeled as "unchanged" for the remainder of the study. - A: 1 month, n=17; 3 months, n=5 - B: 1 month, n=14, 3 months, n=0

Author, Year	Intervention, Comparator
Cakir 2014	A.Continuous Ultrasound (n=20) Application of a therapeutic ultrasound device to affected knee. Additionally, all patients were instructed to perform home exercises including isometric exercises, muscle strength exercises and stretching exercises at least 3 times per week. No. of Treatments: 5 times/week for 2 weeks (10 total) Length of Treatments: 12 minutes Frequency: 1 MHz Intensity: 1 W/cm2 Device: 5-cm2 head B.Pulsed Ultrasound (n=20) Identical treatment protocol except device was set to a pulsed output. Pulse Ratio: 1:4 C.Sham Ultrasound (n=20) Identical treatment protocol except the device's power switch was off.
Carlsson 2001	A.Acupuncture (n=34): standard needle acupuncture (n=18) or electroacupuncture (n=16) Needle acupuncture was given to points of the lower back (local points) and to some points on the lower limbs and forearms or hands (distal points). The number of needles was successively increased from eight (four local and four distal needles) to 14 to 18 during the first three or four treatments. The "de-qi" feeling of numbness, soreness, heaviness, and warmth was sought in all instances, mostly at a needle-tip depth of 2 to 3 cm. The needles were stimulated three times during the 20-minute treatment sessions to restore de-qi feelings. The needles were usual disposable, stainless steel needles with a diameter between 0.30 and 0.32 mm (gauge, 29–30) and a length between 30 and 70 mm (1–3 inches). Electroacupuncture: two or three sessions of manual acupuncture were given initially (to avoid temporary exacerbation of pain), followed by treatments consisting of electrical stimulation of four needles (one pair per side) in the low back. The stimulation frequency was approximately 2 Hz every 2.5 seconds, and was interrupted by a 15-Hz train for 2.5 seconds (dense–disperse) at a perceived but not painful stimulation intensity. We used a Chinese acupuncture electrostimulator (Multiple Electronic Acupunctoscope; WQ-10C, Beijing, China) for which the output could be approximately monitored by a flashing light. In addition, a similar number of needles as in the manual acupuncture group were inserted and manually activated. Primary course of treatment 8 sessions over 2 months, then followup treatment at 3 months and 6 months B.Placebo (sham TENS) (n=16): Mock transcutaneous electrical nerve stimulation (TENS) given by an impressive, stationary, but disconnected GRASS (gradient-recalled acquisition in a steady state) stimulator attached to two large TENS electrodes. The electrodes were placed on the skin over the most intensely painful area in the low back. During stimulation, flashing lamps were displayed and visible to the patient.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Cakir 2014	A vs B vs. C Age: 57 vs. 58 vs. 57 Female: 70% vs. 80% vs. 85% Race: NR Mean Duration of Chronicity: 4.0 (2.9) vs. 5.1 (2.1) vs. 4.5 (3.8) Physical Function (WOMAC): 55.7(13.4)vs. 52.4(11.9) vs. 52.5(15.4) Pain (WOMAC): 15.9(4.3) vs. 14.5(3.1) vs. 14.9(4.3) Pain at Rest (VAS): 57.9(20.2) vs. 55.7(17.8) vs. 53.6(19.1); Pain on Movement (VAS): 75.5(18.3) vs. 73.0(19.9) vs. 72.2(21.8); Disease Severity (VAS): 73.9(19.2) vs. 67.9(18.7) vs. 68.4(20.5);	WOMAC physical function (scale 0-68: higher score=worse function) Stiffness WOMAC pain (range 0-20: higher score=greater pain) Pain at rest (VAS, 0-10; higher score=greater pain) Pain on Movement (VAS, 0-10; higher score=greater pain) Disease Severity (VAS, 0-10; higher score=greater disability)	6 months
Carlsson 2001	Age: 50 years* Female: 66%* Race: NR Pain duration (mean): 9.5 years* Employment status: retired 34%, sick leave 40%, working full time 24%, unemployed 2% Common LBP of presumed muscular origin: 78% Number of treatment modalities tried prior to study (mean): 2.8 Previous lumbar surgery: 10% * no significant difference among groups	Global assessment by independent observer (pain improved, unchanged, or worse) Pain (0-100 VAS) Analgesic intake: number tablets taken Sleep quality (good, slightly disturbed by pain and woke 1 or 2 times, or badly disturbed by pain and work more than twice) Level of activity at work or at home	1, 3, and ≥6 months (based on primary course of treatment)

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Cakir 2014	A vs. B vs. C 6 months Physical Function (WOMAC): 32.6(11.3) vs. 37.1(6.2) vs. 35.5(8.1); AvsB: MD -4.5(95%CI -10.34 to 1.34) p=0.127; AvsC: MD -2.9 (95%CI -9.19 to 3.39) p=0.357 Pain (WOMAC): 9.5(2.6) vs. 11.3(2.2) vs. 11.1(2.6); AvsB: MD -1.8 (95%CI -3.34 to -0.26) p=0.023; AvsC: MD -1.6 (95%CI -3.26 to 0.06) p=0.059 Pain at Rest (VAS): 21.4(17.8) vs. 20.2(14.1) vs. 22.3(14.2); AvsB: MD 1.2 (95%CI -9.08 to 11.48) p=0.814; AvsC: MD 1.2 (95%CI -9.08 to 11.48) p=0.814 Pain on Movement (VAS): 38.7(16.2) vs. 37.5(24.1) vs. 38.1(27.0); AvsB: MD 1.2 (95%CI -11.95 to 14.35) p=0.854; AvsC: MD 0.6 (95%CI -13.65 to 14.85) p=0.933 Disease Severity (VAS): 30.0(11.6) vs. 32.5(10.7) vs. 29.5(11.0); AvsB: MD -2.5 (95%CI -9.64 to 4.64) p=0.483; AvsC: MD 0.5(95%CI -6.74 to 7.74) p=0.899
Carlsson 2001	A vs. B Baseline Pain intensity a.m. (0-100 VAS): 57 vs. 46 Sleep quality slightly or badly disturbed: 88% (30/34) vs. 75% (12/16) Analgesic intake (tablets per week): 31 (SD 21.5) vs. 23 (SD 17.5) Work full time: 21% (7/34) vs. 25% (4/16) 1 month Global assessment "pain improved": 47% (16/34) vs. 13% (2/16), RR 3.76 (95% CI 0.98 to 14.4) Pain intensity a.m. (0-100 VAS): 50 vs. 60 3 month outcomes: Global assessment "pain improved": 44% (15/34) vs. 13% (2/16), RR 6.87 (95% CI 1.87 to 25.1) Pain intensity a.m. (0-100 VAS): 42 vs. 56 ≥6 months outcomes: Global assessment "pain improved": 41% (14/34) vs. 13% (2/16), RR 3.29 (95% CI 0.85 to 12.8) Pain intensity a.m. (0-100 VAS): 41 vs. 50 Analgesic intake (tablets per week): 21.4 (SD 21.1) vs. 21.5 (SD 16.0) Work full time: 32% (11/34) vs. 31% (5/16)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Cakir 2014	NR
Carlsson 2001	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Cakir 2014	NR	"No patient reported any complaint leading to non-compliance"
Carlsson 2001	NR	Withdrawals: NR* Withdrawals due to AEs: NR Serious AEs: NR Nonserious AEs: NR *Excluded at followup for assessment as "worse" or "unchanged" A vs. B *(cumulative)* - 1 month: 17/34 vs. 14/16 - 3 months: 22/34 vs. 14/16

Author, Year	Funding Source	Quality	Comments
Cakir 2014	Financial support provided by Ege University for this project. No conflicts of interest have been reported by the authors or by any individuals in control of the content of this article.	Fair	
Carlsson 2001	Partial support by grant No. 05658 from the Swedish Medical Research Council project.	Poor	The results were not reported clearly. Means and percent changes were not reported as values, just as graphs without any numbers for actual result. - Figure 5

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Cash 2015, Sephton 2007	United States, setting not reported	Inclusion Criteria: Women aged 18 and older, able to attend a weekly group with a physician verified diagnosis of fibromyalgia. Exclusion Criteria: NR	Randomized: 91 Treated: 82.3% (42/51) Analyzed: 90 (ITT) Attrition: 25% (23/91)

Author, Year	Intervention, Comparator
Cash 2015, Sephton 2007	A. Mindfulness-based Stress Reduction [MBSR] (n=51) 8-week group-based program with one 2.5 hour session/week including instruction in techniques, meditation, and simple yoga positions to encourage relaxation. Participants were asked to complete daily practices with workbook and audiotapes for 45 min a day for 6 days a week. 42 participants (82%) attended 4+ sessions, with mean attendance of 5.5 sessions. B. Waitlist control group (n=39) Participants were offered the MBSR program only after the conclusion of the study and followup.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Cash 2015, Sephton 2007	A vs. B Age: NR Female: 100% vs. 100% Race: NR Mean duration of chronicity: NR Physical Functioning (FIQ): 1.3 (.72) vs. 1.2 (.75) Pain VAS: 68.1 (25.4) vs. 69.2 (19.6) Beck Depression Inventory (BDI) Total: 15.6(7.0) vs. 14.7(6.9) Cognitive Subscale BDI (0-45): 6.4(4.3) vs. 6.1(4.1) Somatic Subscale BDI (0-45): 8.4(3.2) vs. 7.7(3.2) Perceived Stress Scale (PSS): 22.0 (6.2) vs. 21.4 (7.4) Stanford Sleep Questionnaire (SSQ): 9.0 (3.2) vs. 9.3 (3.1) FIQ Severity: 67.5 (15.8) vs. 62.5 (18.1) Fatigue Symptom Inventory (FSI): 6.1 (1.4) vs. 6.1 (1.7)	Primary: Fibromyalgia Impact Questionnaire (FIQ, range 0-100: higher scores indicate severity of symptoms) Severity (FIQ, range 0-100: higher scores indicate severity of symptoms) Physical Functioning (FIQ, range 0-10: higher scores indicate severity of symptoms) Pain (VAS, range 0-100mm: higher scores indicate severity of pain) Beck Depression Inventory (BDI; total:0-63, higher scores indicate severity of depressive symptoms) Perceived Stress Scale (PSS, range 0-40: higher scores indicate severity of perceived stress) Stanford Sleep Disorders Questionnaire (SDQ: scoring information unavailable) Fatigue Symptom Inventory (FSI, range 0-10: higher scores indicate severity of fatigue)	2 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Cash 2015, Sephton 2007	A vs. B 2 months: Physical Functioning (FIQ): 1.2 (.74) vs. 1.2 (.76); MD 0.0 (95%CI -0.32 to 0.32) p=1.00 Pain VAS: 65.2 (25.0) vs. 65.1 (22.1); MD 0.1 (95%CI -9.96 to 10.16) p=0.98 Symptom Severity (FIQ): 67.5 (15.8) vs. 62.5 (18.1); MD 5.0 (95%CI -2.12 to 12.12) Beck Depression Inventory (BDI): 13.3(7.5) vs. 14.8(8.1); MD -1.5 (-4.76 to 1.76) p=0.36 Perceived Stress Scale (PSS): 20.2 (6.6) vs. 20.8 (6.5); MD -0.60 (95%CI -3.37 to 2.17) p=0.668 Stanford Sleep Questionnaire (SSQ): 8.4 (4.0) vs. 9.5 (2.7); MD -1.10 (95%CI -2.58 to 0.38) p=0.14 Fatigue Symptom Inventory (FSI): 5.5 (1.8) vs. 6.0 (1.9); MD -0.50 (95%CI -1.28 to 0.28) p=0.206

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Cash 2015, Sephton 2007	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Cash 2015, Sephton 2007	NR	NR

Author, Year	Funding Source	Quality	Comments
Cash 2015, Sephton 2007	NR	Poor	Sephton 2007 was focused on depression, BDI is from that publication

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Castel 2012	Spain Setting NR	Inclusion: FM diagnosis based on ACR 1990 criteria, age 18-65 Exclusion: additional severe chronic medical pain conditions, suicidal ideation, severe psychopathology, moderate-to-severe cognitive impairment	Randomized: 64 Analyzed: 48 Attrition: 25%(16/64)

Author, Year	Intervention, Comparator
Castel 2012	A.CBT plus standard pharmacological care (n=26). CBT conducted in groups (except for session 2, which was individual); 14 weekly 2 hour sessions. CBT included education about FM and pain, autogenic training, cognitive restructuring, CBT for insomnia, assertiveness training, activity pacing, pleasant activity scheduling, goal setting, and relapse prevention. Subjects were given a manual and CD to practice autogenic training at home. No difference was found between attendance in A (mean of 12.3 sessions and SD of 1.7) vs B (mean of 12.0 sessions, SD of 2.6). B.Control (n=22): standard pharmacological care: conventional pharmacological management, including analgesics, antidepressants, anticonvulsants, and myorelaxants

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Castel 2012	A vs B Age: 50 vs 49 Female: 94% vs 100% White: 100% vs 100% Pain duration, years: 13.6 (9.2) vs 11.6 (6.9) FIQ: 62.7 (2.8) vs 66.1 (3.0) Pain NRS: 6.1 (0.3) vs 6.9 (0.3) HADS: 23.2 (1.4) vs 24.2 (1.5) MOS Sleep quantity: 6.0 (0.3) vs 5.5 (0.3) MOS Sleep index problems: 30.4 (1.5) vs 27.9 (1.6)	FIQ (0-100, higher scores=greater impact of FM; MCID 14%) Pain intensity NRS (mean of three 0-10 ratings of maximum, minimum, and usual pain intensity in last week, 0-10, higher scores=greater pain; MCID 30%) Hospital Anxiety and Depression Scale (HADS; scale NR, higher scores=greater psychological distress) MOS Sleep quantity (scale NR) MOS Sleep index problems (scale NR)	Immediately post-treatment, then 3 and 6 months later.

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Castel 2012	A vs B <u>3 months, ITT analysis using LOCF method:</u> *Proportion of patients with minimal clinically significant difference compared with baseline:* FIQ: 55.9% (19*/34) vs 20% (6*/30), p<0.01; OR 5.1 (95% CI 1.7 to 15.6); RR 2.8 (95% CI 1.3 to 6.1) Pain: 14.6% (5*/34) vs 10% (3*/30), p=NS (NR); RR 1.5 (95% CI 0.4 to 5.7), p=0.57 *n's back calculated using % and baseline N for each group *Mean (SD)* FIQ: 52.8 (3.3) vs 66.3 (3.5); MD -13.5 (95% CI -15.478 to -11.522), p<0.0001 Pain NRS: 5.9 (0.3) vs 6.8 (0.3); MD -0.9 (95% CI -1.075 to -0.725), p<0.0001 HADS: 15.4 (1.3) vs 22.3 (1.4); MD -6.9 (95% CI -7.685 to -6.115), p <0.0001 MOS Sleep quantity: 6.9 (0.2) vs 5.5 (0.3); MD 1.4 (95% CI 1.254 to 1.546), p <0.0001 MOS Sleep index problems: 40.1 (1.6) vs 28.8 (1.7); MD 11.3 (95% CI 10.340 to 12.260), p <0.0001 <u>6 months, ITT analysis using LOCF method:</u> *Proportion of patients with minimal clinically significant difference compared with baseline:* FIQ: 58.8% (20*/34) vs. 20% (6*/30), p<0.01; OR 5.7 (95% CI 1.9, 17.8); RR 2.9 (95% CI 1.4, 6.3) Pain: 17.6% (6*/34) vs. 13.3% (4*/30), p=NS (NR); RR 1.3 (95% CI 0.4, 4.2), p=0.64 *n's back calculated using % and baseline N for each group *Mean (SD)* FIQ: 50.5 (3.5) vs 68.5 (3.7); MD -18.0 (95% CI -20.095 to -15.905), p<0.0001 Pain NRS: 5.7 (0.4) vs 6.8 (0.4); MD -1.1 (95% CI -1.333 to -0.867), p<0.0001 HADS: 15.7 (1.3) vs 23.7 (1.4); MD -8.0 (95% CI -8.785 to -7.215), p <0.0001 MOS Sleep quantity: 6.7 (0.2) vs 5.6 (0.3); MD 1.1 (95% CI 0.954 to 1.246), p <0.0001 MOS Sleep index problems: 39.9 (1.5) vs 28.0 (1.6); MD 11.9 (95% CI 10.998 to 12.802), p <0.0001

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Castel 2012	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Castel 2012		Adverse events NR Withdrawals NR

Author, Year	Funding Source	Quality	Comments
Castel 2012	NR	Poor	RRs for 3 month followup results were calculated

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Castel 2013	Spain 1 center Patients recruited from rheumatologists	Inclusion: female, FM diagnosis based on 1990 ACR criteria; age 18-60; 3-8 years of schooling Exclusion: other severe chronic medical pain condition; psychiatric or psychological treatment in past 3 years for severe psychopathology; inflammatory rheumatic disease; cognitive, sensorial, or physical impairment limitation to perform the treatments; pending legal resolution for disability	Randomized: 155 Analyzed: 88 Attrition: 43% (67/155)
Castel 2013/Salvat 2017	Spain 1 center Patients recruited from rheumatologists	Inclusion: female, FM diagnosis based on 1990 ACR criteria; age 18-60; 3-8 years of schooling Exclusion: other severe chronic medical pain condition; psychiatric or psychological treatment in past 3 years for severe psychopathology; inflammatory rheumatic disease; cognitive, sensorial, or physical impairment limitation to perform the treatments; pending legal resolution for disability	Randomized: 155 Analyzed: 88 Attrition: 43% (67/155)

Author, Year	Intervention, Comparator
Castel 2013	A.Multidisciplinary treatment (n=53): Conventional pharmacological treatment, including analgesics, antidepressants, benzodiazepine and non-benzodiazepine hypnotics; group CBT and group physical therapy (1 hour CBT and 1 hour physical therapy) 2 days/week for a total of 24 sessions. CBT included education, cognitive restructuring, CBT for insomnia, assertiveness training, goal setting, activity pacing, pleasant activity scheduling, and relapse prevention. Physical therapy emphasized aerobic capacity, muscle strengthening and flexibility, and hydrokinesiotherapy in a heated pool. Participants attended a mean of 22.3 (SD 1.8) of the CBT sessions and a mean of 21.6 (SD 2.2) of the physical therapy sessions. B.Conventional pharmacological treatment (n=35): Conventional pharmacological treatment, including analgesics, antidepressants, benzodiazepine and non-benzodiazepine hypnotics.
Castel 2013/Salvat 2017	A. Multidisciplinary treatment (n=53): Conventional pharmacological treatment, including analgesics, antidepressants, benzodiazepine and non-benzodiazepine hypnotics; group CBT and group physical therapy (1 hour CBT and 1 hour physical therapy) 2 days/week for a total of 24 sessions. CBT included education, cognitive restructuring, CBT for insomnia, assertiveness training, goal setting, activity pacing, pleasant activity scheduling, and relapse prevention. Physical therapy emphasized aerobic capacity, muscle strengthening and flexibility, and hydrokinesiotherapy in a heated pool. Participants attended a mean of 22.3 (SD 1.8) of the CBT sessions and a mean of 21.6 (SD 2.2) of the physical therapy sessions. B. Conventional pharmacological treatment (n=35): Conventional pharmacological treatment, including analgesics, antidepressants, benzodiazepine and non-benzodiazepine hypnotics.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Castel 2013	A vs B Age, years: 49 vs 49 Female: 100% vs 100% Pain duration, years: 12.5 vs 10.8 FIQ: 64.6 (16.0) vs 66.6 (17.4) Pain intensity (NRS): 6.8 (1.4) vs 7.1 (1.6) HADS: 21.9 (8.0) vs 23.2 (8.1) Sleep index problems: 29.0 (8.9) vs 27.9 (8.1)	Fibromyalgia Impact Questionnaire (FIQ) (scale NR, higher scores=greater impact of FM) FIQ clinically significant improvement: cutoff=14% Pain numerical rating scale (NRS), mean of maximum, minimum, and usual pain intensity in past week (0-10 scale, higher scores=greater pain) Clinically significant pain improvement: 30% cutoff Hospital Anxiety and Depression Scale (HADS) (scale NR, higher scores=greater psychological distress) MOS Sleep scale sleep problems index (scale NR, higher scores=worse sleep)	3, 6, 12 months
Castel 2013/Salvat 2017	A vs B Age, years: 49 vs 49 Female: 100% vs 100% Pain duration, years: 12.5 vs 10.8 FIQ: 64.6 (16.0) vs 66.6 (17.4) Pain intensity (NRS): 6.8 (1.4) vs 7.1 (1.6) HADS: 21.9 (8.0) vs 23.2 (8.1) Sleep index problems: 29.0 (8.9) vs 27.9 (8.1) WONCA total score, median (IQR): 27.0 (23.0 to 31.0) vs 28.0 (25.0 to 32.0)	Fibromyalgia Impact Questionnaire (FIQ) (scale NR, higher scores=greater impact of FM), FIQ clinically significant improvement: cutoff=14%, WONCA total score (9-45, higher score=lower function), WONCA physical function (1-5, higher score=lower function), WONCA daily activites (1-5, higher score=lower function), Pain numerical rating scale (NRS), mean of maximum, minimum, and usual pain intensity in past week (0-10 scale, higher scores=greater pain), Clinically significant pain improvement: 30% cutoff, Hospital Anxiety and Depression Scale (HADS) (scale NR, higher scores=greater psychological distress), MOS Sleep scale sleep problems index (scale NR, higher scores=worse sleep)	3, 6, 12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Castel 2013	A vs B <u>3 months</u> FIQ: 55.5 (19.3) vs 64.6 (17.6), p<0.05, (MD -9.1, 95% CI -14.9 to -3.2) p=0.0026 Minimally clinically significant FIQ improvement: 48.1% vs 23.0%, [OR = 3.1, 95% CI 1.6 to 5.9] Pain NRS: 6.4 (1.9) vs 6.8 (1.8), (MD -0.4, 95% CI -1.0 to 0.2) p=0.18 Minimally clinically significant pain improvement: 13.6% vs 10.8%, [OR = 1.3, 95% CI 0.5 to 3.3] HADS: 15.2 (9.1) vs 20.6 (8.5), p<0.001, (MD -5.4, 95% CI -8.2 to -2.6) p=0.0002 Sleep problems: 40.5 (10.4) vs 31.2 (9.4), (MD 9.3, 95% CI 6.1 to 12.5) p<0.0001 <u>6 months</u> FIQ: 55.8 (20.9) vs 67.8 (18.4), p <0.05 (MD -12.0, 95% CI -17.2 to -6.8) p<0.0001 Minimally clinically significant FIQ improvement: 42% vs 19%, p < 0.01 [OR = 3.1, 95% CI 1.5 to 6.4] Pain NRS: 6.4 (1.9) vs 7.0 (1.9), p >0.05, (MD -0.6, 95% CI -1.2 to 0.004), p=0.051 Minimally clinically significant pain improvement: 16% vs 5%, p <0.05 [OR = 3.4, 95% CI 1.04 to 10.8] HADS: 16.2 (9.3) vs 21.5 (8.5), p < 0.0001, (MD -5.3, 95% CI -8.1 to -2.5) p=0.0003 Sleep problems: 38.7 (10.5) vs 29.0 (8.9), p < 0.0001, (MD 9.7, 95% CI 6.6 to 12.8) p<0.0001 <u>12 months</u> FIQ: 58.8 (20.5) vs 69.6 (17.2), p > 0.05, (MD -10.8, 95% CI -16.8 to -4.8) p=0.0005 Minimally clinically significant FIQ improvement: 27% vs 4%, p < 0.0001 [OR = 8.8, 95% CI 2.5 to 30.9] Pain NRS: 6.7 (1.6) vs 7.1 (1.8), p >0.05, (MD -10.8, 95% CI -16.8 to -4.8) p=0.0005 Minimally clinically significant pain improvement: 8.6% vs 0, p < 0.05 [OR = 0.5, 95% CI 0.4 to 0.6] HADS: 17.1 (9.9) vs 22.8 (9.2), p <0.01, (MD -5.7, 95% CI -8.7 to -2.7) p=0.0003 Sleep problems: 36.3 (11.0) vs 28.8 (8.6), p < 0.0001, (MD 7.5, 95% CI 4.3 to 10.7) p<0.0001
Castel 2013/Salvat 2017	

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Castel 2013	
Castel 2013/Salvat 2017	A vs B <u>3 months</u> FIQ: 55.5 (19.3) vs 64.6 (17.6), p<0.05, (MD -9.1, 95% CI -14.9 to -3.2) p=0.0026 Minimally clinically significant FIQ improvement: 48.1% vs 23.0%, [OR = 3.1, 95% CI 1.6 to 5.9] WONCA total score, mean (95% CI)*: 23.7 (22.5 to 25.0) vs 26.5 (25.1 to 27.9), p<0.005 WONCA physical function, mean (95% CI)*: 2.71 (2.51 to 2.95) vs 3.20 (2.95 to 3.41), p NR WONCA daily activities, mean (95% CI)*: 2.88 (2.70 to 3.05) vs 3.20 (3.00 to 3.39), p NR Pain NRS: 6.4 (1.9) vs 6.8 (1.8), (MD -0.4, 95% CI -1.0 to 0.2) p=0.18 Minimally clinically significant pain improvement: 13.6% vs 10.8%, [OR = 1.3, 95% CI 0.5 to 3.3] HADS: 15.2 (9.1) vs 20.6 (8.5), p<0.001, (MD -5.4, 95% CI -8.2 to -2.6) p=0.0002 Sleep problems: 40.5 (10.4) vs 31.2 (9.4), (MD 9.3, 95% CI 6.1 to 12.5) p<0.0001 <u>6 months</u> FIQ: 55.8 (20.9) vs 67.8 (18.4), p <0.05 (MD -12.0, 95% CI -17.2 to -6.8) p<0.0001 Minimally clinically significant FIQ improvement: 42% vs 19%, p < 0.01 [OR = 3.1, 95% CI 1.5 to 6.4] WONCA total score, mean (95% CI)*: 23.6 (22.4 to 24.9) vs 27.3 (25.9 to 28.6), p<0.005 WONCA physical function, mean (95% CI)*: 2.69 (2.48 to 2.90) vs 3.38 (3.12 to 3.60), p NR WONCA daily activities, mean (95% CI)*: 2.97 (2.80 to 3.15) vs 3.28 (3.10 to 3.47), p NR Pain NRS: 6.4 (1.9) vs 7.0 (1.9), p >0.05, (MD -0.6, 95% CI -1.2 to 0.004), p=0.051 Minimally clinically significant pain improvement: 16% vs 5%, p <0.05 [OR = 3.4, 95% CI 1.04 to 10.8] HADS: 16.2 (9.3) vs 21.5 (8.5), p < 0.0001, (MD -5.3, 95% CI -8.1 to -2.5) p=0.0003 Sleep problems: 38.7 (10.5) vs 29.0 (8.9), p < 0.0001, (MD 9.7, 95% CI 6.6 to 12.8) p<0.0001 <u>12 months</u> FIQ: 58.8 (20.5) vs 69.6 (17.2), p > 0.05, (MD -10.8, 95% CI -16.8 to -4.8) p=0.0005 Minimally clinically significant FIQ improvement: 27% vs 4%, p < 0.0001 [OR = 8.8, 95% CI 2.5 to 30.9] WONCA total score, mean (95% CI)*: 23.5 (22.1 to 24.8) vs 26.4 (24.9 to 27.9), p<0.005 WONCA physical function, mean (95% CI)*: 2.72 (2.49 to 2.96) vs 3.33 (3.05 to 3.62), p NR WONCA daily activities,mean (95% CI)*: 2.87 (2.69 to 3.06) vs 3.32 (3.10 to 3.55), p NR Pain NRS: 6.7 (1.6) vs 7.1 (1.8), p >0.05, (MD -10.8, 95% CI -16.8 to -4.8) p=0.0005 Minimally clinically significant pain improvement: 8.6% vs 0, p < 0.05 [OR = 0.5, 95% CI 0.4 to 0.6] HADS: 17.1 (9.9) vs 22.8 (9.2), p <0.01, (MD -5.7, 95% CI -8.7 to -2.7) p=0.0003 Sleep problems: 36.3 (11.0) vs 28.8 (8.6), p < 0.0001, (MD 7.5, 95% CI 4.3 to 10.7) p<0.0001

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Castel 2013		Adverse events: NR Withdrawals: NR
Castel 2013/Salvat 2017		Adverse events: NR Withdrawals: NR

Author, Year	Funding Source	Quality	Comments
Castel 2013	Foundation Marato TV3	Poor	
Castel 2013/Salvat 2017	Foundation Marato TV3, grant number 070910	Fair	Given instructions in Column I, 3 month results were not abstracted *Values estimated from figure

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Castel 2015 Same population as Castel 2013 (above), Subgroup analysis by BMI			Randomized: 130 Analyzed: 89 Attrition: 32% (41/130)

Author, Year	Intervention, Comparator
Castel 2015 Same population as Castel 2013 (above), Subgroup analysis by BMI	A.Multidisciplinary treatment (n=53): Conventional pharmacological treatment, including analgesics, antidepressants, benzodiazepine and non-benzodiazepine hypnotics; CBT delivered by clinical psychologist and physical therapy delivered by physiotherapist in group format (1 hour CBT and 1 hour physical therapy) 2 days/week for a total of 24 sessions. CBT included education, cognitive restructuring, CBT for insomnia, assertiveness training, goal setting, activity pacing, pleasant activity scheduling, and relapse prevention. Physical therapy emphasized aerobic capacity, muscle strengthening and flexibility, and hydrokinesiotherapy in a heated pool. B.Conventional pharmacological treatment (n=36): Conventional pharmacological treatment, including analgesics, antidepressants, benzodiazepine and non-benzodiazepine hypnotics.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Castel 2015 Same population as Castel 2013 (above), Subgroup analysis by BMI	A vs B BMI < 25 Age: 48 vs 49 Female: 100% vs 100% FIQ: 65.1 (13.3) vs 66.9 (13.0) Pain NRS: 6.8 (1.2) vs 7.4 (1.3) HADS: 22.9 (8.0) vs 21.8 (7.8) MOS Sleep quantity: 5.7 (1.4) vs 4.6 (1.2) MOS Sleep problems index: 28.3 (8.5) vs 24.6 (6.1) BMI 25.0-29.9 Age: 50 vs 48 Female: 100% vs 100% FIQ: 59.8 (17.2) vs 57.7 (15.8) Pain NRS: 6.3 (1.3) vs 6.1 (2.1) HADS: 20.9 (8.1) vs 20.8 (8.7) MOS Sleep quantity: 5.9 (1.5) vs 5.8 (1.4) MOS Sleep problems index: 32.4 (8.4) vs 31.7 (9.1) BMI ≥30 Age: 51 vs 50 Female: 100% vs 100% FIQ: 64.7 (14.4) vs 67.2 (17.2) Pain NRS: 7.3 (1.3) vs 7.2 (1.2) HADS: 20.2 (8.4) vs 24.3 (8.5) MOS Sleep quantity: 5.0 (1.7) vs 5.2 (1.3) MOS Sleep problems index: 28.9 (9.1) vs 27.1 (7.8)	Fibromyalgia Impact Questionnaire (FIQ) (0-100 scale, higher scores=greater impact of FM) Pain numerical rating scale (NRS), mean of maximum, minimum, and usual pain intensity in past week (0-10 scale, higher scores=greater pain) Hospital Anxiety and Depression Scale (HADS) (scale NR, higher scores=greater psychological distress) MOS Sleep scale sleep quantity (scale NR, higher scores=worse sleep) MOS Sleep scale sleep problems index (scale NR, higher scores=worse sleep)	3, 6, and 12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Castel 2015 Same population as Castel 2013 (above), Subgroup analysis by BMI	A vs B BMI < 25 (n = 23 vs. 18; ITT analysis using LOCF) 3 months: *Proportion of patients achieving minimum clinically significant difference:* FIQ: 56.5% (13/23) vs 16.7% (3/18); RR 3.3 (95% CI1.1 to 10.1), p=0.01 Pain NRS: 17.4% (4/23) vs 0% (0/18); RR NC *Mean (SD)* FIQ: 51.8 (20.4) vs 66.8 (15.2), (MD -15.0, 95% CI -26.7 to -3.3) p=0.013 Pain NRS: 6.4 (1.9) vs 7.1 (1.0), (MD -0.7, 95% CI -1.7 to 0.3) p=0.17 HADS: 14.6 (9.6) vs 21.7 (9.0), (MD -7.1, 95% CI -13.0 to -1.2) p=0.02 MOS Sleep quantity: 6.7 (1.1) vs 5.5 (1.6), (MD 1.2, 95% CI 0.3 to 2.1) p=0.007 MOS Sleep problems index: 42.3 (9.0) vs 27.8 (7.2), (MD 14.5, 95% CI 9.2 to 19.8) p<0.0001 6 months: *Proportion of patients achieving minimum clinically significant difference:* FIQ: 47.8% (11/23) vs. 16.7% (3/18); RR 2.9 (95% CI 0.9, 8.8), p=0.04 Pain intensity: 8.7% (2/23) vs. 16.7% (3/18); RR 0.5 (95% CI 0.1, 2.8), p=0.44 *Mean (SD)* FIQ: 56.5 (21.3) vs 66.1 (17.2), (MD -9.6, 95% CI -22.1 to 2.9) p=0.13 Pain NRS: 6.9 (1.6) vs 6.7 (1.5), (MD 0.2, 95% CI -0.8 to 1.2) p=0.69 HADS: 16.2 (10.1) vs 22.1 (9.0), (MD -5.9, 95% CI -12.0 to 0.2) p=0.06 MOS Sleep quantity: 6.3 (1.4) vs 5.0 (2.0), (MD 1.3, 95% CI 0.2 to 2.4) p=0.019 MOS Sleep problems index: 39.0 (10.1) vs 27.9 (5.4), (MD 11.1, 95% CI 5.8 to 16.4) p=0.0001 12 months: *Proportion of patients achieving minimum clinically significant difference:* FIQ: 52.2% (12/23) vs. 5.6% (1/18); RR 9.4 (95% CI 1.3, 65.7), p=0.002 Pain intensity: 13% (3/23) vs. 16.7% (3/18); RR 0.8 (95% CI 0.2, 3.4), p=0.75 *Mean (SD)* FIQ: 52.0 (23.2) vs 66.7 (15.4), (MD -14.7, 95% CI -27.5 to -1.9) p=0.026 Pain NRS: 6.6 (1.6) vs 7.0 (1.6), (MD -0.4, 95% CI -1.4 to 0.6) p=0.43 HADS: 14.4 (9.2) vs 21.6 (9.7), (MD -7.2, 95% CI -13.2 to -1.2) p=0.020 MOS Sleep quantity: 6.7 (1.3) vs 5.5 (1.6), (MD 1.2, 95% CI 0.3 to 2.1) p=0.012 MOS Sleep problems index: 42.1 (9.6) vs 28.6 (6.4), (MD 13.5, 95% CI 8.2 to 18.8) p<0.0001

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Castel 2015 Same population as Castel 2013 (above), Subgroup analysis by BMI	A vs B BMI 25.0-29.9 (n = 29 vs. 20; ITT analysis using LOCF) 3 months: *Proportion of patients achieving minimum clinically significant difference:* FIQ: 44.8% (13/29) vs 30% (6/20); RR 1.5 (95% CI 0.7 to 3.3), p=0.30 Pain NRS: 13.8% (4/29) vs 20% (4/20); RR 0.7 (95% CI 0.2 to 2.4), p=0.57 *Mean (SD)* FIQ: 53.4 (18.8) vs 57.4 (19.8), (MD -4.0, 95% CI -15.2 to 7.2) p=0.48 Pain NRS: 6.2 (2.1) vs 5.6 (2.4), (MD 0.6, 95% CI -0.7 to 1.9) p=0.36 HADS: 12.9 (8.1) vs 18.7 (8.7), (MD -5.8, 95% CI -10.7 to -0.9) p=0.021 MOS Sleep quantity: 6.5 (1.5) vs 5.9 (1.5), (MD 0.6, 95% CI -0.3 to 1.5) p=0.17 MOS Sleep problems index: 42.5 (9.5) vs 33.7 (9.9), (MD 8.8, 9% CI 3.1 to 14.5) p=0.003 6 months: *Proportion of patients achieving minimum clinically significant difference:* FIQ: 51.7% (15/29) vs. 0% (0/20); RR NC Pain intensity: 24.1% (7/29) vs. 0% (0/20); RR NC *Mean (SD)* FIQ: 50.5 (19.1) vs 58.7 (20.0), (MD -8.2, 95% CI -19.6 to 3.2) p=0.15 Pain NRS: 6.0 (2.0) vs 6.0 (2.2), (MD 0.0, 95% CI -1.2 to 1.2) p=1.00 HADS: 13.8 (8.7) vs 18.3 (8.4), (MD -4.5, 95% CI -9.5 to 0.5) p=0.08 MOS Sleep quantity: 6.6 (1.1) vs 5.8 (1.1), (MD 0.8, 95% CI 0.16 to 1.4) p=0.016 MOS Sleep problems index: 42.4 (8.5) vs 32.9 (10.1), (MD 9.5. 95% CI 4.1 to 14.9) p=0.0009 12 months *Proportion of patients achieving minimum clinically significant difference:* FIQ: 31.0% (9/29) vs. 5% (1/20); RR 6.2 (95% CI 0.9, 45.2), p=0.03 Pain intensity: 17.2% (5/29) vs. 5% (1/20); RR 3.4 (95% CI 0.4, 27.3), p=0.20 *Mean (SD)* FIQ: 56.1 (20.1) vs 64.5 (19.6), (MD -8.4, 95% CI -20.0 to 3.2) p=0.15 Pain NRS: 6.2 (1.9) vs 6.2 (2.3), (MD 0.0, 95% CI -1.2 to 1.2) p=1.00 HADS: 14.2 (9.3) vs 20.3 (9.9), (MD -6.1, 95% CI -11.7 to -0.5) p=0.033 MOS Sleep quantity: 6.4 (1.4) vs 5.7 (1.1), (MD 0.7, 95% CI -0.1 to 1.5) p=0.068 MOS Sleep problems index: 40.5 (8.7) vs 31.4 (11.0), (MD 9.1, 95% CI 3.4 to 14.8) p=0.0023

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Castel 2015 Same population as Castel 2013 (above), Subgroup analysis by BMI	A vs B BMI ≥30 (n = 17 vs. 23; ITT analysis using LOCF) 3 months: *Proportion of patients achieving minimum clinically significant difference:* FIQ: 52.9% (9/17) vs 21.7% (5/23); RR 2.4 (95% CI 1.0 to 6.0), p=0.04 Pain intensity:11.8% (2/17) vs 13% (3/23); RR 0.9 (95% CI 0.2 to 4.8), p=0.90 *Mean (SD)* FIQ: 53.2 (17.7) vs 64.0 (18.9), (MD -10.8, 95% CI -22.7 to 1.1) p=0.07 Pain intensity: 6.5 (1.6) vs 7.0 (1.9), (MD -0.5, 95% CI -1.7 to 0.7) p=0.39 HADS: 14.0 (8.6) vs 18.9 (9.2), (MD -4.9, 95% CI -10.7 to 0.9) p=0.10 MOS Sleep quantity: 6.3 (1.6) vs 5.5 (1.6), (MD 0.8, 95% CI -0.2 to 1.8) p=0.13 MOS Sleep problems index: 42.3 (9.0) vs 31.1 (9.4), (MD 11.2, 95% CI 5.2 to 17.2) p=0.0005 6 months: *Proportion of patients achieving minimum clinically significant difference:* FIQ: 41.2% (7/17) vs.4.3% (1/23); RR 9.5 (95% CI 1.3 to 70.0) p=0.045 Pain intensity: 17.6% (3/17) vs. 4.3% (1/23); RR 4.1 (95% CI 0.5 to 35.7) p=0.17 *Mean (SD)* FIQ: 56.5 (20.9) vs 73.9 (19.0), (MD -17.4, 95% CI -30.2 to -4.6) p=0.009 Pain NRS: 6.5 (2.3) vs 7.5 (2.1), (MD -1.0, 95% CI -2.4 to 0.4) p=0.16 HADS: 15.3 (7.9) vs 22.6 (9.6), (MD -7.3, 95% CI -13.1 to -1.5) p=0.015 MOS Sleep quantity: 6.2 (1.7) vs 5.5 (1.3), (MD 0.7, 95% CI -0.3 to 1.7) p=0.15 MOS Sleep problems index: 40.5 (9.2) vs 27.3 (9.5), (MD 13.2, 95% CI 7.1 to 19.3) p=0.0001 12 months: *Proportion of patients achieving minimum clinically significant difference:* FIQ: 41.2% (7/17) vs.4.3% (1/23); RR 9.5 (95% CI 1.3, 69.9), p=0.005 Pain intensity: 11.8% (2/17) vs. 4.3% (1/23); RR 2.7 (95% CI 0.3, 27.5), p=0.38 *Mean (SD)* FIQ: 56.8 (20.4) vs 74.9 (13.9), (MD -18.1, 95% CI -29.1 to -7.1) p=0.002 Pain NRS: 6.8 (1.5) vs 7.5 (2.0), (MD -0.7, 95% CI -1.9 to 0.5) p=0.23 HADS: 14.5 (10.8) vs 23.6 (11.0), (MD -9.1, 95% CI -16.2 to -2.0) p=0.01 MOS Sleep quantity: 6.2 (1.9) vs 5.8 (1.3), (MD 0.4, 95% CI -0.6 to 1.4) p=0.43 MOS Sleep problems index: 40.0 (10.1) vs 29.3 (8.3), (MD 10.7, 95% CI 4.8 to 16.6) p=0.0007	Withdrawals: NR Adverse events: NR

Author, Year	Funding Source	Quality	Comments
Castel 2015 Same population as Castel 2013 (above), Subgroup analysis by BMI	Foundation Marato TV3	Poor	P values were not reported for the comparisons listed in the Results column. There was a significant overall treatment X time interaction effect for pain intensity ($p < 0.01$), HADS ($p < 0.0001$), sleep index problems ($p < 0.0001$). No significant interactions were found for BMI X group treatment X time for any measure. Not enough room in subquestion a column so the different BMI strata were included in the 3 separate results columns INCLUDE FOR KQ6 - Special Populations

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Castien 2011	The Netherlands (multicenter)	Inclusion Criteria: >18 to 65 years old, diagnosed with CTTH according to IHS classification Exclusion criteria: Rheumatoid arthritis, suspected malignancy, pregnancy, intake of triptans, ergotamines, or opioids ≥ 10 days per month, simple analgesics ≥ 15 days per month for ≥ 3 months, manual therapy treatment within 2 months of enrollment	Randomized: 82 Treated: 80 Analyzed: 75 Attrition: 9% (7/82)

Author, Year	Intervention, Comparator
Castien 2011	A.Manual therapy (n=38) No. sessions: Max of 9 over 8 weeks Length of sessions: 30 min Segments targeted: Cervical, thoracic, and lumbar spinal segments Description of technique: combination of 3 approaches: mobilizations, craniocervical muscle exercises and posture correction B.Usual Care (n=37) General practitioner provided information and advice, first prescribing life-style changes. Analgesics or NSAIDs were prescribed and pain medication was changed as needed. Treatment spanned on average 2-3 visits

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Castien 2011	A vs. B Age (SD): 40 vs 40 years Female: 78% vs 78% Race: NR Mean duration of chronicity: 12.5 (10.7) vs. 13.1 (12.3) Mean frequency of headache, days (SD): 23.7 (6.8) vs. 24.0 (7.0) days per month Patients who had prior preventative treatments: NR Patients who overused medications: NA* Mean number of analgesic medications used at baseline (SD): 1.3 (2.8) pills per week NSAIDs 3.2 (4.5) pills per week analgesics HIT-6 (36-78 points): 62.6(5.4) vs. 61.2(6.0); MD 1.4 (95%CI -1.23 to 4.02) p=0.291 HDI (0-100 points): 39.6 (21.9) vs. 44.2(22.9); MD -4.6 (95%CI -14.91 to 5.71) p=0.377 Average pain intensity (0-10): 6.3(1.9) vs 5.7(1.5); MD 0.60 (95% CI -0.19 to 1.39) p=0.134 *See exclusion criteria	Proportion of patients with 50% reduction in headache frequency; Headache Impact Test-6 (HIT-6, range 36-78: from little to no impact to severe impact); Headache Disability Inventory (HDI, range 0-100: higher scores indicate severity of symptoms); Mean Headache frequency (days with headache in 2 week time period); Mean Headache intensity (Numeric Rating Scale, range 0-10: higher scores indicate severity of pain); Mean Headache Duration Analgesic/NSAID use; Healthcare Resource Utilization	4.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Castien 2011	A vs B 4.5 Months Proportion of patients with ≥50% reduction in headache frequency, (n/N): 81.6% (31/38) vs. 40.5% (15/37); RR 2.01 (95% CI 1.32 to 3.05) p=0.003 Δ from baseline, Headache Impact Test-6 (36-78) (SD): –10.6(8.4) vs. –5.5(8.6) p=0.012; MD -5.0 (SEM 1.97) (95% CI –9.02 to –1.16) p=0.012 Δ from baseline, Headache Disability Inventory (0-100) (SD): –20.0(22.6) vs. –9.9(18.0) p=0.037; MD–10.1(SEM 4.74) (95% CI –19.5 to –0.64) p=0.037 Δ from baseline, mean headache frequency (days/14 days (headache diary)) (SD): –9.1(4.2) vs. –4.1(4.4) p<0.001; MD –4.9(SEM 0.99) (95% CI –6.95 to –2.98) p<0.001 Δ from baseline, mean headache pain intensity (0-10 NRS) (SD): –3.1(2.8) vs. –1.7(2.5) p=0.027; MD –1.4 (SEM 0.63) (95% CI –2.69 to –0.16) p=0.027 Δ from baseline, mean headache duration (hrs./day) (SD): –7.0(10.4) vs. –3.5(7.3); p=0.095; MD 3.5 (SEM 2.1) (95% CI –7.71 to –0.63) p=0.095 Proportion who considered themselves improved/much improved (n/N): 86.8% (33/38) vs. 37.8% (14/37); MD 62.5% (48.4-79.3%); RR 2.29 (95%CI 1.49 to 3.53) p=0.00 Proportion who used ≥1 sick leave day (n/N): 7.9% (3/38) vs. 32.4% (12/37) p<0.05; RR 0.23 (95%CI 0.07 to 0.79) p=0.008 Proportion who used any additional health care (i.e., physical therapy, medical specialists, other) (n/N): 13.2% (5/38) vs. 59.4% (22/37) p<0.05; RR 0.22 (95%CI 0.093 to 0.522) p=0.000 Proportion who used additional physical therapy (n/N): 2.6% (1/38) vs. 40.5% (15/37) p<0.05; RR 0.064 (95%CI 0.01 to 0.47) p=0.0001 Proportion who used additional medical specialist care (n/N): 2.6% (1/38) vs. 16.2% (6/37) p<0.05; RR 0.16 (95%CI 0.02 to 1.28) p=0.044 Proportion who used additional "other" health care" (n/N): 7.8% (3/38) vs. 2.7% (1/37) p<0.05 RR 2.92 (95%CI 0.31 to 26.8) p=0.32 Use of analgesics/NSAIDs (decreased, no change, increased intake of tablets): Data NR: "differences were not stat. diff. between/within groups" Use of analgesics/NSAIDs (decreased, no change, increased intake of tablets): Data NR: "differences were not stat. diff. between/within groups"

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Castien 2011	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Castien 2011	NR	"No adverse events were reported in both intervention groups."

Author, Year	Funding Source	Quality	Comments
Castien 2011	NR	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Castro-Sanchez 2011[a]	Spain	Inclusion Criteria: Adults age 40 to 65, agreement to attend evening therapy sessions, limitation of usual activities due to pain on at least 1 day in the previous 30 days, and/or moderate or worse average pain level (<=4 on a 10-point scale according to article; we assume they meant >4). Exclusion Criteria: Receipt of non-pharmaceutical therapies; presence of infection, fever, hypotension, treatment-limiting respiratory disorders; and alterations in cutaneous integrity.	Randomized: 94 Treated: 94 Analyzed: 86 Attrition: 8.5% (8/94)

Author, Year	Intervention, Comparator
Castro-Sanchez 2011[a]	A.Myofascial Release (n=45) Deep fascia release No. of Regions: Temporal region, suboccipital release, compression-decompression of temporomandibular join, global release of cervicodorsal fascia, release of pectoral region, diaphragm release (transverse slide), transverse diaphragmatic plane, lumbosacral decompression, release of psoas fascia and release of the lumbar square. No. of Treatments: 2/week for 20 weeks Length of Treatments: 1 hour with 10 myofascial release modalities B.Sham short-wave and Ultrasound Electrotherapy (n=41) No. of Treatments: 2/week for 20 weeks Length of Treatments: 30 minutes

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Castro-Sanchez 2011[a]	A vs. B Age (SD): 55 vs 54 years Female: NR Race: NR Mean duration of chronicity: NR Total FIQ: 64.95 (18.2) vs. 63.94(16.4) Number of Days Feeling Good (FIQ): 1.84(1.56) vs. 2.04(2.10) Pain (FIQ): 9.2(0.6) vs 8.9(1.1) Fatigue (FIQ): 8.1(1.5) vs. 8.6(1.3) Tiredness on waking: 8.5(2.3) vs. 7.9(2.6) Stiffness: 7.8(1.9) vs. 6.9(2.7) Pain: McGill Pain Questionnaire (MPQ): Sensory (0-33): 19.3(9.2) vs. 19.9(10.6) Affective (0-12): 5.6(3.4) vs. 4.9(4.2) Sensory+Affective (0-45): 24.9 (12.6) vs. 25.3(10.7) Pain (VAS): 9.13(0.8) vs 8.90 (1.3) p=0.219 Clinical Global Impression Severity Scale: 6.25(0.73) vs. 5.92(0.84) Clinical Global Impression Improvement Scale: -5.38(0.79) vs. -5.47(0.46)	Fibromyalgia Impact Questionnaire Total (FIQ, 0-100) Number of Days Feeling Good (FIQ, 0-10): Pain (FIQ, 0-10) Fatigue (FIQ, 0-10) Tiredness on waking (FIQ, 0-10) Stiffness (FIQ, 0-10) McGill Pain Questionnaire (MPQ): Sensory (MPQ, 0-33) Affective (MPQ, 0-12) Sensory+Affective (MPQ, 0-45) Clinical Global Impression Severity Scale (Likert, 1-7, higher scores indicate severity of illness) Clinical Global Impression Improvement Scale (Likert, 1-7, higher scores indicate severity of illness)	6 Months, 12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Castro-Sanchez 2011[a]	A vs. B Intermediate Term (6 months) Fibromyalgia Impact Questionnaire (FIQ): Total (FIQ, 0-100): 58.60(16.3) vs. 64.08(18.1) p=0.048; MD -5.5 (95% CI -12.9 to 1.9) p=0.143 Number of Days Feeling Good (FIQ, 0-10): 2.88(1.56) vs. 2.01(1.44) p=0.036 ; MD 0.87(95% CI 0.2 to 1.5) p=0.009 Pain (FIQ, 0+I8-10): 8.5(0.7) vs. 8.0(1.3) p=0.042; MD 0.5 (95% CI 0.06 to 0.9) p=0.027 Fatigue (FIQ, 0-10): 7.4(1.9) vs. 8.5(1.7) p=0.037; MD -1.1 (95% -1.9 to -0.3) p=0.006 Tiredness on waking (FIQ, 0-10): 7.5(1.9) vs. 7.6(1.8) p=0.724; MD -0.1 (95% CI -0.8 to 0.6) p=0.80 Stiffness (FIQ, 0-10): 6.9(2.5) vs. 7.8(2.4) p=0.043; MD -0.9 (95% CI -1.9 to 0.1) p=0.092 McGill Pain Questionnaire (MPQ): Sensory (0-33): 17.3(7.8) vs. 20.7 (7.1); p=0.042; MD -3.4 (95% CI -6.6 to -0.19) p=0.038 Affective (0-12): 4.5(2.9) vs. 5.2(3.8); p=0.042; MD -0.7 (95% CI -2.14 to 0.74) p=0.337 Sensory+Affective (0-45): 21.9(7.2) vs. 26.2(6.8) p=0.022; MD -4.3(95% CI -7.3 to -1.3) p=0.005 Pain (VAS, 0-10): 8.25(1.13) vs. 8.94(1.34); p=0.043; MD -0.69 (95% CI -1.22 to -0.16) p=0.011 Clinical Global Impression Severity Scale (Likert, 1-7): 5.28(0.97) vs. 5.98(0.84) p=0.048; MD -0.7 (95% CI -1.09 to -0.31) p=0.0006 Clinical Global Impression Improvement Scale (Likert, 1-7): 5.62(0.88) vs. 6.30(0.97) p=0.046; MD -0.68 (95% CI -1.08 to -0.28) p=0.0010 Long Term (12 months) Fibromyalgia Impact Questionnaire (FIQ): Total (FIQ, 0-100): 62.80(20.1) vs. 65.01(19.8) p=0.329; MD -2.21(95%CI -10.78 to 6.36) p=0.609 Number of Days Feeling Good (FIQ, 0-10): 2.55(1.76) vs. 1.99(1.62) p=0.047; MD 0.56 (95%CI -0.17 to 1.29) p=0.129 Pain (FIQ, 0-10): 8.8(0.5) vs. 8.7(0.7) p=0.519; MD 0.10 (95%CI -0.16 to 0.36) p=0.445 Fatigue (FIQ, 0-10): 7.8(2.3) vs. 8.8(1.6) p=0.038; MD -1.00 (95%CI -1.86 to -0.14) p=0.023 Tiredness on waking (FIQ, 0-10): 7.7(2.2) vs. 7.7(1.9) p=0.791; MD 1.00 (95%CI -0.89 to 0.89) p=1.000 Stiffness (FIQ, 0-10): 7.3(2.5) vs. 7.8(2.1) p=.089; MD -0.50 (95%CI -1.50 to 0.50) p=0.321 McGill Pain Questionnaire (MPQ): Sensory (MPQ, 0-33): 18.2(8.3) vs. 21.2(7.9) p=0.038; MD -3.00 (95%CI -6.48 to 0.48) p=0.090 Affective (MPQ, 0-12): 4.8(3.6) vs. 5.1(2.9) p=0.232; MD -0.3 (95%CI -1.71 to 1.11) p=0.673 Sensory+Affective (MPQ 0-45): 23.2(7.6)vs 26.7(6.9) p=0.036; MD -3.50(95%CI -6.62 to -0.37) p=0.028 Pain (VAS, 0-10): 8.74(1.08) vs. 8.92(0.96) p=0.306; MD -0.18 (95%CI -0.62 to 0.26) p=0.418 Clinical Global Impression Severity Scale (Likert, 1-7): 5.49(0.74) vs. 6.17(0.91) p=0.147; MD -0.68 (95%CI -1.03 to -0.32) p=0.0003 Clinical Global Impression Improvement Scale (Likert, 1-7): 5.83(1.24) vs. 6.49(0.89) p=0.049; ; MD -0.66 (95%CI -1.13 to -0.19) p=0.006

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Castro-Sanchez 2011[a]	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Castro-Sanchez 2011[a]	NR	"None of the 94 participants reported adverse effects"

Author, Year	Funding Source	Quality	Comments
Castro-Sanchez 2011[a]	This research received no specific grant from any funding agency in the public, commercial, or not for-profit sectors.	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Castro-Sanchez 2011[b]	Spain	Inclusion Criteria: Adults age 18 to 65, no regular physical activity and agreement to attend evening therapy sessions. Exclusion Criteria: Nonagreement to study participation; receipt of other nonpharmacologic therapies; presence of cardiac, renal or hepatic insufficiency; cardiovascular event during previous year and presence of peripheral arterial or venuous insufficiency, physical or psychological disease, infection fever, hypotension, respiratory alterations limiting treatment application; skin integrity alterations and failure to comply with prescribed pharmaceutical therapy.	Randomized: 64 Treated: 59 Analyzed: 59 Attrition: 8% (5/64)

Author, Year	Intervention, Comparator
Castro-Sanchez 2011[b]	A.Massage-Myofascial Release (n=30) Massage-Myofascial release therapy weekly 90-minute session for 20 weeks. Massage-Myofascial Release at insertion of the temporal muscle, release of falx cerebri by frontal lift, release of tentorium cerebelli by synchronization of temporals, assisted release of cervical fascia, release of anterior thoracic wall, release of pectoral region, lumbosacral decompression, release of gluteal fascia, transversal sliding of wrist flexors and fingers and release of quadriceps fascia. B.Sham Magnotherapy (n=29) Weekly 30-minute session of disconnected magnotherapy for 20 weeks. Patients laid in prone position, magnotherapy was applied on cervical area (15 min) and lumbar area (15 min).

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Castro-Sanchez 2011[b]	A vs. B Age: 49 vs 46 years Female: 94% vs 96% Race: NR Mean duration of chronicity: NR SF-36: Physical Function: 5.23* (5.36) vs 50.24 (8.47); *the number reported is 5.23 but it is assumed that this is a typo Physical Role: 25.97(7.32) vs. 26.36 (6.25) Body Pain: 76.56(6.31) vs. 78.93(11.43) Pain Intensity (VAS)*: 9.1 vs. 9.6 State-Trait Anxiety Inventory (STAI) State Anxiety*: 23.1 vs. 22.2 Trait Anxiety*: 25.9 vs. 26.5 Pittsburgh Quality of Sleep Index Questionnaire (PSQI) No. of Patients with Severe Problems Pittsburgh Subjective Quality (PSQI): 80% (24/30) vs. 65.5% (19/29) No. of Patients with Severe Problems Sleep Latency (PSQI): 93.3% (28/30) vs. 86.2% (25/29) No. of Patients with Severe Problems Sleep Duration (PSQI): 76.6% (23/30) vs. 93.1% (27/29) No. of Patients with Severe Problems Habitual Sleep Efficiency (PSQI): 66.6% (20/30) vs. 82.7% (24/29) No. of Patients with Severe Problems Sleep Disturbance (PSQI): 63.3% (19/30) vs. 58.6% (17/29) No. of Patients with Severe Problems Daily Dysfunction (PSQI): 6.6% (2/30) vs. 10.3% (3/29) Beck Depression Inventory (BDI)*: 2.5 vs. 2.5 SF-36: Vitality: 60.85(6.41) vs. 59.42(5.32); p=.301; MD 1.43 (95%CI -1.65 to 4.51) p=0.356 Social Function: 64.03(8.03) vs. 64.42(13.22); p=.639; MD -0.39 (95%CI -6.07 to 5.29) p=0.891 General Health: 67.82(5.21) vs. 68.78(7.22); p=.203; MD -0.96 (95%CI -4.23 to 2.31) p=0.559	Primary: Pain (VAS, range 0-10) Secondary: State-Trait Anxiety Inventory (STAI) State Anxiety (range 20-80, higher scores indicate higher anxiety levels): Trait Anxiety (range 20-80, higher scores indicate higher anxiety levels): No. of Patients with Severe Problems on Pittsburgh Quality of Sleep Index Questionnaire (PSQI, range 0-21: higher scores indicate worse sleep) Beck Depression Inventory (BDI; total:0-63, higher scores indicate severity of depressive symptoms) SF-36 Quality of Life Questionnaire (SF-36, range 0-100: higher scores indicate optimal health status)	1 month, 6 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Castro-Sanchez 2011[b]	6 months Pain (VAS)*: 8.7 vs. 9.7 State-Trait Anxiety Inventory (STAI) State Anxiety*: 22.0 vs. 23.0 Trait Anxiety*: 25.8 vs. 26.2 Pittsburgh Quality of Sleep Index Questionnaire (PSQI): No. of Patients with Severe Problems Pittsburgh Subjective Quality (PSQI): 66.6% (20/30) vs. 24.1% (7/29) No. of Patients with Severe Problems Sleep Latency (PSQI): 50% (15/30) vs. 62% (18/29) No. of Patients with Severe Problems Sleep Duration (PSQI): 56.6% (17/30) vs. 93.1% (27/29) No. of Patients with Severe Problems Habitual Sleep Efficiency (PSQI): 46.6% (14/30) vs. 75.9% (22/29) No. of Patients with Severe Problems Sleep Disturbance (PSQI): 53.3% (16/30) vs. 72.4% (21/29) No. of Patients with Severe Problems Daily Dysfunction (PSQI): 46.6% (14/30) vs. 20.7% (6/29) Beck Depression Inventory (BDI)*: 2.3 vs. 2.5 SF-36 Quality of Life Questionnaire (SF-36, all subscales range 0-100) Physical Function (SF-36): 48.20(7.43) vs. 51.19(6.32), p=0.281; MD -2.99 (95%CI -.659 to 0.612) p=0.102 Physical Role (SF-36): 25.49(8.41) vs. 27.53(6.25), p=0.213; MD -2.04 (95%CI -5.91 to 1.83) p=0.296 Body Pain (SF-36): 75.63(8.22) vs. 77.84(9.66), p=0.293; MD -2.21 (95%CI -6.88 to 2.46) p=0.347 General Health (SF-36): 67.53(7.24) vs. 68.13(6.44), p=0.401; MD -0.60 (95%CI -4.18 to 2.98) p=0.738 Vitality (SF-36): 62.15(9.32) vs. 58.93(7.65), p=0.312; MD 3.22(95%CI -1.23 to 7.67) p=0.153 Social Function (SF-36): 61.27(7.53) vs. 63.96(9.71), p=0.088; MD -2.69 (95%CI -7.21 to 1.83) p=0.238 Emotional Role (SF-36): 49.11(7.33) vs. 46.90(9.38), p=0.219; MD 2.21 (95%CI -2.17 to 6.59) p=0.317 Mental Health (SF-36): 76.46(10.12) vs. 80.03(12.43), p=0.126; MD -3.57 (95%CI -9.47 to 2.33) p=0.231 *The values Pain (VAS), STAI, and BDI have been estimated from figures presented in the study report.

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Castro-Sanchez 2011[b]	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Castro-Sanchez 2011[b]	NR	

Author, Year	Funding Source	Quality	Comments
Castro-Sanchez 2011[b]		Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Cedraschi 2004	Switzerland 1 university hospital rheumatology center	Inclusion: FM diagnosis based on 1990 ACR criteria, fluent in French Exclusion: Medical disorder requiring immediate treatment or preventing physical activity or participation in pool sessions	Randomized: 164 analyzed: 129 Attrition: 21% (35/164)
Chen 2014	Taiwan Number of centers unclear Setting type NR	Aged 40 or older with bilateral moderate knee OA* and popliteal cyamella. Exclusion criteria NR	Randomized: 60 Treated: 60 Analyzed: 51 Attrition: 15% (9/60)

Author, Year	Intervention, Comparator
Cedraschi 2004	A.Multidisciplinary treatment (n=61): 6-week program, 12 90-minute group sessions, twice a week for 6 weeks. Program included pool sessions led by physiotherapist, relaxation exercises, low impact exercise led by physiotherapist, sessions on activities of daily living led by occupational therapist, and education. Team consisted of rheumatologist, psychologist, physiotherapist, occupational therapist. 19% withdrew, 60% completed ≥10 sessions. B.Waiting list (n=68): Usual care. Offered A after the 6-month followup.
Chen 2014	A.Exercise (n=30): 3 sessions per week for 8 weeks. Sessions consisted of a 20 minutes of hot packs and 5 minutes of passive range of motion exercises on a stationary bike, followed by an isokinetic muscle-strengthening exercise program B.Control (n=30): Details NR

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Cedraschi 2004	A vs B Age 49 vs 50 Female: 93% vs 93% Symptom duration, years: 8.4 vs 9.5 FIQ total score: 5.5 (1.3) vs 5.6 (1.6) FIQ Physical Function: 4.2 (2.0) vs 4.5 (2.2) FIQ Pain: 6.3 (1.9) vs 6.0 (2.1) FIQ Depression: 5.5 (3.1) vs 5.9 (3.5) FIQ Anxiety: 6.4 (2.6) vs 7.1 (2.7) Regional Pain Score: 63.9 (18.0) vs 67.0 (15.7) Psychological General Wellbeing Index subscales: Anxiety: 11.4 (5.3) vs 10.8 (5.4) Depression: 8.3 (3.4) vs 7.6 (4.0) Psychological General Wellbeing Index total score: 45.9 (17.6) vs 44.0 (19.3) SF-36 Physical Function: 41.8 (18.1) vs 46.8 (19.4)	FIQ total score (0-10, higher scores=greater impact of FM) FIQ Physical Function (0-10, higher scores=greater impact of FM on physical function) FIQ Pain (0-10, higher scores=greater pain) FIQ Depression (0-10, higher scores=greater depression) FIQ Anxiety (0-10, higher scores=greater anxiety) Regional Pain Score (0-105, higher score=more pain) Psychological General Wellbeing Index total score 0-110, higher scores=worse wellbeing) Psychological General Wellbeing Index subscales: Anxiety (0-110, higher scores=greater anxiety) Depression (0-110, higher scores=greater depression) SF-36 Physical Function (0-100, higher scores=better function)	6 months
Chen 2014	A vs B† Age: 63 Females: 85% Duration of knee pain: 10-144 months Lequesne Index: 7.8 (1.2) vs 8.0 (1.1) Pain VAS: 5.5 (1.4) vs 5.6 (1.4)	Lequesne Index (0-26, higher score=higher dysfunction); pain VAS (0-10, higher score=higher pain)	6 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Cedraschi 2004	A vs B <u>6 months</u> FIQ total score: 4.9 (1.4) vs 5.5 (1.5), p =0.03, (MD -0.6, 95% CI -1.1 to -0.1) p=0.021 FIQ Physical Function: 4.3 (2.1) vs 4.8 (2.5), p = 0.58, (MD -0.5, 95% CI -1.3 to 0.3) p=0.22 FIQ Pain: 6.1 (2.1) vs 6.6 (2.1), p = 0.03, (MD -0.5, 95 % CI -1.2 to 0.2) p=0.18 FIQ Depression: 4.6 (3.1) vs 6.1 (3.4), p = 0.03, (MD -1.5. 95% CI -2.6 to -0.4) p=0.010 FIQ Anxiety: 5.1 (2.9) vs 6.7 (3.0), p = 0.08, (MD -1.6, 95% CI -2.6 to -0.6) p=0.0026 Regional Pain Score: 62.6 (20.7) vs 68,4 (15.1), p = 0.39, (MD -5.8, 95% CI -12.1 to 0.5) p=0.07 Psychological General Wellbeing Index subscales: Anxiety: 13.0 (6.2) vs 10.3 (5.6), p = 0.01, (MD 2.7, 95% CI0.6 to 4.8) p=0.01 Depression: 9.0 (3.6) vs 7.7 (4.2), p = 0.13, (MD 1.3, 95% CI -0.1 to 2.7) p=0.06 Psychological General Wellbeing Index total score: 51.1 (19.4) vs 43.8 (20.9), p = 0.03, (MD 7.3, 95% CI 0.2 to 14.3) p=0.04 SF-36 Physical Function: 42.2 (19.8) vs 43.9 (19.6), p = 0.29, (MD -1.7, 95% CI -8.6 to 5.2) p=0.63
Chen 2014	A vs B Lequesne Index: 5.4 (1.7) vs 7.6 (1.6), (MD -2.2, 95% CI -3.1 to -1.3) p<0.001 Pain VAS: 4.0 (1.4) vs 6.5 (1.3), (MD -2.5, 95% CI -3.3 to -1.7) p<0.001

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Cedraschi 2004	
Chen 2014	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Cedraschi 2004		A vs B Withdrawals: 19% (16/84) vs 0 Adverse events: 2% (2/84) vs 0
Chen 2014		Intolerable knee pain: 10% (3/30) vs 0% (0/30) RR=inf, p=0.08

Author, Year	Funding Source	Quality	Comments
Cedraschi 2004	Swiss National Foundation for Research	Poor	
Chen 2014	Grant from the National Science Council Taiwan (NSC: 99-2314-B-037-011-MY3)	Poor	*Defined as Altman III: patients over 40 years of age, knee pain, osteophytes, crepitus, and morning stiffness more than 30 minutes without bony enlargement †All baseline characteristics were reported for all four groups combined (n=120) Study also included an exercise+US group (n=30) and exercise+ESWT group (n=30) that data was not abstracted for because interventions were considered additive MDs and p values calculated by

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Cherkin 2001	USA Number of centers: 7 Setting: Outpatient offices of CAM practitioners in HMO network	Inclusion: Age 20-70 years Primary care physician visit for low back pain Exclude: Sciatica Acupuncture or massage for back pain within the past year Back care from a specialist or CAM provider Severe clotting disorders or anticoagulant therapy Cardiac pacemakers Underlying systemic or visceral disease Pregnancy Involvement with litigation or compensation claims for back pain Inability to speak English Severe or progressive neurologic deficits Lumbar surgery within the past 3 years Recent vertebral fracture Serious comorbid conditions Bothersomeness of back pain rated <4 on a scale of 0-10	Randomized: 184 Treated: 94 Analyzed: 184 Attrition: 0% (0/184)

Author, Year	Intervention, Comparator
Cherkin 2001	A.Needle acupuncture (n=94): Traditional Chinese Medical (TCM) acupuncture treatment for up to 10 visits over 10 weeks using protocol; permitted basic TCM needling techniques, electrical stimulation and manual manipulation of the needles, indirect moxibustion, infrared heat, cupping, and exercise recommendations; did not allow massage (including acupressure), herbs, and treatments not considered common TCM practice; number and location of needles were decided by provider. B.Self-care education (n=90): Patients were mailed high-quality and relatively inexpensive educational materials designed for persons with chronic low back pain: a book and 2 professionally produced videotapes (self-management of back pain, exercise demonstrations); materials included information about back pain and its treatment, techniques for controlling and preventing pain and for improving quality of life, and suggestions for coping with the emotional and interpersonal problems often accompanying chronic illness.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Cherkin 2001	A vs. B Age: 54 vs. 44 Female: 52% vs. 44% Race - White: 82% vs. 89% Pain has lasted <1 year: 57% vs. 62% >90 days of LBP in the past 6 months: 63% vs. 66% Baseline Symptom bothersomeness score during past week: 6.2 vs. 6.1 Baseline Roland Disability Scale: 12.8 vs. 12.0 Baseline SF-12 Physical Health Scale: 37.0 vs. 36.5 Baseline SF-12 Mental Health Scale: 48.8 vs. 48.8 ≥1 work-loss day due to LBP in past month: 26% vs. 26% >7 days restricted activity due to LBP in past month: 48% vs. 1% Previous hospitalization for back problem: 11% vs. 7% Previous lower back operation: 5% vs. 8% Pain travels below knee: 24% vs. 30% Symptoms most of past 24 hours: 53% vs. 62% Previous acupuncture for LBP: 3% vs. 4% Previous massage for LBP: 14% vs. 19% Used medication for LBP in the past week: 69% vs. 63% Taking narcotic analgesics: 9% vs. 9%	Symptom bothersomeness scale (0-10) Modified Roland Disability Scale (RMDQ): 0-23 SF-12 physical health summary scale SF-12 mental health summary scale ≥1 work-loss day due to LBP in past month >7 days restricted activity due to LBP in past month	9.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Cherkin 2001	A vs. B Baseline Symptom bothersomeness (0-10): 6.2 (95% CI 5.8-6.5) vs. 6.1 (95% CI 5.7-6.5) RDQ (0-23): 12.8 (95% CI 11.7-13.8) vs. 12.0 (95% CI 10.9-13.0) SF-12 physical component (0-100): 37.0 (SD 9.4) vs. 36.5 (SD 9.6) SF-12 mental component (0-100): 48.8 (10.7) vs. 48.8 (10.9) ≥1 work-loss day due to LBP in past month: 26% vs. 26% >7 days restricted activity due to LBP in past month: 48% vs. 41% Medication use: 69% vs. 63% 9.5 months Symptom bothersomeness scale: 4.5 (95% CI 3.8 to 5.2) vs. 3.8 (95% CI 3.1 to 4.5), p*=0.002 RDQ (0-23): 8.0 (95% CI 6.6 to 9.3) vs. 6.4 (95% CI 5.1 to 7.7), p*=0.05 SF-12 physical health: no significant difference, data not provided SF-12 mental health: no significant difference, data not provided ≥1 work-loss day due to LBP in past month: no significant difference, data not provided >7 days restricted activity due to LBP in past month: no significant difference, data not provided Medication use: 51% vs. 62%, p<0.05 *p adjusted for baseline values: bothersomeness score, Roland Disability Scale score, pain below the knee, >90 days of back pain in the past 6 months, satisfaction with back care, sex and age. Health care utilization during the year after randomization, mean (SD) Differences across all 3 groups of study (acupuncture, massage, and self-care) were not significant (p=0.15-0.69) A vs. B Provider visits: 1.9 (3.7) vs. 1.5 (4.0) LBP medication fills: 4.4 (8.9) vs. 4.0 (8.6) Imaging studies: 0.2 (0.4) vs. 0.1 (0.4) Cost of services (1998 $): 252 (46) vs. 200 (45)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Cherkin 2001	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Cherkin 2001	NR	A vs. B Withdrawals: 4.3% (4/94) vs. 7.8% (7/90) Withdrawals due to AEs: NR Serious AEs: None in any group Nonserious AEs: 11% vs. 0%

Author, Year	Funding Source	Quality	Comments
Cherkin 2001	Supported by grants from Group Health Cooperative, The Group Health Foundation, Seattle, Washington; the John E. Fetzer Institute, Kalamazoo, Michigan; and grant HS09351 from the Agency for Healthcare Research and Quality, Rockville, Maryland.	Fair	No interactions between treatments and baseline RDQ, baseline symptom bothersomeness scale score, pain below knee but not meeting criteria for sciatica, >90 days of back pain in last 6 months, satisfaction with back care, sex, and age in final model Study has arm for massage intervention, not included here since separate type of intervention.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Cherkin 2001	US Number of centers unclear Outpatient	Age 20-70 Primary care visit for low back pain Exclude: Sciatica Acupuncture or massage for back pain within the past year Back care from a specialist or complementary and alternative medicine provider Severe clotting disorders or anticoagulant therapy Cardiac pacemaker Underlying systemic or visceral disease Pregnancy Involvement with litigation or compensation claims for back pain Lumbar surgery within past 3 years Recent vertebral fracture Serious comorbid conditions Bothersomeness of back pain rated <4 on 0-10 scale	Randomized: 262 Treated: 252 Analyzed: 262 Attrition at 1 year: 5% (13/262)

Author, Year	Intervention, Comparator
Cherkin 2001	A: Mixed massage (n=78): Combinations of manipulation of soft tissues, including Swedish (71%), deep-tissue (65%), neuromuscular (45%), trigger and pressure point (48%) techniques. Prohibited "energy techniques" (Reiki) and meridian techniques (acupressure, shiatsu) that would have effects similar to acupuncture and approaches deeper to specialized (craniosacral). Up to 10 sessions over 10 weeks B: Attention control (self-care education) (n=90): Book, 2 professionally produced videotapes, 40-minute self-management of back-pain video, and 25-minute exercise video. Included information about back pain, treatment, techniques for controlling and preventing pain and for improving quality of life.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Cherkin 2001	Age: 46 vs. 44 years Female: 69% vs. 56% White: 82% vs. 89% LBP care >1 year ago: 81% vs. 85% Pain lasted > 1 year: 64% vs. 62% RDQ mean: 11.8 vs. 12.0 Used medication for LBP in last week: 73% vs. 63%	Primary outcomes: Bothersomeness of back pain, leg pain, numbness or tingling in prior week, 0-10 scale, score for most bothersome symptom was used (higher number=more bothersome) Modified RDQ: positive answers to 23 questions on limitation of daily activities attributable to back pain (higher number=more dysfunction) Secondary outcomes: Disability: National Health Interview Survey questions modified to refer specifically to back-related restrictions. Healthcare utilization: automated HMO data Medication use SF-12 Physical and Mental Health summary scales Number of days of aerobic exercise and back exercise in pervious week	10.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Cherkin 2001	A vs. B, mean (95% CI) <u>Baseline</u> Modified RMDQ (0-23): 11.8 (10.8 to 12.7) vs. 12.0 (10.9 to 13.0) Symptom bothersomeness (0-10): 6.2 (5.8 to 6.6) vs. 6.1 (5.7 to 6.5) SF-12 Mental Component Score: no differences, data not shown <u>10.5 months</u> Modified RMDQ (0-23): 6.8 (5.5 to 8.1) vs. 6.4 (5.1 to 7.7), p=0.03* Symptom bothersomeness (0-10): 3.2 (2.5 to 3.9) vs. 3.8 (3.1 to 4.5), p=0.003* Low back pain medication, mean (SD): 2.5 (3.6) vs. 4.0 (8.6), p=0.69 *Adjusted for baseline RMDQ score

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Cherkin 2001	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Cherkin 2001	NR	Serious Adverse Events: 0 Significant discomfort or pain shortly after treatment: 13% in massage group

Author, Year	Funding Source	Quality	Comments
Cherkin 2001	Group Health Cooperative and AHRQ	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Cherkin 2009	USA Number of centers: 2 Setting: 2 integrated health care delivery systems	18-70 years old Plans to continue enrollment in health plan ≥1 primary care visit for LBP within the past 3–12 months Non-specific, uncomplicated low back pain Exclude: Previous acupuncture for any reason LBP lasting <3 months Mild symptoms (VAS for bothersomeness <3 on 0-10 scale) Specific causes of back pain (cancer, fractures, spinal stenosis, infections) Complicated back problems (sciatica, prior back surgery, medico-legal issues) Possible contraindications for acupuncture (coagulation disorders, cardiac pacemaker, pregnancy, seizure disorder) Conditions making treatment difficult (paralysis, psychoses) Conditions that might confound treatment effects or interpretation of data (severe fibromyalgia, rheumatoid arthritis, concurrent care from other providers)	Randomized: 641 Treated: 315 Analyzed: 638 Attrition: 0.5% (3/641)

Author, Year	Intervention, Comparator
Cherkin 2009	A.Needle acupuncture (individualized) (n=157): 10 treatments over 7 weeks with individualized Traditional Chinese Medical (TCM) acupuncture. Diagnostician acupuncturist prescribed therapy after evaluation using TCM diagnostic techniques. Needles were sterile disposable 32-gauge (0.25 mm) at least 1.5 inches long. Therapy could include any acupoints accessible with participant lying prone, and could use any number of needles, depth of insertion, or needle manipulation; average treatment with 10.8 needles (range 5-20) and retained 18 minutes (range 15-20) on 74 distinct points (half on the Bladder meridian) at a depth of 1-3 cm. Use of electrostimulation, moxibustion, herbs or other non-needle adjuncts were prohibited. B.Needle acupuncture (standardized) (n=158): 10 treatments over 7 weeks with a standardized acupuncture prescription for chronic LBP. Acupoints included 8 commonly used for LBP: Du 3, Bladder 23-bilateral, low back ashi point, Bladder 40-bilateral, Kidney 3-bilateral). Needles were sterile disposable 32-gauge (0.25 mm) at least 1.5 inches long, inserted to elicit "de qi", left in place for 20 minutes with stimulation by twirling the needles at 10 minutes and just prior to removal. C.Sham acupuncture (n=162): 10 treatments over 7 weeks with simulated acupuncture using a toothpick in a needle guide tube at the 8 acupoints used in the standardized treatment. Insertion was simulated by holding the skin taut around each acupoint and placing a standard acupuncture needle guide tube containing a toothpick against the skin. The toothpick was tapped gently, twisted slightly to simulate an acupuncture needle grabbing the skin, and then quickly withdrawn while the acupuncturist kept his or her fingers against the skin for a few additional seconds to imitate the process of inserting the needle to the proper depth. Simulation was to imitate needles left in place for 20 minutes with stimulation at 10 minutes and just prior to removal. Stimulation was imitated by the acupuncturist touching each acupoint with the tip of a toothpick without the guide tube, rotating the toothpick clockwise then counterclockwise less than 30 degrees. Withdrawal of the needle was simulated by tightly stretching the skin around each acupoint, pressing a cotton ball on the skin then touching the skin with the toothpick (without guide tube) and quickly pulling the toothpick away using the same hand movements as in regular needle withdrawal. D.Usual care (n=161): No study-related care. Any care was that which they and their physicians chose, mostly medications, primary care, and physical therapy visits. All: Participants in all groups received a self-care book with information on managing flare-ups, exercise, and life-style modifications.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Cherkin 2009	A vs. B vs. C vs. D Age: 47 vs. 49 vs. 47 vs. 46 Female: 68% vs. 56% vs. 60% vs. 64% - White: 67% vs. 69% vs. 72% vs. 65% - Hispanic origin: 7% vs. 9% vs. 8% vs. 8% Chronic pain for ≥1 year: 69% vs. 74% vs. 60% vs. 70% Baseline modified RDQ: 10.8 vs. 10.8 vs. 9.8 vs. 11.0 Baseline VAS (0-10 VAS): 5.0 vs. 5.0 vs. 4.9 vs. 5.3 Baseline SF-36 physical health score: 41 vs. 42 vs. 42 vs. 42 Baseline SF-36 mental health score: 53 vs. 54 vs. 54 vs. 53 Medication use in past week: 62% vs. 62% vs. 63% vs. 65% Reduced activity ≥7 days in last 3 months due to LBP: 29% vs. 23% vs. 22% vs. 27% Reduced activity >7 days in last 4 weeks due to LBP: 27% vs. 25% vs. 20% vs. 28% Kept in bed or lying down ≥1 day in last 4 weeks due to LBP: 17% vs. 22% vs. 21% vs. 22%	Modified Roland Morris Disability Questionnaire (0-23) Symptom bothersomeness (0-10, higher score = more bothersome) Self-reported medication use for back pain in the prior week SF-36 physical component (0-100) SF-36 mental component (0-100) Cost of health services for LBP during the year following randomization	4.5 months, 10.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Cherkin 2009	A vs. B vs. C vs. D <u>Baseline</u> Modified RDQ (0-23): 10.8 (5.2) vs. 10.8 (5.6) vs. 9.8 (5.2) vs. 11.0 (5.2) Symptom bothersomeness (0-10): 5.0 (2.5) vs. 5.0 (2.3) vs. 4.9 (2.4) vs. 5.2 (2.4) SF-36 physical component: 41 (9) vs. 42 (8) vs. 42 (8) vs. 42 (8) SF-36 mental component: 53 (8) vs. 54 (8) vs. 54 (7) vs. 53 (8) Medication use in past week <u>4.5 months</u> Modified RDQ (0-23): 6.8 (5.5) vs. 6.7 (5.8) vs. 6.4 (6.0) vs. 8.4 (6.0), adjusted difference -0.41 (95% CI -1.53 to 0.70) for A vs. C, -0.36 (95% CI -1.48 to 0.75) for B vs. C, -1.86 (95% CI -2.98 to -0.75) for A vs. D, and -1.81 (95% CI -2.94 to -0.68) for B vs. D ≥3 point decrease on RMDQ: 62% vs. 58% vs. 58% vs. 44% Symptom bothersomeness (0-10): 3.8 (2.5) vs. 3.7 (2.6) vs. 3.5 (2.7) vs. 4.4 (2.6), adjusted difference 0.24 (95% CI -0.35 to 0.83) for A vs. C, 0.07 (95% CI -0.52 to 0.66) for B vs. C, -0.54 (95% CI -1.13 to -0.06) for A vs. D, and -0.71 (95% CI -1.31 to -0.11) for B vs. D ≥2 point decrease in symptom bothersomeness: 49% vs. 44% vs. 48% vs. 41% <u>10.5 months</u> Modified RDQ (0-23): 6.0 (5.4) vs. 6.0 (5.8) vs. 6.2 (5.8) vs. 7.9 (6.5), adjusted difference -1.10 (95% CI -2.23 to 0.04) for A vs. C, -0.84 (95% CI -1.95 to 0.28) for B vs. C, -2.08 (95% CI -3.22 to -0.94) for A vs. D, and -1.82 (95% CI -2.95 to -0.69) for B vs. D ≥3 point decrease on RMDQ: 65% vs. 65% vs. 59% vs. 50% Symptom bothersomeness (0-10): 3.7 (2.6) vs. 3.5 (2.7) vs. 3.4 (2.7) vs. 4.1 (2.6), adjusted difference 0.17 (95% CI -0.42 to 0.76) for A vs. C, -0.03 (95% CI -0.61 to 0.55) for B vs. C, -0.45 (95% CI -1.04 to 0.15) for A vs. D, and -0.65 (95% CI -1.24 to -0.06) for B vs. D ≥2 point decrease in symptom bothersomeness: 52% vs. 49% vs. 50% vs. 47% SF-36 physical component: No differences, data not provided SF-36 mental component: No differences, data not provided >7 days with cutting down on activities due to LBP in the past month: A, B and C 5-7% vs. D 18%, p=0.0005 Missed work/school for >1 day in past month: A, B and C 5-10% vs. D 16%, p=0.01 Mean total costs of back-related health services: $160-221 across groups, p=0.65 Differences adjusted for baseline outcome measure, site, age group (18-29, 30-39, 40-49, 50-59, 60-71) and gender.

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Cherkin 2009	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Cherkin 2009	NR	A vs. B vs. C vs. D Withdrawals: 16% (25/157) vs. 13% (20/158) vs. 10% (17/162) vs. 0% (0/161) Withdrawals due to AEs: <1% (1/157) vs. <1% (1/158) vs. 0% (0/162) vs. 0% (0/161) Serious AEs: <1% (1/638); participant's group not specified Nonserious AEs: 3.8% (6/157) vs. 3.8% (6/158) vs. 0% (0/162) vs. 0% (0/162)

Author, Year	Funding Source	Quality	Comments
Cherkin 2009	Funded through an NIH Cooperative Agreement (U01 AT 001110) with the National Center for Complementary and Alternative Medicine (NCCAM). Seirin acupuncture needles used in the study were donated by Lhasa OMS (Weymouth, Massachusetts).	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Cherkin, 2011	US Number of centers: 1 Outpatient	Age 20 to 65 years with LBP 3+ months without 2 or more pain- free weeks and pain bothersomeness rated at least 3 on a scale of 0 to 10 Exclude: specific causes of back pain, sciatica, back surgery in the past 3 years, or medicolegal issues, conditions making treatment difficult	Randomized: 402 Analyzed: 366 Attrition: 8.9% (36/402)

Author, Year	Intervention, Comparator
Cherkin, 2011	A. Structural massage (n=132): 10 weekly treatments, myofascial, neuromuscular, and other soft-tissue techniques, 75 to 90 minutes, follow-up visits lasting 50 to 60 minutes B. Relaxation massage (n=136): 10 weekly treatments, effleurage, petrissage, circular friction, vibration, rocking and jostling, and holding, 7 to 20 minutes on back and lower rear area, 2.5-minute relaxation exercise to be done at home C. Usual care (n=133)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Cherkin, 2011	A vs. B vs. C Mean age: 46 vs. 47 vs. 48 years Female: 66% vs. 65% vs. 62% Race: 86% vs. 87% vs. 86% white LBP for at least 1 year: 77% vs. 72% vs. 78% Mean days with LBP in past the 6 months: 133 vs. 128 vs. 131 LBP bothersomeness, VAS (0-10): 5.6 vs. 5.6 vs. 5.8 Disability, mean RDQ score: 10.1 vs. 11.6 vs. 10.5 NSAIDS in past week: 50% vs. 57% vs. 55% Narcotic analgesics in past week: 17% vs.17% vs. 13% Mean SF-12 physical health component: 40 vs. 38 vs. 39 Mean SF-12 mental health component: 50 vs. 50 vs. 50	Modified RDQ (0-23) Symptom bothersomeness (0 =“not at all” to 10 = “extremely”) Opioid use in last week for LBP Global rating of improvement (7 point categorical scale) Health care costs	3.5 and 9.5 months

Author, Year	Results - Subquestion a (vs. Sham, no treatment, waitlist, attention control)
Cherkin, 2011	A vs. B vs. C <u>Baseline</u> Symptom bothersomeness (0-10): 5.6 (SD 1.5) vs. 5.6 (SD 1.8) vs. 5.8 (SD 1.6) Modified RDQ (0-23): 10.1 (SD 5.0) vs. 11.6 (SD 5.0) vs. 10.5 (SD 5.3) SF-12 Mental Component Summary (0-100): 50 (SD 9) vs. 50 (SD 10) vs. 50 (SD 9) SF-12 Physical Component Summary (0-100): 40 (SD 9) vs. 38 (SD 8) vs. 39 (SD 8) Opioids use in last week for LBP: 17% (22/132) vs. 17% (23/136) vs. 13% (17/133) <u>3.5 months</u> Symptom bothersomeness (0-10): 4.2 (95% CI 3.9 to 4.5) vs. 4.3 (95% CI 3.9 to 4.7) vs. 4.6 (95% CI 4.2 to 5.0), adjusted difference -1.4 (95% CI -1.9 to -0.8) for A vs. C and -1.4 (95% CI -2.6 to -0.2.) for B vs. C Modified RDQ (0-23): 6.7 (95% CI 6.0, 7.5) vs. 6.4 (95% CI 5.5, 7.2) vs. 8.2 (95% CI 7.3, 9.0), adjusted difference -1.4 (95% CI -2.6 to -0.3) for A vs. C and -1.8 (95% CI -3.0 to -0.6) for B vs. C Opioid use in last week for LBP: 5.0% (95% CI 3.4, 7.5) vs. 4.6% (95% CI 2.7, 8.1) vs. 5.2% (3.1, 8.7) Global rating of improvement "much better" or "gone": 27.4% (95% CI 21.0, 35.7) vs. 29.4% (95% CI 22.7, 38.2.) vs. 10.9 (95% CI 6.5, 18.1), RR 2.5 (95% CI, 1.4, 4.5) for A vs. C and RR 2.7 (95% CI 1.5, 4.8) for B vs. C <u>9.5 months</u> Symptom bothersomeness (0-10): 4.6 (95% CI 4.2 to 5.0) vs. 3.9 (95% CI 3.5 to 4.3) vs. 4.2 (95% CI 3.8 to 4.6) Modified RDQ (0-23): 7.2 (95% CI 6.4, 7.9) vs. 6.0 (95% CI 5.2, 6.9) vs. 7.4 (95% CI 6.6,8.3), adjusted difference -0.3 (95% CI -1.4 to 0.9) for A vs. C and -1.4 (95% CI -2.6 to -0.2) for B vs. C SF-12 Mental Component Summary (0-100): 52.4 (95% CI 50.9, 53.8) vs. 53.5 (95% CI 52.2, 54.8) vs. 51.9 (95% CI 50.2, 53.6) SF-12 Physical Component Summary (0-100): 37.7 (95% CI 36.8, 38.7) vs. 37.9 (95% CI 37.0, 38.7) vs. 37.7 (95% CI 36.8, 38.6) Opioid use in last week for LBP: 4.8% (95% CI 3.1, 7.3) vs. 4.9% (95% CI 3.1, 7.9) vs. 4.9% (95% CI 2.7, 8.7) Global rating of improvement "much better" or "gone": 26.1% (95% 19.8, 34.6) vs. 36.2% (95% CI 29.1, 45.0) vs. 20.5 (95% CI 14.5, 29.0), RR 1.3 (95% CI 0.8, 2.0) for A vs. C and RR 1.8 (95% CI 1.2, 2.6) for B vs. C Health care costs (median): $38 (range $0 to $1443) vs. $78 (range $0 to $3764) vs. $25 (range $0 to $8082)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Cherkin, 2011	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawls
Cherkin, 2011	NR	Adverse events possibly related to massage (primarily pain): 7% (9/131) vs. 4% (5/134) vs. NR

Author, Year	Funding source	Quality	Comments
Cherkin, 2011	NCCAM	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Cherkin, 2016 and 2017 and Herman, 2017	US, Washington Number of centers: multiple Clinic and Outpatient	Nonspecific low back pain persisting for >3 months, pain bothersomeness >4 on a scale of 0 to 10, and pain interference with activities ≥3 on a scale of 0 to 10 Exclude: Back pain specific diagnosis (spinal stenosis), compensation or litigation issues, difficulty participating unable to speak English, unable to attend classes at the scheduled time and location), or who rated pain bothersomeness <4 and/or pain interference with activities <3 on 0–10 scales	Randomized: 342 Treated: 264 Analyzed: 341* Attrition: 23% (78/342) *1 patient missing baseline data excluded 276 participants (81%) at 2 year followup

Author, Year	Intervention, Comparator
Cherkin, 2016 and 2017 and Herman, 2017	A.Mindfulness-based stress reduction (n=113): 8 week program, once weekly for 2 hours, based on curriculum developed at University of Massachusetts, optional 6 hours retreat B.Cognitive behavioral therapy (n=116): Group education, instruction and practice in changing dysfunctional thoughts, settings, and working towards behavioral goals, relaxation skills, activity pacing, and pain coping strategies. Use of The Pain Survival Guide between sessions, 2 hours/week for 8 weeks C.Usual care (n=112)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Cherkin, 2016 and 2017 and Herman, 2017	A vs. B vs. C Age (mean): 50 vs. 49 vs. 49 years Female: 61% vs. 59% vs. 66% Race: White: 84% vs. 83% vs. 80% Asian: 4% vs. 5% vs. 3% African-American: 4% vs. 4% vs. 3% Other: 9% vs. 8% vs. 15% Hispanic: 4% vs. 9% vs. 7% Duration of symptoms: 1 year since one week without LBP 80% vs. 80% vs. 76% Medication use for LBP in past week: Any medication: 73% vs. 76% vs. 73% Opioids: 12% vs. 11% vs. 11%	Modified Roland Disability Questionnaire (RDQ) 23 (versus original 24) higher scores (range 0–23) indicate greater functional limitation Depression (PHQ-8) range, 0–24; higher scores indicate greater severity Pain bothersomeness (range 0-10) Patient Global Impression of Change scale, improvement in pain on a 7-point scale (“completely gone, much better, somewhat better, a little better, about the same, a little worse, and much worse”) Quality of life (SF-12) 12-item Short-Form Health Survey (SF-12) (0–100 scale; lower scores indicate poorer health status)	4.5, 10, and 22 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Cherkin, 2016 and 2017 and Herman, 2017	**A vs. B vs. C** <u>Baseline, mean (SD)</u> Modified RMDQ (0-23): 11.8 (4.7) vs. 11.5 (5.0) vs. 10.9 (4.8) Pain bothersomeness (0-10): 6.1 (1.6) vs. 6.0 (1.5) vs. 6.0 (1.6) PHQ-8 (0-24): 5.7 (4.0) vs. 5.7 (4.4) vs. 5.3 (3.8) SF-12 Physical component (0-100): 38.2 (7.5) vs. 39.4 (8.6) vs. 39.7 (7.6) SF-12 Mental component (0-100): 40.6 (8.1) vs. 39.4 (8.2) vs. 39.8 (7.4) <u>4.5 months, mean change from baseline</u> Modified RMDQ (0-23): -4.33 (95% CI -5.16, -3.51) vs. -4.38 (95% CI -5.3, -3.47) vs. -2.96 (95% CI -3.79, -2.14); p=0.03 ≥30% improvement in RMDQ: 60.5% (95% CI 52.0, 70.3) vs. 57.7% (95% CI 49.2, 67.6) vs. 44.1% (95% CI 35.9, 54.2); p=0.04 Pain bothersomeness (0-10): -1.48 (95% CI -1.86, -1.11) vs. -1.56 (95% CI -2.02, -1.11) vs. -0.84 (95% CI -1.21, -0.46); p=0.02 ≥30% improvement in pain bothersomeness: 43.6% (95% CI 35.6, 53.3) vs. 44.9% (95% CI 36.7, 55.1) vs. 26.6% (95% CI 19.8, 35.9); p=0.01 PHQ-8 (0-24): -1.32 (95% CI -1.81, -0.83) vs. -1.80 (95% CI -2.35, -1.26) vs. -0.64 (95% CI -1.23, -0.06); p=0.02 SF-12 Physical component (0-100): 3.58 (95% CI 2.15, 5.01) vs. 3.78 (95% CI 2.56, 5.00) vs. 3.27 (95% CI 2.09, 4.44); p=0.84 SF-12 Mental component (0-100): 0.45 (95% CI -0.85, 1.76) vs. 2.13 (95% CI 0.86, 3.40) vs. −1.11 (95% CI −2.39, 0.17); p=0.002 Used medications for LBP (38% used opioids): 43.4% (95% CI 35.9, 52.6) vs. 50.9% (95% CI 43.4, 59.7) vs. 54.2 (95% CI 46.2, 63.6); p=0.18 Global Improvement (pain much better/gone): 26.2% (95% CI 19.3, 35.7) vs. 30.1% (95% CI 22.7, 39.9) vs. 13.6% (95% CI 8.6, 21.5); p=0.01 <u>10 months</u> Modified RMDQ (0-23): −5.3 (95% CI −6.16, −4.43) vs. −4.78 (95% CI −5.67, −3.89) vs. −3.43 (95% CI −4.33, −2.52); p=0.01 ≥30% improvement in RMDQ: 68.6% (95% CI 60.3, 78.1) vs. 58.8% (95% CI 50.6, 68.4) vs. 48.6% (95% CI 40.3, 58.6); p=0.01 Pain bothersomeness: -1.95 (95% CI -2.32, -1.59) vs. -1.76 (95% CI -2.14, -1.39) vs. -1.10 (95% CI -1.48, -0.71); p=0.005 ≥30% improvement in pain bothersomeness: 48.5% (95% CI 40.3, 58.3) vs. 39.6% (95% CI 31.7, 49.5) vs. 31.0% (95% CI 23.8, 40.3); p=0.02 PHQ-8: −1.51 (95% CI −2.09, −0.92) vs.−1.72 (95% CI −2.28, −1.16) vs. −0.88 (95% CI −1.50, −0.27); p=0.13 SF-12 Physical component: 3.87 (95% CI 2.55, 5.19) vs. 3.79 (95% CI 2.55, 5.03) vs. 2.93 (95% CI 1.70, 4.16); p=0.50 SF-12 Mental component: 2.01 (95% CI 0.74, 3.28) vs. 1.81 (95% CI 0.59, 3.03) vs. 0.75 (95% CI −0.58, 2.08); p=0.36 Used medications for LBP (38% used opioids): 46.8% (95% CI 39.2, 55.9) vs. 42.1% (95% CI 34.9, 50.9) vs. 52.9% (95% CI 45.1, 62.0); p=0.17 Global Improvement (pain much better/gone): 30.0% (95% CI 22.6, 39.8) vs. 31.9% (95% CI 24.5, 41.6) vs. 18.0% (95% CI 12.1, 26.7); p=0.048 All office based and outpatient care (number of visits, change from prior year): -1.1 (95% CI -5.7, 3.7) vs. 1.5 (95% CI -3.8, 8.1) vs. -1.6 (95% CI -11.1, 3.2); A vs. C: difference 3.1 (95% CI -4.3,13.7) and B vs. C: difference 0.5 (95% CI -6.4, 9.6); no differences in ED visits, hospital inpatient stays, pharmacy prescriptions, imaging visits, productivity Total costs: $5580 (95% CI $3465, $8343) vs. $6428 (95% CI $3676, $10262) vs. $6,304 (95% CI $4193, $9805) <u>22 months, mean change from baseline</u> Modified RDQ: −4.09 (95% CI−5.08, −3.10) vs. −4.59 (95% CI−5.60 to −3.57) vs. −2.74 (95% CI−3.81, −1.68), adjusted difference in change from baseline, A vs. C: -1.35 (95% CI -2.80 to 0.11) and B vs. C: −1.84 (−3.32 to −0.37) ≥30% improvement in modified RDQ: 55.4% (95% CI 46.9, 65.5) vs. 62.0% (95% CI 53.5, 71.7) vs. 42.0% (95% CI 33.8, 52.2); A vs C: RR 1.32 (95% CI 1.00 to 1.74) and B vs. C: RR 1.48 (95% CI 1.13, 1.92) Pain bothersomeness: −1.57 (95% CI −1.97, −1.17) vs. −1.79 (−2.21 to −1.37) vs.−1.25 (95% CI −1.69, −0.81), adjusted difference in change from baseline, A vs. C: -0.32 (95% CI -0.92 to 0.28) and B vs. C: -0.54 (95% CI -1.15 to 0.07) ≥30% improvement in pain bothersomeness: 41.2% (95% CI 33.2 to 51.0) vs. 39.6% (95% CI 31.4, 49.8) vs. 31.1% (95% CI 23.9 to 40.5); A vs. C: RR 1.32 (95% CI 0.95 to 1.85) and B vs. C: RR 1.27 (95% CI 0.90 to 1.79)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Cherkin, 2016 and 2017 and Herman, 2017	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Cherkin, 2016 and 2017 and Herman, 2017	NR	Serious adverse events: 0% 30/103 (29%) adverse event of temporarily increased pain with yoga (part of MBSR). 10/100 (10%) adverse event of increased pain with progressive muscle relaxation (part of CBT).

Author, Year	Funding Source	Quality	Comments
Cherkin, 2016 and 2017 and Herman, 2017	National Center for Complementary & Integrative Health of the National Institutes of Health	Fair	38% of patients received baseline opioids. Pearled from Anheye, 2017 Secondary analysis in Turner, 2016. Mindfulness-based stress reduction and cognitive behavioral therapy for chronic low back pain: similar effects on mindfulness, catastrophizing, self-efficacy, and acceptance in a randomized controlled trial. PMID: 27257859+O55

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Chiu 2011	Hong Kong, outpatient, single-site	Inclusion Criteria: Between ages of 18 to 70 years old, with history of neck pain >3 months, can read Chinese. Exclusion criteria: history of injury to neck or upper back from T1 to T6, inflammatory conditions (e.g. rheumatoid arthritis), previous surgery to the neck, history of malignancy, congenital abnormality of the spine, other concurrent musculoskeletal problems, receiving concurrent treatment (e.g. physiotherapy manipulation, chiropractor or bone setter) or received training because of the neck pain in prior 3 months.	Randomized: 79 Treated: 45 Analyzed: 79(ITT) Attrition: 49.3% (39/79)
Cho 2013	Korea Number of centers: 3 Setting: Hospital	Age 18-65 years Chronic LBP for at least the last 3 months VAS for bothersomeness of LBP ≥5 Nonspecific, uncomplicated LBP with intact neurological examination Exclude: Sciatic pain Pain mainly below the knee Serious spinal disorders, including malignancy, vertebral fracture, spinal infection, inflammatory spondylitis and cauda equina compression History of previous spinal surgery Scheduled surgery for a chronic disease that could interfere with treatment effects (e.g., cardiovascular disease, diabetic neuropathy, fibromyalgia, rheumatoid arthritis, dementia, and epilepsy) Acupuncture treatment of LBP in the previous month Conditions that could compromise the safety of acupuncture (e.g., clotting disorders, taking anticoagulant agent, pregnancy, and seizure disorders) Severe psychiatric or psychological disorder History of use of corticosteroids, narcotics, muscle relaxants, or herbal medicine to treat LBP.	Randomized: 130 Treated: 57 Analyzed: 116 Attrition: 11% (14/130)

Author, Year	Intervention, Comparator
Chiu 2011	A.Intermittent Cervical Traction (ICT) (n=39) No. sessions: Twice/week for 6 wks Length of sessions: 20 min Segments targeted: Description of technique: Received ICT using Tru-Trac series 92B machine under supervision of exp. physiotherapist. Parameters: traction poundage ranging from 10-20% of patient body weight, holding time 10-25 seconds; resting time 20-50% of holding; resting poundage 20-40% of traction poundage. traction indvidualized within these ranges at physiotherapist' discretion B.Infrared Irradiation Control (n=34) No. sessions: Twice/week for 6 wks Length of sessions: 20 min Description: Received only infrared irradiation as a placebo heat treatment. Posterior aspect of patients' neck were exposed in a sitting position, and head was well supported by pillows. Center of infra-red lemp was placed directly above the spinous process of C4. Positioned so that patients reported just minimal warmth over the back of their neck.
Cho 2013	A. Needle acupuncture (n=57): 12 sessions, approximately 2 per week for 6 weeks, of individualized acupuncture treatment. Acupuncture points according to the 3 types of meridian patterns: gallbladder, bladder, or mixed meridian pattern. Other acupuncture points could be used according to the diagnosis. Needles were sterile, disposable stainless steel, 40 x 0.25 mm, with the same tube used for the sham acupuncture device. Needles were inserted perpendicular to a depth of 5-20 mm, followed by manual stimulation by bidirectional rotation to induce Deqi sensation, then left in place for 15-20 minutes. B: Sham acupuncture (n=59): 12 sessions, approximately 2 per week for 6 weeks, of sham acupuncture treatment, using nonpenetrating semi-blunt sham needles. 8 predefined points at the lower back unrelated to traditional acupuncture points were used. All: No additional therapy, such as analgesics or physical treatments were allowed. Acupuncturists had ≥3 years experience with specialization in Korean Rehabilitation Medicine. At the 1st visit, participants were given an exercise manual for patients with LBP and instructed about appropriate posture and exercises; patients were requested to do exercises every day and maintain correct posture.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Chiu 2011	A vs. B* Age (SD): 50.9(10.5) vs. 46.8(10.4) Female: 65.2% vs. 76.5% Race: NR Mean duration of chronicity, years: NR NPQ Disability (0-100): 46.1(14.5) vs. 38.5(8.0); ns NPS Pain Severity(0-10): 5.8(1.9) vs. 5.2(2.0); ns *Baseline data only provided for 23/39 intervention participants and 17/40 control patients.	Northwick Park Neck Pain Questionnaire (NPQ, range 0-100: higher scores indicate greater disability) verbal Numerical Pain Scale Pain Severity (NPS, range 0-10: higher scores indicate severity of pain)	intermediate post-intervention, 1.5 months
Cho 2013	A vs. B Age: 42 vs. 42 Female: 83% vs. 86% Baseline pain (0-10 VAS): 6.5 vs. 6.4 Baseline Korean ODI: 28.2 vs. 24.2 Baseline SF-36: 107.7 vs. 110.4 Baseline BDI: 11.3 vs. 11.8	Symptom bothersomeness (0-10 VAS, higher=more bothersome) Pain intensity (0-10 VAS) ODI, Korean version, excludes the sex life item (scale unclear) SF-36 total, Korean version (scale unclear) Beck Depression Inventory, Korean version (0-63)	1.5 and 4 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Chiu 2011	A vs B 1.5 months NPQ Disability: 31.4(12.7) vs. 29.6(15.5); p > 0.05, 95%CI, 29.66-37.50, power=0.15 * NPS Pain Severity: 3.5(2.6) vs. 2.8(2.0); p > 0.05, 95%CI, 3.29-4.50, power=0.17* *Results of two-way repeated measures ANOVA
Cho 2013	A vs. B, mean (SD) Baseline Symptom bothersomeness (0-10 VAS): 6.44 (1.50) vs. 6.32 (1.14) Pain (0-10 VAS): 6.52 (1.41) vs. 6.37 (1.18) ODI, Korean version (scale unclear): 28.23 (10.54) vs. 24.17 (10.5) SF-36 total (scale unclear): 107.72 (18.93) vs. 110.41 (15.91) Beck Depression Inventory (0-63): 11.33 (5.51) vs. 11.75 (8.10) 1.5 months Symptom bothersomeness (0-10 VAS): 2.83 (2.34) vs. 3.99 (2.06) Pain (0-10 VAS): 2.78 (2.32) vs. 4.06 (2.19) ODI: 15.5 vs. 15.5 (estimated from graph), proportion improvement 0.43 (0.33) vs. 0.28 (0.50), p=0.051 SF-36: 126 vs. 121 (estimated from graph), proportion improvement 0.21 (0.22) vs. 0.11 (0.14), p=0.005 BDI: 6 vs. 7.5 (estimated from graph), proportion improvement 0.48 (0.48) vs. 0.30 (0.62), p=0.096 4 months Symptom bothersomeness (0-10 VAS): 2.85 (2.44) vs. 3.63 (2.37) Pain (0-10 VAS): 2.79 (2.44) vs. 3.52 (2.53) ODI: 15.3 vs. 15.3 (estimated from graph), 0.4 (0.38) vs. 0.24 (1.10), p=0.202 SF-36: 126 vs. 124 (estimated from graph), 0.20 (0.23) vs. 0.14 (0.15), p=0.093 BDI: 6 vs. 7 (estimated from graph), 0.44 (0.58) vs. 0.36 (0.66), p=0.486 *Proportion improvement = [(score at baseline) - (score at followup)] / (score at baseline)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Chiu 2011	NR
Cho 2013	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Chiu 2011	NR	NR
Cho 2013	NR	A vs. B Withdrawals: 9% (6/65) vs. 9% (6/65) Withdrawals due to AEs: NR Serious AEs: None were reported Nonserious AEs: 10 events vs. 17 events (total 16 participants)

Author, Year	Funding Source	Quality	Comments
Chiu 2011	NR	Poor	
Cho 2013	Funding support from the Korean Health Industry Development Institute.	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Cho 2014	Korea Single hospital	Men or women aged 25–55 years; neck pain or stiffness lasting for ≥3 months; (3) a score of ≥5 on the visual analogue scale (VAS) at baseline. Excluded: Received acupuncture or NSAID for neck pain within the past 3 months; serious medical disease or cancer; history of spinal trauma, had undergone surgery on the neck or had systematic neurological or other skeletal disorders; pregnant or breast feeding.	Randomized: 45 Treated: 45 Analyzed: 38 Attrition: 16% (7/45)
Chow 2006	Australia Large single suburban medical center of 17 general practitioners	≥18 years of age; chronic neck pain of more than 3 months duration; able to attend a full course of 14 treatments given twice a week; able to understand the nature of the trial and were naive to treatment with LLLT (except laser acupuncture). Exclusion: Current litigation or compensation; neurological signs in the upper limbs relating to nerve entrapment or impingement from the cervical spine; unable to discontinue temporarily any activity which exacerbated the pain; pregnancy; prior cervical spine surgery; systemic rheumatic disease; neck pain which was part of a widespread pain syndrome involving other areas; photosensitivity or had other illnesses precluding involvement for practical reasons.	Randomized: 90 Treated: 84 Analyzed:: 84 Attrition:7% (6/90)

Author, Year	Intervention, Comparator
Cho 2014	A.Acupuncture and NSAIDs group (n=15), acupuncture 3x/week and zaltoprofen (80mg) 3x/day B.Acupuncture alone (n=15), bilateral cervical points SI9, SI10, SI11, SI12, SI14, BL11, BL12, TE14, TE15, TE16, TE17 and GB21; and extremity points SI3, SI4 and BL65 3x/week for 3 weeks. C.Zaltoprofen (80mg) alone (n=15),3x/day for 3 weeks.
Chow 2006	A.Active GaAlAs laser therapy (n=45), (wavelength of 830 nm and power of 300 mW in continuous wave mode at a Power Density (PD) of 0.67 W/cm2) 2x/week for 7 consecutive weeks, maximum half hour per treatment. Up to 50 tender points in the neck were treated for 30 seconds per point. B.Sham laser (n=45)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Cho 2014	A vs B vs C Age: 39 vs 38 vs 39 years Female: 53 vs 60 vs 80 Pain: 6.7 (0.7) vs 6.1 (0.5) vs 7.1 (1.3) NDI: 23.2 (5.9) vs 22.3 (4.0) vs 26.3 (5.0) SF-36: 85.2 (1.2) vs 86.2 (2.0) vs 84.2 (1.7) BDI: 28.7 (4.8) vs 30.7 (5.6) vs 33.1 (7.8) EQ-5D: 7.4 (1.7) vs 7.4 (1.5) vs 7.5 (1.3)	Pain intensity week prior to assessment (scale, 0-10, higher score=greater pain) NDI: (scale 0-50, higher score greater disability) Beck Depression Inventory (scale 0-63, higher score, more severe the depression) Short-Form 36 (SF-36) (scale 0-100, higher score=better QoL) EQ-5D (scale 0-1, lower score, greater disability)	1 month
Chow 2006	A vs B Age: 57 vs 55 years Female: 64% vs 67% Pain duration: 17 vs 13 years Pain (0-10): 5.9 vs 4.0	Pain intensity (VAS 0-10, higher score worse pain) Northwick Park Neck pain Questionnaire (NPNQ) (scale: 0-100%, higher percentage the greater the disability) Neck Pain and Disability Scale (NPAD) (scale: 0-100, higher score = greater disability) McGill Pain Questionnaire (MPQ) (scale: 0-33 sensory, 0-12 affective, @1-5 present pain intensity; higher score = greater pain) Short-Form 36 (SF-36) (scale 0-100, higher score=better QoL)	1 month

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Cho 2014	
Chow 2006	A vs B (within group difference from baseline and 95% CI) <u>1 month</u> NPNQ: -3.5 (-5.1 to 1.9) vs -0.6 (-1.8 to 0.6), MD -3.0 (-5.0 to 0.9) p<0.005 NPAD: -15.2 (-20.4 to -9.9) vs -3.1 (-7.6 to -1.4), MD -12.1 (-19.3 to -4.8) p<0.001 Pain (VAS 0-10): -2.7 (-3.3 to 2.1) vs 0.3 (-0.4 to 0.9), MD 3.0 (-3.8 to -2.1) p<0.001 MPQ sensory: -3.4 (-5.4 to -1.4) vs -1.9 (-4.1 to -0.40), diff -1.5 (-4.5 to 1.5), p=0.32 MPQ affective: -1.3 (-2.3 to -0.4) vs -0.7 (-2.1 to 0.6), MD -0.6 (-2.3 to 1.1), p=0.497 MPQ VAS: -2.1 (-3.0 to -1.1) vs 0.1 (-0.9 to 0.7), MD -2.2 (-3.5 to -0.9), p<0.001 Improved pain <-3 (%): 40% vs 7%, RR 6.0 (95% CI 1.9 to 19.0) SF36 Physical: 3.2 (0.6 to 5.7) vs -1.3 (-3.9 to 1.4), MD 4.5 (0.7 to 8.2),p<0.022 SF 36 Mental: 2.4 (0.3 to 5.1) vs 5.4 (2.1 to 8.6), MD -2.9 (-7.2 to 1.3), p=0.065

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Cho 2014	B vs C <u>1 month</u> Pain (0-10): 4.5 (2.2) vs 3.8 (1.6), MD 0.7 (95% CI -0.74 to 2.14), p=0.328 NDI: 17.3 (5.7) vs 17.7 (5.4), MD -0.40 (95% CI -4.55 to 3.75), p=0.845 BDI: 28.5 (7.3) vs 27.2 (6.3), p=0.606 SF-36: 88.6 (1.5) vs 84.3 (1.1), p=ns EQ-5D: 7.3 (1.9 vs 6.7 (1.7), p=ns
Chow 2006	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Cho 2014		NR
Chow 2006		A vs B (number of patients) Mildly increased pain: 35, 29, p=0.16 Moderately increased pain: 27, 23, p=0.40 Severely increased pain: 14, 12, p=0.64 Increased pain elsewhere: 35, 28, p=0.11 Mild headache: 27, 24, p=0.5 Moderately increased headache: 18, 13, p=0.27 Severe headache: 10, 10, p=1.0 Nausea: 9, 19, p=0.02* Light-headed/dizzy: 16, 20, p=0.39 Tingling in extremity: 8, 6, p=0.56 ‘‘Spaced-out’’ feeling: 14, 10, p=0.34 Sleepiness: 18, 19, p=0.83 Tiredness: 24, 21, p=0.53 Skin sensitivity: 6, 4, p=0.50 Jaw pain: 3, 2, p=0.65 Intercurrent infection: 11, 8, p=0.44 Stiffness: 9, 2, p=0.02* Depression: 2, 3, p=0.65

Author, Year	Funding Source	Quality	Comments
Cho 2014	Program of the Kyung Hee University for young medical researcher in 2009 (KHU-20100763).	Poor	Missing values imputed via Stochastic Regression
Chow 2006	NR	Good	Last observation carried forward for analysis

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Clarke-Jenssen 2014	Norway 1 outpatient Rheumatology clinic	Inclusion: ACR 1990 criteria for FM, age 18-60 years, independent in activities of daily living, capable of participating in light exercise group on land and in warm water, understand written and oral Norwegian Exclusion: Serious physical or psychiatric diagnosis, alcohol or drug abuse, pregnant or breast-feeding, receiving more than 50% disability pension	Randomized: 129 Analyzed: 129 Attrition: 9% (12/129)

Author, Year	Intervention, Comparator
Clarke-Jenssen 2014	A.Aerobic exercise on land and in warm water, stretching, relaxation, education, provided in groups 5 days per week for 4 weeks, provided in warm climate (n=42) B.Aerobic exercise on land and in warm water, stretching, relaxation, education, provided in groups 5 days per week for 4 weeks, provided in cold climate (n=43) C.Usual Care (n=44): received no intervention as was treated "as usual"

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Clarke-Jenssen 2014	A vs C: Age: 46 (9) vs 45 (9) Female: 88% vs 96% Years of symptoms: 17 (12) vs 12 (9) 6-minute walk test, meters: 517(95% CI 493 to 541) vs 504 (95% CI 481 to 526) Pain VAS: 6.6 (95% CI 6 to 7.3) vs 6.6 (95% CI 6 to 7.2) B vs C: Age: 46 (8) vs 45 (9) Female: 93% vs 96% Years of symptoms: 13 vs 12 years 6-minute walk test, meters: 527 (95% CI 503 to 550) vs 504 (95% CI 481 to 526) Pain VAS: 6.9 (95% CI 6.3 to 7.5) vs 6.6 (95% CI 6 to 7.2)	Fibromyalgia Impact Questionnaire (FIQ; 0-100, higher scores = greater impact of FM on daily life) Pain VAS (0-10, higher scores=higher pain) Hospital Anxiety and Depression Scale (HADS; 0-21, higher scores=greater anxiety and depression) SF-36 Physical (0-100, higher scores=better qualify of life) SF-36 Mental (0-100; higher scores=better quality of life)	3 and 12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Clarke-Jenssen 2014	A vs C: 3 months, between-group difference in change from baseline: FIQ: not significant Pain VAS: -1.2 (95% CI -2.2 to -0.1), p=0.02 HADS: not significant SF-36 Physical: not significant SF-36 Mental: not significant 12 months, between-group difference in change from baseline: FIQ: not significant Pain VAS: 0.1 (95% CI -0.9 to 1.1), p=0.45 HADS: not significant SF-36 Physical: not significant SF-36 Mental: not significant B vs C: 3 months, between-group difference in change from baseline: FIQ: not significant Pain VAS: -0.9 (95% CI -1.9 to 0.2), p = 0.12 HADS: not significant SF-36 Physical: not significant SF-36 Mental: not significant 12 months, between-group difference in change from baseline: FIQ: not significant Pain VAS: 0 (95% CI -1 to 1), p=0.99 HADS: not significant SF-36 Physical: not significant SF-36 Mental: not significant

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Clarke-Jenssen 2014	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Clarke-Jenssen 2014		NR

Author, Year	Funding Source	Quality	Comments
Clarke-Jenssen 2014	Section for Climate Therapy, Oslo University Hospital, Rikshospitalet, writing of article supported by the Norwegian Fibromyalgia Association	Fair	Missing data at followup were replaced by baseline values on measures Values were not reported for many of the outcome variables, but the authors reported that the group comparisons were not statistically significant for these measures.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Costa 2009	Australia 1 center Outpatient	Patients aged 18 to 80 with nonspecific low back pain localized below the costal margin and above the inferior gluteal folds, symptoms of at least 3 months duration, and currently seeking care for low back pain Exclude: Spinal pathology, pregnancy, nerve root compromise, previous spinal surgery, major surgery scheduled during study period, contraindication to exercise, ultrasound, or shortwave therapy	Randomized: 154 Treated: 154 Analyzed: 154 Attrition: 6% (9/154)
Da Costa 2005	Canada Patients referred by hospital or community rheumatologists Newspaper ads	Inclusion: Female, confirmed diagnosis of FM Exclusion: diseases that precluded participation in exercise, contraindications to exercise, change in medication in past 2 weeks, regular participation in moderate intensity exercise more than 30 minutes three times per week.	Randomized: 80 Analyzed: 61 Attrition: 24% (19/80)

Author, Year	Intervention, Comparator
Costa 2009	A.Neuromuscular re-education (motor control education) (n=77): Twelve 30 minute sessions over 8 weeks, 2 sessions per week in the first month and 1 session per week in the second month. Sessions were personalized to each patient and consisted of exercises designed to improve function of specific muscles in the low back and control posture and movement. B.Placebo (n=77): Twelve 25 minute sessions over 8 weeks, 2 sessions per week in the first month and 1 session per week in the second month. Sessions consisted of 20 minutes detuned shortwave diathermy and 5 minutes of detuned ultrasound.
Da Costa 2005	A.Exercise (n=28): Over 12 weeks, subjects met 4 times with exercise physiologist. The first visit was 90 minutes; other visits were 30 minutes at 1, 3, and 9 weeks after the initial visit. The exercise prescription for a home-based program was individualized and included aerobic exercise, stretching, and strength exercises. B.Usual care (n=33): "receiving their usual care" (no further details provided); patients were asked to record exercise activity (in case they had engaged in exercise outside study protocol) weekly during the 12-week intervention phase and monthly thereafter.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Costa 2009	A vs B Age: 55 vs 53 years Female: 58% vs 62% Duration of symptoms (weeks): 334.8 vs 328.2 Work status: Full-time: 8% vs 17% Part-time: 7% vs 4% Not working: 26% vs 16% Not seeking employment: 60% vs 64% General health status: Excellent: 4% vs 10% Very good: 23% vs 16% Good: 49% vs 57% Fair: 18% vs 9% Poor: 5% vs 8% Depression Anxiety Stress Scales (0-42): Depression: 11.4 (12.9) vs 11.2 (13.4) Anxiety: 11.9 (11.1) vs 11.8 (12.2) Stress: 14.1 (11.8) vs 14.4 (12.5) PSFS: 3.3 (1.7) vs 3.3 (!.8) RMDQ: 13.1 (5.0) vs 13.4 (4.9) Pain VAS: 6.8 (2.1) vs 6.6 (2.0) Global impression of recovery: -1.9 (2.5) vs -2.1 (2.4)	Patient-Specific Functional Scale (0-10, higher score=lower disability) RDQ (0-24, higher score=higher disability Pain (0-10 VAS, higher score=higher pain) Global impression of recovery (-5 to +5, higher score=higher recovery)	Short-term and intermediate term 4 and 10 months
Da Costa 2005	A vs B 49 (8.7) vs 52 (10.8) Female: 100% vs 100% Symptom duration, years: 10.5 (8.4) vs 11.2 (7.6) Years since diagnosis: 3.8 (4.5) vs 4.9 (4.1) FIQ: 55.1 (15.0) vs 48.6 (17.7) Upper body pain VAS: 49.5 (15.5) vs 47.4 (18.9) Lower body pain VAS: 47.0 (25.8) vs 47.0 (23.9) SCL-90 R GSI: 64.3 (6.3) vs 64.4 (7.9)	Fibromyalgia Impact Questionnaire (FIQ; 0-100, higher scores=more severe symptoms and disability) Pain VAS, past week, upper body (0-100, higher scores=greater pain) Pain VAS, past week, lower body (0-100, higher scores=greater pain) Symptom Checklist 90-R GSI (SCL 90-R; 30-81, higher scores=greater psychological distress)	3 and 9 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Costa 2009	0
Da Costa 2005	A vs B, mean change from baseline 3 months (n = 33 vs. 36): FIQ: -7.8 (95% CI -13.9 to -1.7) vs -0.04 (95% CI -5.2 to 5.1), p = 0.053 Pain VAS, upper body: -10.6 (95% CI -17.8 to -3.4) vs -1.9 (95% CI -6.9 to 3.2), p = 0.048 Pain VAS, lower body: -8.21 (95% CI -15.7 to -0.74) vs -2.0 (95% CI -9.4 to 5.4), p=0.24 SCL 90-R GSI: -0.02 (95% CI -0.3 to -0.04) vs -0.07 (95% CI -0.2 to 0.05), p=0.26 9 months (n = 28 vs. 33): FIQ: -10.1 (95% CI -16.1 to -4.0) vs -0.024 (95% CI -4.4 to 3.9), p = 0.009 Pain VAS, upper body: -7.9 (95% CI -14.3 to -1.4) vs 2.4 (95% CI 3.7 to 8.5), p = 0.02 Pain VAS, lower body: -5.6 (95% CI -13.3 to 2.2) vs -0.29 (95% CI -8.6 to 8.0), p = 0.35 SCL 90-R GSI: -0.16 (95% CI -0.28 to 0.35) vs -0.09 (95% CI -0.21 to 0.03), p=0.39

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Costa 2009	NR
Da Costa 2005	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Costa 2009	NR	A vs B Increased pain: 4% (3/77) vs 3% (2/77), (RR 1.5, 95% CI 0.26 to 8.7)
Da Costa 2005		NR

Author, Year	Funding Source	Quality	Comments
Costa 2009	Research & Development grant from the University of Sydney and the Physiotherapy Research Foundation-Australian Physiotherapy Association	Fair	
Da Costa 2005	The Arthritis Society	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Dias 2003	Brazil 1 center Geriatric outpatient	Aged 65 or older with a diagnosis of knee OA fulfilling ACR criteria Exclude: History of previous knee surgery for OA, hip or knee arthroplasty	Randomized: 50 Treated: 50 Analyzed: 47 Attrition: 6% (3/50)
Dilek 2013	Turkey 1 center Outpatient	ACR criteria for bilateral hand osteoarthritis Exclude: Acute inflammation, trauma or open wounds, steroid drug or NSAID intake, sensory deficits, muscle weakness, malignancy, Raynaud disease and phenomenon, atrophic skin, palmar tenosynovitis, trigger finger, Dupuytren contracture, collagen diseases, inflammatory arthritic diseases, high acute phase reactants, steroid or hyaluronan injection to joints, history of physical therapy, coagulation disorders	Randomized: 56 Treated: 56 Analyzed: 46 Attrition: 18% (10/56)
Djavid 2007	Iran Number of centers: 1 Outpatient clinic and patients home	Patients 20 - 60 years, with low back pain for 12 weeks, able to give consent, understand instructions, and co-operate with treatment. Exclude: patients with degenerative disc disease, disc herniation, fracture, spondylosis, and spinal stenosis, neurological deficits, abnormal laboratory findings, systemic or psychiatric illness, and pregnancy.	Randomized: 61 Treated: 53 Analyzed: 53 Attrition: 13% (8/61)

Author, Year	Intervention, Comparator
Dias 2003	A.Exercise (n=25): 12 exercise sessions twice a week for the 6 month study period in addition to three supervised walks of 40 minutes each week. Exercise sessions consisted stretching, concentric and eccentric isotonic progressive resistance exercises, and closed kinetic chain weight-bearing exercises B.Control group (n=25): Subjects were instructed to follow the instructions given at an educational session that all participants attended (see information below) All patients: One-hour educational session consisting of a lecture on disease characteristics, joint protection, pain management, and strategies to overcome difficulties in activities of daily life
Dilek 2013	A.Dip-wrap paraffin bath therapy (n=24): patients dip both hands into 50°C paraffin bath 10 times, paraffin left on for 15 minutes, treatment administered 5 days per week for 3 weeks B.Control group (n=22): Details NR All patients: received information about joint-protection techniques, only allowed paracetamol intake, asked to keep a drug diary
Djavid 2007	A.GaAs laser (n=16): 810 nm wavelength, 50 mW, continuous wave, and 0.2211 cm2 spot area laser applied to 8 points in the paravertebral region (L2 to S2-S3) at dose of 27 J/cm2, twice weekly for 6 weeks B.Low level laser therapy plus exercise (n=19) C.Sham laser therapy plus exercise (n=18); included strengthening, stretching, mobilizing, coordination and stabilization of the abdominal, back, pelvic, and lower limb muscles, first exercise session conducted by physiotherapist and the rest were at home

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Dias 2003	A vs B Age, median: 74 vs 76 Female: 84% vs 92% Lequesne Index, median: 12 vs 12.5 HAQ, median: 1 vs 1 SF-36 functional capacity, median: 55 vs 45 SF-36 physical role limitation, median: 25 vs 50 SF-36 bodily pain, median: 74 vs 74 SF-36 general health, median: 87 vs 77 SF-36 vitality, median: 90 vs 85	Lequesne Index of Knee OA Severity (0-24, higher score=higher severity of OA); HAQ (0-80, higher score=higher disability); SF-36 (0-100, higher score=higher quality of life)	Immediately post-intervention (treatment of 6 months)
Dilek 2013	A vs B Age: 59 vs 60 Female: 83% vs 91% Symptom duration (mos): 64.4 (57.2) vs 67.6 (55.9) Heberden nodules (no): 4.5 (2.5) vs 4.0 (2.6) Bouchard nodules (no): 0.0 (1.3) vs 0.0 (2.2) AUSCAN function: 16.2 (7.0) vs 17.1 (8.4), p=0.37 AUSCAN pain: 10.7 (3.3) vs 9.8 (5.7), p=0.42 VAS at rest median (IQR): 5.0 (4.0-5.0) vs 4.0 (3.0-8.0), p=0.71 VAS at ADL median (IQR): 7.0 (7.0-9.0) vs 8.0 (6.0-8.0), p=0.88	AUSCAN function (0-36, higher score=worse pain): DFI (0-30, higher score=worse function): AUSCAN pain (0-20, higher score=worse pain): pain VAS at rest (0-10, higher score=worse pain): pain VAS during ADL (0-10, higher score=worse pain)	2.25 months
Djavid 2007	A vs. B vs. C Age: 40 vs. 38 vs. 36 years Female: 5% vs. 7% vs. 2% Duration of LBP: 29 months vs. 29 months vs. 25 months	Pain severity (VAS) (score: 0–10) measures intensity of pain (a higher were indicates higher pain intensity) Lumbar range of motion (ROM) Schober Test (centimeters) Oswestry Disability Index (ODI) (score: 0–50)	Short term 6 weeks

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Dias 2003	A vs B Lequesne Index, median: 4.3 vs 13, p=0.001 HAQ, median: 0.3 vs 1.1, p=0.006 SF-36 functional capacity, median: 77.5 vs 40, p<0.001 SF-36 physical role limitation, median: 92.5 vs 75, p=0.001 SF-36 bodily pain, median: 100 vs 0, p=0.002 SF-36 general health, median: 100.5 vs 51, p=0.021 SF-36 vitality, median: 93.5 vs 87, p=0.027
Dilek 2013	A vs B <u>2.25 month outcomes</u> AUSCAN function: 13.8 (7.0) vs 17.8 (8.4), p value NR (MD -4, 95% CI -8.58 to 0.58) p value NR DFI: Values NR, p=0.05 AUSCAN pain: 6.5 (4.0) vs 9.5 (4.5) (MD -3, 95% CI -5.5 to -0.5) p=0.05, p=0.07 for ITT Pain VAS at rest, median (IQR): 0.0 (0.0-3.0) vs 5.0 (1.0-6.0), p=0.003, p<0.001 for ITT Pain VAS during ADL, median (IQR): 5.0 (3.0-6.5) vs 7.0 (5.0-8.0); p=0.09, p=0.05 for ITT
Djavid 2007	A vs. B, mean (SD) <u>1.5 months</u> Pain (0-10 VAS): 4.4 (2.0) vs. 2.4 (1.4), difference in change from baseline -0.9 (95% CI -2.5 to 0.7) Oswestry Disability Index (0-100): 20.8 (4.4) vs. 16.8 (3.7) difference in change from baseline -4.4 (95% CI -11.4 to 2.5)

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Dias 2003	
Dilek 2013	
Djavid 2007	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Dias 2003		NR
Dilek 2013		NR
Djavid 2007	A vs. C, mean (SD) <u>Baseline</u> Pain (0-10 VAS): 7.3 (1.7) vs. 6.3 (2.0) Oswestry Disability Index (0-100): 33.0 (8.4) vs. 31.8 (7.9) <u>1.5 months</u> Pain (0-10 VAS): 4.4 (2.0) vs. 4.3 (1.6), difference in change from baseline -0.9 (95% CI -2.5 to 0.7) Oswestry Disability Index (0-100): 20.8 (4.4) vs. 24.1 (5.2), difference in change from baseline -4.4 (95% CI -11.4 to 2.5)	None

Author, Year	Funding Source	Quality	Comments
Dias 2003	Grants from the Brazilian Government Funding Agency--CAPES	Poor	
Dilek 2013	Suppliers: Sammons Preston, 1000 Remington Blvd, Bolingbrook, IL 60440; Baseline, Trent Building, South Buckout St, Irvington, NY 10533; SPSS Inc, 233 S Wacker Dr, 11th Fl, Chicago, IL 60606; NCSS LLC, 329 North 1000 East, Kaysville, UT 84037	Fair	Outcomes not reported: ROM, grip and pinch strength, painful and tender joint counts, paracetamol intake Mean differences calculated. No substantial differences between baseline measurements were noted
Djavid 2007	NR	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Ebadi 2012	Iran Single center	18 to 60 years of age with nonspecific chronic low back pain Exclude: nerve root systems, systemic disease and specific conditions, medications for psychological problems, pregnant	Randomized: 50 Analyzed: 50 Attrition: 18% (12% vs. 24%) at 8 weeks
Ebneshahidi 2005	Iran, three sites (outpatient)	Inclusion Criteria: CTTH, no treatment in the previous two weeks Exclusion Criteria: Other causes of chronic headache, patients with papilloedema, pulsating headaches, systemic disorders, contraindications.	Randomized: 50 Treated: 50 Analyzed: 50 Attrition: 0%

Author, Year	Intervention, Comparator
Ebadi 2012	A: Ultrasound 1.5 W/cm ^{2} at 1 MHz; duration based on Grey's formula, 10 sessions over 4 weeks (n=25) B: Sham ultrasound, same technique as A but no US (n=22)
Ebneshahidi 2005	A.Low-Energy Laser Acupuncture (n=25) Laser acupuncture No. of Sessions: 3 times/week for 10 sessions Length of Sessions: NR Output wave length: 830nm; Maximum intensity: 39mW/cm squared on 8 acupoints. Acupoints: GB14, GB20, LI4, LU7 bilaterally (totaling 8 points) B.Sham Laser Acupuncture (n=25) Same procedure except power output was set to zero

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Ebadi 2012	A vs. B Mean age: 31 vs. 37 years 25% vs. 50% female Race: Not reported Pain intensity (mean, 0-100 VAS): 47 vs. 49 Functional Rating Index (mean, 0-100): 41 vs. 44	Pain (mean, 0-100 VAS) Functional Rating Index (0-40)	1 month
Ebneshahidi 2005	A vs B Age: 33 vs 39 years (p=0.04) Female: 80% vs 80% Race: NR Duration of symptoms: NR Median Number of Headache Days/Month (IQR): 20 (15.0) vs. 18 (15.0) p=0.5 Median VAS (IQR): 10 (3.0) vs. 10 (1.0) p=0.1 Median Duration of Attacks (IQR): 10 (4.0) vs. 8 (4.5) p=0.02	Number of Headache Days/Month; Headache Intensity (VAS; 0-10: higher scores indicate severity of pain); Duration of Attacks (hours)	1 2 and 3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Ebadi 2012	A vs. B, mean (SD) Baseline Pain (0-100 VAS): 46.6 (17.7) vs. 49 (16) Functional Rating Index (mean, 0-40): 40.8 (14.6) vs. 43.9 (16.9) 1 month Pain (0-100 VAS): 27.7 (14.4) vs. 25.5 (9.9), p=0.48 Functional Rating Index (0-40): 22.8 (7.8) vs. 30.5 (11.9), p=0.004
Ebneshahidi 2005	A vs. B 1months Δ Number of Headache Days/Month, median (IQR): -15 (16.5) vs. -2 (5.0) p<0.001 Δ in Headache Intensity (VAS), median (IQR): -5 (3.8) vs. -1 (2.0) p<0.001 Δ Duration of Attacks (hours), median (IQR): -6 (4.5) vs. -1 (2.0) p<0.001 2months Δ Number of Headache Days/Month, median (IQR): -10 (20.0) vs. 0 (5.0) p<0.001 Δ in Headache Intensity (VAS), median (IQR): -3 (4.0) vs. 0 (1.5) p<0.001 Δ Duration of Attacks (hours), median (IQR): -4 (6.0) vs. 0 (0.5) p<0.001 3months Δ Number of Headache Days/Month, median (IQR): -8 (21.5) vs. 0 (0.0) p<0.001 Δ in Headache Intensity (VAS), median (IQR): -2 (6.3) vs. 0 (0.0) p<0.001 Δ Duration of Attacks (hours), median (IQR): -4 (7.5) vs. 0 (0.0) p<0.001

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Ebadi 2012	NR
Ebneshahidi 2005	NA

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Ebadi 2012	NR	NR
Ebneshahidi 2005	NA	No adverse events were reported in either group.

Author, Year	Funding Source	Quality	Comments
Ebadi 2012	Tehran University of Medical Sciences	Fair	
Ebneshahidi 2005	NR	Fair	Did not compute MD for these outcomes because they were reported in medians and IQRs

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Ettinger 1997 FAST trial (index study)	United States, 2 centers, academic medical centers	Inclusion criteria: age 60 years or older; pain in the knee(s) on most days of the month; difficulty with at least one of the following because of knee pain: walking 0.4 km; climbing stairs; getting in and out of a car, bath, orbed; rising from a chair; or performing shopping, cleaning, or self-care activities; and radiographic evidence of knee osteoarthritis. Exclusion criteria: baseline ADL disability; the presence of a medical condition that precluded safe participation in an exercise program (e.g., recent myocardial infarction or stroke, severe chronic obstructive pulmonary disease, or congestive heart failure); inflammatory arthritis; regular exercise participation (1 time per week for at least 20 minutes); and inability to walk on a treadmill or walk, unassisted, 128 m in 6 minutes; participating in another research study; or resided in a long-term care facility	Randomized: 439 Treated: 439 Analyzed: 364 Attrition: 17% (75/439)
Falcao 2008	Brazil 1rheumatology outpatient clinic	Inclusion: Met ACR 1990 criteria for FM, female, age 18-65, 4+ years of formal education, no previous treatment for FM Exclusions: other rheumatic disease; known hypersensitivity to amitriptyline, cyclobenzaprine, or paracetamol; using psychotropic drug; psychiatric disease; work-related litigation	Randomized: 60 Analyzed: 51 Attrition: 15% (9/60)

Author, Year	Intervention, Comparator
Ettinger 1997 FAST trial (index study)	A.Aerobic Exercise Program (n=144), 3-month facility-based walking program of 3 times per week for 1 hour. Each session consisted of a 10-minute warm-up and cool-down phase, including slow walking and flexibility stretches, and a 40-minute period of walking at an intensity equivalent to 50% to 70% of the participants' heart rate reserve. Followed by 15-month home-based walking program. B.Resistance Exercise Program (n=146), 3-month supervised facility-based program, with 3 one-hour sessions per week, and a15-month home-based program. Each session consisted of a 10-minute warm-up and cool-down phase and a 40-minute phase consisting of 2 sets of 12 repetitions of 9 exercises. C.Attention Control (n=149), attended, during the first 3 months, monthly group sessions on education related to arthritis manage-ment, including time for discussions and social gathering. Later, participants were called bimonthly (months 4-6) or monthly (months 7-18) to maintain health updates and provide support
Falcao 2008	A.Amitriptyline plus CBT (n=25): amitriptyline 12.5/mg per day during first week, then increase dose to 25 mg/day. Those with intolerance or side effects to amitriptyline were given cyclobenzaprine 5 mg/day in the first week and then 10 mg/day. Subjects were also allowed to use paracetamol if they had pain. Routine medical visits once a week for 10 weeks for brief discussions with the doctors. Immediately after each visit, they had a CBT session, consisting of progressive relaxation training with electromyographic biofeedback, cognitive restructuring, and stress management. Subjects who missed >20% of the treatment sessions and those who started new medications or did not come for evaluation were excluded from analysis. B.Amitriptyline only (control) (n=26): amitriptyline 12.5/mg per day during first week, then increase dose to 25 mg/day. Those with intolerance or side eff+E66ects to amitriptyline were given cyclobenzaprine 5 mg/day in the first week and then 10 mg/day. Subjects were also allowed to use paracetamol if they had pain. Routine medical visits once a week for 10 weeks for brief discussions with the doctors.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Ettinger 1997 FAST trial (index study)	A vs. B vs. C Age: 69 vs. 68 vs. 69 years Female: 69% vs. 73% vs. 69% African-American: 24% vs 28% vs 26% Education, >12 years: 54% vs. 52% vs. 62% BMI >30: 50% vs. 49% vs. 58%	Physical Disability. New disability questionnaire was developed for use in FAST that combined 23 questions drawn from previous studies that assessed difficulty with activities of daily living. The scale used a Likert scale from 1 (usually done with no difficulty) to 5 (unable to do). A composite disability score was created by averaging scores on all 23 items. Pain. Intensity of knee pain during the past week on 6 activities of daily living on a Likert scale from 1 (no pain) to 6 (excruciating pain) during the 6 activities. Scores for each activity were averaged to give summary pain intensity scores for both ambulation and transfer activities.	3 (immediately post treatment), 6, and 15 months
Falcao 2008	A vs B Age: 45 vs 46 Female: 100% vs 100% White: 80% vs 77% Disease duration, years: 3.5 (2.4) vs 3.7 (4.8) FIQ: 64.9 (15.5) vs 69.6 (11.4) Pain VAS: 6.9 (2.3) vs 7.0 (2.3) Beck Depression Inventory: 20.6 (10.0) vs 25.8 (8.5) State-Trait Anxiety Inventory, state scale: 47.4 (3.2) vs 48.3 (2.7) SF-36 physical capacity: 45.4 (24.2) vs 48.8 (25.0) SF-36 Pain: 28.0 (17.5) vs 27.9 (17.7) SF-36 Mental Health: 44.0 (20.4) vs 38.3 (19.7)	FIQ (0-100, higher scores=greater impact of FM) Pain VAS (0-10, higher scores=greater pain) Beck Depression Inventory (BDI; 0-63, higher scores=greater depression) State-Trait Anxiety Inventory, state scale (20-80, higher scores=greater anxiety) SF-36 Physical Capacity (0-100, higher scores=better outcomes) SF-36 Pain (0-100, higher scores=better outcomes) SF-36 Mental Health (0-100, higher scores=better outcomes)	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Ettinger 1997 FAST trial (index study)	A vs B vs C Physical Disability, adjusted mean (SE) over all timepoints Total: 1.72 (0.04) vs 1.74 (0.04) vs 1.90 (0.03) Ambulation subscale: 2.22 (0.06) vs 2.37 (0.07) vs 2.64 (0.06) Transfers subscale: 1.75 (0.05) vs 1.72 (0.05) vs 1.92 (0.06) Pain, adjusted mean (SE) overall timepoints 2.14 (.05) vs 2.21 (.06) vs 2.40 (.05)
Falcao 2008	

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Ettinger 1997 FAST trial (index study)	NR
Falcao 2008	A vs B 3 months FIQ: 38.7 (24.8) vs 42.8 (27.2), MD -4.1 (95% CI -18.765 to 10.565), p=0.58 Pain VAS: 4.4 (3.7) vs 5.1 (3.9), MD -0.7 (95% CI -2.841 to 1.441), p=0.51 Beck Depression Inventory: 10.6 (9.3) vs 15.6 (12.2), MD -5.0 (95% CI -11.122 to 1.122), p=0.11 State-Trait Anxiety Inventory, state scale: 45.8 (2.5) vs 46.8 (2.3), MD -1.0 (95% CI -2.351 to 0.351), p=0.14 SF-36 physical capacity: 59.6 (32.3) vs 54.0 (29.9), MD 5.6 (95% CI -11.905 to 23.105), p=0.52 SF-36 Pain: 48.4 (25.6) vs 45.5 (23.0), MD 2.9 (95% CI -10.783 to 16.583), p=0.67 SF-36 Mental Health: 69.9 (19.2) vs 56.2 (28.2), MD 13.7 (95%CI 0.070 to 27.330), p =0.049

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Ettinger 1997 FAST trial (index study)	NR	A vs B vs C Falls: 14% (2/144) vs 14% (2/146) vs 0% (0/149) A vs C: RR=inf. , p=0.15 B vs C: RR = inf. , p=0.15 Death: 0% (0/144) vs 0% (0/146) vs 0.7% (1/149)
Falcao 2008		A vs B Withdrawals: 17% (5/30) vs 13% (4/30) Adverse events: NR

Author, Year	Funding Source	Quality	Comments
Ettinger 1997 FAST trial (index study)	Claude D. Pepper Older Americans Independence Center of Wake Forest University through grant P60AG10484 from the National Institutes of Health, and by the General Clinical Research Cen¬ ter grant M01-RR00211.	Fair	Original report of FAST Trial Outcomes are reported from a single repeated measures analysis of covariance model.
Falcao 2008	NR	Fair	Note that baseline data were reported only for the sample who completed treatment and all assessment, not for the sample randomized.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Fary 2011	Australia, setting not reported	Inclusion Criteria: Confirmed diagnosis of knee OA (by American College of Rheumatology criteria), persistent and stable pain(unchanging for better or worse) for minimum of 3 months prior to study entry, with baseline pain score of at least 25mm on a 100mm VAS. Exclusion Criteria: Exclusion for coexisting inflammatory arthropathies, contraindications to electrical stimulation, skin disorders in the vicinity of the knee to be treated, total knee replacement scheduled during the study period, and/or insufficient English to follow instructions and complete forms.	Randomized: 70 Treated: 67 Analyzed: 70 (ITT) Attrition: 4.2% (3/70)
Ferreira, 2007	Australia Number of centers: 3 Outpatient clinic physical therapy	Patients with non-specific low back pain for at least 3 months, 18 to 80 years old, with written informed voluntary consent Exclude: patients with neurological signs, specific spinal pathology (e.g. malignancy, or inflammatory joint or bone disease) or previous back surgery	Randomized: 240 Treated: 240 Analyzed: 240 Attrition: 8% (211/240)

Author, Year	Intervention, Comparator
Fary 2011	A.Pulsed Electrical Stimulation (PES) (n=34) Patients were provided with an electrical stimulator modified to provide pulsed, asymmetrically biphasic, exponentially decreasing waveform stimulation. Patients were asked to wear the device 7 hours daily for 26 weeks. All patients were advised to continue their usual treatment for OA. Frequency: 100Hz Pulse Width: 4msec Device: 120mm X 80mm silicone electrodes inserted into 175mm X 100mm calico pockets Positions: 2 (anterior distal thigh and anterior to knee joint) B.Placebo Electrical Stimulation (n=36) An identical placebo device was provided but the current flow was programmed to turn off after 3 minutes. This was subsensory and thus not detectable by participants allocated to placebo group. All patients were advised to continue their usual treatment for OA.
Ferreira, 2007	A: Spinal manipulative therapy (n=80): Joint mobilization or manipulation of the spine or pelvis, 12 sessions over 8 weeks B: Motor control exercise (n=80): Exercises to improve trunk muscles (contraction of transversus abdominis and multifidus muscles), 12 sessions over 8 weeks C: General exercise (n=80): Exercises with a physical therapist in 8 person classes, 12 times for 1 hour over 8 weeks

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Fary 2011	A vs B Age: 71 vs. 69 years Female: 50% vs. 44% Race: NR Mean Duration of Chronicity: 12.6 vs. 11.4 years Analgesic Medication Use: 34% vs. 51% Total (WOMAC): 36(16.8) vs. 34 (14.6) Function (WOMAC): 35 (17.6) vs. 34(16.5) Stiffness (WOMAC): 45(20.9) vs. 41(18.7) Pain Subscale (WOMAC): 35(16.3) vs. 36(18.1) Pain (VAS, 0–100mm): 51 (17.2) vs. 52 (18.2) SF-36 Physical Component: 37.0(8.5) vs. 36.5(9.1) SF-36 Mental Component: 52.7(11.0) vs. 53.7(11.2) Patient's Global Assessment of Disease Activity (VAS 0–100mm): 44(19.3) vs. 47 (24.5)	WOMAC, all scores normalized to 0-100; higher score=worse symptoms) WOMAC total WOMAC physical function subscale WOMAC stiffness subscale WOMAC pain subscale Pain on VAS (0-100; higher score=worse pain) SF-36 Physical Component Summary Score (SF-36, 0–100, higher score=improved state) SF-36 Mental Component Summary Score (SF-36, 0–100, higher score=improved state)	6.5 months
Ferreira, 2007	A vs. B vs. C Age: 54 vs. 52 vs. 55 years Female: 70 % vs. 66% vs. 70% Low back pain duration 3–12 months: 28% vs. 24% vs. 21% Low back pain duration 13–36 months: 18% vs. 29% vs. 14% Low back pain duration >36 months: 55% vs. 48% vs. 65%	Patient-Specific Functional Scale (PSFS): 3 (unable to perform activities) to 30 (able to perform activities at pre-injury level) Pain (Average pain intensity over the last week, a visual analogue scale, 0 = no pain 10 = worst pain possible) Roland Morris Disability Questionnaire (RDQ) (0=no disability to 24=severe disability)	4 and 10 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Fary 2011	A vs. B 6.5 months Proportion of Patients who achieved MCID(≥-9.1) in Function (WOMAC): 38% (13/34) vs. 39% (12/36); Proportion Difference 1% (22%, 22%); RR 1.15 (95%CI 0.61 to 2.15) p=0.671 Proportion of Patients who achieved MCID (≥-20mm) in Pain (VAS): 56% (19/34) vs. 44% (16/36); RR 1.26 (95%CI 0.784 to 2.01) p=0.342 mean Δ in Total (WOMAC): 6(16.0) vs. 7 (15.5); MCD –1.3 (–8.8, 6.3) mean Δ in Function (WOMAC): 5(16.5) vs. 7(16.2); MCD –1.9 (95%CI –9.7 to 5.9) mean Δ in Stiffness (WOMAC): 9(21.5) vs. 5(19.3); MCD 3.7 (95%CI –6.0 to 13.5) mean Δ in Pain Subscale (WOMAC): 5(20.4) vs. 10(18.4); MCD –5.6 (95%CI –14.9 to 3.6) mean Δ in Pain (VAS, 0–100mm): 20(20.7) vs.19(31.1); MCD 0.9 (95%CI –11.7 to 13.4) mean Δ in SF-36 Physical Component Summary Score: –1.0(5.6)vs. –2.6(7.3); MCD 1.7 (95%CI –1.5 to 4.8) mean Δ in SF-36 Mental Component Summary Score: –1.2(9.3) vs. –2.4(8.1); MCD 1.2 (95%CI –2.9 to 5.4)
Ferreira, 2007	NR

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Fary 2011	NR
Ferreira, 2007	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Fary 2011	NR	18% (6/34) in the treatment group vs. 17% (6/36) in the control group experienced localized, mild rashes; RR 1.06 (95%CI 0.378 to 2.97) p=0.914
Ferreira, 2007	A vs. B vs. C, mean (SD) <u>Baseline</u> Patient Specific Functional Scale (3-30): 11.2 (4.6) vs. 10.7 (4.0) vs. 10.1 (4.2) Pain (0-10 VAS): 6.2 (2.0) vs. 6.3 (2.0) vs. 6.5 (2.1) RDQ (0-24): 12.4 (5.7) vs. 14.0 (5.3) vs. 14.1 (5.5) <u>4 months</u> Patient Specific Functional Scale (3-30): 17.3 (7.0) vs. 16.4 (6.6) vs. 15.0 (7.4), difference 0.7 (95% CI -1.3 to 2.7) for A vs. B and 1.7 (95% CI -0.4 to 3.,8) for A vs. C Pain (0-10 VAS): 4.3 (2.6) vs. 4.3 (2.6) vs. 4.8 (2.6), difference 0.0 (95% CI -0.9 to 0.8) for A vs. B and -0.5 (95% CI -1.4 to 0.3) for A vs. C RDQ (0-24): 7.7 (6.2) vs. 8.4 (6.4) vs. 10.1 (7.0), difference 0.2 (95% CI -1.5 to 1.9) for A vs. B and -0.9 (95% CI -2.7 to 0.9) for A vs. C <u>10 months</u> Patient Specific Functional Scale (3-30): 15.2 (6.8) vs. 15.7 (6.8) vs. 13.9 (7.2), difference -0.8 (95% CI -2.9 to 1.2) for A vs. B and 0.3 (95% CI -1.7 to 2.3) for A vs. C Pain (0-10 VAS): 4.9 (2.7) vs. 4.9 (2.9) vs. 5.2 (2.8), difference 0.1 (95% CI -0.8 to 1.0) for A vs. B and -0.2 (95% CI -1.1 to 0.6) for A vs. C RDQ (0-24): 9.2 (6.6) vs. 8.8 (6.5) vs. 9.6 (6.9), difference 1.8 (95% CI 0.0 to 3.6) for A vs. B and 1.2 (95% CI -0.6 to 3.0) for A vs. C	No adverse events were reported

Author, Year	Funding Source	Quality	Comments
Fary 2011	Supported by an Arthritis Australia and State & Territory Affiliate Grant and a Physiotherapy Research Foundation Research Seeding grant, and by a Curtin University School of Physiotherapy Early Career Researcher grant to Dr. Fary. Dr. Fary was recipient of an Australian Government Postgraduate PhD scholarship and a Curtin University School of Physiotherapy Movement Through Life Top-Up scholarship.	Good	
Ferreira, 2007	Arthritis Foundation of New South Wales, the Motor Accidents Authority of New South Wales, and the University of Sydney	Fair	Non-specific low back pain greater than 3 months

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Fontaine 2010 2011	United States University medical center Arthritis Center, newspaper ads, clinicaltrials.gov	Met 1990 American College of Rheumatology diagnostic criteria for FM, age 18 or older, not meeting US Surgeon General's 1996 recommendations for physical activity Exclude: medical conditions that could preclude active participation, plans to change medication that might affect mood, intent to seek professional attention for anxiety or depression during study period	Randomized: 84 Analyzed: 53 Attrition: 37% (31/84)
Fukuda 2011	Brazil, two site, hospital	Inclusion Criteria: Patients >40 years old with primary grade II or II knee OA based on Gupta and colleagues radiographic criteria, and had had joint or anterior knee pain for at least 3 months Exclusion Criteria: Patients were exclude if they had a history of surgery or any invasive procedure of the affected knee, physical therapy for knee injuries or any medication that had changed in the last 3 months, or other diseases affection functional nd patients who presented any contraindication for application of PSW treatment, especially metallic implants, pacemakers, lack of sensitivity or tumor.	Randomized: 86 Treated: 86 Analyzed: 51 Attrition: 41% (35/86)

Author, Year	Intervention, Comparator
Fontaine 2010 2011	A.Lifestyle Physical Activity (n=30): 6, 60-minute group sessions over 12 weeks. Goal was to help subjects increase moderate-intensity physical exercise by accumulating short bursts of physical activity (e.g.,, walking, yard work, climbing stairs) throughout the day to 30 minutes 5-7 days per week. B.Fibromyalgia Education attention control condition (n=23): met monthly for 3 months. Included education about FM and social support.
Fukuda 2011	A.Low-dose Pulsed Short Wave (PSW) (n=32) Patients received a pre-calibrated device set to output a specific frequency and pulse duration. Patients administered the device with a care provider nearby but without direct input from care provider. No. of Treatments: 3 applications per week for 3 weeks (9 total) Length of Treatment: 19 minutes per session Total Energy: 17 kJ Frequency: 27.12 MHz Mean Power Output: 14.5 W Pulse Duration: 400 microseconds Pulse Frequency: 145 Hz Positions: Anterior area of the thigh, 5 cm above superior border of the patella B.High-dose PSW (n=31) Treatment characteristics were identical to Group A except length of treatment (and received total energy) were doubled No. of Treatments: 3 applications per week for 3 weeks (9 total) Length of Treatment: 38 minutes per session Total Energy: 33 kJ C.Sham (n=23) Treatment characteristics were identical to Group A except the device was kept in standby mode without any electrical current applied. No. of Treatments: 3 applications per week for 3 weeks (9 total) Length of Treatment: 19 minutes per session

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Fontaine 2010 2011	A vs B Age: 46 vs 49 Female: 94% vs 100% Race, white: 78% vs 82% Years since diagnosis: 5.9 vs 9.6, p=0.007 Fibromyalgia FIQ: 67.5 (12.0) vs 69.7 (13.4) Pain VAS: 54.6 (25.6) vs 58.9 (25.0) CES-D: 23.4 (8.6) vs 24.0 (10.0), p=0.06	Fibromyalgia Impact Questionnaire Pain VAS (0-100, higher score=greater current pain) Center for Epidemiological Studies Depression Scale (CES-D; higher score=greater depression)	6 and 12 months
Fukuda 2011	A. vs B. vs. C Age: 62 vs. 63 vs. 57 Female: 100% Race: NR Mean Duration of Chronicity: NR KOOS Symptoms Subscale: 46.5 (19.8) vs. 47.0 (18.0) vs. 42.0 (17.9); KOOS Daily Activities Subscale: 45.8(19.8) vs. 51.7(19.1) vs. 45.7(16.3) KOOS Recreational Activities Subscale: 16.6(10.3) vs. 15.3(17.6) vs. 18.2(15.0) KOOS Pain Subscale: 37.4(17.4) vs. 42.5(16.0) vs. 38.0(13.5) Numerical Pain Rating Scale (NPRS) 7.1(2.8) vs. 6.7(2.5) vs. 7.7(1.4) KOOS Quality of Life Subscale: 26.1(12.0) vs. 32.4(15.0) vs. 27.8(29.7)	Primary Knee Injury and Osteoarthritis Outcome Score (KOOS, higher scores on the KOOS represents better function) KOOS Symptoms Subscale (range, 0-100) KOOS Daily Activities Subscale (range, 0-100) KOOS Recreational Activities Subscale (range, 0-100) KOOS Pain Subscale (range, 0-100) Numerical Pain Rating Scale (NPRS, range 0-10: higher scores indicate severity of pain) Secondary KOOS Quality of Life Subscale	12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Fontaine 2010 **2011**	A vs B 6 months: FIQ: 65.3 (17.0) vs 63.9 (24.5), p NR; MD 1.4 (95% CI -10.047 to 12.847), p =0.81 Pain VAS: 54.9 (21.0) vs 49.4 (27.1), p NR; MD 5.5 (95% CI -7.756 to 18.756), p=0.41 CES-D: 18.1 (8.1) vs 19.9 (12.5), p NR; MD -1.8 (95% CI -7.494 to 3.894), p=0.53 12 months: FIQ: 64.4 (20.9) vs 65.1 (25.8), p NR; MD -0.7 (95% CI -13.576 to 12.176), p=0.91 Pain VAS: 51.6 (22.0) vs 50.9 (27.2), p NR CES-D: 19.8 (10.1) vs 20.6 (12.9), p NR; MD -0.8 (95% CI -7.139 to 5.539), p=0.80
Fukuda 2011	A vs. C 12 months KOOS Symptoms Subscale: 61.6 (19.7) vs. 40.7 (11.2); MD 20.9 (95% 8.92 to 32.88) p=0.001 KOOS Daily Activities Subscale: 68.9 (20.2) vs. 41.6 (16.9); MD 27.30 (95% 13.73 to 40.87) p<0.001 KOOS Recreational Activities Subscale: 24.6 (25.4) vs. 11.0 (7.1); MD 13.6 (95% -0.73 to 27.93) p=0.062 KOOS Pain Subscale: 57.5 (21.0) vs. 33.0 (9.9); MD 24.5 (95% 12.12 to 36.88) p<0.001 Numerical Pain Rating Scale (NPRS): 5.7 (3.0) vs. 7.5 (1.6); MD -1.8 (95% -3.60 to 0.00) p=0.050 KOOS Quality of Life Subscale: 31.8 (10.7) vs. 33.0 (12.8); MD -1.2 (95% -9.55 to 7.15) p=0.772 B vs. C 12 months KOOS Symptoms Subscale: 54.9 (21.6) vs. 40.7 (11.2); MD 14.2 (95% 1.21 to 27.19) p=0.033 KOOS Daily Activities Subscale: 51.9 (15.0) vs. 41.6 (16.9); MD 10.30 (95% -1.24 to 21.84) p=0.078 KOOS Recreational Activities Subscale: 15.9 (17.6) vs. 11.0 (7.1); MD 4.9 (95% -5.32 to 15.12) p=0.336 KOOS Pain Subscale: 57.6 (16.1) vs. 33.0 (9.9); MD 24.6 (95% 14.59 to 34.61) p<0.001 Numerical Pain Rating Scale (NPRS): 5.2 (2.1) vs. 7.5 (1.6); MD -2.3 (95% -3.68 to -0.92) p=0.002 KOOS Quality of Life Subscale: 41.2 (20.6) vs. 33.0 (12.8); MD 8.2 (95% -4.55 to 20.95) p=0.199

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Fontaine 2010 2011	
Fukuda 2011	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Fontaine 2010 2011		NR
Fukuda 2011	NR	Went on to have a Total Knee Replacement (TKR) during 12 month followup: 3.1% (1/32) vs. 6.5% (2/31) vs. 4.3% (1/23)

Author, Year	Funding Source	Quality	Comments
Fontaine 2010 2011	NIH NIAMS	Fair	Details regarding subjects, baseline characteristics, and study methods were reported in Fontaine 2010 (Arthritis Research and Therapy 2010). I abstracted that information from Fontaine 2010 because it was not reported in Fontaine 2011. There was a significant treatment X time effect for A vs B from baseline to post-intervention (p=0.008 favoring A over B) and from post-intervention to the 6-month followup (p=0.015, favoring B over A) on the FIQ. "the significant effects of LPA on physical activity, function, and pain found during the 12-week trial were not maintained at 6- and 12-month followup."
Fukuda 2011	NR	Poor	A 12 month followup was not performed for the no treatment group because after the treatment phase ended they were referred to traditional physical therapy; therefore, this arm was excluded due to insufficient followup (immediately post-intervention period only).

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Giannotti 2014	Italy Centers and setting NR	Inclusion: FM diagnosis based on ACR 2010criteria, age 35-65, body mass index 18-35 Exclusion: diabetes, other rheumatic diseases including severe osteoarthritis and severe osteoporosis, use of assistive device to perform daily activities, orthopedic surgery in past year, attendance in physical therapy and rehabilitation treatments or change in usual FM pharmacologic therapy in past 3 months	Randomized: 41 Analyzed: 32 Attrition: 22% (9/41)
Gibson 1985	UK, London Number of centers: 1 Clinic	Patients with chronic low back pain >2 months but <12 months. Exclude: Patients with history of numbness, paresthesia, radicular pain, and neurological deficit.	Randomized: 109 Treated: 108 Analyzed: 108 Attrition: 16% (18/109)
Giombini 2011	Italy	Inclusion Criteria: Inclusion criteria were age 60 and above of both sex; mono or bilateral moderate knee OA (Kellgren and Lawrence grading system II and III), knee pain for at least 6 months and no more than 4 years; independent ambulation without a walking aid; no previous knee surgery or injection of glucocorticoid and/or hyaluronic acid in the last 3 months, no physiotherapy treatment for knee problems in the last month. Exclusion Criteria: Exclusion criteria were tumors, joint disease involving the knee such as rheumatic or psoriatic arthritis, joint infections, previous lower limb fractures, neurologic disorders, neck or low back pain with referred pain to the study knee, impaired cutaneous thermal sensitivity, previous deep vein thrombosis. Patients with a cardiac pacemaker or metallic knee implants were not recruited to avoid possible interactions between electromagnetic fields produced by the hyperthermia equipment and these devices.	Randomized: 63 Treated: 55 Analyzed: 54 (ITT) Attrition: 14.2% (9/63)

Author, Year	Intervention, Comparator
Giannotti 2014	A.Rehabilitation protocol combining physical exercise and education 2 days a week (60 minutes per session) for 10 weeks (n=20). Sessions were conducted in a group and supervised by a physiotherapist. Strengthening exercises intensified from session 8, and from session 15, aerobic exercises were added. Exercises included stretching, strengthening, active and passive mobilization, spine flexibility, and aerobic training. Goal was to improve cardiovascular endurance, muscle strength and stretch, and joint range of motion. Subjects were instructed to perform at home the exercise program at least 3 times per week. B.Control group that did not receive A (n=12)
Gibson 1985	A: Spinal osteopathic manipulation (n=41), once weekly for 4 weeks, including passive articulation of stiff spinal segments and manipulation of the vertebra facet of sacroiliac joints using minimal rotation B: Short wave diathermy (SWD) (n=34), 3 times weekly for 4 weeks C. Placebo, detuned SWD (n=34)
Giombini 2011	A.Microwave Diathermy (n=29) All participants received hyperthermic treatment (application of superficial heat and electromagnetic energy) from an ALBA Hyperthermia System. No. of Treatments: 3 per week for 4 weeks (12 total) Length of Treatments: 30 minutes each Power Output: 50 W Water Pad Temperature: 38 degrees Celsius Pilot Temperature: 41 degrees Celsius B.Sham Diathermy (n=25) All treatment parameters were identical except the device was set to off, but patients were unable to distinguish sham from real treatment.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Giannotti 2014	A vs B Age: 53 vs 51 Female: 95% vs 92% Duration of FM symptoms before diagnosis, years: 8 vs 7 FIQ (mean, 0-100): 62.7 (14.4) vs 59.1 (15.6) Pain VAS: 6.1 (2.1) vs 6.1 (1.6) Sleep VAS: 6.8 (2.7) vs 6.9 (3.5)	FIQ (Italian version) (0-100, higher scores= higher impairment) Pain VAS (0-10, higher scores=greater pain) Sleep VAS (0-10, higher scores=greater sleep problems)	1 and 6 months
Gibson 1985	A vs. B vs. C Age (mean): 34 vs. 35 vs. 40 years Female: 61% vs. 47% vs. 32% Race: NR Pain (median, 0-100 VAS): 35 vs. 45 vs. 48 Using analgesics: 25% vs. 18% vs. 50%	Pain scores (100 mm horizontal visual analogy scale and spinal tenderness 0-3, none, mild, moderate, severe) Pain intensity Need for analgesics	2 months
Giombini 2011	A. vs B. Age: 67 vs. 67 years Female: 65.7% vs. 67.8% Race: NR Mean Duration of Chronicity: Total (WOMAC): 103.1 (27.6) vs. 101.3 (23.4) Pain (WOMAC): 19.2 (7.3) vs. 18.5 (7.1) Stiffness (WOMAC): 9.7 (4.1) vs. 9.7 (3.6) Activities of Daily Living (WOMAC): 74.3(18.9) vs. 73.1(18.3)	Primary: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, higher scores indicate greater pain, stiffness or functional limitation) Total (WOMAC, range 0-120) Physical Function (WOMAC, range 0-85) Stiffness (WOMAC, range 0-10 Pain(WOMAC, range 0-25)	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Giannotti 2014	A vs B 1 month: FIQ: 55.5 (12.2) vs 50.9 (20.0), p NR; MD 4.6 (95% CI -6.38 to 15.58), p=0.40 Pain VAS: 5.3 (2.5) vs 5.5 (2.4), p NR; MD -0.20 (95% CI -1.87 to 1.47), p = 0.81 Sleep VAS: 4.6 (3.1) vs 5.0 (3.1), p NR; MD -0.40 (95% CI -2.51 to 1.71) 6 months: FIQ: 48.8 (17.4) vs 56.9 (14.5), p NR; MD -8.1 (95% CI -20.3, 4.1) Pain VAS: 5.8 (2.0) vs 5.4 (2.9), p NR; MD 0.4 (95% CI -1.4, 2.2) Sleep VAS: 6.3 (3.0) vs 6.1 (3.4) vs 6.9 (1.6), p NR; MD 0.20 (95% CI -2.15 to 2.55, p =0.86
Gibson 1985	A vs. B vs. C <u>Baseline</u> Pain (median [range], 0-100 VAS): 35 (4-90) vs. 45 (5-82) vs. 48 (10-96) Using analgesics: 25% (10-41) vs. 18% (6/34) vs. 50% (17/34) <u>3-months</u> Pain (median [range], 0-100 VAS): 13 (0-90) vs. 35 (0-90) vs. 6 (0-90) Using analgesics: 18% (7/38) vs. 7% (2/27) vs. 22% (7/32)
Giombini 2011	<u>A vs. B</u> <u>3 months</u> Mean Δ in Total (WOMAC): -46.8(27.2) vs. -0.4(12.7); MD -46.4 p<0.01 Mean Δ in Pain (WOMAC): -8.6(6.0) vs. -0.6(3.0); MD -8.1 p<0.01 Mean Δ in Stiffness (WOMAC): -5.2(3.8) vs. -0.1(2.9); MD -5.1 p<0.01 Mean Δ Function (WOMAC): -33(19.7) vs. 0.3(9.8); MD -33.2 p<0.01

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Giannotti 2014	
Gibson 1985	NR
Giombini 2011	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Giannotti 2014		A vs B Adverse events: 0 vs 0 Withdrawals: NR
Gibson 1985	NR	Not reported
Giombini 2011	NR	No serious adverse effects occurred during the trial, except for two patients in the treatment group who reported a transient aggravation of symptoms, which did not induce them to drop out from the study.

Author, Year	Funding Source	Quality	Comments
Giannotti 2014	NR	Poor	Article reported within-group changes over time, but not treatment X time comparisons
Gibson 1985	Arthritis and Rheumatism Council	Poor	
Giombini 2011		Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Goldby 2006	United Kingdom, two-site, hospital	Inclusion Criteria: All subjects had chronic low back disorder, with the current episode lasting for a minimum of 12 weeks, were aged between 18 and 65 years, and able to read and write English. Exclusion Criteria: All patients with nonmechanical low back pain were excluded. Additional exclusion for Spinal stenosis, spondylolisthesis grades III or IV, or recent fractures; significant or worsening signs of neurologic deficit; evidence of inflammatory joint disease; lower limb pathology likely to influence leg pain intensity; present or past history of metastatic disease; medically unsuitable for participation in the exercise class; chronic pain syndrome or a history of 2 operative interventions for low back pain; history of anxiety neurosis; and pregnancy.	Randomized: 323 Treated: 213 Analyzed: Attrition: 3 months - 38% (123/323) 6 months - 46.1% (149/323) 12 months - 46.4% (150/323) 24 months - 71.8% (232/323)

Author, Year	Intervention, Comparator
Goldby 2006	A.Neuromuscular re-education (motor control exercise) (n=84) Participants gathered in classes of 12 participants and were exposed to a functionally progressive exercise class that emphasized the selective retraining of various muscle groupings. No. of Treatments: weekly sessions for 10 weeks (10 total) Length of Treatments: 1 hour B.Manual Therapy (n=89) Physiotherapists treated patients according to clinical reasoning. They were not allowed to prescribe exercises nor electrophysical methods. Patients were discharged at the discretion of the physiotherapist or to a maximum of 10 interventions. No. of Treatments: 1-10 sessions (physiotherapists discretion) Length of Treatments: NR C.Attention control (education) (n=40) Physiotherapists explained the contents of an educational booklet. No. of Treatments: 1 initial consultation with physiotherapist Additionally, patients in all 3 groups attended The Back School, which consisted of 1 group specific 3-hour question and answer session on anatomy and physiology, biomechanics and lifting, pathologies, and advice on education, exercise and general fitness.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Goldby 2006	A vs. B vs. C Age: 43 vs. 41 vs. 41 years Female: 68% vs. 70% vs. 68% Race: 79.8% vs. 75.3% vs. 61.5% Mean Duration of Chronicity: 11.5 vs. 11.1 vs. 12.5 years ODI: 40.47 (15.62) vs. 39.17 (13.73) vs. 33.54 (12.21) LBO: 43.86 (13.97) vs. 44.02 (13.16) vs. 47.55 (15.58) Back Pain (NRS): 45.75 (27.54) vs. 55.67 (28.35) vs. 37.6 (33.99) Leg Pain (NRS): 27.54 (31.93) vs. 27.74 (34.71) vs. 21.0 (31.94) NHP: 162.18 (105.5) vs. 163.22 (118.98) vs. 139.61 (89.81)	Primary: Oswestry Disability Index (ODI, range 0-100) Low Back Outcome Score (0-75, higher=better status) Back Pain (0-100 NRS, higher scores indicate worse pain) Leg Pain (0-100 NRS, higher scores indicate worse pain) Secondary: Nottingham Health Profile (NHP) (range unclear, usually scored 0 to 100, 100=maximal distress)	Short, intermediate, and long-term 3 months, 6 months, 12 months, and 24 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Goldby 2006	A vs. C <u>Baseline</u> ODI (0-100): 40.47 (15.62) vs. 33.54 (12.21) Low Back Outcome Score (0-75): 43.86 (13.97) vs. 47.55 (15.58) Back Pain (0-100 NRS): 45.75 (27.54) vs. 37.6 (33.99) Leg pain (0-100 NRS): 27.54 (31.93) vs. 21.0 (31.94) Nottingham Health Profile:162.18 (105.5) vs. 139.61 (89.81) Medication use: 51.2% vs. 50% <u>3 months</u> ODI: 31.00 (17.07) vs. 28.1 (17.34), difference 2.9 (95% CI -3.89 to 9.69) Low Back Outcome Score: 50.92 (15.05) vs. 54.4 (16.88), difference -3.48 (95% CI -9.67 to 2.71) Back Pain (0-100 NRS): 28.81 (28.14) vs. 34.4 (36.43), difference -5.59 (95% CI -17.86 to 6.68) Leg Pain (0-100 NRS): 15.96 (24.83) vs. 12.85 (26.8), difference 3.11 (95% CI -6.96 to 13.18) Nottingham Health Profile: 94.97 (99.35) vs. 94.32(85.41), difference 0.65 (95% CI -36.97 to 38.27) Medication use: 29.9% vs. 35.1% <u>6 months</u> ODI: 25.81 (17.82) vs. 23.9 (17.75), difference 1.91 (95% CI -6.28 to 10.10) Low Back Outcome Score (0-75): 55.42 (14.15) vs. 57.85(15.8), difference -2.43 (95% CI -9.14 to 4.28) Back Pain (0-100 NRS): 23.16 (27.43) vs. 30.25 (31.68), difference -7.09 (95% CI -20.22 to 6.04) Leg Pain (0-100 NRS): 12.77 (23.89) vs. 7.0 (17.43), difference 5.77 (95% CI -4.56 to 16.09) Nottingham Health Profile: 76.3 (75.46) vs. 77.50 (90.5), difference -1.20 (95% CI -37.76 to 35.36) Medication use: 23.9% vs. 24% <u>12 months</u> ODI: 24.76 (17.44) vs. 26.9 (19.6), difference -2.14 (95% CI -10.14 to 5.86) Low Back Outcome Score: 53.86 (15.27) vs. 50.95 (18.55), difference 2.91 (95% CI -4.29 to 10.11) Back Pain (0-100 NRS): 29.23 (28.1) vs. 30 (34.95), difference -0.77 (95% CI -14.13 to 12.59) Leg Pain (0-100 NRS): 16.23 (26.17) vs. 1.75(6.74), difference 14.48 (95% CI 4.51 to 24.45) Nottingham Health Profile: 70.06 (78.48) vs. 87.47 (107.11), difference -17.41 (95% CI -56.12 to 21.30) Medication use: 16.9% vs. 39.3% <u>24 months</u> ODI: 27 (21) vs. 27 (18); difference 0.00 (95% CI -11.44 to 11.44) Low Back Outcome Score: 54.7 (16.1) vs. 55.2 (13.4), difference -0.5 (95% CI -9.20 to 8.20) Back Pain (0-100 NRS): 35.4 (29) vs. 50.9 (33.7), difference -15.50 (95% CI -33.06 to 2.06) Leg Pain (0-100 NRS): 21.6 (32.1) vs. 17.8 (31.5), difference 3.8 (95% CI -14.44 to 22.04) Nottingham Health Profile: 82 (103.8) vs. 83 (106.3), difference -1.00 (95% CI -60.85 to 58.85) Medication use: 8.8% vs. 45.5%

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Goldby 2006	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Goldby 2006	NR	NR

Author, Year	Funding Source	Quality	Comments
Goldby 2006	"Professional Organizational funds were received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript"	Fair	(EB) There is no mention of radiculopathy in the inclusion or exclusion criteria but Leg Pain is an outcome. No further information is provided. Abstract states that data were collected at baseline, and 3, 6, 12, and 24 months *after* intervention.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Gowans 2001	Canada Advertisements in Rheumatology clinic or large urban teaching hospital and local FM support group newsletters	Inclusion: FM diagnosis based on ACR 1990 criteria Exclusion: high blood pressure or symptomatic cardiac disease, other serious systemic disease, intent to change medications for anxiety or depression, or seek professional treatment for anxiety or depression during study period, enrolled in or intent to begin aerobic exercise program	Randomized: 57 analyzed: 50 Attrition: 12% (7/57)
Groessl, 2017	US Number of centers 1 Outpatient	Age > 18 years with chronic LBP diagnosis > 6 months Exclude: Back surgery in the last 12 months, back pain from systemic conditions, morbid obesity, acute sciatica/nerve compression, chronic lumbar radicular pain, serious unstable coexisting medical or psychiatric conditions, potential metastatic disease, positive Romberg test, or practiced yoga in the last year	Randomized: 152 Treated: 150 Analyzed: 150 Attrition: 0.01% (2/152)
Gudavalli 2006	US, Illinois Number of centers: 1 Outpatient clinic	Patients with LBP from L1 to SI joint for more that 3 months, palpatory tenderness over one or more lumbar zygapophyseal joints, no narcotic use during treatment phase , no NSAID use and/or muscle relaxant use 24 hours prior to baseline or outcome measure assessment Exclude: Patients younger than 18 years with central nervous system disease, contraindication to manual therapy, severe osteoporosis, lumbar fracture, systemic disease potentially affecting the musculoskeletal system, failed fusion surgery with unstable components, inability to undergo physical therapy or flexion–distraction therapy , psychiatric illnesses or lack of cognitive abilities, current and known substance abuse, not fluent and/or illiterate in the English language, morbidly obese, pregnant, receiving care for LBP other providers, chiropractor or physical therapist in past 6 months, not willing to stop LBP care at other clinics, New York Heart Association Classification grade III or IV	Randomized: 235 Treated: 235 Analyzed: 235 Attrition: 17% (197/235)

Author, Year	Intervention, Comparator
Gowans 2001	A.Supervised exercise group (n=27): 3 hospital-based exercise classes per week for 23 weeks. Classes consisted of 10 minutes stretching and 20 minutes of aerobic exercise. Classes for the first 6 weeks were held in a warm therapeutic pool. At 7 weeks, subjects progressed to 2 walking classes in a gym and one pool class. Subjects were taught to maintain their heart rates at 60-75% of age-adjusted maximum heart rates during the aerobic component. Mean attendance at exercise classes over the 23-week period was 55% (range 7-91%). B.Control group (n=23): continued ad libitum activity
Groessl, 2017	A. Hatha yoga (n=75): Two 60 minute sessions per week for 12 weeks, 15–20 minutes of home practice on days without sessions B. Wait list (n=75): Usual care, with yoga started after 6 months
Gudavalli 2006	A.Flexion–distraction (FD) (n=123): Slow manual traction and mobilization, 2–4 times per week for 4 weeks. B.Active trunk exercise program (ATEP) (n=112): Flexion or extension exercises, weight training, flexibility exercises, and cardiovascular exercises dependent on patient symptoms, 2–4 times per week for 4 weeks.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Gowans 2001	A vs B Age, years: 45 vs 50, p<0.05 Female: 89% vs 87% Duration of symptoms, years: 9.6 vs 8.4 Duration of diagnosis, years: 2.8 vs 4.2 FIQ: 57.7 (11.7) vs 56.6 (12.9) 6-minute walk test: 427.8 (89.0) vs 414.1 (81.6) BDI: 22.9 (12.2) vs 21.3 (9.8) STAI: 47.4 (15.9) vs 47.0 (14.6)	FIQ excluding job items (0-80, higher scores=greater impairment) 6-minute walk test (higher scores=greater distance walked) Beck Depression Inventory (0-63; higher scores=greater depression) State version of State-Trait Anxiety Inventory (20-80, higher scores=greater anxiety)	Immediately post-intervention (6 months)
Groessl, 2017	A vs. B Mean age: 53 vs. 54 years Female: 27% vs. 25% Race: African American or black: 21% vs. 13% White: 47% vs. 52% Native American: 1.3% vs. 1.3% Hispanic: 20% vs. 20% Asian/Pacific Islander: 4% vs. 8% Years of LBP: 15.4 vs. 14.6 Current opioid mediication use: 56% vs. 47%	RDQ (0–24) Pain intensity, Brief Pain Inventory (0–10) Opioid medication use Other medical treatments for pain	Short term 3.5 months
Gudavalli 2006	A vs B Age: 42 vs. 41 years Female: 34% vs. 41% Race Caucasian: 83% vs. 82% Hispanic: 4% vs. 6% African American: 7% vs. 6% Asian: 7% vs. 4% Other: 0% vs. 2% Pain VAS (0-100), mean (SD): 38.00 (2.01) vs. 35.70 (1.96) Roland Morris, mean (SD): 6.64 (0.43) vs. 6.84 (0.42) SF-36 Physical component score, mean (SD): 41.77 (0.74) vs.42.71 (0.84) SF-36 Mental component score mean (SD): 51.18 (0.83) vs. 48.49 (1.19) Zung depression score, mean (SD): 43.34 (0.81) vs. 45.06 (0.89) Radiculopathy: 18% vs. 21%	Pain (0-100 VAS) RDQ (0-24)	2, 5, and 11 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Gowans 2001	A vs B 6 months, ITT analysis: FIQ: 48.6 (16.2) vs 54.9 (13.0), p<0.05; MD -6.3 (95% CI -14.8, 2.2) , p=0.14 BDI: 16.9 (10.8) vs 21.3 (10.3), p<0.05; MD -4.4 (95% CI -10.4, 1.6), p=0.15 STAI: 41.3 (14.2) vs 51.7 (13.1), p<0.05; MD -10.4 (95% CI -18.2, -2.6), p = 0.01 p-values reported are from independent t-tests (A vs. B) of change scores (23 weeks–baseline)
Groessl, 2017	Baseline, mean (SD) RDQ (0-24): 9.40 (5.15) vs. 10.3 (5.87) Pain intensity, Brief Pain Inventory (0-10): 4.64 (1.76) vs. 4.68 (2.16) Opioid medication use: 19% (14/75) vs. 21% (16/75) Other medical treatments for pain: 56% (42/75) vs. 47% (35/75) 3.5 months, change from baseline RDQ (0-24): - 3.37 (95% CI -4.51 to -2.23) vs. -0.89 (95% CI-2.02 to 0.23); between group difference - 2.48 (95% CI- 4.08 to -0.87) Pain intensity, Brief Pain Inventory (0-10): -0.44 (95% CI- 0.78 to - 0.11) vs. 0.15 (95% CI -0.18 to 0.47); between-group difference -0.59 (95% CI -1.05 to -0.13) Opioid medication use: 9% (7/75) vs. 7% (5/75), p=0.40 Other medical treatments for pain: 39% (29/75) vs. 37% (28/75), p=0.42
Gudavalli 2006	NR

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Gowans 2001	
Groessl, 2017	NR
Gudavalli 2006	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Gowans 2001		A vs B Withdrawals: 10% (3/30) vs 11% (3/27) Adverse Events: NR
Groessl, 2017	NR	None reported.
Gudavalli 2006	A vs. B, mean (SD) <u>Baseline</u> Pain (0-100 VAS): 38.00 (2.01) vs. 35.70 (1.96) RDQ (0-24): 6.64 (0.43) vs. 6.84 (0.42) <u>2 months</u> Pain (0-100 VAS): 16.52 (2.95) vs. 12.04 (2.53) RDQ (0-24): 3.50 (0.50) vs. 3.75 (0.51) <u>5 months</u> Pain (0-100 VAS): 18.26 (2.64) vs. 8.92 (2.89) RDQ (0-24): 3.89 (0.46) vs. 3.42 (0.50) <u>11 months</u> Pain (0-100 VAS): 17.10 (2.55) vs. 12.36 (2.43) RDQ (0-24): 3.90 (0.53) vs. 3.77 (0.44)	No adverse events or side effects reported.

Author, Year	Funding Source	Quality	Comments
Gowans 2001	Toronto Hospital Auxiliary Women's Health Project on Women and Arthritis	Poor	Authors reported analyses were intent-to-treat but did not include subjects who withdrew after randomization in baseline data analyses.
Groessl, 2017	Veteran Affairs Rehabilitation Research and Development (Grant #RX000474)	Fair	
Gudavalli 2006	Health Resources and Services Administration (HRSA) Grant # R18 AH 10001	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Gur 2004	Turkey Setting NR	Age 17–55 years; pain lasting at least 1 year affecting work or daily activity, arising from the neck and shoulder girdle; between 1-10 myofascial tender points in the shoulder-girdle. Exclusion: Fibromyalgia; patients aged below 17 or above 55 years; mental retardation; neurological deficits involving the upper limbs; advanced osteopathic or arthropathic disorder of the cervical spine or the shoulder; cardiovascular disease, hypertension, coagulopathy, ulcer, recent severe hemorrhage, renal insufficiency, severe hepatic disease, neoplasia, epilepsy, cutaneous pathology or pain of central origin, and pregnancy.	Randomized: 60 Treated: 58 Analyzed:: 54 Attrition:10% (6/60)
Gusi 2006	Spain Members of local FM association	Inclusion: female with FM diagnosis according to ACR 1990 criteria Exclusion: severe spine disorder such as prolapsed disk or spinal stenosis; history of severe trauma, frequent migraines, peripheral nerve entrapment, inflammatory rheumatic disease, severe psychiatric illness; other disease that prevents physical loading; pregnancy; attendance at another psychological or physical therapy	Randomized: 35 Treated: 35 Analyzed: 34 Attrition: 3% (1/35)

Author, Year	Intervention, Comparator
Gur 2004	A.Active Ga-As laser therapy (n=28), (20 W maximum output per pulse, 904 nm, 200 nanoseconds maximum pulse duration, 2.8 kHz pulse frequency,11.2 mW average power, and 1 cm2 surface) daily for 2 weeks, 3 minutes each myofascial tender point, approximately 2 J/cm2 energy density. B.Sham laser (n=26)
Gusi 2006	A.Exercise (n=17): exercise in waist-high warm pool 3 times per week for 12 weeks. Each 1 hour session included 10 minutes warmup, 10 minutes aerobic exercise at 65-75% of maximal heart rate, 20 minutes of overall mobility and lower-limb strength exercises, another set of 10 minutes of aerobics, and 10 minutes cooldown. Heart rate was monitored with a pulse meter. At the end of the 12-week therapy, all subjects were instructed to avoid physical exercise for the next 12 weeks. The 18 participants randomized attended >34 of the 36 sessions. B.Control (n=17): Normal daily activities, which did not include any form of exercise related to those in the therapy.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Gur 2004	A vs B Age: 32 vs 31 years Female: 82% (total pop only) Pain duration: 43 vs 43 months Pain at rest: 7.43 (2.65) vs 6.87 (1.96) Pain at movement: 7.43 (2.65) vs 7.19 (2.52) NPAD: 65.36 (24.83) vs 68.52 (28.39) NHP: 78.92 (20.23) vs 75.47 (26.15) BDI: 21.56 (13.49) vs 20.81 (12.25) Married: 40% vs 37% Employed: 12% vs 17% Student: 21% vs 25% Secondary education or better: 54% vs 47%	Neck Pain and Disability Scale (NPAD) (scale: 0-100, higher score = greater disability) Pain at rest (VAS 0-10, higher score worse pain) Pain at movement (VAS 0-10, higher score worse pain) Nottingham Health Profile (NHP) (scale 0-100, lower score greater disability) Beck Depression Inventory (BDI) (scale 0-63, higher score, more severe the depression)	2.5 months
Gusi 2006	A vs B Age, years: 51 vs 51 Female: 100% vs 100% Duration of symptoms, years: 24 vs 19 Pain VAS (mean, 0-100): 63.1 (26.0) vs 63.9 (25.0) EQ-5D (mean, 0-1): 0.29 (0.28) vs 0.32 (0.32) EQ-5D Pain/discomfort: 2.5 (0.5) vs 2.5 (0.5) EQ-5D Anxiety/depression: 2.2 (0.6) vs 2.2 (0.6)	Pain VAS (0-100; higher scores=worse pain) EQ-5D (0-1; 0=death, 1=full functional quality of life) EQ-5D Mobility (1-3; higher scores=more problems) EQ-5D Pain/discomfort (1-3, higher scores=more problems) EQ-5D Anxiety/depression (1-3, higher scores=more problems)	6 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Gur 2004	A vs B <u>2.5 months</u> NPAD (0-100): 41.14 (28.34) vs 63.29 (24.50), MD -22.15 (95%CI -36.7 to -7.6), p=0.004 NHP (0-100): 56.41 (29.18) vs 72.48 (24.66), MD -16.1 (95% CI -30.9 to -1.3), p=0.034 BDI: 14.72 (13.19) vs 21.38 (10.65), MD -6.66 (95% CI -13.24 to -0.08), p=0.047 Pain at rest (0-10) 4.18 (2.65) vs 6.29 (3.52), MD -2.11 (95% CI -3.80 to -0.42), p=0.016 Pain at movement (0-10): 5.26 (1.49) vs 7.28 (3.03), MD -2.02 (95%CI -3.31 to -0.73), p= 0.003
Gusi 2006	A vs B 6 months (mean hange from baseline (95% CI)) (p is for difference between groups): Pain VAS: -1.6 (95% CI -12.7 to 0.9) vs 0.9 (95% CI -7.3 to 9.2), p=0.69 EQ-5D: 0.14 (95% CI -0.03 to 0.32) vs -0.02 (-0.17 to 0.13), p=0.14 EQ-5D Mobility: -0.2 (-0.5 to -0.1) vs 0.1 (95% CI -0.2 to 0.3), p=0.056 EQ-5D Pain/discomfort: -0.1 (95% CI -0.4 to 0.3) vs 0 ((95% CI -0.3 to 0.3), p=0.79 EQ-5D Anxiety/depression: -0.5 ((95% CI -0.8 to -0.1) vs 0 (95% CI -0.2 to 0.2), p=0.01

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Gur 2004	
Gusi 2006	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Gur 2004		NR
Gusi 2006		A vs B Withdrawals: 6% (1/18) vs 0/17 Adverse events: 1 non-study related in A; no others reported

Author, Year	Funding Source	Quality	Comments
Gur 2004	NR	Fair	
Gusi 2006	European Social Funds and Regional Government of Extremadura (Spain)	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Haake 2007	Germany Number of centers: 340 Outpatient	Age ≥18 years Clinical diagnosis of chronic low back pain for ≥6 months Mean Von Korff Chronic Pain Grade Score (CPGS) of grade ≥1 Hannover Functional Ability Questionnaire (HFAQ) score <70% No previous acupuncture for treatment of chronic low back pain Ability to speak, read, and write German Exclude: Treatment with needle acupuncture for any other indication within the last year Previous spinal fracture, or disc or spinal surgery Infectious or tumorous spondylopathy Systemic bone or joint disorders Scoliosis or kyphosis Sciatica or chronic pain from other disease Hemorrhagic disorders or anticoagulant therapy Skin disease in the area of acupuncture Abuse of drugs or pain medication Pregnancy Epilepsy Patient included in any other studies	Randomized: 1162 Treated: 387 Analyzed: 1161 Attrition: <1% (1/1162)

Author, Year	Intervention, Comparator
Haake 2007	A.Acupuncture (n=387): 10-15 sessions* of acupuncture of 30 minutes each. Needling fixed points and additional points (from a prescribed list) chosen individually on the basis of traditional Chinese medicine diagnosis, including tongue diagnosis. Body needle acupuncture without electrical stimulation or moxibustion using 0.25 x 40 mm or 0.35 x 50 mm needles. 14-20 needles were inserted to a depth of 5-40 mm depending on location. Induction of de Qi was elicited by manual stimulation. For acute episodes of pain, only rescue medication was permitted; strictly defined as nonsteroidal anti-inflammatory drugs to be taken on no more than 2 days per week up to the maximum daily dose during the therapy period, and only 1 day per week during followup. B.Sham acupuncture (n=387): 10-15 sessions* of sham acupuncture, 30 minutes each. Body needle acupuncture without electrical stimulation or moxibustion using 0.25 x 40 mm or 0.35 x 50 mm needles. Acupuncture on either side of the lateral part of the back and on the lower limbs was standardized, avoiding all known verum points or meridians. 14-20 needles were inserted, but superficially (1-3 mm) and without stimulation. For acute episodes of pain, only rescue medication was permitted; strictly defined as nonsteroidal anti-inflammatory drugs to be taken on no more than 2 days per week up to the maximum daily dose during the therapy period, and only 1 day per week during followup. C.Usual care (n=388): Multimodal treatment according to German guidelines: 10 sessions with physician or physiotherapist who administered physiotherapy, exercise, etc. Physiotherapies were supported by nonsteroidal anti-inflammatory drugs or pain medication up to the maximum daily dose during the therapy period. Rescue medication was identical to that for the acupuncture groups. * Ten 30-minute sessions, generally 2 sessions per week, and 5 additional sessions if after the 10th session patients experienced a 10-50% reduction in pain intensity on the Von Korff Chronic Pain Grade Scale.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Haake 2007	A vs. B vs. C Age: 50 vs. 49 vs. 51 Female: 57% vs. 64% vs. 58% Race: NR Duration of back pain: 8.1 vs. 7.7 vs. 8.1 years Baseline CPGS: 67.7 vs. 67.8 vs. 67.8 Baseline HFAQ: 46.3 vs. 46.3 vs. 46.7 Baseline SF-12, physical component: 31.8 vs. 31.5 vs. 31.6 Baseline SF-12, mental component: 46.6 vs. 46.6 vs. 47.1	Treatment response: ≥33% improvement in pain or ≥12% improvement in function Von Korff Chronic Pain Grade Scale (0-100) Hannover Functional Ability Questionnaire: 0-100 (higher score = better function) SF-12 physical and mental component Global assessment of therapy effectiveness by patient: 1 (very good) to 6 (fail)	1.5 and 4.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Haake 2007	A vs. B vs. C <u>Baseline</u> Von Korff Chronic Pain Grade Scale (0-100): 67.7 (13.9) vs. 67.8 (13.2) vs. 67.8 (14.6) Hannover Functional Ability Questionnaire (0-100): 46.3 (14.7) vs. 46.3 (15.3) vs. 46.7 (14.5) SF-12 physical component (0-100): 31.8 (6.8) vs. 31.5 (6.9) vs. 31.6 (6.8) SF-12 mental component (0-100): 46.6 (12.3) vs. 46.6 (11.5) vs. 47.1 (11.6) <u>1.5 months</u> Treatment response: 55.0% (213/387) vs. 51.9% (201/387) vs. 41.9% (162/387), RR 1.05 (95% CI 0.93 to 1.21) for A vs. B and RR 1.31 (95% CI 1.13 to 1.52) for A vs. C Von Korff Chronic Pain Grade Scale (0-100): 45.4 (19.4) vs. 48.5 (19.5) vs. 54.8 (18.4) Hannover Functional Ability Questionnaire (0-100): 65.4 (22.9) vs. 61.3 (22.7) vs. 56.0 (22.0) SF-12 physical component (0-100): 40.3 (10.1) vs. 39.2 (9.7) vs. 36.1 (8.9) SF-12 mental component (0-100): 50.5 (11.1) vs. 50.2 (11.0) vs. 48.6 (11.6) Global assessment (1-6): 2.8 (1.3) vs. 3.1 (1.4) vs. 3.6 (1.3) <u>4.5 months</u> Treatment response: 47.6% (184/387) vs. 44.2% (171/387) vs. 27.4% (106/387), RR 1.08 (95% CI 0.92 to 1.25) for A vs. B and RR 1.74 (95% CI 1.43 to 2.11) for A vs. C Von Korff Chronic Pain Grade Scale (0-100): 40.2 (22.5) vs. 43.3 (23.0) vs. 52.3 (21.2) Hannover Functional Ability Questionnaire (0-100): 66.8 (23.1) vs. 62.2 (23.0) vs. 55.7 (22.7) SF-12 physical component summary (0-100): 41.6 (10.5) vs. 39.5 (10.1) vs. 35.8 (9.5) SF-12 mental component summary (0-100): 50.7 (11.1) vs. 50.9 (10.8) vs. 49.2 (11.8) Global assessment (1-6): 2.8 (1.3) vs. 3.0 (1.4) vs. 3.5 (1.3)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Haake 2007	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Haake 2007	NR	A vs. B vs. C Withdrawals: 2.6% (10/387) vs. 2.8% (11/387) vs. 5.9% (23/388), RR 0.91 (95% 0.39 to 2.12) for A vs. B and RR 0.44 (95% CI 0.21 to 1.14) for A vs. C Withdrawals due to AEs: NR Serious AEs: 3% (12/387) vs. 3% (12/387) vs. 4% (16/387), RR 1.00 (95% CI 0.45 to 2.20) for A vs. B and RR 0.75 (95% CI 0.36 to 1.56) for A vs. C Clinically relevant AEs: 22.6% (257/1162) overall, no difference between groups (p=0.81)

Author, Year	Funding Source	Quality	Comments
Haake 2007	German public health insurance companies: Allgeme- ine Ortskrankenkasse, Betriebskrankenkasse, Innungskran-kenkasse, Bundesknappschaft, Bundesverband der Land-wirtschaftlichen Krankenkassen, and Seekasse.	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Haas 2014	US, Oregon Number of centers: 1 Outpatient clinic	Patients 18+ years old, current episode of LBP of mechanical origin 3+ months duration, some LBP on 30 days in the previous 6 weeks and a minimum LBP index of 25 on a 100-point scale. Exclude: Patients who received manual therapy within 90 days or for contraindications to study interventions, patients with active cancer, spine pathology, inflammatory arthropathies, autoimmune disorders, anticoagulant conditions, neurodegenerative diseases, pain radiating below the knee, organic referred pain, pregnancy, and disability compensation.	Randomized: 400 Treated: 391 Analyzed: 391 Attrition: 2.3% (9/400)

Author, Year	Intervention, Comparator
Haas 2014	A.Spinal manipulation (n=100) 6 sessions over 6 weeks with 12 minimal massage (control) sessions; manipulation consisted of manual thrust (high velocity, low amplitude) spinal manipulation predominantly in the side-posture position, lighter thrust manipulation including use of spring-loaded table and segmental low-velocity mobilization permitted for acute exacerbation of back pain B.Spinal manipulation (n=100): 12 sessions over 6 weeks with 6 minimal massage sessions C. Spinal manipulation (n=100): 18 sessions over 6 weeks D: Attention control (minimal massage) (n=100): 18 treatment visits, 3 times per week for 6 weeks; 5 minutes of light massage All treatment sessions consisted of 5 minutes of hot pack, 5 minutes of SMT and 5 minutes of very low-dose (subtherapeutic) pulsed ultrasound (20% duty cycle with 0.5 watts/cm2)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Haas 2014	A vs. B vs. C vs. D Mean age (years): 41 vs. 42 vs. 41 vs. 41 Female: 49% vs. 49% vs. 52% vs. 49% Nonwhite or Hispanic: 18% vs. 11% vs. 16% vs. 14% Pain (0–100 VAS) mean (SD): 51.0 (18.2) vs. 51.6 (17.5) vs. 51.5 (16.8) vs. 52.2 (16.3) Modified Von Korff functional disability (0–100) mean (SD): 44.8 (24.0) vs.46.1 (23.4) vs.45.2 (21.8) vs. 45.2 (21.8) SF-12 physical health component mean (SD): 43.8 (8.9) vs. 44.3 (8.4) vs.42.3 (8.8) vs. 43.0 (9.5) SF-12 mental health component mean (SD): 48.6 (10.5) vs. 47.6 (11.2) vs. 49.4 (9.6) vs. 50.2 (10.5) EuroQoL (0–100 Visual Analog Scale) mean (SD): 48.6 (10.5) vs. 47.6 (11.2) vs. 49.4 (9.6) vs. 50.2 (10.5) Nonprescription medication use (times in last 4 weeks): 8.9 (10.8) vs. 9.5 (10.0) vs. 7.6 (9.4) vs. 7.6 (10.0)	Von Korff pain intensity (0–100) Von Korff functional disability (0–100, lower scores=less disability) SF-12 physical health component (norm-based mean=50) SF-12 mental health component (norm-based mean=50) EuroQol Health State (0–100 VAS, higher score is more favorable)	4 months and 10.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Haas 2014	A vs. B vs. C vs. D, mean (SD) <u>Baseline</u> Von Korff pain intensity (0–100): 51.0 (18.2) vs. 51.6 (17.5) vs. 51.5 (16.8) vs. 52.2 (16.3) Von Korff functional disability (0–100): 44.8 (24.0) vs.46.1 (23.4) vs.45.2 (21.8) vs. 45.2 (21.8) SF-12 physical component summary (norm-based mean=50): 43.8 (8.9) vs. 44.3 (8.4) vs.42.3 (8.8) vs. 43.0 (9.5) SF-12 mental health component mean (norm-based mean=50): 48.6 (10.5) vs. 47.6 (11.2) vs. 49.4 (9.6) vs. 50.2 (10.5) EuroQoL (0–100): 48.6 (10.5) vs. 47.6 (11.2) vs. 49.4 (9.6) vs. 50.2 (10.5) <u>4 months</u> Von Korff pain intensity (0-100): 32.5 (19.8) vs. 33.7 (20.5) vs. 32.1 (20.5) vs. 34.9 (20.6), adjusted difference -1.7 (95% CI -6.9 to 3.4) for A vs. D, -0.8 (95% CI -6.0 to 4.4) for B vs. D, and -2.4 (95% CI -7.6 to 2.9) for C vs. D Von Korff functional disability (0-100): 25.6 (21.7) vs. 24.0 (20.4) vs. 24.1 (20.3) vs. 27.1 (25.2), adjusted difference -1.4 (95% CI -7.2 to 4.5) for A vs. D, -3.4 (95% CI -9.3 to 2.4) for B vs. D, and -2.9 (95% CI -8.8 to 2.9) for C vs. D SF-12 physical component summary (norm-based mean=50): 50.5 (10.1) vs. 51.4 (9.1) vs. 50.9 (9.4) vs. 50.0 (11.1), adjusted difference 0.0 (95% CI -2.4 to 2.3) for A vs. D, -0.8 (95% CI -3.2 to 1.6) for B vs. C, and -1.3 (95% CI -3.6 to 1.1) for C vs. D SF-12 mental component summary (norm-based mean=50): 52.8 (10.2) vs. 50.8 (11.8) vs. 51.3 (11.2) vs. 51.8 (10.9), adjusted difference -2.1 (95% CI -4.2 to 0.0) for A vs. D, -0.7 (95% CI -2.8 to 1.3) for B vs. D, and -0.1 (95% CI -2.2 to 2.1) for C vs. D EuroQoL (0-100): 77.8 (15.5) vs. 77.0 (15.4) vs. 74.5 (16.7) vs. 73.9 (17.5), difference -2.9 (95% CI -6.9 to 1.0) for A vs. D, -1.4 (95% CI -5.5 to 2.6) for B vs. D, and -1.5 (95% CI -5.8 to 2.7) for C vs. D Von Korff pain intensity improved >=50%:40.4% vs. 40.2% vs. 42.0% vs. 36.8%, adjusted difference 3.7% (95% CI -10.0 to 17.4%) for A vs. D, 3.2% (95% CI -10.5 to 16.9%) for B vs. D, and 4.9% (95% CI -8.7 to 18.4%) for C vs. D Von Korff functional disability improved >=50%: 51.5% vs. 59.8% vs. 54.0% vs. 49.5%, adjusted difference 2.5% (95% CI -11.5 to 16.5%) for A vs. D, 10.4% (95% CI -3.4 to 24.3%) for B vs. D, and 4.8% (95% CI -9.1 to 18.6%) for C vs. D 10.5 months (see row below)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Haas 2014	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Haas 2014	NR	No SAEs; 4 participants had increased back pain. One withdrew due to exacerbation from lifting a child.

Author, Year	Funding Source	Quality	Comments
Haas 2014	National Center for Complementary and Alternative Medicine (NCCAM) National Institutes of Health (U01 AT001908)	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Haas 2014 (continued)			
Harkapaa 1989	Finland Number of centers In patient and outpatient	Patients with physically strenuous work and chronic or recurrent LBP for >2 years and LBP caused sick leave Exclusion criteria not reported	Randomized: 476 Treated: 459 Analyzed: 459 Attrition: 4% (20/476)
Hegedus 2009	Hungary 1 center	Inclusion: Between the ages of 30 and 65. Knee pain >40mm on VAS and mild to moderate knee OA confirmed by radiographs Exclusion: Considerable varus or valgus deformity, ankylosis, intense synovitis, gonitis, Kellgren-Lawrence stage 4, and contraindications to laser therapy.	Randomized: 35 Treated: 27 Analyzed: 27 Attrition: 8/35=23%

Author, Year	Intervention, Comparator
Haas 2014 (continued)	
Harkapaa 1989	A.Inpatient multidisciplinary rehabilitation (n=156): Groups sessions, 4 Swedish back school sessions, 15 sessions of back exercises, 9 sessions of relaxation exercises, heat/electrotherapy, discussion groups on coping, discussion on back care, stretching, massage and strengthening and physical exercises for 3 weeks; total hours not reported B.Outpatient multidisciplinary rehabilitation (n=150): 15 session back treatment same as above with program conducted at work or local health center, twice weekly for 2 months; total hours not reported C. Usual care (n=153): Exam and questionnaire plus oral instructions for ergonomics and back exercise
Hegedus 2009	A.Low Level Laser Therapy (n=18) 50mW, continuous wave laser. Treatment provided over the femoral and tibial condyles. Total does of 48 J/cm2 per session. Twice a week for four weeks. B.Placebo (n=17) Placebo probe used twice a week for four weeks.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Haas 2014 (continued)			
Harkapaa 1989	A vs. B vs. C Age (mean): 45 vs. 45 vs. 45 years Female: 37% vs. 39% vs. 35% Race: NR Continuous LBP during the past year: 42% vs. 39% vs. 41% Use of analgesics: 62% vs. 65% vs. 67%	Pain Index (0-400, sum of 4 0-100 VAS scales) LBP Disability Index (0-45, higher score=more disabled)	1 month
Hegedus 2009	A and B (for n=27 completers only) Age: 49 Female: 81% A vs B Mean Pain VAS (SD): 5.75 vs 5.62	Pain (VAS 0-10; higher score=greater pain)	2 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Haas 2014 (continued)	10.5 months (from row above) Von Korff pain intensity (0-100): 30.7 (22.4) vs. 31.9 (22.5) vs. 28.7 (20.5) vs. 36.5 (21.8), adjusted difference -5.4 (95% CI -11.1 to 0.4) for A vs. D, -4.6 (95% CI -10.3 to 1.2) for B vs. D, and -7.6 (95% CI -13.2 to -2.0) for C vs. D Von Korff functional disability (0-100): 22.6 (22.4) vs. 22.4 (21.2) vs 19.1 (18.7) vs. 28.0 (23.7), adjusted difference -5.2 (95% CI -10.9 to 0.5) for A vs. D, -5.9 (95% CI -11.8 to -0.1) for B vs. D, and -8.8 (95% CI -14.4 to -3.3) for C vs. D SF-12 physical component summary (norm-based mean=50): 50.8 (11.0) vs. 52.6 (10.3) vs. 52.5 (8.5) vs. 50.7 (12.0), adjusted difference -0.3 (95% CI -2.1 to 2.7) for A vs. D, -1.4 (95% CI -4.0 to 1.2) for B vs. D, and -2.2 (95% CI -4.5 to 0.2) for C vs. D SF-12 mental component summary (norm-based mean=50): 50.4 (11.5) vs. 50.6 (12.7) vs. 50.4 (11.7) vs. 51.3 (12.0), adjusted difference -0.2 (95% CI -2.7 to 2.3) for A vs. D, -1.1 (95% CI -3.7 to 1.6) for B vs. D, and 0.3 (95% CI -2.3 to 2.9) for C vs. D EuroQoL (0-100): 77.1 (17.0) vs. 77.3 (15.3) vs. 77.2 (14.9) vs. 74.8 (17.0), adjusted difference -1.3 (95% CI -5.4 to 2.7) for A vs. D, -0.9 (95% CI -4.9 to 3.1) for B vs. D, and -3.3 (95% CI -7.2 to 0.5) for C vs. D Von Korff pain intensity improved >=50%: 47.5% vs. 41.2% vs. 48.0% vs. 37.9%, adjusted difference 10.2% (95% CI -3.5 to 23.9%) for A vs. D, 3.9% (95% CI -9.8 to 17.6%) for B vs. D, and 10.6% (95% CI -3.2 to 24.4%) for C vs. D Von Korff functional disability improved >=50%: 57.6% vs. 57.7% vs. 62.0% vs. 58.9%, adjusted difference -1.1% (95% CI -14.8 to 12.6%) for A vs. D, -1.4% (95% CI -15.4 to 12.6%) for B vs. D, and 2.7% (95% CI -11.0 to 16.5%) for C vs. D Differences adjusted for baseline covariates and using imputed data
Harkapaa 1989	A vs. B <u>Baseline</u> Pain Index (0-400): 184.9 (76.9) vs. 178.6 (81.8) vs. 175.8 (87.3) LBP Disability Index (0-45): 16.7 (7.9) vs. 17.6 (7.4) vs. 16.7 (8.4) <u>1 month</u> (estimated from graph, SD not reported) Pain Index (0-400): 127 vs. 145 vs. 160, p<0.001 for A vs. C and p<0.04 for B vs. C LBP Disability Index (0-45): 13.8 vs. 14.7 vs. 17.3, p<0.004 for A vs. C and p<0.01 for B vs. C
Hegedus 2009	A vs B Mean Pain VAS: 1.18 vs 4.12, MD= -2.94* *standard deviation not reported

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Haas 2014 (continued)	
Harkapaa 1989	
Hegedus 2009	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Haas 2014 (continued)		
Harkapaa 1989		NR
Hegedus 2009	NR	NR

Author, Year	Funding Source	Quality	Comments
Haas 2014 (continued)			
Harkapaa 1989	RAY of Finland and Social Insurance Institution in Finland	Poor	
Hegedus 2009	NR	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Helminen 2015	Finland, single site, primary care	Inclusion Criteria: Patients aged between 35 and 75 years with clinical symptoms and radiographic grading (Kellgren–Lawrence 2–4) of knee osteoarthritis were eligible. Exclusion Criteria: Exclusion for severe psychiatric or psychological disorders that had led to hospitalization or an inability to work, previous or planned lower extremity joint surgery, and other back or lower limb pain symptoms that had been more aggravating than the knee pain.	Randomized: 111 Treated: 111 Analyzed: 111 (ITT) 3 month: 90.9% (101/111) 12 months: 88.2% (98/111) Attrition: 11.7% (13/111)

Author, Year	Intervention, Comparator
Helminen 2015	A.Cognitive-Behavioral Training (CBT) (n=55) Patients undertook group (7-13 people each) sessions of CBT led by trained psychologist and physiotherapist. Practices included knowledge building, problem solving, skills training and homework assignments. In addition all patients were instructed to continue regular care. No. of Treatments: weekly sessions for 6 weeks (6 total) Length of Treatment: 2 hours/session B.Usual Care (n=56) Both the intervention and control group continued usual care from their general practitioners.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Helminen 2015	A vs B Age: 64.5 vs. 63 Female: 71% vs. 68% BMI: Race: NR Mean Duration of Chronicity: 6.6 (4.5) vs. 8.9 (8.7) WOMAC Pain: 57.6 (53.9−61.3) vs. 56.4 (52.9−60.0) WOMAC Stiffness: 63.1 (57.2−69.0) vs. 62.0 (56.6−67.4) WOMAC Function: 53.0 (48.1−57.9) vs. 48.4 (43.1−53.7) NPRS avg. last week: 6.6 (6.1−7.0) vs. 6.4 (5.9−6.8) NPRS worst last week: 8.0 (7.6−8.4) vs. 7.5 (7.1−7.9) NPRS average 3 months: 6.8 (6.3−7.3) vs. 6.6 (6.1−7.0) NPRS worst 3 months: 8.2 (7.9−8.6) vs. 8.0 (7.6−8.3) HRQoL, 15D: 0.82 (0.80−0.84) vs. 0.83 (0.80−0.86) RAND-36 Physical Functioning: 44.4 (38.5−50.3) vs. 49.8 (44.2−55.5) RAND-36 Role-Physical: 35.2 (24.9−45.5) vs. 38.4 (27.7−49.2) RAND-36 Bodily Pain: 51.0 (46.4−55.7) vs. 53.6 (48.5−58.6) RAND-36 General Health: 50.8 (46.3−55.3) vs. 56.7 (51.4−62.0) RAND-36 Vitality: 62.2 (57.4−67.0) vs. 67.1 (62.3−71.8) RAND-36 Social Functioning: 73.4 (66.4−80.4) vs. 82.5 (76.5−88.5) RAND-36 Role-Emotional: 68.5 (57.2−79.8) vs. 75.8 (65.9−85.6) RAND-36 Emotional Well-Being: 78.1 (74.0−82.3) vs. 81.4 (77.8−85.0) RAND-36 Health Change: 40.9 (35.7−46.2) vs. 45.0 (38.3−51.7) Beck Depression Inventory (0−63): 6.1 (4.8−7.4) vs. 5.8 (4.5−7.1) Beck Anxiety Inventory (0−63): 9.0 (7.2−10.8) vs. 7.1 (5.7−8.5)	WOMAC Physical Function (0-100; higher score=worse function) WOMAC Stiffness (r0-100; higher score=worse stiffness) WOMAC Pain 0-100; higher score=greater pain) Numeric Pain Rating Scales (NPRS, range 0-10; higher score=greater pain) Beck Depression Inventory (BDI, range 0-63; higher score=worse depression) Beck Anxiety Inventory (BAI, range 0-63; higher score=worse anxiety) Health Related Quality of Life 15D (HRQoL, range: 0-1) Quality of Life RAND-36 (each subscale ranged 0-100, higher scores indicate better health)	3 and12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Helminen 2015	A vs. B Post-Treatment Average (3-12 months) WOMAC Function: 36.5 (30.6−42.3) vs. 36.7 (31.0−42.4); MD −0.3 (95%CI −8.3 to 7.8) WOMAC Stiffness: 46.2 (39.6−52.9) vs. 49.0 (43.3−54.7); MD −2.7 (95% −11.4 to 5.9) WOMAC Pain: 35.6 (30.0−41.1) vs. 39.5 (33.7−45.2); MD −3.9 (95% −11.8 to 4.0) NPRS avg. last week: 5.0 (4.3−5.6) vs. 4.9 (4.3−5.5); MD 0.02 (95%CI −0.89 to 0.93) NPRS worst last week: 6.1 (5.4−6.7) vs. 5.9 (5.3−6.5); MD 0.1 (95%CI −0.8 to 1.1) NPRS average 3 months: 5.2 (4.6−5.8) vs. 5.4 (4.8−6.0); MD −0.2 (95%CI −1.0 to 0.6) NPRS worst 3 months: 6.4 (5.9−7.0) vs. 6.6 (6.0−7.1); MD −0.1 (95%CI −0.9 to 0.7) Beck Depression Inventory (0−63): 5.8 (4.7−6.8) vs. 5.9 (4.1−7.7); MD −0.1 (95%CI −2.2 to 2.0) Beck Anxiety Inventory (0−63): 8.0 (6.5−9.5) vs. 7.1 (5.4−8.8); MD 0.9 (95%CI −1.3 to 3.1) HRQoL, 15D: 0.82 (0.80−0.85) vs. 0.85 (0.83−0.88); MD −0.03 (95%CI −0.06 to 0.00) RAND-36 Physical Functioning: 48.0 (41.5−54.6) vs. 49.4 (43.6−55.2); MD −1.4 (95%CI −10.2 to 7.3) RAND-36 Role-Physical: 44.4 (34.5−54.4) vs. 44.5 (33.9−55.1); MD −0.09 (95%CI −14.4 to 14.3) RAND-36 Bodily Pain: 57.3 (51.5−63.0) vs. 57.4 (52.0−62.8); MD −0.1 (95%CI −8.0 to 7.7) RAND-36 General Health: 53.1 (48.6−57.7) vs. 58.2 (52.2−64.1); MD −5.0 (95%CI −12.3 to 2.3) RAND-36 Vitality: 62.7 (57.2−68.2) vs. 67.5 (61.8−73.3); MD −4.8 (95%CI −12.6 to 3.1) RAND-36 Social Functioning: 75.0 (68.2−81.8) vs. 82.8 (77.6−88.0); MD −7.8 (95%CI −16.4 to 0.81) RAND-36 Role-Emotional: 67.9 (58.1−77.8) vs. 74.7 (65.3−84.0); MD −6.7 (95%CI −20.2 to 6.8) RAND-36 Emotional Well-Being: 75.3 (71.1−79.5) vs. 78.5 (73.7−83.3); MD −3.2 (95%CI −9.5 to 3.1) RAND-36 Health Change: 46.6 (40.6−52.6) vs. 47.4 (41.5−53.3); MD −0.8 (95%CI −9.2 to 7.6)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Helminen 2015	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Helminen 2015	NR	"No adverse events were recorded in either of the study groups."

Author, Year	Funding Source	Quality	Comments
Helminen 2015	This study has been supported by an EVO and a VTR grant from Kuopio University Hospital	Fair	Values reported for follow up are an aggregated "post-treatment average" reflecting all outcome values over 12 month period with no specific values for 3- or 12-month follow up sessions.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Hinman 2014	Australia, community recruitment, ? 1 center	Inclusion Criteria: 50 years or older knee pain > 3 months knee pain most days with average severity of 4 or more on 0-10 NRS morning stiffness <30 minutes Exclusion: in online table (need to access)	Randomized: 282 Treated: 248 Analyzed: 282 (analyzed all regardless of follow up) Attrition: 24.5% (69/282)

Author, Year	Intervention, Comparator
Hinman 2014	A.Needle acupuncture (n=70): combination of Western and traditional Chinese acupuncture; standardized set of acupoints; acupuncturists selected from points around the knee as well as distal points (other points could be used at acupuncturists discretion); initial treatment permitted a maximum of 6 points (4 on the study limb and 2 additional points chosen per protocol); in other treatments, points were added and varied as clinically indicated. Needles were left in while patient rested. Sessions were 20 minutes in duration, 1-2x/week for 12 weeks, with 8 to 12 sessions in total B.laser acupuncture (n=71): combination of Western and traditional Chinese acupuncture; delivered to selected points using standard Class 3B laser devices (measured output 10mW and energy output 0.2 J/point), with a red nonlaser light at the probe tip that lit up in active and sham modes C.Control/no treatment (n=71): did not receive acupuncture; patients randomized to this group continued in an observational study, unware they were in an acupuncture trial D.sham laser acupuncture (n=70): same as true laser but no laser was emitted, only red nonlaser light at the probe tip lit up. For all acupuncture and sham groups, patients were exposed to 20 minute treatments 1-2/week for 12 weeks, with 8 to 12 sessions in total

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Hinman 2014	A vs B vs. C vs. D Age: 64 vs. 63 vs. 63 vs. 64 years Female: 46% vs. 39% vs. 56% vs. 56% Race: NR Duration of symptoms ≥ 10 years: 41% vs. 38% vs. 27% vs. 50% Unilateral symptoms: 36% vs. 34% vs. 49% vs. 37% Opioid use: 1% vs. 3% vs. 1% vs. 1% Previous acupuncture for knee pain: 7% vs. 13% vs. 7% vs. 3% Previous injection therapy for knee pain: 11% vs. 8% vs. 8% vs. 17% Previous surgery for knee pain: 37% vs. 34% vs. 32% vs. 39% WOMAC function: 31.3 (11.8) vs. 27.0(11.3) vs. 26.1 (12.4) vs. 27.5 (12.4) NRS activity restriction: 5.0 (2.5) vs. 4.3 (2.3) vs. 4.1 (2.5) vs. 4.5 (2.6) WOMAC pain: 9.0 (3.3) vs. 8.3 (3.1) vs. 7.8 (3.4) vs. 8.6 (3.5) NRS average pain overall: 5.3 (1.9) vs. 4.9 (1.9) vs. 5.1 (2.1) vs. 5.0 (2.1) NRS pain on walking: 5.5 (2.0) vs. 4.8 (2.0) vs. 4.8 (2.1) vs. 5.2 (2.2) NRS pain on standing: 4.6 (2.2) vs. 3.8 (2.1) vs. 4.1 (2.4) vs. 4.3 (2.3) AQoL-6D: 0.72 (0.15) vs. 0.70 (0.16) vs. 0.77 (0.16) vs. 0.73 (0.15) SF-12 PCS: 36.6 (9.0) vs. 37.6 (10.3) vs. 39.2 (9.0) vs. 37.9 (9.6) SF-12 MCS: 51.3 (11.4) vs. 52.5 (11.1) vs. 55.6 (10.2) vs. 52.4 (19.5)	WOMAC function subscale (0-68; higher score=worse function; MCID = 6 nonnormalized units); WOMAC pain subscale (0-20; higher score=worse pain; MCID ≥12% improvement from baseline); Average knee pain over previous week (NRS, 0-10; higher score=greater pain; MCID = 1.8 points); Average knee pain with standing and walking (NRS, 0-10; higher score=greater pain; MCID = 1.8 points) Average daily activity restriction over previous week (NRS, 0-10; higher score=more restriction) Assessment of Quality of Life instrument version 2 (AQol-6D; scale −0.04 to 1.00, higher scores= better quality of life; MCID = 0.06) Physical and Mental Component Summary scores (PSC and MSC) of the 12-item Short Form Health Survey (SF-12, scale 0-100, higher scores=better status; MCID ≥12% improvement from baseline).	9 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Hinman 2014	A vs. C, 9 months WOMAC Function: 22.4 (14.1) vs. 23.6 (13.4); adjusted MD -3.7 (95% CI -8.2, 0.8), p=0.11 Activity restriction, NRS: 3.4 (2.9) vs. 4.1 (2.7); **adjusted MD -1.1 (95% CI -2.1, -0.2), p=0.02** WOMAC Pain: 6.7 (4.0) vs. 7.4 (4.1); adjusted MD -1.4 (95% CI -2.7, 0.0), p=0.05 Overall Pain, NRS: 4.0 (2.7) vs. 4.6 (2.6); adjusted MD -0.7 (95% CI -1.6, 0.2), p=0.14 Pain on walking, NRS: 4.1 (2.9) vs. 4.4 (2.6); adjusted MD -0.6 (95% CI -1.5, 0.4), p=0.27 Pain on standing, NRS: 3.7 (2.9) vs. 4.0 (2.6); adjusted MD -0.5 (95% CI -1.4, 0.5), p=0.35 AQoL-6D: 0.74 (0.17) vs. 0.77 (0.16); adjusted MD: -0.01 (95% CI -0.07, 0.05), p=0.67 SF-12 PCS: 41.7 (10.8) vs. 38.9 (11.2); adjusted MD 2.3 (95% CI -1.7, 6.3), p=0.26 SF-12 MCS: 51.1 (11.0) vs. 54.4 (10.2); adjusted MD -0.9 (95% CI -5.2, 3.4), p=0.67 Opioid use: 0% (0/70) vs. 1% (1/71) B vs. C, 9 months WOMAC Function: 22.6 (13.1) vs. 23.6 (13.4); adjusted MD −1.7(95%CI −5.1 to 1.8), p=0.340 Activity restriction, NRS: 3.7 (2.8) vs. 4.1 (2.7); adjusted MD −0.8(95%CI −1.7 to0.1), p=0.090 WOMAC Pain: 7.1 (4.1) vs. 7.4 (4.1); adjusted MD −1.0(95%CI −2.1 to 0.2), p=0.100 Overall Pain, NRS: 4.0 (2.5) vs. 4.6 (2.6); adjusted MD −0.8(95%CI −1.5 to −0.1), p=0.030 Pain on walking, NRS: 4.1 (2.6) vs. 4.4 (2.6); adjusted MD −0.6(95%CI −1.4 to 0.2), p=0.160 Pain on standing, NRS: 3.8 (2.6) vs. 4.0 (2.6); adjusted MD −0.4(95%CI −1.2 to 0.4), p=0.310 AQoL-6D: 0.73 (0.17) vs. 0.77 (0.16); adjusted MD 0.00(95%CI −0.05 to 0.04), p=0.870 SF-12 PCS: 38.8 (10.2) vs. 38.9 (11.2); adjusted MD 0.8(95%CI −2.4 to 4.0), p=0.620 SF-12 MCS: 52.1 (9.8) vs. 54.4 (10.2); adjusted MD −1.7(95%CI −5.0 to 1.6), p=0.320 Opioid use: 2% (1/71) vs. 1% (1/71) B vs. D, 9 months WOMAC Function: 22.6 (13.1) vs. 21.6 (13.6); adjusted MD 1.1 (95% CI -4.8, 7.0), p=0.71 Activity restriction, NRS: 3.7 (2.8) vs. 3.9 (2.6); adjusted MD -0.1 (95% CI -01.1, 1.0), p=0.93 WOMAC Pain: 7.1 (4.1) vs. 6.9 (4.0); adjusted MD 0.0 (95% CI -1.9, 1.9), p=0.96 Overall Pain, NRS: 4.0 (2.5) vs. 3.9 (2.5); adjusted MD 0.0 (95% CI -0.9, 1.0), p=0.94 Pain on walking, NRS: 4.1 (2.6) vs. 4.2 (2.6); adjusted MD 0.0 (95% CI -1.0, 1.1), p=0.94 Pain on standing, NRS: 3.8 (2.6) vs. 3.5 (2.9); adjusted MD 0.5 (95% CI -0.7, 1.6), p=0.42 AQoL-6D: 0.73 (0.17) vs. 0.74 (0.16); adjusted MD: 0.01 (95% CI -0.05, 0.08), p=0.70 SF-12 PCS: 38.8 (10.2) vs. 38.2 (9.9); adjusted MD 0.4 (95% CI -3.8, 4.5), p=0.86 SF-12 MCS: 52.1 (9.8) vs. 52.8 (9.1); adjusted MD -0.6 (95% CI -5.4, 4.2), p=0.81 Opioid use: 2% (1/71) vs. 0% (0/70)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Hinman 2014	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals

Hinman 2014	NR	Adverse events reported for group A only ("few, mild and transient"):
		increased knee pain: 10% (n=5/57);
		pain in other areas: 2% (n=1/57);
		tingling: 2% (n=1/57);
		tiredness: 2% (n=1/57);
		swelling: 2% (n=1/57);
		sensitive skin: 0%;
		nausea or dizziness: 0%
		
		B vs. D ("few, mild and transient"):
		increased knee pain: 12% (7/59) vs. 3% (2/61); RR 3.6 (95% CI 0.8, 16.7), p=0.08;
		pain in other areas: 2% (1/59) vs. 2% (1/61)
		tingling: 2% (1/59) vs. 2% (1/61)
		nausea or dizziness: 2% (1/59) vs. 2% (1/61)
		tiredness: 0% (0/59) vs. 2% (1/61)
		sensitive skin: 2% (1/59) vs. 0% (0/61)
		swelling: 0% (0/59) vs. 0% (0/61)

Author, Year	Funding Source	Quality	Comments
Hinman 2014	Australian National Health and Medical Research Council	Good - vs. sham Fair - vs. no treatment	Results are for the ITT analysis with multiple imputation for missing data; adjusted for baseline value of the measure Adverse events were reported in eTable 3 of supplemental data; Also reported at 9 months in eTable 3: medication use (defined as medications purchased over previous 4 weeks for knee pain) to include analgesics, NSAIDs, COX-2 inhibitors, Glucosamine, and fish oil; use of cointerventions to include physical therapy, surgery, acupuncture, exercise, and hydrotherapy

Author, Year	Country Number of centers and setting	Inclusion/Exclusion Criteria	Number randomized, analyzed Attrition
Ho 2017	China 1 center Hospital	18-65 years old, no history of abdominal acupuncture, and VAS score ≥3 for neck pain casued by one or more of the following: neck pain, stiffness, or tenderness, pain around the neck with radiation towards the occiput or shoulder or ROM limited by neck pain, or neck pain with denegerative joint disease or cervical sponylosis or both. Exclude: Illness due to visceral pain in the neck, serious spinal disorders, previous neck surgery or plan to get neck surgery during study, chronic diseases that could interfere with abdominal acupuncture, cancer diagnosis, chief pain complaint other than neck pain, unsafe conditions for abdominal acupuncture, abdominal scars interfering with acupoints, severe psychiatric or psychological disorders, acupuncture treatment within 1 month to study start with conflicting or ongoing co-interventions, participation in other clinical trials during study, pending neck-related litigation or disability claims, inability to answer questionnaires and non-responsiveness towards the assesor, pregnancy and breast feeding	Randomized: 154 Treated: 154 Analyzed: 154 Attrition: 0% (0/154)

Author, Year	Intervention, Comparator
Ho 2017	A. Acupuncture (n=77): 30 sessions of abdominal acupuncture 3 times a week for 2 weeks. The acupuncture points CV12, CV4, KI17, and ST24 were needled for 30 minutes with a infrared therapeutic lamp placed 30 cm above the naval B. Sham acupuncture (n=77): : 30 sessions of sham abdominal acupuncture 3 times a week for 2 weeks. Blunt sham needles were non-penetratively administered at non-acupuncture points.

Author, Year	Study participants	Outcome measures	Duration of followup
Ho 2017	A vs B Age: 46 vs 45 Female: 81% vs 83% Pain duration (years): 6.0 vs 6.0 Cervical radiography findings: Normal: 21% vs 33% Cervical lordosis abnormality: 51% vs 51% Narrowing of disc space: 52% vs 49% Other degenerative changes: 57% vs 62% Use of pain-relief medications: 15% vs 13% Previous acupuncture use: 42% vs 44% NPQ, mean (SD): 41.3 (13.6) vs 41.0 (14.7) Pain VAS, mean (SD): 6.4 (1.5) vs 6.1 (1.8) SF-36 physical functioning, mean (95% CI): 47.4 (45.9 to 48.9) vs 49.4 (47.9 to 50.8) SF-36 role-physical, mean (95% CI): 42.1 (40.5 to 43.7) vs 44.2 (42.5 to 45.9) SF-36 bodily pain, mean (95% CI): 35.1 (33.8 to 36.4) vs 36.6 (35.3 to 37.8) SF-36 general health, mean (95% CI): 36.7 (34.8 to 38.5) vs 38.3 (36.3 to 40.3) SF-36 vitality, mean (95% CI): 43.2 (41.2 to 45.1) vs 43.3 (41.1 to 45.5) SF-36 social functioning, mean (95% CI): 42.2 (40.2 to 44.2) vs 45.0 (43.2 to 46.8) SF-36 role-emotional, mean (95% CI): 41.7 (39.3 to 44.0) vs 44.4 (42.2 to 46.7) SF-36 mental health, mean (95% CI): 43.9 (42.1 to 45.7) vs 44.5 (42.1 to 46.9) SF-36 PCS, mean (95% CI): 40.9 (39.6 to 42.2) vs 42.7 (41.4 to 43.9) SF-36 MCS, mean (95% CI): 42.9 (40.9 to 45.0) vs 44.3 (42.0 to 46.6)	NPQ (0 to 100, higher score=higher disability); pain VAS (0-10, higher score=higher pain); SF-36 subscales (0-100, higher score=higher quality of life)	1 and 3 months

Author, Year	Results - Subquestion a (vs. Sham, no treatment, waitlist, attention control)
Ho 2017	A vs B <u>1 month</u> NPQ, mean Δ (95% CI): -11.9 (-14.6 to -9.2) vs -3.3 (-5.5 to -1.0), MD -8.7 (95% CI -12.1 to -5.2) p<0.001 Pain VAS, mean Δ (95% CI): -2.4 (-2.8 to -1.9) vs -0.6 (-0.9 to -0.2), MD -1.8 (95% CI -2.4 to -1.2) p<0.001 SF-36 physical functioning, mean Δ (95% CI): 2.3 (1.3 to 3.3) vs -0.1 (-1.4 to 1.1), MD 2.5 (95% CI 0.9 to 4.0), p=0.007 SF-36 role-physical, mean Δ (95% CI):3.3 (1.9 to 4.7) vs 0.3 (-1.5 to 2.1), MD 3.0 (95% CI 0.8 to 5.3) p=0.024 SF-36 bodily pain, mean Δ (95% CI): 5.9 (4.4 to 7.3) vs 3.0 (1.2 to 4.8), MD 2.9 (95% CI 0.6 to 5.1), p=0.041 SF-36 general health, mean Δ (95% CI): 3.5 (2.2 to 4.8) vs 0.2 (-1.2 to 1.7), MD 3.3 (95% CI 1.3 to 5.2) p=0.004 SF-36 vitality, mean Δ (95% CI): 3.6 (2.0 to 5.2) vs 1.9 (0.1 to 3.7), MD 1.7 (95% CI -0.7 to 4.1) p NR SF-36 social functioning, mean Δ (95% CI): 3.5 (1.9 to 5.0) vs 0.4 (-1.2 to 2.0), MD 3.1 (95% CI 0.8 to 5.3) p=0.022 SF-36 role-emotional, mean Δ (95% CI): 2.0 (0.2 to 3.8) vs -1.2 (-3.3 to 1.0), MD 3.2 (95% CI 0.4 to 5.9) p NR SF-36 mental health, mean Δ (95% CI): 1.9 (0.4 to 3.4) vs 0.0 (-1.8 to 1.8), MD 1.9 (95% CI -0.5 to 4.2) p NR SF-36 PCS, mean Δ (95% CI): 4.1 (3.0 to 5.3) vs 1.3 (0.1 to 2.5), MD 2.8 (95% CI 1.2 to 4.5), p=0.003 SF-36 MCS, mean Δ (95% CI): 2.0 (0.5 to 3.5) vs -0.3 (-2.0 to 1.4), MD 2.3 (95% CI -0.0 to 4.5) p NR <u>3 months</u> NPQ, mean (95% CI): 29.4 (26.2 to 32.6) vs NR Pain VAS, mean (95% CI): 4.2 (3.7 to 4.8) vs NR SF-36 physical functioning, mean (95% CI): 50.1 (48.7 to 51.5) vs NR SF-36 role-physical, mean (95% CI): 44.7 (43.0 to 46.3) vs NR SF-36 bodily pain, mean (95% CI): 41.2 (39.6 to 42.9) vs NR SF-36 general health, mean (95% CI): 40.8 (38.7 to 42.8) vs NR SF-36 vitality, mean (95% CI): 45.9 (43.7 to 48.2) vs NR SF-36 social functioning, mean (95% CI): 46.7 (44.9 to 48.4) vs NR SF-36 role-emotional, mean (95% CI): 44.1 (42.1 to 46.0) vs NR SF-36 mental health, mean (95% CI): 44.5 (42.6 to 46.4) vs NR SF-36 PCS, mean (95% CI): 45.4 (43.9 to 46.8) vs NR SF-36 MCS, mean (95% CI): 44.5 (42.5 to 46.5) vs NR

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Ho 2017	NR

Author, Year	**Results - Subquestion c** (vs. Exercise)	**Adverse events including withdrawls**
Ho 2017	NR	A vs B Transient bruising: 11/77 (14.2%) vs 0/77 (0%)

Author, Year	Funding source	Quality	Comments
Ho 2017	The developmental reserve of Pok Oi Hospital - The Chinese University of Hong Kong Chinese Medicine Centre for Training and Research (Shatin)	Fair	Type of pain-relief medication being taken at baseline was not specified

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Hoeksma 2004	The Netherlands 1 center Outpatient	Diagnosis of hip OA fulfilling ACR criteria Exclude: Bilateral symptoms, fear of manipulative surgery, age <60 or >85 years, lower back pain, severe cardiopulmonary disease	Randomized: 109
Holroyd 1991	United States, single site, clinic	Inclusion Criteria: Diagnosis of CTTH, >=3 days of headache/week, suffered from headaches for at least 1 year Exclusion Criteria: Prodromal symptoms commonly associated with vascular headache, frequent unilateral pulsing or throbbing pain, typical sudden or abrupt headache onset, indication of sinus headaches, headaches associated with a disease state or head trauma, or aggravated by analgesic abuse, free from prophylactic headache medication for at least 3 months before entering the study.	Treated: 103

Author, Year	Intervention, Comparator
Hoeksma 2004	A.Manual therapy (n=56): 2 sessions per week for 5 weeks with 9 sessions in total. Sessions consisted of stretching followed by traction manipulation in each limited position (high velocity thrust technique). B.Exercise therapy (n=53): 2 sessions per week for 5 weeks with 9 sessions in total. Sessions implemented exercises for muscle functions, muscle length, joint mobility, pain relief, and walking ability and were tailored to the specific needs of the patient. Instructions for home exercises were given.
Holroyd 1991	A.Cognitive Behavioral Therapy (n=19) Primarily home-based treatment protocol No. of Treatments: Total of 3 sessions over 8 week treatment period. Length of Treatment: 1 hour B.Amitriptyline therapy (n=17) Individualized dosage at 25, 50, or 75 mg/day

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Hoeksma 2004	A vs B Age: 72 vs 71 Females: 68% vs 72% Symptom duration: 1 month to 1 year: 39% vs 28% 1 year to 2 years: 21% vs 25% 2 years to 5 years: 16% vs 28% 5 years to 10 years: 18% vs 15% > 10 years: 5% vs 4% Radiographic deterioration: 0 (no OA): 9% vs 8% 1 (mild OA): 13% vs 11% 2 (moderate OA): 34% vs 43% 3 (severe OA): 45% vs 38% HHS: 54 (15) vs 53 (14) SF-36 physical function: 42.1 (23) vs 41.4 (21) SF-36 role physical function: 27.0 (38) vs 24.7 (36) SF-36 bodily pain: 41.1 (18) vs 37.9 (18) Pain at rest VAS: 22.5 (23) vs 23.0 (26) Pain walking VAS: 34.0 (22) vs 28.8 (22)	HHS (0-100, higher score=higher function); SF-36 physical function (0-100, higher score=worse function); SF-36 role physical function (0-100, higher score=worse function); SF-36 bodily pain (0-100, higher score=less pain); pain at rest VAS (0-100, higher score=higher pain); pain walking VAS (0-100, higher score=higher pain)	3 and 6 months
Holroyd 1991	A+B Age: 32.3 years Female: 80% Race: NR Duration of symptoms: 10.7 years % of Headache-Free Days: 18.0 (16.0) vs. 18.5 (14.3) Headache Index Scores (0-10): 2.17 (0.96) vs. 2.04 (0.94) Headache Pain Peak Scores(0-10): 6.41 (1.67) vs. 6.36 (1.23) Mean Number of Analgesic Tablets: 0.82 (0.89) vs. 1.59 (1.77) Depression (BDI): 9.26 (5.41) vs. 7.69 (5.88) Anxiety(STPI): 22.63 (6.04) vs. 20.62 (6.82) Anger(STPI): 20.68 (5.65) vs. 19.06 (5.08) Physical Complaints(WPSI): 20.53 (8.16) vs. 20.94 (7.87)	% of Headache-Free Days; Proportion of Patients who Substantially Improved (>66% reduction;) Proportion of Patients who Moderately Improved (33- 66% reduction); Headache Index (mean headache recording for an assessment period): measure of the average level of pain (range 0-10: higher scores=more incapacitating the pain); Headache Peak (highest pain rating for each week averaged across an assessment period): measure of patient's most intense pain (range 0-10; higher scores=more intense the pain) Mean Number of Analgesic Tablets (weighted by medication potency); Beck Depression Inventory (BDI; total: 0-63, higher scores indicate severity of depressive symptoms); State-Trait Personality Inventory (STPI, range 20-80: higher scores indicate higher anxiety levels); Wahler Physical Symptom Inventory (WPSI)	1 month

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Hoeksma 2004	
Holroyd 1991	NA

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Hoeksma 2004	
Holroyd 1991	A vs. B 1 month % of Headache-Free Days: 54.7 (27.5) vs 42.3 (32.9); MD 12.4 (95%CI -8.06 to 32.86) p=0.227 Proportion of Patients who showed Substantial Improvement (>66% reduction): 37% (7/19) vs. 18% (3/17); RR 2.09 (95%CI 0.79 to 2.23) p=0.270 Proportion of Patients who showed Moderate Improvement (33-66% reduction): 53% (10/19)vs. 35% (6/17); RR 1.49(95%CI 0.80 to 2.03) p=0.306 Headache Index Scores (0-10): 0.96 (0.65) vs 1.49 (1.11); MD -0.53 (95%CI -1.14 to 0.08) p=0.086 Headache Peak Scores: 4.33 (2.35) vs. 4.55 (1.98); MD -0.22 (95%CI -1.70 to 1.26) p=0.765 Mean Number of Analgesic Tablets: 0.26 (0.52) vs. 0.82 (1.17); MD -0.56 (95%CI -1.16 to 0.04) p=0.067 Depression (BDI): 5.16 (4.65) vs. 5.56 (5.85); MD -0.4 (95%CI -3.96 to 3.16) p=0.821 Anxiety (STPI): 18.37 (4.60) vs. 19.06 (5.16); MD -0.69 (95%CI -3.99 to 2.62) p=0.674 Anger (STPI): 19.47 (5.96) vs. 17.44 (5.85); MD 2.03 (95%CI -1.98 to 6.04) p=0.311 Physical Complaints (WPSI): 16.05 (8.33) vs. 20.50 (7.27); MD -4.45(95%CI -9.78 to 0.87) p=0.099

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Hoeksma 2004	A vs B 3 months HHS: 68.4 (17) vs 56.0 (15), (Adj MD 11.1, 95% CI 4.0 to 18.6) SF-36 physical function: 45.3 (23) vs 46.6 (21), (Adj MD -2.1, 95% CI -11.7 to 7.7) SF-36 role physical function: 25.4 (43) vs 29.8 (33), (Adj MD -23.5 to 10.2) SF-36 bodily pain: 47.4 (25) vs 46.1 (20), (Adj MD -3.2, 95% CI -13.1 to 6.8) Pain at rest VAS: 19.1 (29) vs 26.9 (28), (Adj MD -7.2, 95% CI -13.8 to -0.5) Pain walking VAS: 16.4 (26) vs 23.7 (21), (Adj MD -12.1, 95% CI -22.9 to -2.5) 6 months HHS: 70.2 (20) vs 59.7 (18), (Adj MD 9.7, 95% CI 1.5 to 17.9) SF-36 physical function: 50.4 (22) vs 45.3 (18), (Adj MD 3.1, 95% CI -4.1 to 10.5) SF-36 role physical function: 36.7 (44) vs 32.4 (35), (Adj MD 2.2, 95% CI -16.8 to 21.1) SF-36 bodily pain: 51.4 (22) vs 49.9 (24), (Adj MD -1.5, 95% CI -11.1 to 7.7) Pain at rest VAS: 14.0 (27) vs 21.6 (30), (Adj MD -7.0, 95% CI -20.3 to 5.9) Pain walking VAS: 17.0 (22) vs 24.3 (28), (Adj MD -12.7, 95% CI -24.0 to -1.9)	Increased complaints: 3/56 (5%) vs 0/53 (0%)
Holroyd 1991	NA	Statistically significant difference in side effects between groups, with 58.8% (10/17) patients who received amitriptyline reporting at least mild side effects (p<.001) vs. 0% (0/19) of the CBT group Withdrawals: One patient (1/20) from the CBT group (due to lack of time) vs. four patients (4/21) in the amitriptyline group due to medication side effects

Author, Year	Funding Source	Quality	Comments
Hoeksma 2004	NR	Fair	Outcomes not reported: walking speed, recovery NRS 0-6, main complaint VAS, stiffness VAS, range of hip joint motion (2 ways)
Holroyd 1991	NR	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Holroyd 2001	United States, two sites (outpatient)	Inclusion criteria: >18 to 65 years old, CTTH according to IHS classification Exclusion criteria: Diagnosis of analgesic-abuse headache; current use of antidepressants or other prophylactics; current psychotherapy; current or planned pregnancy or breastfeeding; medical contraindication to amitriptyline; migraine headache >1 day/month; pain disorder other than headache as primary pain problem; medical disorder req. immediate treatment, failure to complete baseline diary recordings	Analyzed: 98

Author, Year	Intervention, Comparator
Holroyd 2001	A.Stress Management Therapy + Placebo (n=34) Psychologist or counselor administered lessons on home-based relaxation and cognitive coping skills No. of Sessions: 3 Length of Sessions: 1 hour B.Placebo (n=26) Followed the same procedure as AM group but with placebo pills. C.Antidepressant Medications (n=44) Low starting dose (12.5 mg increased to 25mg, then 50mg) with the possibility to switch to nortriptyline

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Holroyd 2001	A vs B vs C Age: 37 vs 38 vs. 36 Sex: 80% vs 79% vs. 66% female Race: 91% vs 98% vs 98% white Duration of symptoms: 12.3 vs. 11.1 vs 11.9 (p=0.44) Frequency of Headache, days per month: 26.5 (0.70) vs. 26.1(0.74) vs. 25.1 (0.72), p=0.57 Headache Index: 2.8 (0.20) vs. 2.7 (0.21) vs. 2.8 (0.18); Avs.B: MD 0.10 (95%CI 0.02 to 0.18) p=0.018; Avs.C: MD 0.0(95%CI -0.07 to 0.07) p=1.000 At least moderately severe headache days/month: 13.5 (1.2) vs. 13.5 (1.2)vs. 14.1 (1.1); Avs.B: MD 0.0(95%CI -0.48 to 0.48) p=1.000; Avs.C: MD -0.6(95%CI -1.05 to -0.15) p=0.009 Weighted Analgesic use: NR Headache Disability Inventory Score(0-100): NR	Days/month with at least moderately severe (≥5 pain rating) headache; Headache Disability Inventory Scores (HDI, range 0-100: higher scores indicate greater severity of symptoms); Headache Index Scores (mean of all headache diary ratings for 1 month period; 0-10; higher score=greater pain); Analgesic Medication Use Scores (weighted by medication potency)	1 month, 6 month

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Holroyd 2001	A vs. B 1 Month Days/month with at least moderately severe headache: MD 2.5 (95% CI -0.1 to 5.2) p=0.03 Headache Disability Inventory Score(0-100): MD 7.3 (95% CI 1.6 to 13.0) p<0.01 Headache Index: MD 0.46 (95% CI 0.02 to 0.89) p=0.02 Weighted analgesic use: MD -1.7 (95% CI -12.0 to 8.6) p=0.37 6 month Patients who experienced ≥50% reductions in Headache Index Scores: 35% (17/49) vs. 29% (14/48); RR 1.18 (95%CI 0.79 to 1.79) p=0.404 Days/month with at least moderately severe headache: MD 5.1 (95% CI 2.3 to 8.0) p=0.001 Headache Disability Inventory Score(0-100): MD 9.3 (95% CI 3.5 to 15.1) p=0.001 Headache Index: MD 0.79 (95% CI 0.30 to 1.28) p<0.01 Weighted analgesic use: MD 11.8 (95% CI 1.5 to 22.1) p=0.01 MDs adjusted for baseline scores.

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Holroyd 2001	A vs. C 1 Month Days/month with at least moderately severe headache: MD -3.5 (95% CI -6.1 to -0.9); p<0.01 Headache Disability Inventory Score(0-100): MD 0.1 (95% CI -5.6 to 5.7); p=0.99 Mean Headache Index: MD -0.54 (95% CI -0.97 to -0.12); p=0.01 Weighted analgesic use: MD -19.4 (95% CI -29.5 to -9.3); p=0.001 6 month Patients who experienced ≥50% reductions in Headache Index Scores: 35% (17/49) vs. 38% (20/53); RR 0.92 (95%CI 0.71 to 1.54) p=0.811 Days/month with at least moderately severe headache: MD 0.1 (95% CI -2.7 to 2.9); p=0.92 Headache Disability Inventory Score(0-100): MD 2.4 (95% CI -3.3 to 8.0); p=0.41 Headache Index: MD -0.13 (95% CI -0.61 to 0.35); p=0.58 Weighted analgesic use: MD -6.2 (95% CI -16.2 to 3.8); p=0.22 MDs adjusted for baseline scores.

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Holroyd 2001		A vs. B vs. C Withdrawals: 15 vs. 22 vs. 9 Withdrawals due to AEs: 2% (1/49) vs. 6% (3/48) vs. 2% (1/53); A vs. B: RR 0.33 (95%CI 0.04 to 3.03) p=0.30; A vs. C: RR 1.08 (95%CI 0.07 to 16.8) p=0.96 Serious AEs: NR Among 187 patients who completed at least the first dose adjustment session*: *Adverse effects**: 80% (78/97) who received antidepressant mediation (9 events reported: dry mouth, drowsiness, weight gain, dizziness, sweating, constipations, abdominal pains, nervousness, increased appetite) vs. 30% (27/90) who received placebo, p=0.001 • Dry mouth: 53% (51/97) vs. 13% (12/90), p=0.001 • Drowsiness: 44% (43/97) vs. 11% (10/90), p=0.001 • All other adverse events were reported in ≤10% of patients in either group. * Data is only reported for the combined groups in which patients received either antidepressant or placebo medication: antidepressant group = SMT + antidepressant (excluded from our analysis) and antidepressant alone; placebo group = SMT + placebo vs. placebo alone.

Author, Year	Funding Source	Quality	Comments
Holroyd 2001	Grant NS32374 from the National Institute of Neurological Disorders and Stroke, National Institute of Health	Poor	This study involved 4 comparator groups, 1 of which was excluded for not meeting our inclusion criteria (stress management + meds = additive). Some patients who received AM also received SMT so AE cannot be separated.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Hondras 2009	US, Iowa Number of centers: 1 Research clinic	Patients 55 years old, with non-specific LBP for 4 weeks and diagnostic classification of 1 (pain without radiation), 2 (pain plus radiation to extremity, proximally), or 3 (pain plus radiation to extremity, distally) according to the Quebec Task Force on Spinal Disorders. Exclude: Patients with frank radiculopathy or neurological signs, comorbid conditions or general poor Health, pregnancy, bleeding disorders, evidence of narcotic or other drug abuse, major clinical depression scores greater than 29 on the Beck Depression Inventory, bone or joint pathology, spinal fractures, tumors, infections, arthropathies, and significant osteoporosis, pacemaker, current or pending litigation related to LBP episode, receiving disability, received SM within the past month; unwilling to postpone use of manual therapies for LBP except those provided in the study (including chiropractic and osteopathic manipulation, physical therapy and massage).	Attrition: 10% (11/109)
Huang 2003	Taiwan, single center, outpatient department of rehabilitation	Inclusion: moderate bilateral knee OA (Altman grade II Exclusion: respiratory or cardiac dysfunction, or combined ankle or hip pain	Randomized: 132 Treated: 132 Analyzed: 122 Attrition: 8% (10/132)

Author, Year	Intervention, Comparator
Hondras 2009	A: Spinal manipulation (n=96): Chiropractic high-velocity low amplitude spinal manipulation, side-lying diversified lumbar spine "adjustment", 12 visits over 6 weeks B: Flexion distraction manipulation (n=95): Chiropractic low-velocity variable amplitude spinal mobilization, flexion distraction technique (Cox technique) with the application of up to 15 slow repetitions (low-velocity variable amplitude loads), 12 visits over 6 weeks C: Usual care (n=49): Consultation with medical provider within 7 days and at week 3 and week 6 plus a questionnaire All groups received home exercise instruction at week 3
Huang 2003	A.Isokinetic Strengthening (n=33) Sixty percent of the average peak torque was selected as the initial dose of isokinetic exercise, and an increasing dose program was used in the initial first to fifth sessions (1 set to 5 sets), and a dose of 6 sets was applied from sixth to the twenty-fourth sessions. Each set consists of 5 repetitions of concentric and eccentric(Con/Ecc) contraction in angular velocity 30°/sec-ond and 120°/second for extensors, and 5 repetitions of eccentric and concentric (Ecc/Con) con-traction in angular velocity 30°/second and 120°/second for flexors. Compliance: 88% (29/33) B.Isotonic Strengthening (n=33) The same protocol was used as in the isokinetic exercise. The isotonic muscle strengthening exercise program consisted of 5 repetitions of Con/Eccat the maximum velocity that the lever arm could achieve. Compliance: 93% (31/33) C.Isometric Strengthening (n=33) The same protocol of was used as in the isokinetic exercise. The speed of passive forward or backward motion was set at 30°/second. Compliance: 93% (31/33) All intervention groups exercised 3 times weekly for 8 weeks. The patients in all groups also received 20 minutes of hot packs and passive range motion exercise by an electric stationary bike (20 cycles per minute) for 5 minutes to both knees before muscle strengthening exercise. D.Control (n=33)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Hondras 2009	A vs. B vs. C Age: 64 vs. 62 vs. 63 years Female: 45% vs. 44% vs. 41% White race: 96% vs. 96% vs. 98% Non-white: 4% vs. 3% vs. 2% SF-36, Physical component summary, mean (SD): 39.1 (8.3) vs. 38.8 (8.1) vs. 40.7 (8.7) SF-36, Mental component summary, mean (SD): 51.7 (8.6) vs. 52.6 (8.7) vs. 52.1 (8.0) RDQ (0-24), mean (SD): 6.5 (4.1) vs. 6.6 (4.6) vs. 5.7 (4.0) Pain (0-100 VAS): 42.1 (23.6) vs. 42.5 (25.2) vs. 42.4 (24.5) SF-36 Physical Function (0-100): 65.3 (22.2) vs. 64.4 (22.2) vs. 67.2 (21.6) Beck Depression Inventory: 7.3 (5.6) vs. 8.2 (6.9) vs. 6.9 (6.3)	RDQ (0-24) Global improvement from baseline (1= no improvement to 10=complete improvement)	1.5 and 4.5 months
Huang 2003	All Patients (not reported by treatment group) Age: 62 (range, 45-77) years Female: 70% Duration of knee pain: range, 0.33 (4 mos.) to 9 years A vs. B. vs. C vs. D. Lequesne Index (n=33 patients per group): 6.9 (1.4) vs. 7.1 (1.2) vs. 6.8 (2.2) vs. 7.2 (1.5) VAS pain (n=66 knees per group): 4.8 (1.4) vs. 4.6 (1.7) vs. 4.7 (1.4) vs. 4.6 (1.3)	Lequesne Index (Scale 1-26, higher score=greater disability) (The disability may be graded as follows: >14 points, extremely severe; 11–13 points, very severe; 8–10 points, severe; 4–7 points, moderate; 1–3 points, mild disability; <7 points is considered acceptable function) Pain Visual Analog Scale after 5 minutes of weight bearing (Scale 0-10, higher score=worse pain)	10 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Hondras 2009	A vs. B vs. C, mean (SD) Baseline RDQ (0-24), mean (SD): 6.5 (4.1) vs. 6.6 (4.6) vs. 5.7 (4.0) 1.5 months RDQ (0-24): adjusted difference -1.5 (95% CI -3.1 to 0.1) for A vs. C and -2.2 (95% CI -3.7 to -0.6) for B vs. C Global improvement from baseline (1-10): adjusted difference 1.3 (95% CI 0.2 to 2.3) for A vs. C and 1.6 (95% CI 0.5 to 2.7) for B vs. C 4.5 months RDQ (0-24): adjusted difference -1.3 (95% CI −2.9 to 0.6) for A vs. C and -1.9 (95% CI -3.6 to -0.2) for B vs. C Global improvement from baseline (1-10): adjusted difference 1.7 (95% CI 0.5 to 2.8) for A vs. C and 1.8 (95% CI 0.6 to 3.0) for B vs. C
Huang 2003	A vs B vs C vs D Lequesne Index, mean (SD) 3.1 (1.6) (n=28) vs 4.0 (1.4) (n=29) vs 4.8 (1.5) (n=30) vs 7.6 (1.5) (n=27); p<0.05 for groups A, B, and C compared with group D A vs. D: MD -4.5 (95% CI -5.3, -3.7), p=0.0001 B vs. D: MD -3.6 (95% CI -4.4, -2.8), p=0.0001 C vs. D: MD -2.8 (95% CI -3.6, -2.0), p=0.0001 VAS Pain, mean (SD) 2.5 (1.8) (n=56 knees) vs 2.0 (1.4) (n=58 knees) vs 3.2 (1.6) (n=60 knees) vs 6.1 (1.3) (n=54 knees); p<0.05 for groups A, B, and C compared with group D

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Hondras 2009	NR
Huang 2003	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Hondras 2009	NR	No serious adverse events.
Huang 2003	NR	A vs B vs C vs D Withdrawals: 3% (1/33) vs 6% (2/33) vs 3% (1/33) vs 18% (6/33) Withdrawals RR (95% CI): A vs D: 0.17 (0.02, 1.3) B vs D: 0.33 (0.07,1.53) C vs D: 0.17 (0.02, 1.3) Stopped therapeutic exercise due to intolerable pain during exercise*: 12.1% (4/33) vs. 6.1% (2/33) vs. 6.1% (2/33) *There was greater treatment compliance in exercise groups B and C, and exercise-induced knee pain was the major factor causing discontinuation of treatment.

Author, Year	Funding Source	Quality	Comments
Hondras 2009	Bureau of Health Professions Health Resources and Services Administration, Rockville, MD (Grant No. 6 R18 HP01423-01)	Fair	
Huang 2003	National Science Council of Taiwan	Poor	Since VAS pain (mean +/- SD) is based on the number of knees and thus is a correlated measures, we cannot calculate a MD.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Huang 2005a **Arthritis & Rheumatism**	Taiwan	Inclusion: bilateral moderate knee OA (Altman grade II Exclusion: NR	Randomized: 70 Treated: 70 Analyzed: 54 Attrition: 23% (16/70)
Huang 2005b **Archives of PM&R**	Taiwan	Inclusion: bilateral moderate knee OA (Altman grade II) with periarticular soft tissue pain Exclusion: NR	Randomized: 60 Treated: 60 Analyzed: 45 Attrition: 25% (15/60)
Jensen 2012 **Wicksell 2013**	Sweden Patient referred from primary care physicians in Stockholm	Inclusion: female, diagnosed with FM by 1990 ACR criteria, age 18-55, pain of at least 40 on 0-100 pain VAS Exclusions: left-handed pregnant, breastfeeding, metal implant, claustrophobia; use of antidepressants, mood stabilizers, analgesics, strong opioids, anticonvulsants, centrally acting relaxants, joint injections, trigger/tender point injections, biofeedback, transcutaneous electrical nerve stimulation, severe psychiatric comorbidity	Randomized: 43 Analyzed: 33 Attrition: 23% (10/43)

Author, Year	Intervention, Comparator
Huang 2005a **Arthritis & Rheumatism**	A.Isokinetic Exercise (n=35) 3 times per week for 8 weeks. Began with 60% of the mean peak torque, increasing dose program was used in the first 5 sessions (1 set to 5 sets), and a dose of 6 sets was applied from the sixth to twenty-fourth sessions, with the density rising from 60% to 80% of the mean peak torque as the patient was able. Each set consisted of 5 repetitions of concentric contraction in angular velocities of 30°/second and 120°/second for extensors, and 5 repetitions of eccentric and concentric (Ecc/Con) contractions in angular velocities of 30°/second and 120°/second for flexors. B.Control (n=35) Warm-up exercises only
Huang 2005b **Archives of PM&R**	A vs B A.Isokinetic Exercise (n=30) 3 times per week for 8 weeks. Began with 60% of the average peak torque. Intensity of isokinetic exercise increased from 1 set to 5 sets during the first through fifth sessions and remained at 6 sets for the remaining 6th through 24th sessions. Each set consisted of 5 repetitions of concentric contraction in angular velocities of 30°/s and 120°/s for extensors, and 5 repetitions of eccentric and concentric contractions in angular velocities of 30°/s and 120°/s for flexors. B.Control (n=30) Heat for 20 minutes and 5 minutes of passive range of motion on bike only.
Jensen 2012 **Wicksell 2013**	A.Acceptance and Commitment Therapy (ACT) (n=19): 12 weekly 90-minute group sessions: exposure to personally important situations and activities previously avoided due to pain and distress, training to distance self from pain and distress. A physician conducted two sessions and a psychologist conducted 10 sessions. B.Waiting list control (n=15)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Huang 2005a **Arthritis & Rheumatism**	All Patients, not reported by treatment group (see comment column regarding study population) Age: 65 (range, 40-77) years Female: 81% Duration of knee pain: range, 0.42 (5 mos.) to 12 years A vs. B. Lequesne Index (n=35 patients per group): 7.6 (1.2) vs. 7.4 (1.1) VAS pain (n=70 knees per group): 5.3 (1.5) vs. 5.4 (1.7)	Lequesne Index (Scale 1-26, higher score=greater disability) (The disability may be graded as follows: >14 points, extremely severe; 11–13 points, very severe; 8–10 points, severe; 4–7 points, moderate; 1–3 points, mild disability; <7 points is considered acceptable function) Pain Visual Analog Scale after 5 minutes of weight bearing (Scale 0-10, higher score=worse pain)	10 months
Huang 2005b **Archives of PM&R**	All Patients, not reported by treatment group (see comment column regarding study population) Age: 62 (range, 42-72) years Female: 81% Duration of knee pain: range, 0.5 (6 mos.) to 11 years A vs. B. Lequesne Index (n=30 patients per group): 6.7 (2.1) vs. 7.0 (1.1) VAS pain (n=60 knees per group): 4.9 (1.5) vs. 4.8 (1.8)	Pain Visual Analog Scale after 5 minutes of weight bearing (Scale 0-10, higher is worse pain) Lequesne Index (Scale 1-26, higher is greater disability)	10 months
Jensen 2012 **Wicksell 2013**	A vs B Age: 45 vs 47 Female: 100% vs 100% Time since FM onset, years: 10.5 vs 11.8 FIQ: 49.3 (9.7) vs 48.7 (12.0) Pain Disability Index: 40.0 (10.9) vs 39.0 (10.2) Pain VAS: 61 (20) vs 65.0 (10) Pain NRS: 4.2 (1.0) vs 4.3 (1.1) BDI: 15.9 (6.3) vs 19.3 (13.0) STAI: 45.7 (12.0) vs 48.0 (15.1) SF-36 Mental: 40.1 (9.1) vs 38.6 (12.4) SF-36 Physical: 25.2 (6.6) vs 29.1 (9.9)	Fibromyalgia Impact Questionnaire (FIQ) (0-100, higher scores= greater impact of FM) Pain Disability Index (scale NR, higher scores= greater disability) Pain VAS: (0-100 mm, higher scores=worse pain in past week) Pain NRS (0-10, higher scores=greater pain) Beck Depression Inventory (BDI): (scale NR, higher scores=greater depression) State-Trait Anxiety Inventory State scale: (STAI-S): (scale NR, higher scores=greater anxiety) SF-36 (0-100, higher scores=better health-related quality of life)	3-4 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Huang 2005a **Arthritis & Rheumatism**	A vs B Lequesne Index, mean (SD) 5.8 (1.8) (n=26) vs 8.1 (1.5) (n=28), p<0.05 MD -2.3 (95% CI -3.2, -1.4), p=0.0001 VAS Pain, mean (SD) 3.9 (1.4) (n=52 knees) vs 6.6 (1.5) (n=56 knees), p<0.05
Huang 2005b **Archives of PM&R**	A vs B Lequesne Index, mean (SD) 5.1 (1.8) (n=21) vs 7.8 (1.7) (n=24) MD -2.7 (95% CI -3.8, -1.6), p=0.0001 VAS Pain, mean (SD) 3.5 (1.7) (n=42 knees) vs 6.0 (1.3) (n=48 knees); p<0.05
Jensen 2012 **Wicksell 2013**	A vs B 3-4 months FIQ: 37.4 (13.4) vs 45.7 (11.1), Cohen's d=0.66 (95% CI -0.06 to 1.37); MD -8.3 (95% CI -17.056 to 0.456), p=0.06 Pain Disability Index: 28.1 (12.5) vs 38.1 (15.4), Cohen's d=0.73 (95% CI -0.00 to 1.44); MD -10.0 (95% CI -19.740 to -0.260), p=0.04 Pain VAS: means NR but group X time interaction p=0.26 Pain NRS: 3.9 (1.1) vs 4.8 (1.1), Cohen's d= 0.82 (95% CI 0.08 to 1.54); MD -0.90 (95% CI -1.674 to -0.126), p = 0.02 BDI: 10.7 (4.8) vs 16.4 (12.5), Cohen's d=0.64 (95% CI -0.08 to 1.35); MD -5.7 (95% CI -12.044 to 0.644), p=0.08 STAI-S: 39.8 (7.5) vs 45.4 (12.8), Cohen's d=0.55 (95% CI -0.17 to 1.26); MD -5.6 (95% CI -12.751 to 1.551), p = 0.12 SF-36 Mental: 46.0 (9.4) vs 34.7 (12.2), Cohen's d=1.06 (95% CI 0.28 to 1.82); MD 11.3 (95% CI 3.761 to 18.839), p =0.005 SF-36 Physical: 28.4 (8.4) vs 31.1 (10.8), Cohen's d=0.28 (95% CI -0.45 to 1.00); MD -2.7 (95% CI -9.401 to 4.001), p =0.42

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Huang 2005a **Arthritis & Rheumatism**	NR
Huang 2005b **Archives of PM&R**	NR
Jensen 2012 **Wicksell 2013**	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Huang 2005a **Arthritis & Rheumatism**	NR	A vs B Withdrawals 11% (4/35) vs 11% (4/35) Discontinuation of exercise due to intolerable pain during exercise: 14% (5/35) vs. NA
Huang 2005b **Archives of PM&R**	NR	A vs B Withdrawals 13% (4/30) vs 13% (4/30) Discontinuation of exercise due to intolerable pain during exercise: 17% (5/30) vs. NA
Jensen 2012 **Wicksell 2013**		Withdrawals A vs B Before treatment 8% (2/25) vs 6% (1/18) During treatment: 12% (3/25 originally randomized) vs 6% (1/18 originally randomized) Adverse events NR

Author, Year	Funding Source	Quality	Comments
Huang 2005a **Arthritis & Rheumatism**	National Science Council of Taiwan	Fair	This trial had a total of 4 arms (N=140 total); 2 were excluded from our analysis because they did not meet our inclusion criteria (additive/combination of treatments): Group II (35 patients) = isokinetic exercise and pulse US treatment for painful periarticular soft tissue; Group III (35 patients) = isokinetic exercise, pulse US treatment for painful periarticular soft tissue, and intraarticular hyaluronan therapy. Since VAS pain (mean +/- SD) is based on the number of knees and thus is a correlated measures, we cannot calculate a MD.
Huang 2005b **Archives of PM&R**	National Science Council of Taiwan (grant no. NSC-92-2314-B-037-067)	Fair	This trial had a total of 4 arms (N=120 total); 2 were excluded from our analysis because they did not meet our inclusion criteria (additive/combination of treatments): Group II (30 patients) = isokinetic exercise and continuous Ultrasound; Group III (30 patients) = isokinetic exercise and pulsed Ultrasound Since VAS pain (mean +/- SD) is based on the number of knees and thus is a correlated measures, we cannot calculate a MD.
Jensen 2012 **Wicksell 2013**	Swedish Society for Medical Research Swedish Council for Working Life and Social Research Swedish Research council Stockholm City council Swedish Rheumatism Association	Fair	Note that the intervention was ACT, a form of CBT but a therapy that differs in content/goals from traditional CBT for pain Wicksell 2013 reports full study results for patient-reported outcome measures; Jensen 2012 reports some patient-reported outcome measures and fMRI results. Jensen 2012 reports 25 randomized to ACT and 18 randomized to WL; Wicksell 2013 did not count the 3 participants who withdrew after randomization and instead reported 23 randomized to ACT and 17 randomized to WL. For purposes of data abstraction, used the originally-reported 25 randomized to CBT and 18 randomized to WL.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Johnson 2007	UK Number of centers: 9 Setting: General practices	18-65 years old Persistent disabling LBP for 3 months, defined as: 1) Pain ≥20 mm (scale: 0-100 mm VAS), and 2) RMDQ disability score ≥5 (scale: 0-24) Exclude Previous consultation for LBP in past 6 months "Red flags" indicating signs of serious pathology Pregnancy or recent childbirth Major rheumatologic, neurologic, neoplastic or other conditions that may prevent full participation in the intervention Previous spinal surgery Major psychiatric illness, diagnosed or such symptoms under investigation History of drug or alcohol abuse in past 5 years	Randomized: 234 Analyzed: - 6 months: 203 - 12 months: 195 Attrition: 16.7% (39/234)
Jousset 2004	France Number of centers: 1 Outpatient clinic	Patients 18 to 50 years with LBP not relieved by conventional treatment, threatened job situation. Exclude: Patients with LBP of specific origin, less than 4 months, spinal surgery, cardiac or respiratory abnormalities after exercise stress tests on bicycle ergometers, psychiatric disorders precluding group participation, or receiving disability pensions	Randomized: 86 Treated: 84 Analyzed: 83 Attrition: 1.2% (1/83)

Author, Year	Intervention, Comparator
Johnson 2007	A.Cognitive behavioral therapy (CBT) program (n=116): 8 group sessions, 2 hours each over 6 weeks in community-based program for active exercise and education led by physiotherapist trained on CBT principles for LBP. Group discussions, case vignettes, and practical (physical) activities, encouraging the self-management of back pain; focused on problem solving, pacing and regulation of activity, challenging distorted cognitions about activity and harm, and helping patients identify helpful and unhelpful thoughts about pain and activity. Weekly homework was assessed and discussed. Patients were to monitor thoughts associated with pain and work to recognize helpful and unhelpful thoughts associated with the behavioral experiments. B.Usual care (n=118): Treated as usual according to their general practitioner. Both: Mailed an educational booklet and audio-cassette containing advice on self-management suitable for patients with persistent LBP. The booklet had 9 "leaflets": pain and activity; pacing; goal setting; stress; posture and body mechanics; guidelines for sleep hygiene; beds and sleeping; flare-up plans; when to see your general practitioner.
Jousset 2004	A.Functional Restoration (n=44) Exercise with physiotherapist; warm-up, stretching, flexibility, aerobic exercises strengthening, muscular endurance, coordination exercises, work simulations, counselling, 6 hours a day, 5 days a week for 5 weeks B.Active Individual Therapy (n=42) Active exercise, flexibility, stretching, strengthening, proprioception exercises, endurance training, jogging, swimming, stretching, 1 hour, 3 times a week for 5

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Johnson 2007	A vs. B Age: 47 vs. 49 Female: 61% vs. 58% Race: NR History of LBP: 90% vs. 87% <1 month LBP prior to consultation: 54% vs. 38% Baseline VAS: 44.9 vs. 51.6 Baseline RMDQ: 10.6 vs. 10.9 Baseline EQ-5D: 0.66 vs. 0.64 12-item General Health Questionnaire score ≥22: 83% vs. 81% Paid employment: 68% vs. 66% Routine and manual occupations: 28% vs. 27%	Pain (0-100 VAS) RDQ (0-24, 0 = no disability) EuroQol EQ-5D (0-1, 1 = perfect health)	6 and 12 months
Jousset 2004	A vs. B Age (mean): 41 vs. 40 years Female: 30% vs. 37% Race: NR Previous surgery 34.9% vs. 14.6%	Pain (0-10 NRS) Dallas Pain Questionnaire, 4 subscales (0-100, higher scores=less favorable) Quebec Disability Scale (0-100, higher score=more disability) Work status Hospital Anxiety Depression scale (0-21), higher score=less favorable)	5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Johnson 2007	A vs. B, mean (SD) <u>Baseline</u> Pain (0-100 VAS): 44.9 (18.2) vs. 51.6 (22.9) RDQ (0-24): 10.6 (3.9) vs. 10.9 (4.0) EQ-5D (0-1): 0.66 (0.22) vs. 0.64 (0.22) <u>6 months</u> Pain (0-100 VAS): 26.1 (23.5) vs. 35.0 (28.4), adjusted difference -4.60 (95% CI -11.07 to 1.88) RDQ (0-24): 6.5 (4.7) vs. 8.0 (5.4), adjusted difference -1.09 (95% CI -2.28 to 0.09) EQ-5D (0-1): 0.75 (0.24) vs. 0.71 (0.25), adjusted difference 0.03 (95% CI -0.05 to 0.10) <u>12 months</u> Pain (0-100 VAS): 27.9 (26.1) vs. 36.4 (27.3), adjusted difference -5.49 (95% CI -12.43 to 1.44) RDQ (0-24): 6.7 (5.6) vs. 8.0 (5.5), adjusted difference -0.93 (95% CI -2.30 to 0.45) EQ-5D (0-1): 0.75 (0.23) vs. 0.71 (0.23), adjusted difference 0.03 (95% CI -0.04 to 0.09) Healthcare cost: mean difference £27 (95% CI -159 to 213) Mean incremental cost-effectiveness ratio: £5,000 per QALY Cost-effectiveness acceptability: 90% probability for cost per QALY ≤ £30,000 Differences adjusted for baseline pain, disability, age, gender, LBP history, and psychological distress
Jousset 2004	NR

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Johnson 2007	NR
Jousset 2004	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Johnson 2007	NR	A vs B Withdrawal: 12.1% (14/116) vs. 20.3% (24/118) Withdrawal due to AEs: NR Serious AEs: NR Nonserious AEs: NR
Jousset 2004	A vs. B , mean (SD) <u>Baseline</u> Pain (0-10 NRS): 5.0 (2.2) vs. 4.6 (2.2) Dallas Pain Questionnaire ADL (0-100): 53.7 (16.7) vs. 50.3 (16.7) Dallas Pain Questionnaire Work/leisure (0-100): 54.0 (20.9) vs. 58.7 (18.2) Dallas Pain Questionnaire Anxiety/depression (0-100): 40.6 (25.3) vs. 31.8 (23.1) Dallas Pain Questionnaire Social interest (0-100): 34.8 (23.9) vs. 26.6 (21.6) Quebec Disability Scale (0-100): 34.6 (15.4) vs. 31.6 (15.9) Hospital Anxiety Depression Scale (0-21): 17.0 (6.5) vs. 14.3 (6.1) <u>5 months</u> Pain (0-10 NRS): 3.1 (2.5) vs. 4.0 (2.8), p=0.01 Dallas Pain Questionnaire ADL (0-100): 36.7 (23.0) vs. 41.5 (24.4), p=0.36 Dallas Pain Questionnaire Work/leisure (0-100): 34.0 (23.8) vs. 41.3 (25.6), p=0.18 Dallas Pain Questionnaire Anxiety/depression (0-100): 21.6 (22.9) vs. 27.8 (22.2), p=0.21 Dallas Pain Questionnaire Social interest (0-100): 19.6 (20.6) vs. 24.3 (26.1), p=0.37 Quebec Disability Scale (0-100): 22.0 (16.0) vs. 22.9 (17.7), p=0.80 Hospital Anxiety Depression Scale (0-21): 12.7 (7.2) vs. 13.4 (6.4), p=0.62 Ability to work: 90.5% (38/42) vs. 80.5% (33/41), p=0.20 Sick leave days: 28.7 (44.6) vs. 48.3 (66.0), p=0.12	NR

Author, Year	Funding Source	Quality	Comments
Johnson 2007	Supported by the Arthritis Research Campaign, Chesterfield, UK and the Epidemiology Unit at the University of Manchester, UK. Charity funds were received in support of the study.	Fair	
Jousset 2004	Union Regionale des Caisses d'Assurance Maladie des Pays de Loire	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Jubb 2008	UK, Rheumatology clinic attendees, 1 center	Inclusion Criteria: 18 years or older symptomatic, radiological knee OA > 6 months w/ inadequate response to 1+ conventional medical treatments Exclusion: previous acupuncture, regnancy other forms of arthritis and the “usual contra-indications for acupuncture”	Randomized: 68 Treated: 64 Analyzed: 62 Attrition: 9% (6/68)

Author, Year	Intervention, Comparator
Jubb 2008	A.Acupuncture (n=34): 10 minutes of manual acupuncture (total of 9 points; 3 cm, 30 gauge solid stainless steel needles; insertion depth of 1-1.5 cm; elicitation of de qi) and 20 minutes of electroacupuncture (10 mins. each on anterior and posterior part of the knee; low frequency, delivered at 6 Hz at a constant current; voltage set just above the pain threshold) B.Sham acupuncture (n=34): sham needle secured to the skin with a plastic ring covered by a sticking plaster (also used for those having verum acupuncture), did not penetrate the skin; dummy mode of the electrical stimulation apparatus was used (produced sound signals but no electrical current). Both groups received 30 minute treatments, 2/week for 5 weeks, with 10 sessions in total

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Jubb 2008	A vs B Age: 64.1 (1.6) vs. 66.1 (1.9) Female: 85% vs. 76% Caucasian: 74% vs. 85% Duration of symptoms: 10 vs. 9.6 years WOMAC pain: 294 (78) vs. 261 (100) WOMAC function: 1028 (277) vs. 979 (313) EuroQoL VAS: 63 (22) vs. 54 (20) Total Body Pain VAS: 49 (24) vs. 49 (26) Night Pain in Knee VAS: 61 (26) vs. 52 (28) Overall Pain in Knee VAS: 63 (19) vs. 53 (25) Weight Pain in Knee VAS: 71 (19) vs. 60 (23)	WOMAC function (0-1700, non-normalized; higher score=worse function) WOMAC pain (0-500, non-normalized; higher score=worse function) Knee Pain on VAS (scale 0-100; higher score=worse pain) EuroQol - VAS (0-100; higher score=best health imaginable)	1 month

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Jubb 2008	A vs. B <u>1 month</u> WOMAC Function (mean Δ from baseline): 137 (95% CI 20 to 255) vs. 134 (95% CI 9 to 258); MD between groups in Δ scores: 4 (-163 to 171), p=NS WOMAC Pain (mean Δ from baseline): 59 (95% CI 16 to 102) vs. 13 (95% CI -22 to 50); MD between groups in Δ scores: 46 (95% CI -9 to 100), p=NS Weight-bearing pain in knee, VAS (mean Δ from baseline): 19 (95% CI 9 to 30) vs. 8 (95% CI -1 to 16); MD between groups in Δ scores: 11 (95% CI -2 to 25), p=NS Overall knee pain, VAS (mean Δ from baseline): 14 (95% CI 5 to 24) vs. 2 (95% CI -6 to 10); MD between groups in Δ scores: 12 (95% CI -1 to 24), p=NS Nighttime knee pain, VAS (mean Δ from baseline): 10 (95% CI -1 to 22) vs. 5 (95% CI -3 to 14); MD between groups in Δ scores: 5 (95% CI -9 to 19), p=NS General body pain, VAS (mean Δ from baseline): 5 (95% CI -5 to 15) vs. -8 (95% CI -1 to 18); MD between groups in Δ scores: 13 (95% CI 0 to 27), p=0.048 EuroQoL - VAS (mean, SD): 63 (24) vs. 52 (26), p=0.98

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Jubb 2008	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Jubb 2008		Withdrawal: 5.9% (2/34) vs. 5.9% (2/34); Withdrawal due to adverse events: 2.9% (1/34) vs. 0% (0/34) (flare of synovitis, not septic); Adverse events (not specified): 11.8% (4/34) vs. 17.6% (6/34); RR 0.67 (95% CI 0.21, 2.2), p=0.50 No adverse events attributable to acupuncture

Author, Year	Funding Source	Quality	Comments
Jubb 2008	University Hospital Birmingham NHS Foundation Trust, UK	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Juhakoski 2011	Finland 2 centers Outpatient	Aged 55-80 years, commitment to two year long study, radiological evidence within 3 years of unilateral or bilateral hip Oawith Kellgren-Lawrence grade ≥ 1, pain in hip region within previous month consistent with ACR criteria Exclude: Total hip replacement, rheumatoid arthritis, cognitive impairment, major surgical operation to lower back or lower limb area within previous 6 mos, acute or subacute lower back pain, cardiovascular or pulmonary disease, chronic disease that would prevent full participation	Randomized: 120 Treated: 118 Analyzed: 113 Attrition: 6% (7/120)

Author, Year	Intervention, Comparator
Juhakoski 2011	A.Exercise+standard care (n=57): 12 supervised strengthening and stretching exercise sessions of 45 minutes once per week, (with instructions to perform exercises 3 times per week for two years) and 4 booster sessions 1 year later. Sessions consisted of warm-up, strengthening and stretching. B.Standard care (n=56): normal routine care offered by patient's own general practitioner, analgesics and physiotherapy All patients: instructional hour-long session on basic principles of non-operative treatment of hip osteoarthritis

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Juhakoski 2011	A vs B Age: 67 vs 66 years Female: 68% vs 72% Duration of symptoms (yrs): 8.3 vs 8.5 Knee OA and/or knee pain: 38% vs 29% Comorbidities (chronic disease): None: 40% vs 43% One: 47% vs 43% Two or more: 13% vs 14% Work status: No longer employed: 77% vs. 67% Part-time employment: 12% vs. 9% Employed: 10% vs. 24% WOMAC function: 24.7 (16.7) vs 28.9 (22.4) RAND-36 (SF-36) physical function: 63.4 (19.8) vs 61.2 (20.8) WOMAC pain: 21.5 (14.8) vs 29.1 (20.2) Weak opioid (i.e. tramadol and codeine) use: Not using: 81.7% vs 84.5% Using less than daily: 13.3% vs 6.9% Using daily: 5.0% vs 8.6%	WOMAC physical function (0-100, higher score=higher disability); SF-36 (0-100, higher score=higher QoL); WOMAC pain (0-100, higher score=higher pain); Weak opioid use; Physician visits attributable to hip OA	3, 9, 15, and 21 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Juhakoski 2011	A vs B 3 months WOMAC function, mean (SE): 22.6 (2.3) vs 30.1 (2.5) (MD -7.5, 95% CI -13.9 to -1.0) WOMAC pain, mean (SE): 23.4 (2.7) vs 28.9 (2.8) (MD -5.5, 95% CI -13.0 to 2.0) Weak opioid use (p=0.73): Not using: 82.5% vs 87.7% Using less than daily: 10.5% vs 8.8% Using daily: 7.0% vs 3.5% 9 months WOMAC function, mean (SE): 24.6 (2.2) vs 27.6 (2.3) (MD -3.0, 95% CI -9.2 to 3.2) WOMAC pain, mean (SE): 22.9 (2.6) vs 25.0 (2.6) (MD -2.1, 95% CI -9.2 to 5.0) Weak opioid use (p=0.12): Not using: 81.0% vs 93.1% Using less than daily: 10.4% vs 1.7% Using daily: 8.6% vs 5.2% No. of doctor up to 9 month followup visits concerning hip OA, mean (SE): 0.5 (0.1) vs 0.8 (0.2), p=0.07 No. of physiotherapy visits up to 9 month followup (i.e. exercise physiotherapy and/or physical therapy modalities) for hip OA, mean (SE): 1.3 (0.2) vs 2.0 (0.3), p=0.05 Six-minute walk (m): 502 vs 491 21 months WOMAC function, mean (SE): 24.4 (2.7) vs 30.0 (2.8) (MD -5.6, 95% CI -12.9 to 1.7) WOMAC pain, mean (SE): 24.1 (2.9) vs 27.9 (3.0) (MD -3.8, 95% CI -12.0 to 4.4) Weak opioid use (p=0.70): Not using: 80.7% vs 85.2% Using less than daily: 12.3% vs 7.4% Using daily: 7.0% vs 7.4% No. of doctor between 9 and 21 month followup visits concerning hip OA, mean (SE): 0.5 (0.1) vs 1.1 (0.2), p=0.05 No. of physiotherapy visits between 9 and 21 month followup (i.e. exercise physiotherapy and/or physical therapy modalities) for hip OA, mean (SE): 0.4 (0.1) vs 1.3 (0.2), p<0.001 Total cost per patient: 1066.3 (331.5) vs 1406.3 (441.8), p=0.13 Total hip replacements: 5 (2 before 9 month followup, 3 between 9 and 21 month followup) vs 8 (3 before 9 month followup, 5 between 9 and 21 month followup) Six-minute walk (m): 498 vs 493 SF-36 data NS but values NR (timing not indicated)

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Juhakoski 2011	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Juhakoski 2011		NR

Author, Year	Funding Source	Quality	Comments
Juhakoski 2011	EVO-grant from Mikkeli Central Hospital	Fair	*Weak opioids evaluated were tramadol and codeine Outcomes not reported: Direct medical costs, use of analgesics, use of NSAIDS, internal rotation and flexion of the hip joint, extensor power of lower limb, 10 m walk test, Timed Up and Go test, the Sock test

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Kankaanpaa 1999	Finland, single site, health center	Nonspecific, chronic LBP for greater than 3 months duration, and no radicular symptoms Exclude: nerve root compression, disc prolapse, severe scoliosis, spondyloarthrosis, pervious back surgery, and other specific and serious causes of back pain	Randomized: 59 Treated: 54 Analyzed: 54 Attrition: 6 month - 15.3% (9/59) 12 month - 16.9% (10/59)
Karst 2000	Germany, number of sites/setting not reported	Inclusion criteria: CTTH according to IHS classification Exclusion criteria: Anticoagulation, predominantly operating factors, rebound analgesic headache syndrome, symptomatic or other concomitant headaches, history of or current migraines	Randomized: NR Treated: NR Analyzed: 39 Attrition: NR

Author, Year	Intervention, Comparator
Kankaanpaa 1999	A.Combined exercise (n=30) Active rehabilitation patients trained in groups of 4 to 5 under supervision of a physiotherapist. Patients learned exercises, stretching and relaxation exercises, behavioral support and ergonomic advice. Four specially designed training units targeted trunk muscle function and coordination. Progressive load increases we added over the course of the 12 weeks. No. of Treatments: 24 sessions over 12 weeks Length of Treatments: 1.5 hours B.Attention Control (n=24) Use of treatment methods, medication dosages and guidance presumed to be of minor efficacy, and thus considered as a placebo. This included thermal therapy and minimal massage from physiotherapists. No. of Treatments: Once weekly for 4 weeks (4 sessions total during the final 4 weeks of the 12 week active group) Length of Treatments: NR
Karst 2000	A. Acupuncture (n=21) No. of treatments: Twice per week for 5 weeks Type of needle: Seirine Btype needle no. 8 (0.3 x0.3 mm) and no. 3 (0.2 x 0.15 mm) Acupoints: GB 20, L 14, LR 3, GB 8, GB 14, GB 21, GB 41, UB 2, UB 10, UB 60 No. of needles: Max of 15 No. of insertions per needle: NR Insertion depth: NR Time length of treatment: 30 min B.Sham Acupuncture (n=18) Blunt placebo needles simulated puncturing sensation without being inserted. Elastic foam was used to shield needle type.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Kankaanpaa 1999	A vs B Age: 40 vs. 39 years Female: 36.6% vs. 33.3% Race: NR Mean Duration of Chronicity: 9.03 vs. 7 Functional Disability (PDI): 13.2 (10.2) vs. 9.5 (8.3) Back Pain Intensity (VAS): 55.2 (22.8) vs. 47.0 (29.3)	Pain and Disability Index (PDI, range 0-70: higher scores indicate worse disability) Back Pain Intensity (VAS, range 0-100mm: higher scores indicate worse pain)	Short term and intermediate term followup 3 and 9 months
Karst 2000	A vs. B Age: 50 vs 47 years Female: 38% vs. 61% Race: NR Mean duration of chronicity: NR Mean frequency of headache: (SD): 26.9 vs 27.2 days/month Patients who had prior preventative treatments: NR Patients who overused medications: NR VAS at baseline: 6.2 (2.2) vs 6.3 (2.2) Mean Analgesic Intake/Month at Baseline: 8.3 (11.8) vs. 10.2 (12.0)	Frequency of headache attacks/month; Headache severity (VAS, range 0-10: higher scores indicate severity of pain); Mean Analgesic Intake/Month	1.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Kankaanpaa 1999	A vs. B, mean (SD) <u>Baseline</u> Pain and Disability Index (0-70): 13.2 (10.2) vs. 9.5 (8.3) Back pain intensity (0-100 VAS): 55.2 (22.8) vs. 47.0 (29.3) <u>3 months</u> Pain and Disability Index (0-70): 5.7 (6.6) vs. 12.6 (10.2), difference -6.9 (95% CI -11.69 to -2.11) Back pain intensity (0-100 VAS): 26.6 (28.4) vs. 43.4 (19.8); difference -16.80 (95% CI -31.12 to -2.47) <u>9 months</u> Pain and Disability Index (PDI): 5.7 (8.1) vs. 11.4 (11.4), difference -5.7 (95% CI -11.31 to -0.09) Back pain intensity (0-100 VAS): 23.9 (17.8) vs. 45.1 (22.2), difference -21.20 (95% CI -32.69 to -9.71)
Karst 2000	<u>A vs. B</u> <u>1.5 Months</u> Frequency of headache attacks/month: 22.1 (10.6) vs. 22.0(9.9); MD 0.10 (95%CI -6.59 to 6.79) p=0.976 Mean Headache Severity VAS (0-10): 4.0(2.5) vs. 3.9(2.7); MD 0.10 (95%CI -11.92 to 12.12) p=0.987 Mean Analgesic Intake/Month: 13.7(17.2) vs. 21.2(27.6); MD -7.5(95%CI -22.20 to 7.20) p=0.308

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Kankaanpaa 1999	NR
Karst 2000	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Kankaanpaa 1999	NR	NR
Karst 2000	NR	NR

Author, Year	Funding Source	Quality	Comments
Kankaanpaa 1999	Ministry of Education and Academy of Finland Fund, The Finnish Medical Society Duodecim; Yrjo Jahnsson Emil Aaltonen and Instrumentarium Science Foundations; and a grant (496115) from Kuopio University EVO Fund.	Fair	
Karst 2000	NR	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Kayiran 2010	Turkey 1 center Outpatient	Aged 16-49 years old, ACR criteria for FM, not receiving any medication or other treatments for FM or any other diseases Exclude: Major health problem, alcohol abuse, psychoactive drug treatment, abnormality in routine laboratory tests	Randomized: 40 Treated: NR Analyzed: 36 Attrition: 10% (4/40)
Kayo 2012	Brazil 1 outpatient rheumatology clinic	Inclusion: women who met ACR 1990 criteria for FM age 30-55, agreed to participate in exercise program and discontinue medication for FM 4 weeks before the study, and at least 4 years of schooling. Exclusion: contra-indication to exercise, medical litigation	Randomized: 90 Analyzed: 68 Attrition: 24% (22/90)

Author, Year	Intervention, Comparator
Kayiran 2010	A.EEG Biofeedback (Neurofeedback) (n=18): 5 sessions based on SMR training protocol per week for 4 weeks. Each session composed of 10 SMR periods lasting for 3 minutes for a total of 30 minutes B.Escitalopram (n=18): 10 mg/day for 8 weeks (control group)
Kayo 2012	A.Walking program (n=30): walking 60 minutes 3 times per week for 16 weeks, supervised by physical therapist. Every 4 weeks, walking duration was increased (25-30 minutes to 50 minutes), as well as the intensity based on heart rate reserve. Heart rate was monitored using a heart rate monitor. B.Muscle strengthening exercise (n=30): muscle strengthening exercise 60 minutes 3 times per week for 16 weeks, supervised by physical therapist. Exercise used free weights and body weight. Exercise load and intensity were increased every 2 weeks. C.Control (no treatment) (n=23)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Kayiran 2010	A vs B Age: 32 vs 32 Female: 100% vs 100% Duration of symptoms (years): 4.6 (2.5) vs 4.9 (2.4) Major depressive disorder, n: 9 vs 10 FIQ: 70 vs 74* Pain VAS, mean (SE): 8.9 (0.2) vs 9.1 (0.2) Hamilton Depression Scale, mean (SE): 16.9 (1.3) vs 20.8 (0.7) Beck Depression Scale, mean (SE): 21.5 (2.6) vs 26.0 (2.2) Hamilton Anxiety Scale, mean (SE): 19.7 (1.4) vs 25.1 (1.3) Beck Anxiety Scale, mean (SE):26.2 (2.4) vs 35.6 (2.4) SF-36*: Physical functioning:40 vs 39 Bodily pain: 28 vs 25 Role-physical: 2 vs 4 Role-emotional: 11 vs 8 Social functioning: 39 vs 25 General mental health: 35 vs 31 General health: 38 vs 51 Vitality: 23 vs 22	FIQ (0-100, higher score=higher disability); pain VAS (0-10, higher score=higher pain); Hamilton Depression Scale (0-50, higher score=more severe symptoms of depression); Beck Depression Scale (0-63, higher score=more severe symptoms of depression); Hamilton Anxiety Scale (0-56, higher score=more severe symptoms of anxiety); Beck Anxiety Scale (0-63, higher score=more severe symptoms of anxiety)	4-5 months
Kayo 2012	A vs C: Age, years: 48 (5.3) vs 46 (6.4) Duration of symptoms, years: 4.0 (3.1) vs 5.4 (3.5) FIQ total: 63.1 (14.7) vs 63.8 (16.7) Pain VAS: 8.6 (1.6) vs 8.4 (1.5) SF-36 Physical Functioning: 39.3 (18.6) vs 35.8 (17.3) SF-36 Mental Health: 51.3 (24.3) vs 46.0 B vs C: Age, years: 46.7 (6.3) vs 46.1 (6.4) Duration of symptoms, years: 4.7 (5.7) vs 5.4 (3.5) FIQ total: 67.3 (16.5) vs 63.8 (16.7) Pain VAS: 8.7 (1.6) vs 8.4 (1.5) SF-36 Physical Functioning: 37.3 (17.6) vs 35.8 (17.3) SF-36 Mental Health: 46.0 (22.8) vs 46.0 (22.2)	FIQ (0-100, higher scores=greater disability) Pain VAS (0-10, higher scores=greater pain) SF-36 (0-100, higher scores=better health status)	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Kayiran 2010	
Kayo 2012	A vs C, ITT analysis (n= 30 vs. 30) 3 months: FIQ: 38.5 vs 57.7; overall group x time interaction ns Pain VAS: 4.8 vs 6.7; overall group x time interaction ns SF-36: NR B vs C, ITT analysis (n= 30 vs. 30) 3 months: FIQ: 50.5 vs 57.7; overall group x time interaction ns Pain VAS: 5.9 vs 6.7; overall group x time interaction ns SF-36: NR

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Kayiran 2010	A vs B <u>4 months</u> FIQ: 19 vs 48*, p NR Pain VAS, mean (SE): 2.6 (0.4) vs 5.3 (0.3), p<0.0001; MD -2.7 (95% CI -3.7 to -1.7), p<0.0001 Hamilton Depression Scale, mean (SE): 6.3 (0.6) vs 13.4 (0.8), p <0.0001; MD -7.1 (95% CI -9.1 to -5.1), p<0.0001 Beck Depression Scale, mean (SE): 4.7 (0.9) vs. 12.3 (0.5), p < 0.0001; MD -7.6 (95% CI -9.7 to -5.5), p<0.0001 Hamilton Anxiety Scale, mean (SE): 7.1 (0.8) vs 15.2 (1.2), p<0.0001; MD -8.1 (95% CI -11.0 to -5.2), p<0.0001 Beck Anxiety Scale, mean (SE): 7.2 (1.2) vs. 16.7 (1.8), p <0.0001; MD -9.5 (95% CI -13.9 to -5.1), p<0.0001 SF-36*: Physical functioning: 77 vs 65, p<0.05 Bodily pain: 70 vs 45, p<0.05 Role-physical: 90 vs 43, p<0.05 Role-emotional: 95 vs 51, p<0.05 Social functioning: 76 vs 65, p<0.05 General mental health: 74 vs 59, p<0.05 General health: 72 vs 28, p<0.05 Vitality: 70 vs 50, p<0.05
Kayo 2012	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Kayiran 2010		NR
Kayo 2012		A vs C: Adverse events: 0 vs 0 Withdrew during treatment: 7% (2/30) vs 7% (2/30) B vs C Adverse events: 0 vs 0 Withdrew during treatment: 23% (7/30) vs 7% (2/30)

Author, Year	Funding Source	Quality	Comments
Kayiran 2010	NR	Poor	*Indicates value was estimated from a graph; SD NR
Kayo 2012	NR	Fair	Means were reported for the VAS Pain, FIQ, and SF-36 Bodily Pain measures, but no other outcome measures. SDs were not reported for any followup outcome measures. The overall treatment X time interactions for the VAS Pain and FIQ were not significant. Overall treatment X time interactions were not reported for the other measures. The analysis included all 90 participants (intention-to-treat anal-ysis) using the last observed response for patients with missing data (carry forward). Efficacy (as-treated) analysis was also performed.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Kerr 2003	UK Number of centers: Unclear Setting: Unclear Patients were recruited as direct referral from general practitioner or from the waitlist of an open referral system for outpatient physiotherapy services operated by local general practitioners and hospitals.	LBP symptoms ≥6 months with or without leg pain No neurologic deficits Exclude Contraindications to acupuncture therapy Age <18 years Pregnancy Underlying systemic disorders Rheumatoid arthritis Osteoarthritis of the spine Cancer	Randomized: 60 Treated: 26 Analyzed: 46 (end of treatment), 40 (4.5 months)
King 2002	United States 1 center University setting	Females with diagnosis of FM fulfilling ACR criteria Exclude: Conditions that precluded ability to exercise, inflammatory arthritis, systemic lupus erythematosus, rheumatoid arthritis	Randomized: NR* Treated: NR* Analyzed: 76 Attrition: Unclear*

Author, Year	Intervention, Comparator
Kerr 2003	A.Acupuncture (n=26): 6 30-minute sessions over 6 weeks using set acupuncture points performed by single provider. 11 needles used for each patient, 0.30 x 50 mm c-type, inserted with until the sensation of "ch'i" was produced, with patient in prone position. Needles were manually rotated to produce "ch'i" sensation again at 10- and 20-minute intervals. Patients were also given a leaflet that included standardized advice and exercises (identical for both groups). B.Placebo (sham TENS) (n=20): 6 30-minute sessions over 6 weeks. Nonfunctioning TENS unit attached to 4 electrodes (3 cm x 3 cm carbon-rubber with self-adhesive gel pads) and placed over the lumbar spine. The unit was switched on but the circuit was broken between the unit and the patient. Patients were also given a leaflet that included standardized advice and exercises (identical for both groups).
King 2002	A.Exercise (n=30‡): 3 supervised exercise sessions per week for 12 weeks. Sessions were based on recommendations from the 1990 American College of Sports Medicine recommendations on quantity and quality of exercise for developing cardiorespiratory fitness in healthy adults. Exercises were aerobic and included both land and water activities. Sessions lasted from 10-15 minutes at the beginning of the treatment period and were 20-40 minutes at the end of the treatment period. B.Control (n=18‡): Subjects were given basic instructions on stretches and coping strategies at the beginning of the treatment period. Subjects were contacted 1-2 times during the treatment period to answer any questions.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Kerr 2003	A vs. B Age: 43 vs 43 Female: 50% vs. 35% Duration of symptoms (mean), months: 86 vs. 73 Baseline MPQ*: 29.0 vs. 28.5 Baseline pain (0-100 VAS): 79.7 vs. 76 Baseline SF-36: 52.3 vs. 47.3	Pain relief (yes/no)	4.5 months
King 2002	A vs B Age: 45 vs 47 Female: 100% vs 100% Duration of symptoms (years): 7.8 vs 9.6 FIQ: 52.4 vs 55.2	FIQ (0-80, higher score=higher disability)	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Kerr 2003	A vs. B <u>4.5 months</u> Pain relief "yes": 91% (21/23) vs. 75% (13/17), RR 1.19 (95% CI 0.89 to 1.60)
King 2002	A vs B FIQ: 47.5 (14.0) vs 51.5 (13.1), p ns; (MD -4.0, 95% CI -12.2 to 4.2) p=0.33

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Kerr 2003	NR
King 2002	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Kerr 2003	NR	A vs. B Withdrawals: 13% (4/30) vs. 33% (10/30); RR 0.90 (95% CI 0.55 to 1.47) Serious AEs: None reported Nonserious AEs: 9% (2/23) vs. 13% (2/17), RR 1.14 (95% CI 0.66 to 1.97)
King 2002		NR

Author, Year	Funding Source	Quality	Comments
Kerr 2003	Grant support from the Department of Health and Social Services for Northern Ireland.	Poor	The only results for scale outcomes are at end of treatment. May be an exclude. Calculated the RR for withdrawals and Nonserious AEs. There are results for within-group change for pre/post-treatment outcomes.
King 2002	Grants from the Medical Services Incorporated Foundation and the Health Services Research and Innovation Fund	Poor	*Total number of patients randomized was 196 over 4 groups, but only 2 groups were of interest. Insufficient information was given to determine the number of subjects randomized and treated for individual groups. Below are the numbers for all patients in the study: Randomized: 196 Treated: 170 Analyzed: 152 (ITT), 95 (completers) Attritions: 22% ITT (44/196), 52% completers (101/196) †Baseline values abstracted are for completers (patients who attended all 3 sessions) because only followup values for the completers population were reported ‡Number included in completers analysis MD and p value calculated

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Lamb 2010 and 2012	UK Number of centers: Unclear Setting: Unclear	Age ≥18 years At least moderately troublesome LBP ≥6 weeks duration Consultation with primary care for LBP within the preceding 6 months Exclude Family doctor concerned for possibility of serious cause for LBP (i.e., infection, fracture, malignancy) Severe psychiatric or psychological disorders Previous participation in a cognitive behavioral intervention for LBP	Randomized: 701 Analyzed: 545 at 3 months; 582 at 6 months; 598 at 12 months Attrition: 22% (156/701) at 3 months; 17% (119/701) at 6 months; 15% (103/701) at 12 months

Author, Year	Intervention, Comparator
Lamb 2010 and 2012	A.Cognitive behavioral treatment (CBT) (n=468): Program consisting of active management advice, individual assessment and group cognitive behavioral treatment. Active management advice: 15-minute session with a nurse or physiotherapist on remaining active, avoiding bed rest, appropriate use of pain medication and symptom management, and patients were given an educational book (The Back Book). Individual assessment: up to 1.5 hour assessment. Group CBT: 6 standardized sessions, 1.5 hours each, targeting behaviors and beliefs about physical activity and avoidance of activity, supplemented with a workbook and led by physiotherapists, nurses, psychologists, and occupational therapists. General practitioners were requested to avoid referral to other treatments while subjects were receiving the intervention, where possible. B.Control (n=233): Active management advice only. 15-minute session with a nurse or physiotherapist on remaining active, avoiding bed rest, appropriate use of pain medication and symptom management, and patients were given an educational book (The Back Book).

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Lamb 2010 and 2012	A vs. B Age: 53 vs. 54 years Female: 59% vs. 61% White race: 88% vs. 88% Duration of back pain (years since first onset): 13 vs. 13 Employed: 51% vs. 47% Unable to work because of LBP: 11% vs. 9% RDQ (0-24): 9 vs. 9 Modified Von Korff disability (0-100): 49 vs. 46 Modified Von Korff pain (0-100): 59 vs. 59 SF-12 Physical component score (0-100): 37 vs. 38 SF-12 Mental component score: 45 vs. 46	Roland Morris Disability Questionnaire (RDQ, 0-24 (higher scores indicate more disability) Modified Von Korff disability (0-100) Modified Von Korff pain (0-100) SF-12 Physical component score (0-100, lower score indicates poorer quality of life) SF-12 Mental component score (0-100) Health care resource use for LBP during followup year	1.5, 4.5, 10.5, and mean 34 months (see Lamb 2012)

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Lamb 2010 and 2012	A vs. B, mean (SD) <u>Baseline</u> RDQ (0-24): 9 (5.0) vs. 9 (4.7) Modified Von Korff disability (0-100): 49 (23.9) vs. 46 (23.8) Modified Von Korff pain (0-100): 59 (19.2) vs. 59 (19.5) SF-12 Physical component score (0-100):37 (9.3) vs. 38 (10.1) SF-12 Mental component score (0-100): 45 (11.5) vs. 46 (11.0) <u>3 months, mean change from baseline (95% CI)</u> RDQ (0-24): -2.0 (-2.43 to -1.58) vs. -1.1 (-1.54 to -0.35).adjusted difference -1.1 (-1.71 to -0.38) Modified Von Korff disability (0-100): -13.2 (-15.74 to -10.59) vs. -8.9 (-12.27 to -5.56), adjusted difference -4.2 (-8.10 to -0.40) Modified Von Korff pain (0-100): -12.2 (-14.56 to -9.83) vs. -5.4 (-8.40 to -2.49), adjusted difference -6.8 (-10.20 to -3.31) SF-12 Physical component score (0-100): 3.7 (2.82 to 4.59) vs. 1.5 (0.26 to 2.83), adjusted difference 2.2 (0.74 to 3.57) SF-12 Mental component score (0-100): 1.3 (0.19 to 2.42) vs. 0 (-1.45 to 1.46), adjusted difference 1.3 (-0.36 to 2.96) <u>4.5 months</u> RDQ (0-24): -2.5 (-3.03 to -1.96) vs. -1.0 (CI -1.67 to -0.40), adjusted difference -1.5 (-2.22 to -0.70) Modified Von Korff disability (0-100): -13.9 (CI -16.25 to -11.55) vs. -5.7 (-9.22 to -2.28), adjusted difference -8.2 (-12.01 to -4.31) Modified Von Korff pain (0-100): -13.7 (-16.20 to -11.29) vs. -5.7 (-8.99 to -2.41), adjusted difference -8.0 (-11.80 to -4.28) SF-12 Physical component score (0-100): 3.6 (2.72 to 4.52) vs. 1.8 (0.54 to 3.08), adjusted difference 1.8 (0.37 to 3.25) SF-12 Mental component score (0-100): 2.5 (1.44 to 3.48) vs. -0.09 (-1.61 to 1.43), adjusted difference 2.6 (0.85 to 4.25) <u>10.5 months</u> RDQ (0-24): -2.4 (-2.84 to -1.89) vs. -1.1 (-1.72 to -0.39), adjusted difference -1.3 (-2.06 to -0.56) Modified Von Korff disability (0-100): -13.8 (-16.28 to -11.39) vs. -5.4 (-8.90 to -1.99), adjusted difference -8.4 (-12.32 to -4.47) Modified Von Korff pain (0-100): -13.4 (-15.96 to -10.77) vs. -6.4 (-9.66 to -3.14), adjusted difference -7.0 (-10.81 to -3.12) SF-12 Physical component score: 4.9 (4.00 to 5.84) vs. 0.8 (-0.52 to 2.11), adjusted difference 4.1 (2.63 to 5.62) SF-12 Mental component score: 0.9 (-0.10 to 1.90) vs. 0.7 (-0.75 to 2.20), adjusted difference 0.2 (-1.48 to 1.84) RDQ improved >=30%: NNT 7; RR 1.4 (1.1 to 1.8) Modified Von Korff disability improved >=30%: NNT 7; RR 1.2 (1.1 to 1.4) Modified Von Korff pain improved >=30%: NNT 7; RR (1.2 (1.1 to 1.3) Total health-care cost per person for LBP including intervention (mean): £421.52 vs. £224.65 Cost per person for study treatments: £187.00 vs. £16.32 Additional benefit in QALYs for CBT intervention: 0.099 Incremental cost per QALY: £1786.00 Probability of CBT intervention being cost effective: 90% at £3000

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Lamb 2010 and 2012	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Lamb 2010 and 2012	NR	A vs. B Withdrawal: 5% (24/468) vs. 6% (14/233) - Loss to followup at 12 months: 10% (45/468) vs. 9% (20/233) Withdrawal due to AEs: <1% (1/468) vs. <1% (1/233) Serious AEs: None reported Nonserious AEs: NR* * 2 subjects withdrew due to claim was hurt by physiotherapist or did not benefit: <1% (1/468) vs. <1% (1/233)

Author, Year	Funding Source	Quality	Comments
Lamb 2010 and 2012	National Institute for Health Research Health Technology Assessment Programme	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Lamb 2012 Extended followup of subjects from Lamb 2010			Randomized: 701 Analyzed: 395 Attrition: 44% (306/701)
Lambeek 2010a	The Netherlands 17 centers Outpatient	Patients aged 18-65 with low back pain for > 12 weeks, were in paid work for ≥ 8 hours per week, and were absent or partially absent from work. Exclude: Patients who had been absent from work for > 2 years, worked temporarily for an employment agency without detachment, specific low back pain due to infection, tumor, osteoporosis, rheumatoid arthritis, fracture, or inflammatory process, lumbar spine surgery within past 6 weeks or planned within 3 months, series psychiatric cardiovascular illness, pregnancy, current lawsuit against employer	Randomized: 134 Treated: 129 Analyzed: 117 Attrition: 13% (17/134)

Author, Year	Intervention, Comparator
Lamb 2012 Extended followup of subjects from Lamb 2010	
Lambeek 2010a	A: Multidisciplinary care (n=66): Intervention consisted of integrated care management by a clinical occupational physician, workplace intervention, and a graded activity program. The integrated care management lasted a maximum of 3 months and consisted of developing a treatment plan to aid the subject in returning to work. The workplace intervention lasted 9 weeks and consisted of an occupational therapist observing patient's in the workplace and developing solutions for work-based obstacles. The graded activity was a program of up to 26 sessions that consisted of teaching patients to manage pain during activity. B: Usual care (n=68): Patients received usual care from their medical specialist, occupational physician, general practitioner, and/or allied health professionals.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Lamb 2012 Extended followup of subjects from Lamb 2010		As above, plus: EuroQol-5 Dimensions (EQ-5D): -0.59 to 1 (lower scores indicate worsening health-related quality of life)	Mean 34 months
Lambeek 2010a	Age: 46 vs 47 Female: 44% vs 40% Demands of work: Physical: 64% vs 62% Mental: 36% vs 38% Absence from work: Partial: 52% vs 53% Full: 49% vs 47%Modified Modified RDQ (0-23): 14.7 (5.0) vs 15.0 (3.6) Pain (0-10 VAS): 5.7 (2.2) vs 6.3 (2.1)	RMDQ (0-24) Pain (0-10 VAS) Number of healthcare visits Medications for back pain Total costs	3 and 9 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Lamb 2012 Extended followup of subjects from Lamb 2010	A vs. B, mean change from baseline (95% CI) RDQ (0-24): -2.9 (-3.42 to -2.38) vs. -1.6 (-2.48 to -0.80), adjusted difference -1.3 (-2.26 to -0.27) Modified Von Korff disability (0-100): -16.7 (-19.43 to -13.93) vs. -11.2 (-15.59 vs. -6.86), adjusted difference -5.5 (-10.64 to -0.27) Modified Von Korff pain (0-100): -17.4 (-20.35 to -14.44) vs. -12.8 (-17.52 to -7.99), adjusted difference -4.6 (-10.28 to 1.00) EQ-5D: 0.07 (0.04 to 0.10) vs. 0.04 (-0.01 to 0.09), adjusted difference 0.03 (-0.03 to 0.08) >1 night in hospital: 2% vs. 4%, p=0.257 GP visit due to LBP: 38% vs. 43%, p=0.356 Missed work because of LBP: 9% vs. 13%, p=0.238 Decreased work hours because of LBP: 3% vs. 6%, p=0.378
Lambeek 2010a	A vs B <u>Baseline, mean (SD)</u> Modified RDQ (0-23): 14.7 (5.0) vs. 15.0 (3.6) Pain (0-10 VAS): 5.7 (2.2) vs. 6.3 (2.1) <u>3 months, mean improvement (SE)</u> Modified RDQ (0-23): 4.8 (0.9) vs 5.0 (0.9), adjusted difference 0.06, 95% CI -2.3 to 2.5 Pain (0-10 VAS): 1.3 (0.4) vs 2.3 (0.4), adjusted difference 0.5, 95% CI -0.6 to 1.6 <u>9 months, mean improvement (SE)</u> Modified RDQ (0-23): 7.2 (0.7) vs 4.4 (0.7), adjusted difference -2.9, 95% CI -4.9 to -0.9 Pain (0-10 VAS): 1.6 (0.4) vs 1.9 (0.4), adjusted difference 0.21, 95% CI -0.8 to 1.2 Medications for back pain (# of patients): 27 vs. 40 General practitioner visits (# of patients): 13 vs. 29 Medical specialist visits (# of patients): 13 vs. 29 Total costs (pounds): 13165 (SD 13600) vs. 18475 (SD 13616), mean difference -5310 (95% CI -10042 to -391)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Lamb 2012 Extended followup of subjects from Lamb 2010	NR
Lambeek 2010a	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Lamb 2012 Extended followup of subjects from Lamb 2010	NR	A vs. B Withdrawal: 40% (187/468) vs. 51% (119/233) Withdrawal due to AEs: NR Serious AEs: NR Nonserious AEs: NR
Lambeek 2010a		None

Author, Year	Funding Source	Quality	Comments
Lamb 2012 Extended followup of subjects from Lamb 2010	NR; Original trial funded by the National Institute for Health Research Health Technology Assessment Programme	Fair	
Lambeek 2010a	VU University Medical Center, TNO Work & Employment, Dutch Health Insurance Executive Council, Stitching Instituut GAK, the Netherlands Organisation for Health Research and Development, support from a grant given to the Work Disability Prevention Canadian Institutes of Health Research (FRN: 53909)	Fair	NOTE: Lambeek 2010b (economic evaluation) did not have any data that was includable *Number of visits was counted over a 12 month time period; starting from baseline, spanning through the 3 month treatment period, and up to the 9 month followup.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Lansdown 2009	York, UK GP practice	Inclusion criteria: ≥50 years old who had consulted their GP in the last 3 years with knee pain, using the READ codes of 'knee pain', 'knee joint pain', 'osteoarthritis-tis of the knee', 'anterior knee pain', 'other knee injury', 'painful right knee' and 'arthralgia'. Exclusion criteria: taking anticoagulants, intra articular steroid injection within 2 months, back pain with referred leg pain, ipsilateral hip OA, skin conditions around knee, RA or having had PT or acupuncture within last year	Randomized: 30 Treated: 29 Analyzed: 21 (ITT n=30) Attrition: 30% (9/30)* *Attrition A vs. B: 13% (2/15) vs. 47% (7/15)
Lansinger 2007	Sweden Multicenter (number of centers unclear) Outpatient	Aged 18-65 years old, non-specific neck pain for >3 months, VAS > 20mm on 0-100mm scale Exclude: Chronic tension-type headache, migraine, traumatic neck injuries, neurologic signs or symptoms, rheumatic diseases, fibromyalgia, physiologic or physical diseases, treatment with antidepressive and anti-inflammatory drugs	Randomized: 139 Treated: 122 Analyzed: 121* Attrition: 28% (39/139)

Author, Year	Intervention, Comparator
Lansdown 2009	A.Acupuncture (n=15): Usual care (below) plus acupuncture using an adapted protocol developed for the treatment of depression, focus on use of clinical judgement; treatment sessions varied in length and content - pragmatic design: mean number of acupoints, 12 (range 4-24); stainless steel needles with diameter 0.2-0.28mm, length 25-50mm, and depth of insertion 3-33mm; de qi was usually elicited; variety of stimulation methods used included tonification and reduction; retention time for needles, 10-30 minutes; auxiliary treatment included moxibustion (3/14, 21%) and acupressure massage (3/14, 21%); life style advice was offered to 11/14 (79%) patients; 1x/week for up to 10 weeks, with 10 max sessions in total; Compliance: 14 (93%) attended 136 appointments, 90% of 150 max; 12 (80%) attended all 10 available sessions. B.Usual care (n=15): any appointments, medications prescribed or over the counter) and interventions sought by participants from any health practitioner
Lansinger 2007	A.Qigong (n=72): 10-12 group sessions of 10-15 people done 1-2 times per week over 3 months. Sessions were 1 hour and consisted of information of the philosophy of medical qigong followed by exercises based on the Biyun method B.Exercise (n=67): 10-12 sessions 1-2 times per week over 3 months. Sessions were 1 hour and individualized to target 30%-70% of a person's maximal voluntary capacity, with exercises aiming to maintain/increase circulation, endurance, and strength. All patients: Ergonomic instructions and a pamphlet containing written information on neck pain

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Lansdown 2009	A vs B Age: 63 vs. 64 years Female: 60% vs. 60% Caucasian: 100% vs. 100% Duration of symptoms: NR WOMAC Total: 31 (15.7) vs. 57.5 (18.2) WOMAC Function: 20.5 (12.7) vs. 26.3 (14.0) WOMAC Pain: 7.3 (2.8) vs. 7.4 (3.7) OKS: 30.9 (9.3) vs. 30.6 (9.3) SF-36 physical functioning: 49.6 (26.6) vs. 48.3 (24.5) SF-36 social functioning: 71.8 (25.2) vs. 70 (23.5) SF-36 role physical: 62.5 (28.4) vs. 52.9 (25.4) SF-36 role mental: 76.7 (26.0) vs. 68.9 (35.6) SF-36 mental health: 76.3 (15.4) vs. 69.3 (18.7) SF-36 vitality: 55 (18.6) vs. 46.3 (24.0) SF-36 pain: 53.1 (18.7) vs. 51.3 (24.3) SF-36 general health: 67.3 (17.0) vs. 55.1 (19.0) EQ5D: 0.61 (0.24) vs. 0.67 (0.15)	WOMAC total (scale 0-96; higher score=worse disability) WOMAC function (scale 0-68; higher score=worse function) WOMAC pain (scale 0-20; higher score=worse pain) Oxford Knee Scale (OKS) (higher score=worse disability) SF-36 (higher score=better quality of life) EQ-5D (higher score=better quality of life)	9.5 months
Lansinger 2007	A vs B Age: 45 vs 43 Female: 73% vs 67% Duration of neck pain: 3 mos-1 year: 15% vs 20% >1 year: 38% vs 37% >5 years: 22% vs 24% >10 years: 25% vs 20% Neck frequency (days/wk), median (range): 7 (2.5-7) vs 7 (1-7) Physical activity: Slightly no exercise: 22% vs 31% Light exercise <4 hr/wk: 45% vs 34% Med to hard exercise 1-4 hrs/wk: 22% vs 29% Hard exercise ≥ 3 hrs/wk: 11% vs 6% Neck Disability Index, median (IQR): 26 (6-60) vs 22 (8-52) Neck pain VAS, median (IQR): 45 (2-100) vs 39 (3-76)	Neck Disability Index (0-100%, higher percent=higher disability) Neck pain VAS (0-100, higher score=higher pain)	6 and 12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Lansdown 2009	A vs. B (mean, SD) <u>9.5 months</u> WOMAC Total: 24.8 (17.1) vs. 25.6 (17.6); adjusted means 23.8 vs. 26.8, adjusted MD -2.94 (95% CI 9.5, -15.4), p=0.624 WOMAC Function: 17.4 (13.9) vs. 17.6 (12.6); adjusted means 16.8 vs. 18.2, adjusted MD -1.36 (95% CI 8.7, -11.4), p=0.778 WOMAC Pain: 4.7 (2.3) vs. 5.3 (3.9); adjusted means 4.4 vs. 5.8, adjusted MD -1.4 (95% CI 0.8, -3.6), p=0.200 OKS: 24.5 (7.5) vs. 28.1 (9); MD -3.6 (95% CI -9.8, 2.6), p=0.24 SF-36 physical functioning: 54.2 (29.5) vs. 55.6 (24.9); MD -1.4 (95% CI -21.8, 19.0), p=0.89 SF-36 social functioning: 81.3 (20.3) vs. 76.6 (20.5); MD 4.7 (95% CI -10.6, 20.0), p=0.53 SF-36 role physical: 71.4 (25.2) vs. 57.8 (27.9); MD 13.6 (95% CI -6.3, 33.5), p=0.17 SF-36 role mental: 79.2 (27.0) vs. 67.7 (18.6); MD 11.5 (95% CI -5.8, 28.8), p=0.19 SF-36 mental health: 73.1 (17.0) vs. 65.0 (19.1); MD 8.1 (95% CI -5.4, 21.6), p=0.23 SF-36 vitality: 58.2 (13.1) vs. 46.9 (17.4); MD 11.3 (95% CI -0.22, 22.8), p=0.05 SF-36 pain: 65.2 (22.3) vs. 65.9 (17.3); MD -0.7 (95% CI -15.6, 14.2), p=0.92 SF-36 general health: 67.7 (18.7) vs. 62.4 (4.2); MD 5.3 (95% CI -4.8, 15.4), p=0.29 EQ5D: 0.66 (0.24) vs. 0.63 (0.19); MD 0.03 (95% CI -0.13, 0.19), p=0.71
Lansinger 2007	

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Lansdown 2009	
Lansinger 2007	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Lansdown 2009		No major AEs reported; 7 minor AEs in acupuncture group (none led to a patient discontinuing treatment): bruising, 7% (1/14); faint, 7% (1/14); worsening of symptoms, 14% (2/14); forgotten needle, 7% (1/14); migraine, 7% (1/14); pain at needle site, 7% (1/14)
Lansinger 2007	A vs B <u>6 months</u> Neck Disability Index, median (range): 22 (0-64) vs 18 (0-56) Neck pain VAS, median (range): 26 (0-90) vs 23 (0-76) <u>12 months</u> Neck Disability Index, median (range): 22 (0-54) vs 18 (0-52) Neck pain VAS, median (range): 28 (0-86) vs 21 (0-86)	NR

Author, Year	Funding Source	Quality	Comments
Lansdown 2009	Medical Research Council	Poor	WOMAC total also include the WOMAC stiffness (scale 0-8) subscale which was not abstracted for the purposes of this report. Adjusted means and MD included baseline scores as covariate; done only for the WOMAC From methods: "All data were collected by post at baseline, and 1, 3 and 12 months post randomization"; if tx was 10 wks, then 1 month = half way through tx; 3 months = 2 wks post-tx; and 12 months = 9.5 months post-tx
Lansinger 2007	Vardal Foundation, the Ekhaga Foundation, the Development Council of Goteborg and Southern Bohuslan, the Swedish Association of Registered Physiotherapists: Minnesfonden, and Renne Eanders Hjalpfond	Poor	Outpatient the same as primary care? Outcomes not included: grip strenght (with validated measure) and ROM *Last value forward

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Larsson 2015	Sweden Number of centers unclear Type of center unclear	Women aged 20-65 with a FM diagnosis fulfilling ACR criteria Exclude: Blood pressure > 160/90 mmHg), knee or hip osteoarthritis confirmed radiologically and affecting activities of daily living , severe somatic or psychiatric disorders, other dominating causes of pain besides FM, alcohol use disorders identification test score > 6, participation in a rehabilitation program within the past year, regular resistance exercise or relaxation exercise two times a week or more, inability to refrain from NSAIDs or hypnotic drugs 48 hours before examinations	Randomized: 130 Treated: 93 Analyzed: 91 Attrition: 30% (39/130)*

Author, Year	Intervention, Comparator
Larsson 2015	A.Relaxation therapy (n=63): Two groups sessions of 5-8 subjects per week for 15 weeks. The intervention was preceded by an individual meeting covering instructions and allowing for adjustments to the intervention. The sessions lasted 25 minutes and consisted of autogenic training guided by physiotherapist and were followed by stretching. B.Resistance exercise (n=67): Two group sessions of 5-7 subjects per week for 15 weeks. The intervention was preceded by an individual meeting going over instructions on the intervention, testing, and modifications of specific exercises. Sessions were based on a resistance exercise program aiming to improve muscle strength, focusing on large muscle groups in the lower extremity.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Larsson 2015	A vs B Age: 52 vs 51 Female: 100% vs 100% Duration of symptoms, years: 9.4 vs 11.1 Medication use: Paracetamol: 70% vs 79% Opioids: 19% vs 19% Antidepressants: 38% vs 48% Anticonvulsants: 3% vs 6% Sedatives: 19% vs 16% Work status: 0%: 41% vs 43% 20-49%: 6% vs 3% 50%: 18% vs 19% 51-79%: 13% vs 12% 100%: 22% vs 22% Sick leave/disability pensions: 25%: 8% vs 13% 50%: 14% vs 24% 75%: 5% vs 3% 100%: 35% vs 31% FIQ: 61.1 (17.3) vs 60.5 (14.4) Pain VAS: 52.4 (18.3) vs 49.3 (23.9) PDI: 35.0 (12.5) vs 35.3 (12.2) SF-36 physical component score: 29.9 (8.1) vs 31.2 (7.9) SF-36 mental component score: 39.6 (12.1) vs 37.7 (12.2)	FIQ (0-100, higher score=lower function); pain VAS (0-100, higher score=worse pain); PDI (0-70, higher score=higher disability from pain); SF-36 physical component score (0-100, higher score=higher quality of life); SF-35 mental component score (0-100, higher score=higher quality of life); patient global impressions of change (1-7, higher score=higher improvement)	13-18 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Larsson 2015	

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Larsson 2015	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Larsson 2015	A vs B FIQ: 55.4 (17.0) vs 57.1 (19.4), (MD -1.7, 95% CI -9.3 to 5.9) p=0.65 Pain VAS: 52.1 (19.5) vs 49.2 (20.8), (MD 2.9, 95% CI -5.5 to 11.3) p=0.50 PDI: 33.7 (10.9) vs 33.0 (11.6), (MD 0.7, 95% CI -4.0 to 5.4) p=0.77 SF-36 physical component score: 32.0 (9.4) vs 32.2 (8.0), (MD -0.2, 95% CI -3.8 to 3.4) p=0.91 SF-36 mental component score: 40.0 (11.9) vs 39.2 (13.9), (MD 0.8, 95% CI -4.6 to 6.2) p=0.89 Patient global impression of change: Values NR but difference was NS	Withdrawal due to increased pain: 7% (5/67) vs 0% (0/63)

Author, Year	Funding Source	Quality	Comments
Larsson 2015	Swedish Rheumatism Association, the Swedish Research Council, the Health and Medical Care Executive Board of Vastra Gotaland Region, ALF-LUA at Sahlgrenska University Hospital, Stockholm County Council, the Norrbacka-Eugenia foundation, and Gothenburg Center for Person Centered Care	Poor	*For analysis, researchers stated that all participants were invited to post-treatment examination regardless of if they had participated in the intervention but only measured values were included in analyses of changes over time between the two groups. There were 17 patients in the exercise intervention and 20 patients in relaxation therapy that did discontinued after randomization. An additional 19 patients in the exercise intervention and 20 patients in the relaxation intervention were lost to followup. Results were presented with n values that indicated patients that discontinued after randomization were still included in analysis and only the values of patients that were lost to followup were not included. MDs and p values calculated using n=43 for the relaxation group and n=48 for the exercise group. P values given by study were calculated by dividing the mean difference between the post-treatment score and baseline score in the intervention group and in the control group by the pooled SD for difference and were not included in abstraction

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Lauche 2016	Germany Setting NR	≥18 years of age; chronic nonspecific neck pain ≥3 consecutive months ≥5 days/week; moderate pain (≥45 mm or higher on VAS 0-100 mm) Excluded: Neck pain caused by trauma, disc protrusion, whiplash, congenital deformity of the spine, spinal stenosis, neoplasm, inflammatory rheumatic disease, neurological disorder, active oncologic disease, severe affective disorder, addiction, and psychosis; pregnant; invasive treatment of the spine in previous 4 weeks or spinal surgery within previous year; initiated /modified drug regimen recently; taking opiates; regular practice of tai chi, Qi gong, or yoga in past 6 months	Randomized: 114 Treated: 104 Analyzed: 114* Attrition: 23% (26/114) *missing values completed via multiple imputation
Laufer 2005	Israel, single-site, outpatient	Inclusion Criteria: Patients age 65 and above; primary OA of one or both knee joints; grade 2-3 knee OA, based on the Kellgren- Lawrence classification, as evidenced by a radiograph and interpreted by a trained rheumatologist blind to treatment allocation; knee pain for at least three months; independent ambulation with or without an assistive device; no physiotherapy treatment for knee problems in the last month; no previous knee surgery or knee joint injection in the last three months; no change in medication in the last month; normal sensation for warmth in the knee region; no other orthopedic or neurological disease that could affect pain and/or disability; and no contraindication to SWD, particularly no presence of metal implants, pacemakers, joint effusion or malignancy. Exclusion Criteria: Anything not fitting inclusion criteria.	Randomized: 115 Treated: 103 Analyzed: 95 Attrition: 17.3% (20/115)

Author, Year	Intervention, Comparator
Lauche 2016	A.Tai chi (Yang style) (n=38) weekly 75-90-min session in a group format for 12 weeks; sessions included warm up, Tai Chi form practice, relaxation period. educational units, breathing exercises, and relaxation music; illustrated written movement sequences for home Tai chi ≥15 mins/day. B.Neck exercises (n=37) weekly 60- 75 min session in a group format for 12 weeks; ergonomic principles, proprioceptive exercises, and isometric and dynamic mobilization, stretching, strengthening neck and core exercises, and relaxation exercises; illustrated written exercises for home use ≥15mins/day. C.Wait list (n=39) continuing usual activities/therapies (Tai chi or neck exercises offered at end of study)
Laufer 2005	A.Low Intensity Pulsed Shortwave Diathermy (n=38) Shortwave diathermy was applied to affected knee(s). Treatments were administered with one of two Curapuls 670 machines (manufactured by Enraf-Nonius, Delft, The Netherlands). No. of Treatments: 3 per week for 3 weeks (9 total) Length of Treatments: 20 minutes each Pulse Duration: 82 µs Pulse Frequency: 110 Hz Peak Power: 200 W (mean 1.8W) Area: anterior aspect of the knee B.High Intensity Pulsed Shortwave Diathermy (n=32) Treatment protocol identical to Group A except with a higher intensity (pulse duration and frequency). Pulse Duration: 300 µs Pulse Frequency: 300 Hz Peak Power: 200 W (mean 18W) Area: anterior aspect of the knee C.Sham Shortwave Diathermy (n=33) Identical treatment except the apparatus was turned on but the power output was not raised.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Lauche 2016	A vs B vs C Age: 52 vs 47 vs 49 years Female: 74% vs 86% vs 82% ars Pain recently (0-100): 54.2 (20.5) vs 46.2 (19.2) vs 51.5 (21.1) Pain considered tolerable (0-100): 21.7 (14.5) vs 20.5 (11.7) vs 20.7 (12.1)	NDI (scale, 0-50) Disability in days (VAS) Everyday function (VAS) Recent pain intensity, pain considered tolerable, pain with motion VAS (scale, 0-100), higher score worse pain) SF-36 PCS, MCS HADS depression	3 months
Laufer 2005	A vs B vs. C Age: 75 vs. 73 vs. 73 Female: 82% vs. 90.6% vs. 67% Race: NR Mean Duration of Chronicity: NR Overall (WOMAC): 5.13(3.49) vs. 4.60(3.40) vs. 5.02(3.40) Pain (WOMAC): 4.89(3.30) vs. 4.43(3.35) vs. 4.97(3.52) Stiffness (WOMAC): 4.87(3.50) vs. 4.25(3.47) vs. 4.92(3.58) Activities of Daily Living (WOMAC): 5.16(3.52) vs. 4.69(3.41) vs. 5.05(3.45)	Primary: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, higher scores indicate greater pain, stiffness or functional limitation) Overall (WOMAC): Pain (WOMAC, range 0-10): Stiffness (WOMAC, range 0-10): Activities of Daily Living (WOMAC, range 0-10):	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Lauche 2016	A vs C <u>3 month outcomes</u> NDI (0-50): 24.3 (14.1) vs 29.4 (12.7), MD -6.6 (95% CI -11.6 to -1.6) Recent pain VAS (0-100): 35.0 (27.7) vs 44.6 (20.0), MD -10.6 (95% CI -20.9 to -0.3) Pain with motion VAS (0-100): 29.1 (19.0) vs 45.5 (19.7), MD -14.3 (95%CI -22.0 to -6.7) SF-36 PCS (0-100): MD 4.1 (95% CI 0.8 to 7.5) SF-36 MCS (0-100): MD 1.0 (95% CI -3.1 to 5.2) B vs C <u>3 month outcomes</u> NDI:25.1 (12.9) vs 29.4 (12.7), MD -4.3 (95% CI -10.2 to 1.6) Recent pain VAS (0-100): 33.1 (20.9) vs 44.6 (20.0), MD -11.5 (95% CI -20.8 to -2.2) Pain with motion VAS (0-100): 34.9 (14.4) vs 45.5 (19.7), MD -10.6 (95%CI -18.5 to -2.7) SF-36 PCS (0-100): MD 2.0 (95% CI -1.55 to 5.55) SF-36 MCS (0-100): MD 0.5 (95% CI -3.9 to 4.9)
Laufer 2005	<u>A vs. C</u> <u>3 months</u> Overall (WOMAC): 4.82(3.71) vs. 4.60(3.58); MD 0.22 (95% CI -1.51 to 1.95) p=0.801 Pain (WOMAC): 4.48(3.58) vs. 4.33(3.69); MD 0.15 (95% CI -1.57 to 1.87) p=0.863 Stiffness (WOMAC): 4.43(3.85) vs. 3.60(3.78); MD 0.83 (95% CI -0.98 to 2.64) p=0.364 Activities of Daily Living (WOMAC): 4.98(3.61) vs. 4.82(3.42); MD 0.16 (95% CI -1.51 to 1.83) p=0.849 <u>B vs. C</u> <u>3 months</u> Overall (WOMAC): 4.56(3.31) vs. 4.60(3.58); MD -0.04 (95% CI -1.75 to 1.67) p=0.963 Pain (WOMAC): 4.09(3.49) vs. 4.33(3.69); MD -0.24 (95% CI -2.02 to 1.54) p=0.788 Stiffness (WOMAC): 3.81(3.28) vs. 3.60(3.78); MD 0.21 (95% CI -1.55 to 1.97) p=0.812 Activities of Daily Living (WOMAC): 4.8(3.25) vs. 4.82(3.42); MD -0.02 (95% CI -1.67 to 1.63) p=0.981

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Lauche 2016	
Laufer 2005	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Lauche 2016	A vs B <u>3 month outcomes</u> NDI:24.3 (14.1) vs 25.1 (12.9), MD: -1.4 (-6.7 to 4.0) Recent pain VAS (0-100): 35.0 (27.7) vs 33.1 (20.9), MD -0.5 (95% CI -11.8 to 10.7) Pain with motion VAS (0-100): 29.1 (19.0) vs 34.9 (14.4), MD -5.6 (95%CI -13.0 to 1.8) SF-36 PCS (0-100): MD -1.6 (95% CI -4.8 to 8.0) SF-36 MCS (0-100): MD -0.3 (95% CI -12.0 to 12.6)	A vs B vs C Likely related to intervention Serious AEs: none Minor AEs: 4 vs 1 vs 0 A: Migraine attack (n=1); Achilles tendon pain (n=3) B. Knee pain (n=1) Total serious AEs to include those not related to intervention: 2 vs 4 vs 0 Total minor AEs: 8 vs 5 vs 0
Laufer 2005	NR	No adverse reactions to the treatment were reported by the subjects.

Author, Year	Funding Source	Quality	Comments
Lauche 2016	NR	Fair - Tai chi vs. wait list Poor - Tai chi vs. Exercise, Exercise vs. waitlist	
Laufer 2005	NR	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Li 2017	China Number of centers NR Type of center NR	Females aged 20-55, daily computer user with constantly or frequently occurring computer-related neck pain for > 1 year, worked on a computer ≥ 3 years, employed, motivated to continue working and rehabilitation, not been sick for >1 month in the last year, working ≥ 20 hours per week, neck pain in the previous 7 days, self-reported pain intesnity of ≥ 2 or 3-7 days on a 0-10 scale.	Randomized: 109 Treated: 109 Analyzed:102 Attrition: 6% (7/109)
Liang 2011	China Outpatient clinic of Guangdong Provincial Hospital of Chinese Medicine 2007-2009	18 to 60 years of age, neck and shoulder pain or stiffness, frequent attacks ≥1/month for ≥6 months, baseline pain between 3-7 points on 10-point VAS scale, no acupuncture within the last 6 months, willing to join the study and sign an informed consent document. Excluded: Received acupuncture due to neck pain in the past 6 months, were unwilling to following the study protocol for treatment or to provide informed consent, cervical or thoracic vertebral trauma, surgery on the neck, neurological disorder, skeletal disorder, fear of acupuncture treatment, pregnant or breast feeding, severe medical disease or cancer.	Randomized: 190 Treated: 183 Analyzed: 178 Attrition: 6% (12/190)
Licciardone 2013	United States Single center	21 to 69 years of age, nonpregnant, low back pain >3 months. Exclude: Cancer, spinal osteomyelitis, spinal fracture, herniated disc, ankylosing spondylitis, cauda equina syndrome, low back surgery in last year, workers' compensation benefits in the last 3 months, ongoing litigation involving back problems, angina or congestive heart failure symptoms with minimal activity, history of stroke or transient ischemic attack in past year, implanted biomedical devices, bleeding or infection in the lower back, corticosteroids in the last month, use of manual treatment of ultrasound in the last 3 months or more than 3 times in the past year, no signs of radiculopathy.	Randomized: 455 Analyzed: 455 Attrition: 7.4% (9.4% vs. 5.9%) at 12 weeks

Author, Year	Intervention, Comparator
Li 2017	A. Progressive resistance training (n=38). At least 3 sessions per week for six weeks. Sessions consisted of four cervical isometric neck resistance exercises, with each exercise repeated 8-12 times. Resistance progressively increased every 2 weeks, starting at 30% of maximal strength and increased to 70%. B. Fixed resistance training (n=35) At least 3 sessions per week for six weeks. Sessions consisted of four cervical isometric neck resistance exercises, with each exercise repeated 8-12 times.Resistnace was fixed at 70% of the participants maximal strength. C. Attention control (n=36). Subjected received information and had weekly discussions about workplace ergonomics, stress management, relaxation, meditation, and diet.
Liang 2011	A. Active acupuncture, traditional Chinese (n=88) 3x/week for 3 weeks (9 treatments total) lasting 20 minutes at the following points: bilateral DU14, SI15 and Ex-HN15. Needles inserted to a depth of 20mm and manipulated until numbness or other acupuncture sensation was felt. B. Sham acupuncture (n=90) for 3x/week for 3 weeks (9 treatments total) lasting 20 minutes 1 cm lateral to the points in treatment A. Needles inserted to a depth of 3 mm without any manipulation. Both groups received infrared irradiation in the cervical area.
Licciardone 2013	A.Ultrasound 1.2 W/cm ^{2} at 1 MHz; six 10 minute treatments over 8 weeks (n=233) B. Sham ultrasound, at 0.1 W/cm ^{2}, treatment otherwise identical to A (n=222) Factorial design, patients also randomized to osteopathic manual treatment vs. sham treatment; no interaction between treatments

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Li 2017	A vs B vs C Age: 36 vs 34 vs 34 BMI: 21 vs 22 vs 22 Years working: 9 vs 9 vs 10 Pain duration (years): 3 vs 4 vs 4 Work (days/week): 5 vs 6 vs 5 Computer use (hours/day): 7 vs 8 vs 7 NDI: 28.3 (6.3) vs 28.9 (6.7) vs 27.8 (6.5) Pain VAS: 5.3 (1.3) vs 5.4 (1.1) vs 5.2 (1.2)	NDI (0 to 100, higher score=greater disability), pain VAS (0-10, higher score=higher pain)	1.5 months
Liang 2011	A vs B Age: 37 vs 37 years Female: 72% vs. 73% ≥5 pain attacks per month: 58% vs 62% NPQ (0-100%): 32.7 (12.5) vs 33.0 (10.6) Pain (0-10): 5.3 (1.9) vs 5.5 (1.6) SF-36 physical functioning: 80.8 (14.8) vs 79.2 (19.1) SF-36 mental: 63.5 (15.4) vs 59.5 (14.4)	Northwick Park Neck pain Questionnaire (NPNQ) (scale: 0-100%, higher percentage the greater the disability) Pain intensity (scale, 0-10, higher score=greater pain) Short-Form 36 (SF-36) (scale 0-100, higher score=better QoL)	1 and 3 month
Licciardone 2013	A vs. B Median age: 38 vs. 43 years 58% vs. 68% female Race: Not reported Pain (median, 0-100 VAS): 44 vs. 44 RDQ (median, 0-24): 5 vs. 5 SF-36 general health (median, 0-100): 72 vs. 67 Duration of LBP >1 year: 51% vs. 49%	RDQ (median, 0-24) SF-36 general health % improvement in pain Lost days of work Very satisfied with back care	1 month

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Li 2017	A vs C 1.5 month NDI: 14.9 (4.9) vs 26.6 (5.4), p<0.05 Pain VAS: 1.9 (0.9) vs 5.1 (1.0), p<0.05 B vs C 1.5 month NDI: 15.8 (4.8) vs 26.6 (5.4), p<0.05 Pain VAS: 2.5 (0.9) vs 5.1 (1.0), p NR
Liang 2011	A vs B 3 months NPNQ: 19.1 (9.9) vs 25.5 (13.7), MD -6.4 (95% CI -9.9 to -2.9), p<0.001 Pain (0-10): 2.9 (1.7) vs 3.2 (1.3), MD -0.3 (95% CI -0.75 to 0.15), p=0.187 SF-36 physical functioning: 84.3 (15.2) vs 85.9 (14.0), p=0.447 SF-36 mental: 67.1 (10.0) vs 61.6 (10.7), p=0.001
Licciardone 2013	A vs. B, median (IQR) Baseline RDQ (0-24): 5 (3-10) vs. 5 (3-9) SF-36 general health (0-100): 72 (56-85) vs. 67 (52-82) 1 month RDQ (0-24): 3 (1-7) vs. 3 (1-7), p=0.93 SF-36 general health (0-100): 72 (52-87) vs. 74 (54-87) ≥50% improvement in pain: RR 1.09 (95% CI 0.88 to 1.35) Lost 1 or more days work in past 4 weeks because of low back pain: 13% vs. 6%; p=0.11 Very satisfied with back care: 55% vs. 55%; p=0.99 Prescription drug use for LBP: 16% vs. 18%, p=0.54 2 months RDQ (0-24): 3 (1-8) vs. 4 (1-7); p=0.76 SF-36 general health (0-100): 72 (54-85) 72 (57-85); p=0.53 ≥50% improvement in pain: RR 1.09 (95% CI 0.88 to 1.35) 3 months RDQ (0-24): 3 (1-7) vs. 3 (1-7) p=0.93 SF-36 general health (0-100): 72 (52-87) vs. 74 (54-87); p=0.66

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Li 2017	NR
Liang 2011	
Licciardone 2013	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Li 2017	NR	"Very few participants complained about the arm or shoulder pain when stretching the thera-bands. No other side effects were heard in the process of training."
Liang 2011		Fainting: n=3 vs n=4 Feeling numb and aching on treated points: n=4 vs n=2 Bleeding: Occurred, but frequency NR
Licciardone 2013	NR	A vs. B Withdrawal due to adverse event: Not reported Any adverse event: 6.0% (14/233) vs. 5.9% (13/222), RR 1.03 (95% CI 0.49 to 2.13) Serious adverse event: 1.3% (3/233) vs. 2.7% (6/222), RR 0.48 (95% CI 0.12 to 1.88)

Author, Year	Funding Source	Quality	Comments
Li 2017	Grant of National Science Foundation of China (81171469 and 81671088)	Fair	Reducion in pain VAS ≥2 was considered a clinically important difference. ANOVA used Least significant difference tests p values reported for outcome measurements, are
Liang 2011	State Ministry of Science and Technology (No. 2006BAI12B04-1) and the Scientific Project supported by Guangdong Provincial Administration of Science and Technology (No. 2006B50107006)	Fair	
Licciardone 2013	National Institutes of Health- National Center for Complementary and Alternative Medicine and the Osteopathic Heritage Foundation	Good	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Little 2008	UK Number of centers: 2 Outpatient	Age 18-65 Primary care visit for low back pain more than three months previously RDQ score ≥4 Current pain for ≥3 weeks Exclude: Previous experience with Alexander technique Clinical indicators of serious spinal disease Current nerve root pain History of psychosis or major alcohol misuse Perceived inability to walk 100 meters	Randomized: 579 Treated: 579 Analyzed: 469
Lund 2008	Denmark, Outpatient General Praction	Inclusion: OA criteria according to The American College of Rheumatology , C-reactive protein within the reference range, and a negative rheumatoid factor. Exclusion: hydrophobia, incontinence, wounds, language or intellectual problems, a history of periarticular knee fracture, total knee replacement, inflammatory joint disease, heart or lung condition and other medical diseases with possible contra-indication of exercise and/or pool therapy, present participation in other clinical or exercise trials, and secondary knee OA.	Randomized: 79 Treated: 71 Analyzed: 70 Attrition: 11% (9/79)

Author, Year	Intervention, Comparator
Little 2008	A: Mixed massage (n=72): Swedish Massage, soft tissue release, and passive and active stretching techniques, one session a week for 6 weeks B: Alexander technique (6 lessons) (n=75) C: Alexander technique (24 lessons) (n=73) D: Exercise (n=72): Exercise prescription at initial visit with target of 30 minutes of regular exercise 5 times per week, up to 3 followup 15-20 minute appointments with practice nurse E: Exercise + massage (n=72) F: Exercise + Alexander technique (6 lessons) (n=71) G: Exercise + Alexander technique (24 lessons) (n=71) H: Normal care (n=72)
Lund 2008	A.Aquatic Exercise (n=27): 2x per week for 8 weeks. warm-up, strengthening/endurance exercise, balance exercise and stretching exercise. Each session lasted 50 min, comprising 10 min warm-up, 20 min resistance exercises, 10 min balance and stabilizing exercises, 5 min lower limb stretches and 5 min cool-down period. Compliance was 92%. B.Land-based Exercise (n=25): 2x per week for 8 weeks. warm-up, strengthening/endurance exercise, balance exercise and stretching exercise. Each session lasted 50 min, comprising 10 min warm-up, 20 min resistance exercises, 10 min balance and stabilizing exercises, 5 min lower limb stretches and 5 min cool-down period. Compliance was 85%. C.Control (n=27): No exercise All 3 groups were asked to continue any other treatment as usual.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Little 2008	Baseline characteristics presented groups of study arms: Controls (H+D) vs. Massage (A+E) vs. Alexander 6 lessons (B+F) vs. Alexander 24 lessons (C+G) Age: 46 vs. 46 vs. 45 vs. 45 Female: 73% vs. 78% vs. 63% vs. 64% Median number of days in pain in past 4 months: 24.5 vs. 28 vs. 28 vs. 28 Baseline Deyo troublesomeness: 3.3-3.4 Baseline RDQ (0-24): 10.8-11.3	Primary outcomes: Disability: RDQ Number of days in pain during the past four weeks Secondary outcomes: Quality of life: SF-36, higher score=better outcome Back pain and disability: VonKorff scale and Deyo "troublesomeness" scale, higher number = worse outcome Back Health Scale: developed by study to measure enablement, 0 (worst) to 7 (best)	10.5 months
Lund 2008	A vs B vs C Age: 65 vs 68 vs 70 years Female: 83% vs 88% vs 66% Duration of OA (median years): 8.5 vs 7.8 vs 4.5 Pain at rest (VAS): 29.8 (23.5) vs 23.3 (18.8) vs 15.5 (20.1) Pain during walking (VAS): 59.8 (18.4) vs. 53.0 (32.6) vs. 48.5 (31.9) KOOS symptom: 50.5 (13.6) vs. 50.9 (12.7) vs. 50.1 (13.6) KOOS pain: 47.1 (15.2) vs. 41.0 (14.8) vs. 37.9 (15.0) KOOS ADL: 44.7 (18.1) vs. 40.6 (13.6) vs. 39.6 (13.2) KOOS Sport: 79.1 (18.4) vs. 75.6 (20.3) vs. 70.0 (22.8) KOOS Quality of Life: 63.7 (11.8) vs 57.0 (12.4) vs 60.8 (13.1)	Pain at rest and during walking with Visual Analog Scale (Scale 0-100, higher is worse pain) Knee Injury and Osteoarthritis Outcome Score questionnaire (KOOS) (Scale 0-100, higher is better symptoms and function)	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Little 2008	A vs. H, mean (SD) <u>Baseline</u> Not reported by randomization group <u>10.5 months</u> RDQ (0-24): NR vs. 9.23 (5.3), difference -0.45 (95% CI -2.3 to 1.39) Number of back pain days in past 4 weeks (median): NR vs. 24 (95% CI 14 to 28), difference -8 (95% CI -20 to 4) SF-36 Physical Component Score (0-100): NR vs. 56.1 (18.6), difference -1.45 (95% CI -9.04 to 6.15) SF-36 Mental Component Score (0-100): NR vs. 64.8 (17.5), difference -2.11 (95% CI -9.37 to 5.16) Von Korff overall (0-10): NR vs. 4.19, difference 0.31 (95% CI -0.52 to 1.14) Von Korff disability (0-10): NR vs. 3.32 (2.25), difference 0.46 (95% CI -0.43 to 1.35) Von Korff pain (0-10): NR vs. 4.74 (2.20), difference 0.29 (95% CI -0.58 to 1.16) Deyo troublesomeness scale (1-5): NR vs. 3.05 (0.80), difference 0.04 (-0.25 to 0.33)
Lund 2008	A vs C 3 months (ITT analysis) KOOS symptom (mean, standard error): 64.1 (2.5) vs. 63.7 (2.5); MD 0.5 (95% CI -6.6, 7.6) KOOS ADL (mean, standard error): 63.0 (2.6) vs. 61.4 (2.6); MD 1.6 (95% CI -5.7, 8.9) KOOS sport (mean, standard error): 24.2 (3.5) vs. 23.5 (3.5); MD 0.7 (95% CI -9.3, 10.7) KOOS quality of life (mean, standard error): 42.8 (2.4) vs. 41.4 (2.4); MD 1.7 (95% CI -5.4, 8.2) KOOS pain (mean, standard error): 60.7 (2.6) vs. 62.6 (2.5); MD -1.5 (95% CI -8.7, 5.8) VAS pain at rest (mean, standard error): 18.1 (2.7) vs. 23.8 (2.7); MD -5.7 (95% CI -13.3, 2.0) VAS pain walking (mean, standard error): 52.9 (3.8) vs. 58.3 (3.5); MD -5.4 (95% CI -16.2, 5.4) B vs C 3 months (ITT analysis) KOOS symptom (mean, standard error): 66.1 (2.6) vs. 63.7 (2.5); MD 2.4 (95% CI -4.8, 9.5) KOOS ADL (mean, standard error): 63.9 (2.7) vs. 61.4 (2.6); MD 2.5 (95% CI -5.0, 9.9) KOOS sport (mean, standard error): 31.6 (3.6) vs. 23.5 (3.5); MD 8.1 (95% CI -2.0, 18.2) KOOS quality of life (mean, standard error): 43.1 (2.5) vs. 41.4 (2.4); MD 1.7 (95% CI -5.3, 8.7) KOOS pain (mean, standard error): 62.0 (2.6) vs. 62.6 (2.5); MD -0.3 (95% CI -7.5, 7.0) VAS pain at rest (mean, standard error): 15.6 (2.8) vs. 23.8 (2.7); **MD -8.1 (95% CI -15.8, -0.4), p=0.039** VAS pain walking (mean, standard error): 50.1 (4.0) vs. 58.3 (3.5); MD -8.2 (95% CI -19.7, 2.7)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Little 2008	NR
Lund 2008	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Little 2008	A vs. D, mean improvement versus usual care (95% CI) 10.5 months RDQ: -0.45 (-2.3 to 1.39) vs. -1.65 (-3.62 to 0.31) Number of back pain days in past 4 weeks (median): -8 (-20 to 4) vs. -11 (-23 to -1) SF-36 Physical Component Score: -1.45 (-9.04 to 6.15) vs. -2.08 (-10.6 to 6.40) SF-36 Mental Component Score: -2.11 (-9.37 to 5.16) vs. 0.72 (-7.38 to 8.81) Von Korff overall: 0.31 (-0.52 to 1.14) vs. -0.19 (-1.09 to 0.72) Von Korff disability: 0.46 (-0.43 to 1.35) vs. 0.05 (-0.92 to 1.02) Von Korff pain: 0.29 (-0.58 to 1.16) vs. -0.31 (-1.26 to 0.63) Deyo troublesomeness scale: 0.04 (-0.25 to 0.33) vs. -0.21 (-0.52 to 0.09)	Increased back pain: 0.7% (1/147) in massage group vs. 0 in all other groups
Lund 2008	NR	A vs B vs C Withdrawals 4% (1/27) vs. 20% (5/25) vs. 7% (2/27) A vs C: RR 0.5 (95% CI 0.05, 5.2) B vs C: RR 2.5 (95% CI 0.6, 12.7) Increased pain during and after exercise: 11% (3/27) vs. 32% (8/25) vs. NR Swollen knees: 0% (0/27) vs. 12% (3/25) vs. NR Withdrawals due to adverse events: 0% (0/27) vs. 12% (3/25) vs. NR

Author, Year	Funding Source	Quality	Comments
Little 2008	Medical Research Council	Fair	
Lund 2008	The Oak foundation, The Research Foundation of the Danish Physiotherapy Association, The Danish Rheumatism Association, The Spies Foundation and H:S Central Research Fund.	Fair	Also report a Completers analysis in Table IV

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Lynch 2012	Canada 1 center Outpatient	Diagnosis of FM fulfilling 1990 ACR criteria, bilateral and widespread pain above and below the waist and axial skeletal pain for at least 3 months, at least 11 of 18 tender points, stable medications for at least 14 days prior, average 7 day pain score of at least 4 on an 11-point NRS Exclude: Already practicing qigong, significant medical disorder that would compromise participant safety	Randomized: 100 Treated: 100 Analyzed: 88 Attrition: 12% (12/100)

Author, Year	Intervention, Comparator
Lynch 2012	A.Qigong (n=53): 1 group session per week for 8 weeks in addition to instructions for subjects to practice qigong daily at home for 45 to 60 minutes. Sessions used Chaoyi Fanhuan Qigong. B.Waitlist (n=47): Subjects continued with their usual care

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Lynch 2012	A vs B Age: 53 vs 52 Female: 94% vs 98% Duration of FM, years: 9.7 vs 9.6 Pain condition comorbidities: Headache: 59% vs 57% Orofacial pain: 43% vs 70% Osteoarthritis: 42% vs 36% Rheumatoid arthritis: 9% vs 9% Other: 30% vs 28% Previous opioid treatment: 42% vs 30% Medication use: Anticonvulsants: 25% vs 30% Antidepressants: 38% vs 32% NSAIDs: 49% vs 57% Opioids: 36% vs 23% Other: 55% vs 60% FIQ: 65.5 (14.4) vs 61.8 (13.4) Pain intensity NRS: 6.5 (1.5) vs 6.6 (1.1) SF-36 physical component score: 30.0 (8.3) vs 32.6 (8.8) SF-36 mental component score: 38.1 (9.6) vs 40.4 (10.1) PSQI: 13.8 (3.0) vs 13.1 (3.8)	FIQ (0-100, higher score=more severe symptoms); pain intensity NRS (0-10, higher score=higher pain); SF-36 physical component score (0-100, higher score=higher quality of life); SF-36 mental component score (0-100, higher score=higher quality of life); PSQI (0-21, higher scores=worse sleep quality)	2 and 4 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Lynch 2012	A vs B <u>4 months</u> FIQ mean Δ from baseline, mean Δ (SD): -16.1 (21.4) vs -4.8 (16.1), (MD -11.3, 95% CI -19.3 to -3.3) p=0.007 Pain intensity NRS mean Δ from baseline, mean Δ (SD): -1.2 (2.1) vs -0.3 (1.6), (MD -0.9, 95% CI -1.7 to -0.1) p=0.02 SF-36 physical component score mean Δ from baseline, mean Δ (SD):4.6 (7.9) vs 0.2 (5.5), (MD 4.4, 95% CI 1.5 to 7.3) p=0.004 SF-36 mental component score mean Δ from baseline, mean Δ (SD): 4.4 (10.1) vs 0.7 (8.7) (MD 3.7, 95% CI -0.3 to 7.7) p=0.07 PSQI mean Δ from baseline, mean Δ (SD): -3.3 (3.4) vs -1.1 (3.3), (MD -2.2, 95% CI -3.6 to -0.8) p=0.003

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Lynch 2012	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Lynch 2012		A vs B Treatment related pain: 2% (1/53) vs 0% (0/47) Plantar fasciitis: 2% (1/53) vs 0% (0/47)

Author, Year	Funding Source	Quality	Comments
Lynch 2012	Pfizer Neuropathic Pain Research Award	Fair	Majority of patients had tried previous treatments including anticonvulsants, antidepressants, nerve blocks/injections, NSAIDs, acupuncture, chiropractic, naturopath/homeopath/osteopath, massage therapy, physiological therapies, psychological therapies MDs were calculated, p values were given by the study. N's used for calculations were n=43 for qigong group and n=45 for wait list group.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
MacPherson 2015	England General Practice	Neck pain lasting ≥3 months and a score of at ≥28% on the Northwick Park Questionnaire (NPQ) for neck pain and associated disability. Excluded: serious underlying pathology, prior cervical spine surgery, psychosis, rheumatoid arthritis, ankylosing spondylitis, osteoporosis, hemophilia, cancer, HIV or hepatitis, current or recent alcohol or drug dependency, compensation or litigation pending, unable to communicate in English, participation in another clinical trial that might interfere with the current study, currently receiving acupuncture for neck pain, attendance at 1-to-1 alexander technique lessons in the past 2 years.	Randomized: 517 Treated: 483 Analyzed: 439 Attrition:15% (78/517)

Author, Year	Intervention, Comparator
MacPherson 2015	A.Needle acupuncture (n=173) at various points, most common (of 259 different points): GB-20, GB-21, LI-4, LIV-3, BL-10, SP-6, and SI-3. Twelve 50 minute session (600 minutes total) plus usual care, once per week initially and once every 2 weeks later. B.Alexander Technique group (n=172): up to 20 one-to-one lessons of 30 minutes' duration (600 minutes total) plus usual care, delivered weekly, with the option of being delivered twice per week initially and every 2 weeks later. C.Usual care (n=171): general and neck pain–specific treatments routinely provided to primary care patients, such as prescribed medications and visits to physical therapists and other health care professionals. All intervention sessions were intended to be delivered within 5 months

Author, Year	Study Participants	Outcome Measures	Duration of Followup
MacPherson 2015	A vs B vs C Age: 52 vs 54 vs 54 years Female: 69% vs 70% vs 69% White: 93% vs 89% vs 89% Employed: 61% vs 59% vs 62% Pain duration (median): 60 vs 60 vs 96 months) NPQ (39.64 (9.71) vs 39.38 (11.91) vs 40.46 (11.60) SF12v2 (n=172 vs 169 vs 169): physical: 39.99 (9.83) vs 39.87 (9.75) vs 40.98 (9.49) mental: 45.07 (11.00) vs 45.63 (12.22) vs 46.59 (10.87)	Northwick Park Neck pain Questionnaire (NPQ) (scale: 0-100%, higher percentage the greater the disability) Short-Form 12v2 (SF-12v2) (scale 0-100, higher score=better QoL)	1 and 7 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
MacPherson 2015	A vs C <u>1 month</u> NPQ* 35.35 vs 40.90, diff: -5.56 (95% CI, -8.33 to -2.78), p=0.001 SF-12v2 physical: data NR, no significant diff SF-12v2 mental: data NR, no significant diff <u>7 months</u> NPQ* 37.07 vs 40.99, diff:-3.92 (95% CI, -6.87 to -0.97), p=0.009 NPQ†: 26.76 vs 31.23 (diff, -4.05; 95%CI -6.70 to -1.41), p=0.004 SF-12v2 physical: 0.68 (95% CI, 1.08 to 2.44), p=0.44 SF-12v2 mental: 1.76 (955 CI, 0.15 to 3.37), p=0.033 B vs C <u>1 month</u> NPQ* 32.65 vs 37.64, diff: -4.98 (95% CI, -7.72 to -2.25), p<0.001 SF-12v2 physical: data NR, no significant diff SF-12v2 mental: data NR, no significant diff <u>7 months</u> NPQ*: 33.39 vs 37.18, diff -3.79 (95% CI, -6.66 to -0.91), p=0.010 NPQ†: 27.14 (15.87) vs 31.23 (14.86) (diff, -3.81; 95%CI -7.24 to -0.39), p=0.030 SF-12v2 physical 0.38 (95% CI, -1..54 to 2.30), p=0.69 SF-12v2 mental: 2.12 (95% CI, 0.42 to 3.82), p=0.016 *primary analysis with baseline score as outcome, repeated measures, n=173 A, vs n=172 B, vs 171 C †secondary analysis with baseline score as covariate, n=150 A vs n=145 B vs n=144 C

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
MacPherson 2015	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
MacPherson 2015		A: Serious AEs: 0/173 (0.0%) Non-serious AEs: 10/173 (5.8%) Bruising, swelling or numbness: 1/173 (0.6%) Muscle spasm: 1/173 (0.6%) Pain: 7/173 (4.0%) Respiratory problems 1/173 (0.6%) B: Serious AEs: 1/172 (0.6%) Pain & incapacity: 1/172 (0.6%) Non-serious AEs: 2/173 (1.2%) Injury at knee: 1/172 (0.6%) Muscle spasm: 1/172 (0.6%) C: Serious AEs: 2/172 (1.2%) Complications after surgery: 1/172 (0.6%) Pain & incapacity: 1/172 (0.6%) Non-serious AEs:0/172 (0.0%)

Author, Year	Funding Source	Quality	Comments
MacPherson 2015	Arthritis Research, UK	Fair	Data are adjusted values with sensitivity analyses. Not sure what to use for meta-analysis.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Mannerkorpi 2009	Sweden Number of centers unclear Primary care centers	Females aged 18-60 years with FM or chronic widespread pain Exclude: Severe somatic or psychiatric disorders, allergy to chlorine, ongoing exercise therapy supervised by a physical therapist or plans to start exercise therapy during study period	Randomized: 166 Treated: 152 Analyzed: 125 Attrition: 25% (41/166)

Author, Year	Intervention, Comparator
Mannerkorpi 2009	A.Exercise and education (n=81 randomized, 75 treated, 63 analyzed): One 45 minute pool exercise session per week for 20 weeks. Sessions w consisted of stretching and aerobic exercises. All patients also attended six 1 hour sessions conducted weekly that introduced strategies to cope with FM symptoms. At each sessions, patients developed a plan for physical activity for the following week and performed a short relaxation exercise. 58% of participants assigned to the program were defined as active participants. B.Education control (n=85 randomized, 77 received allocated intervention, 62 analyzed): six 1 hour sessions conducted weekly that introduced strategies to cope with FM symptoms. At each sessions, patients developed a plan for physical activity for the following week and performed a short relaxation exercise. 66% of participants assigned to the program were defined as active participants.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Mannerkorpi 2009	A vs B Age: 45 vs 47 Female: 100% vs 100% Employment: Not working: 55% vs 62% Working part-time: 35% vs 27% Working full-time: 10% vs 11% FIQ: 61.6 (16.42) vs 66.6 (15.3) FIQ pain subscale: 67.7 (16.8) vs 70.4 (20.1) HADS depression scale: 6.4 (4.0) vs 7.8 (3.6) HADS anxiety scale: 8.1 (5.5) vs 9.1 (4.8) SF-36 physical component score: 30.8 (8.1) vs 29.4 (8.0) SF-36 mental component score: 40.9 (13.8) vs 36.6 (12.3) SF-36 physical functioning: 56.6 (19.0) vs 50.9 (18.3) SF-36 role-physical: 22.8 (32.2) vs 15.2 (26.0) SF-36 bodily pain: 28.6 (14.3) vs 25.7 (16.1) SF-36 vitality: 28.4 (21.1) vs 24.2 (16.7)	FIQ (0-100, higher score=higher disability); FIQ pain subscale (0-100, higher score=higher pain); HADS depression subscale (0-21, higher score=higher symptoms of depression); HADS anxiety subscale (0-21, higher score=higher symptoms of anxiety); SF-36 physical component score (0-100, higher score=higher quality of life); SF-36 mental component score (higher score=higher quality of life)	6-7 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Mannerkorpi 2009	A vs B FIQ, mean change from baseline (SD): -3.9 (15.5) vs -4.5 (14.3), p=0.04 FIQ pain subscale, mean change from baseline (SD): -6.5 (23.7) vs -2.5 (19.9), p=0.018 HADS depression scale, mean change from baseline (SD): -0.4 (3.3) vs 0.0 (3.2), p=0.99 HADS anxiety scale, mean change from baseline (SD): -0.7 (3.3) vs 0.4 (3.8), p=0.15 SF-36 physical component score, mean change from baseline (SD): 2.9 (8.6) vs 1.3 (7.9) , p=0.13 SF-36 mental component score, mean change from baseline (SD): 0.5 (13.9) vs 1.3 (11.3), p=0.15 SF-36 physical functioning, mean change from baseline (SD): 2.2 (14.5) vs 1.3 (16.9), p=070 SF-36 role-physical, mean change from baseline (SD): 12.1 (40.7) vs 9.3 (43.6), p = 0.72 SF-36 bodily pain, mean change from baseline (SD): 5.0 (21.1) vs 3.6 (18.2), p = 0.24

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Mannerkorpi 2009	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Mannerkorpi 2009		NR

Author, Year	Funding Source	Quality	Comments
Mannerkorpi 2009	The Swedish Research Council, The Health and Medical Care Executive Board of Vastra Gotaland Region, The Länsförsäkringsbolagens Research Foundation, The Rheumatic Pain Society in Goteborg/RiG, The Goteborg Region Foundation for Rheumatology Research/GSFR and ALF at Sahlgrenska University Hospital	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Martin 2006	United States, Single-Site	Inclusion Criteria: Confirmed diagnosis of Fibromyalgia Exclusion Criteria: Patients with prior experience of acupuncture or a bleeding diathesis, cognitive ability to read consent form and complete survey instruments, and within geographic range that allowed for participation in treatment over 3-week period.	Randomized: 50 Treated: 50 Analyzed: 49 Attrition: 2% (1/50)

Author, Year	Intervention, Comparator
Martin 2006	A.Acupuncture (n=25) No. of Treatments: 6 treatments over 2 to 3 weeks Length of Treatments: NR Acupoints: Standardized for all patients, bilateral points at LI-4, ST-36, LR-2, SP-6, P-6, HT-7 Electrical Stimulation at 2 Hz for LI-4 and ST-36, and 10Hz at axial points along the bladder meridian No. of Needles: 18 needles (first 3 sessions) or 20 (final 3 sessions) B.Sham Acupuncture (n=24) Procedure protocol was identical but with sham needles. Patients were positioned so they could not see the treatments.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Martin 2006	A vs B Age: 48 vs. 52 years; p=.30 Female: 100% vs. 96% Race: 96% vs. 100% white Mean Duration of Chronicity: NR Total (FIQ, 0-80): 42.4 (11.0) vs. 44.0 (9.8) Physical Function (FIQ): 4.1(2.4) vs 3.6(2.5) Well-Being (FIQ): 3.3(2.7) vs. 2.7(2.0) Pain (FIQ): 6.2(2.2) vs. 6.5(1.8) Fatigue (FIQ): 7.6(2.1) vs. 7.6(1.8) Sleep (FIQ): 6.9(2.1) vs. 7.3(2.4) Stiffness (FIQ): 7.2(1.9) vs. 6.8(2.0) Anxiety (FIQ): 4.2(2.9) vs. 5.5(2.2) Depression (FIQ): 2.9(3.0) vs. 4.0(3.1) Pain Severity (MPI): 40.4 (10.3) vs. 43.0(7.7) Interference (MPI): 42.6(11.5) vs. 36.9(11.7) Life Control (MPI): 51.4(5.4) vs. 49.5(7.3) Affective Distress (MPI): 42.6(7.7) vs. 46.1(8.1) General Activity Level (MPI): 55.7(8.1) vs. 56.6(8.2)	Fibromyalgia Impact Questionnaire (FIQ, range 0-80: higher scores represent severity of disability) Well-Being (FIQ, 0-10) Pain (FIQ, 0-10) Fatigue (FIQ, 0-10) Sleep (FIQ, 0-10) Stiffness (FIQ, 0-10) Anxiety (FIQ, 0-10) Depression (FIQ, 0-10) Multidisciplinary Pain Inventory (MPI): Pain Severity (MPI) Interference (MPI) Life Control (MPI) Affective Distress (MPI) General Activity Level (MPI)	1 and 7 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Martin 2006	A vs. B 1 month Total (FIQ, 0-80): 34.8(12.1) vs. 42.2(10.2) p=0.007; MD -4.9 (95% CI, -8.7 to -1.2) p=0.01 Physical Function (FIQ, 0-10): 3.7(2.5) vs 3.3(2.3), p=0.96; MD –0.4 (95% CI, –1.1 to 0.3) p=0.28 Well-Being (FIQ, 0-10): 4.6(2.9) vs. 3.1(2.4), p=0.10; MD 0.8 (95% CI, –0.4 to 2.0) p=0.18 Pain (FIQ, 0-10): 4.7(2.4) vs. 5.9(2.3), p=0.09; MD –0.8 (95% CI, –1.8 to 0.2) p=0.14 Fatigue (FIQ, 0-10): 5.6(2.7) vs. 7.7(2.1), p=0.001; MD –1.2 (95% CI, –2.1 to –0.4) p=0.007 Sleep (FIQ, 0-10): 5.9(3.1) vs. 6.8(2.2), p=0.28; MD –0.7 (95% CI, –1.8 to 0.5) p=0.25 Stiffness (FIQ, 0-10): 5.8(2.7) vs. 6.6(2.9), p=0.11; MD –1.0 (95% CI, –2.3 to 0.3) p=0.16 Anxiety (FIQ, 0-10): 2.6(2.3) vs. 5.1(2.6), p<0.05; MD –1.1 (95% CI, –2.0 to –0.2) p=0.02 Depression (FIQ, 0-10): 2.0(2.4) vs 3.7(2.7), p=0.06; MD –0.7 (95% CI, –1.6 to 0.3) p=0.18 Pain Severity (MPI): 34.2(11.4) vs. 41.6(9.1), p=0.03; MD–4.6 (95% CI, –8.7 to –0.5) p=0.03 Interference (MPI): 38.3(11.9) vs. 34.9 (10.6); p=0.96; MD 0.1 (95% CI, –3.4 to 3.6) p=0.97 Life Control (MPI): 52.8(5.7) vs. 50.7(6.1), p=0.30; MD 1.2 (95% CI, –1.3 to 3.8) p=0.34 Affective Distress (MPI): 38.9(8.6) vs. 45.9(9.3), p0.03; MD –2.2 (95% CI, –5.2 to 0.9) p=0.17 General Activity Level (MPI): 55.4(9.2) vs. 58.3(8.4), p=0.12; MD–1.2 (95% CI, –3.8 to 1.4) p=0.38 7 months Total (FIQ, 0-80): 38.1(12.1) vs 42.7(9.6), p=0.24; MD –4.3 (95% CI, –7.7 to –0.9) p=0.02 Physical Function (FIQ, 0-10): 3.5(2.5) vs. 3.3(2.2), p=0.85; MD –0.3 (95% CI, –0.9 to 0.3) p=0.27 Well-Being (FIQ, 0-10): 3.8(2.9) vs. 3.6(2.3); p=0.99; MD 0.4 (95% CI, –0.6 to 1.4) p=0.41 Pain (FIQ, 0-10): 5.5(2.3) vs. 6.4(2.1), p=0.25; MD –0.7 (95% CI, –1.5 to 0.3) p=0.07 Fatigue (FIQ, 0-10): 7.0(2.4) vs. 7.6(1.9), p=0.35; MD –0.9 (95% CI, –1.6 to –0.2) p=0.02 Sleep (FIQ, 0-10): 6.1(2.9) vs. 6.3(2.5), p=0.89; MD –0.3 (95% CI, –1.3 to 0.6) p=0.49 Stiffness (FIQ, 0-10): 6.5(2.7) vs. 6.8(1.9), p=0.61; MD –0.6 (95% CI, –1.6 to 0.4) p=0.26 Anxiety (FIQ, 0-10): 3.3(2.7) vs. 4.8(3.0), p=0.31; MD –1.1 (95% CI, –1.9 to –0.2) p=0.02 Depression (FIQ, 0-10): 2.2(2.6) vs. 3.6(3.1), p=0.29; MD –0.7 (95% CI, –1.6 to 0.2) p=0.14 Pain Severity (MPI): 37.3(13.1) vs. 41.4(8.4), p=0.37; MD –3.8 (95% CI –7.5 to –0.2) p=0.05 Interference (MPI): 37.7(12.2) vs. 35.5(12.1), p=0.78; MD 0.1 (95% CI, –3.2 to 3.4) p=0.95 Life Control (MPI): 52.8(6.4) vs. 53.6(5.0), p=0.37; MD 0.0 (95% CI, –2.1 to 2.1) p=0.98 Affective Distress (MPI): 41.7(9.9) vs. 43.0(8.4), p=0.73; MD –1.1 (95% CI, –3.9 to 1.7) p=0.44 General Activity Level (MPI): 58.1(9.1) vs. 59.5(8.7), p=0.53; MD –0.6 (95% CI, –3.1 to 1.8) p=0.61

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Martin 2006	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Martin 2006	NR	4% (2/50) experienced mild vasovagal symptoms 2% (1/50) experienced a pulmonary embolism believed to be unrelated to treatment

Author, Year	Funding Source	Quality	Comments
Martin 2006	This work was supported by Mayo Foundation and the Mayo Anesthesia Clinical Research Unit. Dr. Martin is supported in part by a Research Starter Grant from the Foundation for Anesthesia Education and Research.	Good	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Martin 2012	Spain 1 hospital pain management unit	Inclusion: FM diagnosis by ACR criteria, age >18 years, continuous chronic pain for at least 6 months Exclusion: severe psychiatric or organic disorder, employment-related legal proceedings related to FM.	Randomized: 180 (90 A, 90 B) Analyzed: 110 (54 A, 56 B) Attrition: 39% (70/180)
Mazzuca 2004	United States	Inclusion Criteria: Eligibility criteria were grade 2 or higher Kellgren and Lawrence (K/L) radiographic severity of tibiofemoral OA in the standing anteroposterior view and a total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score 8 (possible range 5–25). Exclusion Criteria: NR	Randomized: 52 Treated: 51 Analyzed: 49 Attrition: 5.7% (3/52)
Messier 2004 ADAPT Trial (same trial as Rejeski 2002; reports pain and function outcomes)	United States 1 center University	Aged 60 or older, BMI greater or equal to 28, knee pain on most days of the month, sedentary lifestyle with less than 20 minutes of formal exercise once a week for the past 6 months, self-reported difficulty in at least one of the following activities due to knee pain: 0.25 mile walk, climbing stairs, bending, stopping, kneeling, shopping, housecleaning, other self-care or daily living activities, radiographic evidence of grad I-III tibiofemoral or patellofemoral OA Exclude: Serious medical condition preventing safe participation in an exercise program, Mini-Mental score less than 24, inability to complete 18 month study, inability to walk without a cane or assistive device, participation in another research study, greater than or equal to 14 alcoholic drinks per week, ST segment depression of at least 2 mm at exercise level of 4 METS or less, hypotension or complex arrhythmias during graded exercise test, inability to complete protocol	Randomized: 158 Treated: 158 Analyzed: 158 Attrition: 17% (27/158)

Author, Year	Intervention, Comparator
Martin 2012	A.Interdisciplinary pain treatment (n=54): current standard pharmacologic care for FM in Spain: amitriptyline maximum dose 75 mg/day, paracetamol maximum dose 4gr/day, and tramadol maximum dose of 400 mg/day. In addition: 6week multidisciplinary treatment delivered by team of physician, clinical psychologist, and physiotherapist and consisting of twice-weekly 105-minute group sessions. Treatment included cognitive-behavioral therapy (cognitive restructuring, breathing and relaxation exercises, communication skills, activity pacing), education, and physiotherapy. 78% (70/90) randomized completed the treatment. B.Control (n=56): current standard pharmacologic care for FM in Spain: amitriptyline maximum dose 75 mg/day, paracetamol maximum dose 4gr/day, and tramadol maximum dose of 400 mg/day
Mazzuca 2004	A.Superficial Heat (sleeve) (n=25) Participants word a cotton and lycra sleeve with a heat retaining polyester and aluminum substrate. Patients were asked to wear the sleeve at least 12 hours each day and to continue their usual OA pain medication(s). B.Placebo Sleeve (n=24) Placebo sleeves and treatment protocol were identical except placebo sleeves did not contain the heat retaining substrate layer.
Messier 2004 ADAPT Trial (same trial as Rejeski 2002; reports pain and function outcomes)	A.Exercise (n=80): Three 1 hour sessions per week done at the study facility for 4 months. After 4 months, participants wanting to do a home-based program had the option to undergo a 2 month transition phase alternating between facility and home sessions, after which they carried out the program at home. Sessions consisted of 15 minutes of aerobic exercises, 15 minutes of resistance-training, an additional 15 minutes of aerobic exercises, and a 15 minute cool down phase. B.Control (n=78): 1 hour sessions monthly for three months consisting of presentations on osteoarthritis, obesity, and exercise and a question and answer session. Monthly phone contact was maintained for months 4-6 and bimonthly phone contact was maintained for months 7-18. During phone calls, researchers gathered information on pain, medication, illnesses, and hospitalizations. On phone calls, participants were also able to ask questions and voice concerns. All subjects: Instructed to continue use of all medications and other treatments as prescribed by their personal physicians

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Martin 2012	A vs B Age: 49 vs 52 years Female: 91% vs 91% Race NR Pain duration: 15 vs 14 years FIQ total: 76.3 vs 76.2 FIQ physical functioning: 5.5 vs 5.4 FIQ Pain: 7.5 vs 7.5 HAD Anxiety: 13.8 vs 13.4 HAD Depression: 10.6 vs 10.6	FIQ total (0-100, higher scores=greater impact of FM on functioning) FIQ physical functioning (0-10, higher scores=greater impact of FM on physical functioning) HAD Anxiety (scale NR) HAD Depression (scale NR)	6 months
Mazzuca 2004	A + B Age: 62.7 Female: 77% Race: 67% white Mean Duration of Chronicity: NR Pain (WOMAC): 15.2 vs. 14.7* Stiffness (WOMAC): 6.5(1.4) Function (WOMAC): 51.8(11.8) *Separate group baseline values not given for Stiffness and Function. Mean pain estimated from graph.	Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, higher scores indicate greater pain, stiffness or functional limitation) Pain (WOMAC, range 5-25) Stiffness (WOMAC, range 2-10) Physical Function (WOMAC, range 17-85)	1 month
Messier 2004 ADAPT Trial (same trial as Rejeski 2002; reports pain and function outcomes)	A vs B Age: 69 vs 69 Female: 74% vs 68% Comorbidities: Obesity (BMI ≥30 kg/m^2): 84% vs 76% Arthritis in other joints: 55% vs 58% Hypertension: 54% vs 46% Coronary heart disease: 34% vs 28% Diabetes: 11% vs 9% Kellgren/Lawrence score: 2.2 (0.8) vs 2.2 (0.09) WOMAC physical function, mean (SEM): 24.0 (1.3) vs 26.0 (1.3) WOMAC pain, mean (SEM): 6.6 (0.4) vs 7.3 (0.4)	WOMAC physical function subscale (0-68, higher score=higher disability); WOMAC pain subscale (0-20, higher score=higher pain)	6 and 18 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Martin 2012	A vs B 6-month outcomes: FIQ total: 70.33 (16.48) vs 76.81 (14.18), p=0.04; MD -6.48 (95% CI -12.2837 to -0.6763), p=0.03 FIQ physical function: 5.19 (1.83) vs 5.92 (1.84), p=0.01; MD -0.73 (95% CI -1.4238 to -0.0362), p=0.04 FIQ pain: 7.24 (2.17) vs 8.22 (1.62), p=0.03; MD -0.98 (95% CI -1.7020 to -0.2580), p=0.008 HADS Anxiety: 13.41 (4.31) vs 12.75 (4.55), p=0.72 HADS Depression: 9.77 (4.09) vs. 10.2 (4.22), p=0.19
Mazzuca 2004	A vs. B 1 month Mean Pain (WOMAC): 13.7 vs. 13.9
Messier 2004 ADAPT Trial (same trial as Rejeski 2002; reports pain and function outcomes)	A vs B 6 months WOMAC physical function, mean*: 22.0 vs 22.0 WOMAC pain, mean (SEM): 6.2 (0.5) vs 6.2 (0.5), (MD 0.0, 95% CI -0.2 to 0.2) p=1.0 18 months WOMAC physical function, mean*: 21.0 vs 22.6 WOMAC physical function, mean Δ (95% CI): 3.1 (1.9 to 6.1) vs 3.4 (0.5 to 6.3) WOMAC pain, mean (SEM): 6.2 (0.5) vs 6.0 (0.5), (MD 0.2, 95% CI 0.04 to 0.4) p=0.01

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Martin 2012	
Mazzuca 2004	NR
Messier 2004 ADAPT Trial (same trial as Rejeski 2002; reports pain and function outcomes)	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Martin 2012		A vs B Dropouts: 40% (36/90) vs 38% (34/90) No adverse events reported
Mazzuca 2004	NR	No adverse events were reported.
Messier 2004 ADAPT Trial (same trial as Rejeski 2002; reports pain and function outcomes)		A vs B Accident related to treatment: 1% (1/80) vs 0% (0/78)

Author, Year	Funding Source	Quality	Comments
Martin 2012	Dept. of Health of the Basque Country	Poor	
Mazzuca 2004		Fair	Only results for mean WOMAC pain were given for 1 month post-treatment follow up. The other scores given were at immediate follow up. Mean pain scores were estimated from a graph.
Messier 2004 ADAPT Trial (same trial as Rejeski 2002; reports pain and function outcomes)	NIH grants from 5p60-AG-10484-07 and M01-RR-00211	Fair	*Means for WOMAC physical function scores were estimated from a graph A diet group (n=73) and a diet+exercise group (n=68) were also included in the study but data was not abstracted Between group MDs calculated

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Miyamoto 2013	Brazil 1 center Outpatient	Patients aged 18 to 60 with chronic nonspecific low back pain for 3 months or greater. Exclude: Contraindication for physical exercise, previous regular Pilates method training, pregnancy, serious spinal pathologies, previous or scheduled spine surgery, low back pain from nerve root compression, physical therapy for low back pain in previous 6 months	Randomized: 86 Treated: 86 Analyzed: 86 Attrition: 0% (0/86)

Author, Year	Intervention, Comparator
Miyamoto 2013	A.Muscle performance (Pilates) (n=43): 2 sessions of 60 minutes a week for 6 weeks. Sessions were individual and were based on the modified Pilates method, with exercises aimed at improving breathing, core stability, motor control, posture, flexibility, and mobility with the spine in neutral position. B.Attention control (education) (n=43): Instructed to not undergo treatments elsewhere. Subjects received twice-weekly phone calls regarding education booklet instructions that all patients received. All subjects: Received an educational booklet containing information on the anatomy of the spine and pelvis, information on low back pain, and recommendations for posture and movements involved in the activities of daily living.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Miyamoto 2013	A vs B Age: 41 vs 38 Female: 84% vs 79% Duration of symptoms (months): 73.3 vs 56.7 Percent done previous physical therapy: 42% vs 2% Percent used previous other treatment: 9% vs 7% Percent using medication: 40% vs 42% RMDQ: 9.7 (4.5) vs 10.5 (5.4) PSFS: 4.9 (1.8) vs 4.3 (1.8) Pain VAS: 6.6 (1.5) vs 6.5 (1.7) Global impression of recovery: -1.0 (2.3) vs -1.0 (2.5)	RMDQ (0-24, higher score=higher disability) Patient-Specific Functional Scale (0-10, higher score=lower disability) Pain (0-10 VAS, higher score=higher pain) Global impression of recovery (-5 to +5, higher score=greater recovery)	Short-term followup 4.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Miyamoto 2013	A vs B, mean (SD) <u>Baseline</u> RDQ: 9.7 (4.5) vs. 10.5 (5.4) Patient-Specific Functional Scale (0-10): 4.9 (1.8) vs. 4.3 (1.8) Pain (0-10 VAS): 6.6 (1.5) vs. 6.5 (1.7) Global impression of recovery (-5 to +5): -1.0 (2.3) vs. -1.0 (2.5) <u>4.5 months</u> RDQ: 4.5 (4.5) vs 6.7 (5.6), adjusted difference -1.4 (95% CI -3.1 to 0.03) Patient-Specific Functional Scale (0-10): 6.9 (1.8) vs 6.1 (2.0), adjusted difference 0.2 (95% CI -0.6 to 1.1) Pain (0-10 VAS): 4.5 (2.2) vs 5.3 (2.3), adjusted difference -0.9 (95% CI -1.9 to 0.1) Global impression of recovery (-5 to +5): 2.4 (1.7) vs 1.7 (2.1), adjusted difference 0.7 (95% CI -0.4 to 1.8)

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Miyamoto 2013	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Miyamoto 2013	NR	None

Author, Year	Funding Source	Quality	Comments
Miyamoto 2013	NR	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Monticone 2013	Italy 1 center Outpatient	Patients older than 18 years with nonspecific low back pain last longer than 3 months. Exclude: Cognitive impairment and all causes of specific chronic low back pain, patients receiving compensation for work-related disabilities, previous participation in cognitive-behavioral intervention for chronic low back pain.	Randomized: 90 Treated: 90 Analyzed: 90 Attrition: 0% (0/90)

Author, Year	Intervention, Comparator
Monticone 2013	A: Multidisciplinary rehabilitation (n=45): 5 weekly 60 minute cognitive-behavioral therapy sessions, and 10 twice weekly 60 minute motor training sessions involving active and passive spine mobilization, stretching, strengthening, and improvement of postural control, program administered by physiatrists, psychologist, and physiotherapists. Then once monthly 60 minute cognitive behavioral session with psychologist for 1 year B: Exercise (n=45): 10 twice weekly 60 minute motor training sessions involving active and passive spine mobilization, stretching, strengthening, and improvement of postural control

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Monticone 2013	A vs B Age: 49 vs 50 Female: 60% vs 56% Comorbidity: None: 47% vs 40% Musculoskeletal: 18% vs 20% Non-musculoskeletal: 11% vs 16% Pain duration, months: 25.2 (11.9) vs 26.3 (11.7) RDQ (0-24): 15.3 (2.9) vs 15.0 (2.9) Pain (0-10 VAS): 7.0 (1.1) vs 7.0 (1.3) SF-36 physical functioning: 47.2 (27.3) vs 48.3 (24.7) SF-36 physical role: 29.4 (35.5) vs 31.1 (32.5) SF-36 physical pain: 38.2 (15.4) vs 41.4 (17.9) SF-36 general health: 34.0 (17.7) vs 36.7 (14.1) SF-36 vitality: 52.0 (16.9) vs 52.6 (15.4) SF-36 social functioning: 50.8 (18.3) vs 51.6 (17.7) SF-36 emotional role: 39.3 (35.0) vs 39.3 (37.8) SF-36 mental health: 50.1 (11.6) vs 52.1 (12.7)	RDQ (0-24) Pain (0-10 VAS) SF-36 subscales(0-100, higher score=higher quality of life)	11 and 23 months (based on time following initial intensive 5 week intervention)

Author, Year	**Results - Subquestion a** (vs. sham, no treatment, waitlist, attention control)
Monticone 2013	

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Monticone 2013	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Monticone 2013	A vs B, mean (SD) <u>Baseline</u> RDQ (0-24): 15.3 (2.9) vs 15.0 (2.9) Pain (0-10 VAS): 7.0 (1.1) vs 7.0 (1.3) SF-36 physical functioning: 47.2 (27.3) vs 48.3 (24.7) SF-36 physical role: 29.4 (35.5) vs 31.1 (32.5) SF-36 physical pain: 38.2 (15.4) vs 41.4 (17.9) SF-36 general health: 34.0 (17.7) vs 36.7 (14.1) SF-36 vitality: 52.0 (16.9) vs 52.6 (15.4) SF-36 social functioning: 50.8 (18.3) vs 51.6 (17.7) SF-36 emotional role: 39.3 (35.0) vs 39.3 (37.8) SF-36 mental health: 50.1 (11.6) vs 52.1 (12.7) <u>11 months</u> RDQ (0-24): 1.3 (1.6) vs. 11.0 (2.0) Pain (0-10 VAS): 1.4 (1.1) vs. 5.3 (1.2) SF-36 physical functioning (0-100): 85.7 (19.6) vs. 62.1 (19.4) SF-36 physical role (0-100): 86.1 (19.2) vs. 60.3 (19.1) SF-36 physical pain (0-100): 79.0 (14.6) vs. 52.0 (16.2) SF-36 general health (0-100): 85.0 (13.8) vs. 56.4 (15.9) SF-36 vitality (0-100): 90.00 (11.7) vs. 55.3 (11.0) SF-36 social functioning (0-100): 91.0 (10.5) vs. 54.4 (11.4) SF-36 emotional role (0-100): 91.1 (14.9) vs. 58.5 (14.5) SF-36 mental health (0-100): 89.8 (13.0) vs. 54.1 (11.9) <u>23 months</u> RDQ (0-24): 1.4 (1.2) vs 11.1 (2.2), difference -9.7, 95% CI -10.4 to -9.0 Pain (0-10 VAS): 1.5 (1.1) vs 6.2 (0.9), difference -4.7, 95% CI -5.1 to -4.3 SF-36 physical functioning (0-100): 87.6 (18.4) vs 65.0 (17.7), difference 22.6, 95% CI 15.0 to 30.1 SF-36 physical role: 88.0 (18.0) vs 62.7 (17.3), difference 25.3, 95% CI 17.9 to 32.7 SF-36 physical pain: 80.4 (13.2) vs 61.8 (13.9), difference 18.6, 95% CI 12.8 to 24.3 SF-36 general health: 86.3 (13.2) vs 63.1 (15.0), difference 23.2, 95% CI 17.3 to 29.1 SF-36 vitality: 91.3 (10.4) vs 56.2 (10.5), difference 35.1, 95% CI 30.7 to 39.5 SF-36 social functioning: 92.3 (9.2) vs 52.5 (10.2), difference 39.8, 95% CI 35.7 to 43.9 SF-36 emotional role: 93.1 (13.5) vs 60.7 (12.9), difference 32.4, 95% CI 26.9 to 37.9 SF-36 mental health: 91.0 (11.3) vs 58.8 (11.8), difference 32.2, 95% CI 27.4 to 37.0)	NR

Author, Year	Funding Source	Quality	Comments
Monticone 2013	NR	Fair	MDs and p values calculated by Spectrum

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Monticone 2014	Italy Number of centers: 1 Outpatient	Patients age >18 Nonspecific chronic (>3 months) LBP Exclude: Central or peripheral neurological signs Cognitive impairment Severe cardiovascular and respiratory comorbidity Prior spine surgery Ambulation deficits due to neurological or orthopedic impairments Pregnant Previous participation in cognitive-behavioral interventions	Randomized: 20 Treated: 20 Analyzed: 20 Attrition: 0%
Morone 2009	US, Pennsylvania Number of centers 1 Clinic and Outpatient	Patients age ≥65 years, MMSE score ≥24, and chronic low back pain (with moderate intensity for ≥3 months) and intact cognition (Mini-Mental Status Exam ≥24) Exclude: non-English speaking, previous participation in mindfulness meditation, serious hearing or vision impairment, medical instability from heart or lung disease, multiple recent falls or inability to stand independently, pain caused by an acute injury within previous 3 months, possible serious underlying illness (unexplained weight loss, fever, or sudden worsening of back pain)	Randomized: 40 Treated: 35 Analyzed: 35 Attrition: 14% (5/35)

Author, Year	Intervention, Comparator
Monticone 2014	A.Multidisciplinary rehabilitation (n=10): 8 weekly 60 minute cognitive-behavioral therapy sessions, and 8 weekly 60 minute motor training sessions administered by physiatrists, psychologist, and physiotherapists B.Exercise (n=10): 8 weekly 60 minute motor training sessions involving active and passive spine mobilization, stretching, strengthening, and improvement of postural control
Morone 2009	A. Mindfulness-based stress reduction (n=16), 8 1.5-hour sessions over 8 weeks B. Attention control (education) (n=19)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Monticone 2014	A vs. B Age (mean): 59 vs. 57 years Female: 7% vs. 4% Race: NR Pain duration (months): 15 vs. 14	Oswestry Disability Index (ODI, 0-100, higher number=greater disability Pain (0-10 NRS) Italian SF-36 (8 scales, each scored 1-100, higher number = better health status) Global perceived effect: treatment satisfaction questions, higher number = worsening of symptoms	3 months
Morone 2009	A vs B Age (mean): 78 vs. 73 years Female: 69% vs. 58% White: 94% vs. 80% African American: 5% vs. 15% Asian: 0% vs. 5% Opioids: 19% vs. 26%	Roland and Morris Disability Questionnaire (RMDQ, range 0–24, higher scores indicate more disability SF-36 Pain Score (10-62) McGill Pain Questionnaire Total Score: Answer range 0–45, lower scores indicate less pain McGill Pain Questionnaire Current Pain Scale: Answer range 0–10, lower scores indicate less pain	4 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Monticone 2014	NR
Morone 2009	A vs. B, Mean <u>Baseline*</u> RDQ (0-24): 8.8 (95% CI 7.8 to 10.0) vs. 11.3 (95% CI 10.1 to 12.7) SF-36 Pain Score (10-62): 39.7 (95% CI 38.0 to 41.2) vs. 40.1 (95% CI 38.5 to 41.2) McGill Pain Questionnaire Total Score (0-45): 15.7 (95% CI 13.8 to 17.3) vs. 16.1 (95% CI 14.1 to 18.1) McGill Pain Questionnaire Current Pain (0-10): 2.9 (95% CI 2.3 to 3.6) vs. 4.4 (95% CI 3.7 to 4.9) <u>4-month outcomes*</u> RDQ: 7.6 (95% CI 6.2 to 8.7) vs. 10.0 (95% CI 8.7 to 11.2); p>0.05 SF-36 Pain Score: 41.4 (95% CI 39.8 to 43.1) vs. 40.5 (95% CI 38.7 to 42.2); p>0.05 McGill Pain Questionnaire Total Score: 12.4 (95% CI 10.4 to 14.6) vs. 12.0 (95% CI 10.2 to 13.7); p>0.05 McGill Pain Questionnaire Current Pain: 2.3 (95% CI 1.6 to 2.8) vs. 3.7 (95% CI 3.1 to 4.3); p>0.05 *age-adjusted mean scores estimated from Figure 2

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Monticone 2014	NR
Morone 2009	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Monticone 2014	A vs. B , mean (SD) <u>Baseline</u> ODI (0-100): 26 (5) vs. 24 (2) Pain (0-10 NRS): 5 (3) vs. 4 (1) SF-36 physical activity (0-100): 41 (7) vs. 43 (5) SF-36 physical role (0-100): (38 (18) vs. 35 (13) SF-36 bodily pain (0-100): 45 (14) vs. 48 (13) SF-36 general health (0-100): 34 (15) vs. 39 (12) SF-36 vitality (0-100): 54 (12) vs. 54 (13) SF-36 social function (0-100): 60 (10) vs. 59 (10) SF-36 emotional role (0-100): 47 (17) vs. 43 (16) SF-36 mental health (0-100): 59 (10) vs. 57 (12) <u>3 months</u> ODI (0-100): 8 (6) vs. 15 (3), p=0.027 Pain (0-10 NRS): 2 (1) vs. 3 (2), p=1.0 SF-36 physical activity (0-100):84 (6) vs. 67 (10), p=0.001 SF-36 physical role (0-100): 80 (16) vs. 59 (11), p=0.034 SF-36 bodily pain (0-100): 65 (12) vs. 55 (7), p=0.261 SF-36 general health (0-100): 71 (5) vs. 55 (8), p=0.018 SF-36 vitality (0-100): 82 (8) vs. 62 (11), p=0.008 SF-36 social function (0-100): 81 (7) vs. 61 (7), p=0.001 SF-36 emotional role (0-100): 77 (16) vs. 57 (16), p=0.007 SF-36 mental health (0-100): 88 (10) vs. 67 (12), p=0.001	Withdrawals: 0 Nonserious AEs: Transitory pain worsening: 3/10 vs. 2/10 Mood alterations: 1/10 vs. 2/10
Morone 2009	NR	No adverse events.

Author, Year	Funding Source	Quality	Comments
Monticone 2014	EuroSpine Task Force on Research	Fair	
Morone 2009	National Institutes of Health	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Morone 2016	US, Pennsylvania Number of centers 1 Clinic	Patients age ≥65 years, MMSE score ≥24, and chronic low back pain (with moderate intensity for ≥3 months) and functional limitations score of ≥11 on the Roland and Morris Disability Questionnaire Exclude: Patients who participated previous mindfulness meditation programs, or had serious illness (malignant neoplasms, infection, unexplained fever, weight loss, or recent trauma) or had moderate to severe depression.	Randomized: 282 Treated: 273 Analyzed: 282 Attrition: 4% (9/282)
Nambi 2014	India Number of centers: 1 Outpatient	Age >18 years Nonspecific LPB for 3 months; Exclude: LBP due to nerve root compressing, disc prolapse, spinal stenosis, tumor, spinal infection, ankylosing spondylosis, spondylolisthesis, kyphosis or structural scoliosis, widespread neurological disorder, pre-surgical candidates Involved in litigation or compensation, Compromised cardiopulmonary system Pregnant BMI >35 Major depression or substance abuse Yoga practitioners	Randomized: 60 Treated: 60 Analyzed:54 Attrition: 10% (6/60)

Author, Year	Intervention, Comparator
Morone 2016	A. Mindfulness-based stress reduction (n=140), 8 1.5-hour sessions over 8 weeks, followed by 6 monthly booster sessions B. Attention control (education) (n=142)
Nambi 2014	A: Iyengar yoga (n=30): 1 hour Iyengar class/week + 30 minute home practice, 5 days/week for 4 weeks; with props; 29 poses introduced in stages simple to progressively more challenging; At end of 4 weeks, participants encouraged to continue Yoga at home. B: Exercise (n=30): Following 5-10 minute warm up (stretching exercises for soft tissue flexibility and range of motion); Taught specific exercises for strengthening abdominal and back muscles (depending on clinical findings) 3 days/week with 5 repetitions in 3 sets with 30-s pause per set; repetitions gradually increased until reaching 15 for 4 weeks: instructed to refrain from other back exercises, strenuous activities outside of normal activities of daily living during study .

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Morone 2016	A vs B Age (mean): 75 vs. 74 Female: 66% vs. 66% White: 70% vs. 71% African American: 30% vs. 27% Asian: 0% vs. 2% Cumulative Illness Rating Scale score, mean (SD): 3.4 (2.1) vs. 3.2 (1.8) Geriatric Depression Scale score: 5.7 (4.3) vs. 6.0 (4.3)	Disability (RMDQ Scores range from 0 to 24, with higher scores indicating increased limitations) Average pain, NRS (0-20) SF-36 Global Health Composite (9 to 67) SF-36 Physical Health Composite (20 to 65)	4.5 months
Nambi 2014	A vs. B Mean age: 44 vs. 43 Female: 63% vs. 43% Race: NR Baseline Pain intensity (10 cm VAS,0= no pain , 10 = worst possible): 6.7 vs. 6.7 Physically unhealthy days (from CDC HRQOL-4): 18 vs. 17.8 Mentally unhealthy days (from CDC HRQOL-4):17.0 vs. 17.4 Activity limitation days (from CDC HRQOL- 4): 16.7 vs. 17.1	Primary outcomes: Pain intensity: Visual Analog Scale, 0-10cm line, higher number = more pain) Health-related quality of life: HRQOL-4, dichotomized answers into fair/poor vs. good/very good/excellent for general health and into 14 days vs. <14 days for frequency of physical distress, mental distress, activity limitation.	5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Morone 2016	A vs. B, mean (SD) <u>Baseline</u> RDQ (0-24): 15.6 (3.0) vs. 15.4 (3.0) Pain (0-20 NRS): 11.0 (4.0) vs. 10.5 (4.2) SF-36 Global Health Composite (9 to 67): 40.5 (8.1) VS. 40.6 (8.8) SF-36 Physical Health Composite (20 to 65): 38.8 (6.6) vs. 38.9 (6.9) <u>4.5 months</u> RDQ: 12.2 (5.1) vs. 12.6 (5.0), adjusted difference -0.4 (95% CI -1.5 to 0.7) Pain (0-20 NRS): 9.5 (5.1) vs. 10.6 (4.7), adjusted difference -1.1 (95% CI -2.2 to -0.01) SF-36 Global Health Composite (9 to 67): 42.4 (8.2) vs. 41.2 (8.5), adjusted difference 0.2 (95% CI -1.9 to 2.4) SF-36 Physical Health Composite (20 to 65): 41.2 (8.2) vs. 41.2 (8.5), adjusted difference -0.1 (95% CI -1.9 to 1.8) RDQ improved ≥2.5 points: 49.2% (58/117) vs. 48.9% (66/135), p=0.97 Pain improved ≥30%: 36.7% (43/117) vs. 26.7% (36/135), p=0.09 Differenced s adjusted for sex and time
Nambi 2014	NR

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Morone 2016	NR
Nambi 2014	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Morone 2016	NR	No adverse events.
Nambi 2014	A vs. B (mean, SD) <u>Baseline</u> Pain intensity (VAS, 0-10): 6.7 (0.9) vs. 6.7 (0.9) Physically unhealthy days: 18.0 (2.5) vs. 17.8 (3.2) Mentally unhealthy days: 17.0 (2.3) vs. 17.4 (2.2) Activity limitation days: 16.7 (2.6) vs. 17.1 (2.5) <u>5 months</u> Pain intensity (VAS, 0-10):1.8 (1.1) vs. 3.8 (0.7), p=0.001 (repeated measures ANOVA) Physically unhealthy days: 2.6 (3.1) vs. 6.9 (3.2), p=0.001 Mentally unhealthy days: 2.1 (2.3) vs. 5.0 (2.0), p=0.001 Activity limitation days: 2.0 (2.2) vs. 5.0 (1.9), p=0.001	NR

Author, Year	Funding Source	Quality	Comments
Morone 2016	National Institutes of Health.	Fair	
Nambi 2014	NR	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Nassif 2011	France 1 center Subjects' workplace (factory)	Workers aged 18 or older in the assembly line of a car manufacturing company with chronic low back pain. Exclude: Recent surgery or pathologic conditions related to the onset of low back pain or interfering with the designed monitoring measurements of the study.	Randomized: 75 Treated: 75 Analyzed: 52 Attrition: 17% (13/75)

Author, Year	Intervention, Comparator
Nassif 2011	A.Exercise (n=37): Three 60 minute group sessions of 2 to 8 participants per week for 8 weeks. In sessions, participants trained major muscle groups through joint flexion and extension, stretching, stability, coordination, and muscle strengthening exercises. B.Usual care (n=38): Subjects received no direct intervention but were free to pursue treatments externally. All subjects: Received medical and paramedical consultation on the benefits of physical activity and proper working posture positions

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Nassif 2011	A vs B Age: 45 vs 45 Female: 11% vs 21% Quebec Back Pain Disability Questionnaire: 57.3 (18.5) vs 36.2 (17.1) RMDQ: 13.9 (4.6) vs 12.3 (5.0) Pain VAS: 4.5 (2.7) vs 4.9 (2.4) Dallas Pain Questionnaire daily activities: 57.3 (16.2) vs 53.2 (19.6) Dallas Pain Questionnaire work and recreation: 54.9 (20.9) vs 48.8 (19.5) Dallas Pain Questionnaire anxiety and depression: 44.7 (19.5) vs 36.5 (23.0) Dallas Pain Questionnaire social: 34.5 (24.9) vs 31.8 (24.1)	Quebec Back Pain Disability Questionnaire (0-100, higher percent=higher disability) RDQ (0-24, higher score=higher disability) Pain (0-10 NRS, higher score=higher pain) Dallas Pain Questionnaire (0-100%, higher percent=higher impact of pain)	Short-term followup 4 months

Author, Year	**Results - Subquestion a** (vs. sham, no treatment, waitlist, attention control)
Nassif 2011	A vs B, mean (SD) <u>Baseline</u> Quebec Back Pain Disability Questionnaire: 40.86 (18.52) vs. 36.16 (17.07) RDQ: 13.91 (4.63) vs. 12.30 (4.95) Pain (0-10 NRS): 4.54 (2.73) vs. 4.92 (2.35) Dallas Pain Questionnaire daily activities (0-100): 57.29 (16.19) vs. 53.16 (19.57) Dallas Pain Questionnaire work and recreation (0-100): 54.85 (20.90) vs. 48.37 (19.54) Dallas Pain Questionnaire anxiety and depression (0-100): 44.73 (19.45) vs. 36.48 (22.96) Dallas Pain Questionnaire social: 34.50 (24.85) vs. 31.75 (24.07) <u>4 months</u> Quebec Back Pain Disability Questionnaire: 27.2 (13.8) vs 30.2 (17.3), difference -3.0 (95% CI -11.7 to 5.7) RDQ: 10.0 (5.1) vs 10.6 (5.4), difference -0.6 (95% CI -3.5 to 2.3) Pain (0-10 NRS): 3.2 (2.3) vs 3.5 (2.5), difference -0.3 (95% CI -1.6 to 1.0) Dallas Pain Questionnaire daily activities: 48.5 (14.6) vs 46.8 (20.2), difference 1.7, 95% CI -8.0 to 11.4) Dallas Pain Questionnaire work and recreation: 38.3 (17.6) vs 37.6 (20.4), difference 0.7 (95% CI -9.9 to 11.3) Dallas Pain Questionnaire anxiety and depression: 31.2 (17.5) vs 28.9 (20.2), difference 2.3 (95% CI -8.2 to 12.8) Dallas Pain Questionnaire social: 25.3 (20.8) vs 22.6 (22.1), difference 2.7, 95% CI -9.3 to 14.7)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Nassif 2011	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Nassif 2011		NR

Author, Year	Funding Source	Quality	Comments
Nassif 2011	Unclear	Poor	MDs and p values calculated by AAI. Baseline values of outcome measures seem different enough to potentially do adj MD

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Natour 2014	Brazil Number of centers unclear Type of center unclear	Patients with a diagnosis of chronic low back pain*, nonspecific low back pain with no signs of a serious underlying condition, no signs of spinal stenosis or radiculopathy, pain that becomes accentuate with physical effort and is relieve with rest, aged 18 to 50, and a pain VAS score between 4 and 7 Exclude: Diagnosis of low back pain due to other causes, fibromyalgia, previous spine surgery, lawsuit, initiation or change to regular physical activity in previous 3 months, body mass index > 30, physical therapy or acupuncture treatment in the previous 3 months	Randomized: 60 Treated: 60 Analyzed: 60 Attrition: 5% (3/60)

Author, Year	Intervention, Comparator
Natour 2014	A.Muscle performance (Pilates) (n=30): 50 minute group sessions of 3-4 subjects 2 times per week for 90 days. Sessions were based on the Pilates method and led by physical educator with experience in the method. B.Usual care (n=30): No additional intervention besides the medication treatment using NSAIDs as described below. All subjects: Instructed to use 50 mg of sodium diclofenac at intervals no shorter than 8 hours when pain VAS was greater than 7

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Natour 2014	A vs B Age: 48 vs 48 Female: 80% vs 77% Employment: Unpaid work: 30% vs 37% Paid work: 70% vs 60% None: 0% vs 3% Physical activity: Walking: 37% vs 27% Workout/dance: 7% vs 13% None: 56% vs 60% RMDQ: 12.1 (5.2) vs 10.6 (5.1) Pain VAS: 5.5 (5.2) vs 5.8 (2.1) SF-36 physical functioning: 57.3 (21.4) vs 58.8 (23.7) SF-36 role physical: 34.3 (38.2) vs 42.7 (40.7) SF-36 bodily pain: 45.9 (18.9) vs 42.9 (21.4) SF-36 general health: 64.4 (18.8) vs 63.7 (23.4) SF-36 vitality: 54.6 (21.5) vs 56.0 (21.2) SF-36 social functioning: 78.1 (23.4) vs 78.6 (28.2) SF-36 role emotional: 73.3 (28.2) vs 78.9 (27.0) SF-36 mental health: 60.1 (23.9) vs 67.1 (21.9)	RMDQ (0-24, higher score=higher disability) Pain (0-10 VAS, higher score=higher pain) SF-36 subscales (0-100, higher score=higher quality of life)	Short-term followup 3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Natour 2014	A vs B, mean (SD) <u>Baseline</u> RDQ: 10.58 (5.12) vs. 12.12 (5.24) Pain (0-10 VAS): 4.79 (2.06) vs. 5.50 (1.25) SF-36 physical functioning: 58.75 (23.69) vs. 57.29 (21.36) SF-36 role physical: 42.70 (40.69) vs. 34.37 (38.17) SF-36 bodily pain: 42.91 (21.40) vs. 45.91 (18.87) SF-36 general health: 63.66 (23.37) vs. 64.37 (18.81) SF-36 vitality: 56.04 (21.21) vs. 54.58 (21.46) SF-36 social functioning: 78.64 (28.18) vs. 78.12 (23.38) SF-36 role emotional: 78.86 (26.97) vs. 73.31 (28.24) SF-36 mental health: 67.06 (21.85) vs. 60.06 (23.85) <u>3 months</u> RDQ: 7.0 (5.4) vs 10.7 (6.2), difference -3.6, p<0.001 Pain (0-10 VAS): 4.2 (2.8) vs 5.8 (2.9), difference -1.6, p<0.001 SF-36 physical functioning: 65.4 (28.0) vs 59.6 (19.0), difference 5.8, p=0.026 SF-36 role physical: 56.4 (34.8) vs 40.0 (31.3), difference 16.4, p=0.086 SF-36 bodily pain: 52.2 (24.6) vs 43.9 (29.1), difference 8.3, p=0.030 SF-36 general health: 65.2 (22.2) vs 62.1 (21.1), difference 3.1, p=0.772 SF-36 vitality: 60.3 (23.4) vs 55.0 (21.7), difference 5.3, p=0.029 SF-36 social functioning: 86.0 (22.8) vs 80.4 (23.3), difference 5.6, p=0.096 SF-36 role emotional: 82.6 (24.2) vs 73.0 (31.5), difference 9.7, p=0.165 SF-36 mental health: 67.9 (22.1) vs 65.3 (23.1), difference 2.6, p=0.243

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Natour 2014	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Natour 2014		A vs B Depression leading to withdrawal: 3% (1/30) vs 0% (0/30)

Author, Year	Funding Source	Quality	Comments
Natour 2014	Grants from Fundacao Amparo a Pesquisa do Estado de Sao Paulo (2007/53423-5)	Fair	*Defined as pain between the lower rib cage and gluteal folds for more than 12 months MDs given by study but were not adjusted for baseline values ES's and 95% CIs only given for parameters that were statistically significantly different between groups with ANOVA

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Nicholas 1991	Australia Number of centers: 1 Setting: Outpatient	20-60 years old Chronic non-malignant LBP >6 months duration Not considered suitable for further invasive treatments No insurance compensation claim due for settlement within 12 months Able to read and speak English Willing to participate in a research-oriented treatment program	Randomized: 58 Analyzed: 39 Attrition: 33% (19/58)

Author, Year	Intervention, Comparator
Nicholas 1991	A.Cognitive treatment + physiotherapy (n=10): 5 weekly 1-hour group sessions of cognitive treatment led by psychologist focused on negative and non-coping cognitions as consequences of persistent pain and treatment failures. Subjects were taught to identify non-coping cognitions, challenge them, and replace them with more appropriate, coping self-statements; as well as distraction techniques. Physiotherapy consisted of 10 sessions, 2 per week (1 hour and 1.5 hours) for 5 weeks, consisting of information, exercises and written handouts. Teaching covered concepts of back anatomy, back-care procedures, related medical terminology, nutrition and weight, and commonly prescribed medications. Exercises were aimed at back-support muscle strengthening, with 4 sessions of mobilization exercise practice. Home exercise practice was recommended but physiotherapists did not check on compliance and did not provide specific reinforcement. B.Behavioral treatment + physiotherapy (n=10): 5 weekly 1-hour group sessions of behavioral treatment led by psychologist focused on consequences of reduced activity level. Subjects were encouraged to decrease medication, identify and work towards long-term behavioral goals and pace activities. Verbal praise was given by the psychologist and group members for progress towards goals as well as for practicing physiotherapy exercises. C.Cognitive treatment and relaxation training + physiotherapy (n=8): Progressive muscle relaxation training was incorporated into the 5 cognitive treatment sessions, with reduced time on cognitive treatment. The cognitive treatment was otherwise the same as for group A. Relaxation training used three 30-minute audiotapes; relaxation technique was not practiced during the sessions, but subjects were given the tapes in order at sessions 1, 2 and 3, respectively. They kept tape 3, were encourage to practice the technique and report progress and difficulties at each session. D. Behavioral treatment and relaxation training + physiotherapy (n=9): Progressive muscle relaxation training was incorporated into the 5 behavioral treatment sessions, with reduced time on behavioral treatment. The behavioral treatment was otherwise the same as for group B. The relaxation training was the same as that for group C. E.Attention-control + physiotherapy (n=10): 5 weekly 1-hour group sessions led by psychologist with group discussion of weekly topics: 1) history of their back complaint; 2) treatments received; 3) effects of back complaints on their family; 4) effects of back complaints on lifestyle and work; and 5) coping methods attempted. No coping methods were taught and no other information given; questions directed back to the group. No reinforcement related to physiotherapy was provided. F.Physiotherapy only (n=11): Physiotherapy as described above. At the end of the first session every week the subject received the physiotherapy exercise sheets from the psychologist; no encouragement or reinforcement on physiotherapy exercises given.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Nicholas 1991	Overall Age: 41 Duration of LBP: 7.0 years Prior back surgery: 37.9%(22/58) Prior nerve block: 32.8% (19/58) Medications used: analgesics 82.8%, minor tranquilizers 36.2%, antidepressants 31% Employment status: employed 8.6% (5/58), unemployed due to pain/disability 75.9%, homemaker 15.5%	Pain (0-5 categorical scale) Beck Depression Inventory (BDI) (0-63, higher number=more severe depression) Sickness Impact Profile (SIP, 0-100%, higher scores=greater dysfunction) State-Trait Anxiety Inventory - State (STAI-S, 20-80) Medication intake: number of types of medication taken over a 1-week period (0-5)	5 and 11 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Nicholas 1991	NR

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Nicholas 1991	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Nicholas 1991	A vs. B vs. C vs. D vs. E vs. F <u>Baseline</u> Pain (0-5 categorical scale): 2.78 (0.41) vs. 2.96 (0.58) vs. 3.80 (0.79) vs. 2.27 (0.54) vs. 2.84 (0.80) vs. 2.77 (0.90) STAI-S (20-80): 52.75 (14.01) vs. 50.78 (9.14) vs. 53.50 (14.98) vs. 40.29 (10.26) vs. 52.89 (10.74) vs. 52.29 (13.10) BDI (0-63): 24.63 (7.25) vs. 19.00 (8.69) vs. 25.13 (10.37) vs. 16.86 (7.92) vs. 15.67 (4.37) vs. 19.29 (7.63) Sickness Impact Profile (0-100): 37.13 (10.75) vs. 34.24 (12.05) vs. 33.41 (8.27) vs. 20.53 (9.69) vs. 27.12 (7.05) vs. 28.06 (7.51) Medication use (0-5): 2.38 (1.32) vs. 1.56 (1.34) vs. 1.38 (0.99) vs. 1.43 (0.50) vs. 1.78 (1.40) vs. 2.00 (1.07) <u>5 months</u> Pain (0-5 categorical scale): 2.18 (0.55) vs. 1.87 (0.73) vs. 3.20 (0.93) vs. 2.22 (0.48) vs. 2.64 (0.90) vs. 3.18 (0.72) STAI-S (20-80): 57.17 (10.30) vs. 37.57 (12.92) vs. 55.71 (10.47) vs. 36.40 (6.28) vs. 41.13 (11.70) vs. 54.00 (12.03) BDI (0-63): 18.67 (9.01) vs. 8.14 (5.77) vs. 16.14 (3.80) vs. 9.00 (6.07) vs. 9.88 (5.46) vs. 19.17 (8.78) Sickness Impact Profile (0-100): 24.42 (11.78) vs. 15.44 (14.12) vs. 25.69 (8.50) vs. 14.86 (9.08) vs. 19.40 (6.89) vs. 29.78 (8.76) Medication use (0-5): 1.50 (1.26) vs. 0.57 (0.73) vs. 1.86 (0.64) vs. 1.60 (1.02) vs. 1.50 (0.71) vs. 1.83 (1.07) <u>11 months</u> Pain (0-5 categorical scale): 2.56 (0.97) vs. 2.66 (1.06) vs. 3.30 (0.83) vs. 1.88 (0.65) vs. 2.70 (0.84) vs. 3.22 (0.69) STAI-S (20-80): 42.83 (9.42) vs. 37.43 (12.26) vs. 47.17 (17.01) vs. 40.67 (11.81) vs. 46.56 (11.51) vs. 53.40 (18.78) BDI (0-63): 18.67 (10.04) vs. 8.00 (5.93) vs. 12.83 (6.69) vs. 13.17 (8.51) vs. 10.56 (5.21) vs. 17.60 (6.09) Sickness Impact Profile (0-100): 23.85 (12.50) vs. 12.80 (8.62) vs. 20.77 (8.29) vs. 12.87 (6.68) vs. 18.94 (12.79) vs. 25.18 (8.08) Medication use (0-5): 1.17 (1.37) vs. 0.71 (0.88) vs. 1.67 (1.37) vs. 1.33 (0.75) vs. 1.44 (0.96) vs. 1.60 (1.49)	Overall Withdrawal: 17% (10/58) at posttreatment; 33% (19/58) at 6- and 12-month follow ups Withdrawal due to AEs: NR Serious AEs: NR. "One [subject] died during the followup period." Nonserious AEs: NR

Author, Year	Funding Source	Quality	Comments
Nicholas 1991	NR	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Nicholas 1992	Australia Number of centers: 1 Setting: Outpatient	20-60 years old Chronic non-malignant LBP >6 months duration Not considered suitable for further invasive treatments No insurance compensation claim due for settlement within 12 months Able to read and speak English Willing to participate in a research-oriented treatment program	Randomized: 20 Analyzed: 17 Attrition: 15% (3/20)
Osteras 2014	Norway 2 centers Outpatient	ACR criteria for features of hand OA or uni-/bilateral OA in the first carpometacarpal joint, FIHOA score ≥5 Exclude: Inflammatory rheumatic disease, steroid injection within 2 mos, recent severe trauma, recent OA surgery, recent major surgery of any type, cognitive dysfunction, language problems	Randomized: 130 Treated: 124 Analyzed: 119 Attrition: 16% (21/130) *29% in treatment group vs. 7% in the control group
Paolucci 2015	Italy	Inclusion: met ACR criteria (year NR) for FM and pharmacologic treatment stable for 3 months Exclusion: baseline FIQ score <51, severe somatic or psychiatric disorders that prevent physical loading, previous spine surgery, vertebral fractures, sciatic pain, neoplasia, currently attending another type of physical therapy, use of antidepressants	Randomized: 37 Analyzed: 32 Treated: 84% (16/19) in A Attrition: 14% (5/37)

Author, Year	Intervention, Comparator
Nicholas 1992	A.Cognitive-behavioral treatment (CBT), progressive muscle relaxation training, + physiotherapy (n=10): CBT treatment in 5 weekly 1-hour group sessions of cognitive treatment led by psychologist focused on negative and non-coping cognitions as consequences of persistent pain and treatment failures. Subjects were taught to identify non-coping cognitions, challenge them, and replace them with more appropriate, coping self-statements; as well as distraction techniques. Relaxation training used three 30-minute audiotapes; relaxation technique was not practiced during the sessions, but subjects were given the tapes in order at sessions 1, 2 and 3, respectively. Patients encouraged to practice the technique and report progress and difficulties at each session. Physiotherapy consisted of 10 sessions, 2 per week (1 hour and 1.5 hours) for 5 weeks, consisting of information, exercises and written handouts. Exercises aimed at back-support muscle strengthening, with 4 sessions of mobilization exercise practice. Home exercise practice was recommended but physiotherapists did not check on compliance and did not provide specific reinforcement. B.Attention-control (n=10) + physiotherapy: 5 weekly 1-hour group sessions led by psychologist who introduced a topic at each session and encouraged group discussion. The topics were: 1) history of their back complaint; 2) treatments received; 3) effects of back complaints on their family; 4) effects of back complaints on lifestyle and work; and 5) coping methods attempted. No coping methods were taught and no other information given by the psychologist. The psychologist deflected questions back to the group, and did not give any reinforcement related to physiotherapy.
Osteras 2014	A.Exercise (n=46): exercises to improve grip strength, improve thumb stability, and maintain finger range of motion, 4 group sessions supplemented by for 3 times weekly at 10 repetitions (weeks 1-2) and 15 repetitions (weeks 3-12) at home B.Usual care (n=64): Subjects received no particular attention, referral, or treatment from the study. They were allowed to receive 'usual care' from a general practitioner
Paolucci 2015	A.exercise (n=16): 10 60-minute rehabilitation sessions, twice a week for 5 weeks. Low-impact aerobic training, 60% of maximum heart rate, for 20 minutes; agility training and balance exercises, postural exercises, hip flexor strengthening, static stretching, diaphragmatic breathing, and relaxation. 84% of participants in A completed all sessions. B.Control (n=16): No rehabilitation interventions, continued normal activities

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Nicholas 1992	Overall Age: 44 Female: 45% (9/20) Duration of LBP: 5.5 years Previous treatments: back surgery 45% (9/20), physiotherapy 85% (17/20), nerve block 35% (7/20) Medications used: analgesics 80% (16/20), minor tranquilizers 30% (6/20), antidepressants 30% (6/20) Employment status: employed 10% (2/20), unemployed due to pain/disability 65% (13/20), homemaker 25% (5/20)	Pain (0-5 categorical scale) Beck Depression Inventory (BDI) (0-63, higher number=more severe depression) Sickness Impact Profile (SIP, 0-100%) Medication intake: number of types of medication taken over a 1-week period (0-5)	5 months
Osteras 2014	A vs B Age: 67 vs 65 Females: 89% vs 91% Fulfilment of ACR criteria for hand OA: 91% vs 91% Self-reported hip OA: 39% vs 46% Self-reported knee OA: 40% vs 51% Other rheumatic disease: 13% vs 15% Severe mental distress: 17% vs 39% FIHOA: 10.8 (5.0) vs 9.8 (4.7) PSFS: 3.5 (2.4) vs 3.9 (2.3) Hand pain NRS 0-10: 4.2 (2.1) vs 3.9 (1.8) Patient global assessment affecting activity: 4.3 (1.9) vs 4.3 (1.8) Patient global assessment affecting ADL: 4.1 (2.0) vs 3.9 (2.0)	FIHOA (0-30, higher score=higher disability): PSFS (0-10, higher score=less disability): hand pain NRS (0-10, higher score=greater pain): patient global assessment of disease activity (0-10, higher score=greater disease activity): patient global assessment of disease activity on ADL (0-10, higher score=great disease activity on ADL): OARSI OMERACT (responder vs non-responder)	3 months
Paolucci 2015	A vs B Age: 50 vs 48 Female: 100% vs 100% Duration of symptoms: NR FIQ total: 64.8 (9.1) vs 63.9 (9.3)	FIQ total score (0-100, higher scores=greater impairment)	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Nicholas 1992	NR
Osteras 2014	A vs B <u>3 months</u> FIHOA: 10.9 (5.4) vs 10.5 (4.9) (Adj MD -0.5, 95% CI -1.9 to 0.8) PSFS: 4.3 (2.5) vs 4.4 (2.6) (Adj MD 0.1, 95% CI -0.7 to 1.0) Hand pain NRS 0-10: 4.3 (2.3) vs 4.3 (2.1) (Adj MD -0.2, 95% CI -0.8 to 0.3) Patient global assessment of disease activity: 4.2 (2.2) vs 4.1 (1.9) (Adj MD 0.1, 95% CI -0.5, 0.7) Patient global assessment of disease activity affecting ADL: 3.8 (2.2) vs 3.8 (2.0) (Adj MD -0.2, 95% CI -0.8 to 0.4) OARSI OMERACT no. of responders: 30% vs 28% (NS)
Paolucci 2015	A vs B 3 months: FIQ total: 53.8 (10.7) vs 64.3 (9.4), p=0.006; MD -10.50 (95% CI -17.77, -3.23), p = 0.006

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Nicholas 1992	NR
Osteras 2014	
Paolucci 2015	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Nicholas 1992	A vs. B. mean (SD) <u>Baseline</u> Pain (0-5 categorical scale): 3.13 (0.88) vs. 2.84 (0.85) Beck Depression Inventory (0-63): 17.33 (7.41) vs. 20.44 (10.62) Sickness Impact Profile (0-100): 30.87 (12.17) vs. 32.10 (13.45) Using medication: 100% (10/10) vs. 90% (9/10) <u>5 months</u> Pain intensity (0-5 categorical scale): 2.89 (0.64) vs. 2.75 (1.11) Beck Depression Inventory (0-63): 14.44 (5.98) vs. 18.50 (9.26) Sickness Impact Profile (0-100): 18.30 (11.18) vs. 25.31 (14.34) Using medication: 44% (4/9) vs. 88% (7/8)	A vs. B Withdrawal: 10% (1/10) vs. 20% (2/10) 6-months Withdrawal due to AEs: NR Serious AEs: NR Nonserious AEs: NR
Osteras 2014		Increased pain and inflammation in one finger (n=1) Increased pain and inflammation in all fingers (n=2) Increased neck/shoulder pain (n=5), one withdrawal from the study (note: study reported all patients that experienced increased neck/shoulder pain had a history of neck/shoulder problems) Adverse events not broken down by intervention group
Paolucci 2015		A vs B Withdrawals: 16% (3/19) vs 11% (2/18) Adverse events: 0 vs 0

Author, Year	Funding Source	Quality	Comments
Nicholas 1992	NR	Fair	The intervention group (A) had both the cognitive and the behavioral treatments described in Nicholas 1991, so not sure if there is overlap in subjects. The attention control condition is described the same as in 1991, so may be same control group? Entered ANOVA results from Table III for the treatment x pre vs. f/u. P-values as reported in the text.
Osteras 2014	The Norwegian Fund for Post-Graduate Training in Physiotherapy through the FYSIOPRIM and the Norwegian Rheumatism Association Research Fund	Poor	OARSI OMERACT responder criteria was either (a) ≥50% improvement in pain or in function and an absolute change ≥20 or (b) at least 2 of the 3: improvement of pain ≥20% and absolute change ≥10, improvement in function ≥20% and absolute change ≥10, or improvement in patient's global assessment ≥20% and absolute change ≥10 Gave information on MCIDs for some outcome measures Outcomes not reported: Hand stiffness NRS 0-10, maximal grip strength, Moberg Pick-up Test, thumb web space
Paolucci 2015	NR	Fair	

Author, Year	Country Number of Centers and Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Paolucci 2016	Italy 1 center Outpatient	Inclusion: Subjects with fibromyalgia who experienced widespread pain for > 3 months and pain with 4 kg/cm^2 pressure at 11 or more of the 18 tender points, ages 18 to 60 years old, and VAS score > 3 for pain. Exclusion: presence of concomitant autoimmune or hematologic diseases, psychiatric disorders, other causes of chronic pain, and other diseases such as epilepsy and tumors, pregnancy, pacemakers, participants currently participating in another type of physical therapy, overlapping painful conditions.	Randomized: 33 Analyzed: 26 Attrition: 21% (7/33)

Author, Year	Intervention, Comparator
Paolucci 2016	Cross-over trial: patients randomized to receive A or B during the first treatment period then patients recevied opposite treatment during the second treatment period (i.e., after crossing over; B vs. A) A. Extremely low-frequency magnetic field first (n=16): 3 thirty minute sessions per week for 4 weeks (12 sessions total). Patients laid on a bed with multi-low-frequency mattress that delivered a magentic field at an intensity of 100 uT and a multifrequency of 1 to 80 Hz. B. Sham extremely low-frequency magnetic field first (n=17): 3 thirty minute sessions per week for 4 weeks (12 sessions total). Patients laid on a bed with multi-low-frequency mattress but no magnetic field was delivered. Washout period: 1 month

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Paolucci 2016	A vs B Age, years: 50 vs 51 Female: 100% vs 100% FM duration, years: 7 vs 5 FIQ: 58.7 (11.3) vs 57.2 (12.3) HAQ: 0.7 (0.3) vs 1.1 (0.8) FIQ pain: NR Pain VAS: 4.9 (1.4) vs 4.8 (1.2) FAS: 6.1 (1.7) vs 6.4 (1.4)	FIQ (0-100, higher score=greater impact of FM); HAQ (0-3, higher score=higher disability); FIQ pain (0-10, higher score=higher pain) pain VAS (0-10, higher score=higher pain); FAS (0-10, higher score=higher pain)	1 month

Author, Year	Results - Subquestion a (vs. Sham, no treatment, waitlist, attention control)
Paolucci 2016	A vs B <u>1 month</u> FIQ: 19.2 (7.3) vs 57.9 (12.5), p<0.001 Percent change from baseline in FIQ: -67.3 (9.9) vs 2.9 (7.4), p<0.001 HAQ: 0.3 (0.2) vs 1.1 (0.9), p=0.03 Percent change from baseline in HAQ: NR FIQ pain: values NR, p<0.001 Pain VAS: 2.2 (1.0) vs 5.3 (1.3), p<0.001 Percent change from baseline in pain VAS: -54.1 (19.9) vs 6.3 (16.0), p<0.001 FAS: 3.2 (1.2) vs 6.1 (1.7), p<0.001 Percent change from baseline in FAS: -46.5 (17.3) vs -4.5 (20.8), p<0.001 B vs A (after cross-over) <u>1 month</u> FIQ: 25.1 (8.5) vs 53.9 (8.7), p<0.001 Percent change from baseline in FIQ: -56.0 (9.4) vs -8.1 (16.5), p<0.001 HAQ: 0.7 (0.7) vs 0.8 (0.3), p=0.41 Percent change from baseline in HAQ: NR Pain VAS: 3.1 (1.6) vs 4.6 (1.3), p=0.02 Percent change from baseline in pain VAS: -39.7 (26.0) vs -9.1 (15.1), p=0.006 FAS: 3.5 (1.9) vs 6.2 (1.0), p=0.002 Percent change from baseline in FAS: -46.9 (22.8) vs -1.2 (15.4), p<0.001

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Paolucci 2016	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawls
Paolucci 2016		No side effects were recorded suring the study

Author, Year	Funding Source	Quality	Comments
Paolucci 2016	No funding		

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Pennix 2001 **FAST trial (substudy in patients with no baseline ADL disability)**	United States, 2 centers, academic medical centers	Inclusion criteria: age 60 years or older; pain in the knee(s) on most days of the month; difficulty with at least one of the following because of knee pain: walking0.4 km; climbing stairs; getting in and out of a car, bath, orbed; rising from a chair; or performing shopping, cleaning, or self-care activities; and radiographic evidence of knee osteoarthritis. Exclusion criteria: baseline ADL disability; the presence of a medical condition that precluded safe participation in an exercise program (e.g., recent myocardial infarction or stroke, severe chronic obstructive pulmonary disease, or congestive heart failure); inflammatory arthritis; regular exercise participation (1 time per week for at least 20 minutes); and inability to walk on a treadmill or walk, unassisted, 128 m in 6 minutes.	Randomized: 250* Treated: 230 Analyzed: 250 Attrition: 0% (0/250) *this article only included patients from the FAST trial would did not have baseline ADL disability

Author, Year	Intervention, Comparator
Pennix 2001 **FAST trial (substudy in patients with no baseline ADL disability)**	A.Aerobic Exercise Program (n=88) 3-month facility-based walking program of 3 times per week for 1 hour. Each session consisted of a 10-minute warm-up and cool-down phase, including slow walking and flexibility stretches, and a 40-minute period of walking at an intensity equivalent to 50% to 70% of the participants' heart rate reserve. Followed by 15-month home-based walking program. B.Resistance Exercise Program (n=82) 3-month supervised facility-based program, with 3 one-hour sessions per week, and a15-month home-based program. Each session consisted of a 10-minute warm-up and cool-down phase and a 40-minute phase consisting of 2 sets of 12 repetitions of 9 exercises. C.Attention Control (n=80) attended, during the first 3 months, monthly group sessions on education related to arthritis manage-ment, including time for discussions and social gathering. Later, participants were called bimonthly (months 4-6) or monthly (months 7-18) to maintain health updates and provide support

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Pennix 2001 **FAST trial (substudy in patients with no baseline ADL disability)**	A vs. B vs. C Age: 70 vs. 69 vs. 69 years Female: 66% vs. 72% vs. 66% African-American: 25% vs 21% vs 28% Education, >12 years: 58% vs. 57% vs. 61% Pain: 2.2 (0.6) vs 2.1 (0.5) vs 2.1 (0.3) Disability: 1.7 (0.5) vs 1.7 (0.5) vs 1.6 (0.4)	Incidence of ADL Disability. Disability assessed using a 30 item physical disability questionnaire and ADL disability was defined as experiencing (yes or no) some or a lot of difficulty or an inability in doing at least one of the follow-ing without help: bathing, eating, dressing, transferring from a bed to a chair, or using the toilet.	15 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Pennix 2001 **FAST trial (substudy in patients with no baseline ADL disability)**	A vs B vs C <u>Cumulative Incidence at 15 months</u> *ADL Disability (overall):* 36.4% (n=88) vs. 37.8% (n=82) vs. 52.5% (n=80) Disability in transferring from a bed to a chair: 29.5% vs. 36.6% vs. 50.0% Disability in bathing: 12.5% vs. 13.4% vs. 27.5% Disability in toileting: 19.4% vs. 13.4% vs. 25.0% Disability in dressing: 5.7% vs. 7.3% vs. 17.5% Disability in eating: 0% vs. 1.2% vs. 5.0%, p=0.02 <u>Adjusted relative risk (RR)* at 15 months</u> *ADL Disability (overall)* A vs. C: RR 0.53 (95% CI 0.33, 0.85), p=0.009 B vs. C: RR 0.60 (95% CI 0.38, 0.97), p=0.04 Disability in transferring from a bed to a chair A vs. C: RR 0.46 (95% CI 0.28, 0.76) B vs. C: RR 0.68 (95% CI 0.42, 1.09) p=0.007 for A/B vs. C Disability in bathing A vs. C: RR 0.31 (95% CI 0.15, 0.68) B vs. C: RR 0.44 (95% CI 0.21, 0.93) p=0.002 for A/B vs. C Disability in toileting A vs. C: RR 0.58 (95% CI 0.29, 1.15) B vs. C: RR 0.61 (95% CI 0.28, 1.31) p=0.13 for A/B vs. C Disability in dressing A vs. C: RR 0.20 (95% CI 0.07, 0.64) B vs. C: RR 0.46 (95% CI 0.17, 1.22) p=0.005 for A/B vs. C Disability in eating: incidence too small to calculate risks. *adjusted for site, race, age, sex, BMI, baseline walking speed, disability, volume of O2 taken up in 1 min/kg at peak exercise, and pain score

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Pennix 2001 **FAST trial (substudy in patients with no baseline ADL disability)**	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Pennix 2001 **FAST trial (substudy in patients with no baseline ADL disability)**	NR	Increased severity of knee OA leading to withdrawal: n=3 (not reported by exercise group)

Author, Year	Funding Source	Quality	Comments
Pennix 2001 **FAST trial (substudy in patients with no baseline ADL disability)**	grant P60AG10484-01 from the National Institute on Aging	Fair	Secondary analysis/outcome of original trial (Ettinger 1997) The Fitness Arthritis and Seniors Trial (FAST) Primary analyses were conducted by ITT using the data of all participants. When analyses were repeated among only those with complete data (n = 188), results were similar: the adjusted RR was 0.55 (95% CI 0.34-0.90; P= .02) for resistance exercise and 0.58 (95% CI, 0.36-0.94; P= .03) for aerobic exercise.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Pennix 2002 **FAST trial (substudy looking at baseline depressive symptoms)**	United States, 2 centers, academic medical centers	Inclusion criteria: age 60 years or older; pain in the knee(s) on most days of the month; difficulty with at least one of the following because of knee pain: walking0.4 km; climbing stairs; getting in and out of a car, bath, orbed; rising from a chair; or performing shopping, cleaning, or self-care activities; and radiographic evidence of knee osteoarthritis. Exclusion criteria: the presence of a medical condition that precluded safe participation in an exercise program (e.g., recent myocardial infarction or stroke, severe chronic obstructive pulmonary disease, or congestive heart failure); inflammatory arthritis; regular exercise participation (1 time per week for at least 20 minutes); and inability to walk on a treadmill or walk, unassisted, 128 m in 6 minutes.	Randomized: 439 Treated: 439 Analyzed: 407 Attrition: 7% (31/438)
Perlman 2012	United States	Inclusion Criteria: Eligible patients were men and women with radiographically established OA of the knee who met American College of Rheumatology criteria, were at least 35 years of age, and had a pre-randomization score of 40 to 90 on the visual analog pain scale. Patients with bilateral knee involvement had the more severely affected knee (determined by the patient) designated as the study knee. Subjects using NSAIDS or other medications to control pain were included if their doses remained stable three months prior to starting the intervention. Exclusion Criteria: Subjects were excluded if they suffered from rheumatoid arthritis, fibromyalgia, recurrent or active pseudogout, cancer, or other serious medical conditions. Subjects were also excluded if they had signs or history of kidney or liver failure; unstable asthma; knee replacement of both knees; reported recent use (4 weeks–1 year prior to enrollment) of oral or intra-articular corticosteroids or intra-articular hyaluronate; or knee arthroscopy or significant knee injury one year prior to enrollment. A rash or open wound over the knee and regular use of massage therapy (greater than once a month) also resulted in exclusion from the study.	Randomized: 125 Treated: 119 Completers: 115 Analyzed: 125 Attrition: 8% (10/125)

Author, Year	Intervention, Comparator
Pennix 2002 **FAST trial (substudy looking at baseline depressive symptoms)**	A.Aerobic Exercise Program (n=149) 3-month facility-based walking program of 3 times per week for 1 hour. Each session consisted of a 10-minute warm-up and cool-down phase, including slow walking and flexibility stretches, and a 40-minute period of walking at an intensity equivalent to 50% to 70% of the participants' heart rate reserve. Followed by 15-month home-based walking program. B.Resistance Exercise Program (n=146) 3-month supervised facility-based program, with 3 one-hour sessions per week, and a15-month home-based program. Each session consisted of a 10-minute warm-up and cool-down phase and a 40-minute phase consisting of 2 sets of 12 repetitions of 9 exercises. C.Attention Control (n=144) attended, during the first 3 months, monthly group sessions on education related to arthritis manage-ment, including time for discussions and social gathering. Later, participants were called bimonthly (months 4-6) or monthly (months 7-18) to maintain health updates and provide support
Perlman 2012	A1. Massage Therapy Group 1 (MT) (n=25) Participants received a uniform massage protocol designed to address symptoms of osteoarthritis of the knee with a series of standard Swedish massage strokes, and specified time allocated to various body regions. All study therapists agreed to the protocol and did not deviate from it. No. of Treatments: 1 per week for 8 weeks (8 total) Length of Treatments: 30 minutes A2. MT Group 2 (n=25) Identical treatment parameters to group A1 except differing 'dosage' of massage. No. of Treatments: twice per week for 4 weeks, then once weekly for four weeks (12 total) Length of Treatments: 30 minutes A3. MT Group 3 (n=25) Identical treatment parameters to group A1 except differing 'dosage' of massage. No. of Treatments: 1 per week for 8 weeks (8 total) Length of Treatments: 60 minutes A4. MT Group 4 (n=25) Identical treatment parameters to group A1 except differing 'dosage' of massage.. No. of Treatments: twice per week for 4 weeks, then once weekly for four weeks (12 total) Length of Treatments: 60 minutes B. Usual Care (n=25) Participants continued with their current treatment without the addition of massage therapy. No. of Treatments:

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Pennix 2002 **FAST trial (substudy looking at baseline depressive symptoms)**	All participants (not reported separately by treatment group) Age: 69 years Female: 70% Education, >12 years: 56% High depressive symptomology on the CES-D (cutoff of 5 points): 22% CES-D: 2.74 vs. 2.74 vs. 2.74	Short Version of Center for Epidemiologic Studies Depression (CES-D) (scale 0-18; higher score=more depression); 23-item self-report disability questionnaire (Scale 1-5; higher score=greater disability); Average knee pain during the past week for six different activities of daily living on a Likert scale (Scale 1-6; higher score=worse pain)	3 (immediately post treatment), 6, and 15 months
Perlman 2012	A1 vs. A2 vs. A3 vs. A4 vs. B Age: 70 vs. 62 vs. 63 vs. 64 vs. 64 Female: 60% vs. 72% vs. 76% vs. 68% vs. 76% Race: 92% vs. 88% vs. 76% vs. 80% vs 88% white Mean Duration of Chronicity: NR Global (WOMAC): 52.9(18.3) vs. 50.2(19.4) vs. 53.6(17.3) vs. 48.0(19.0) vs. 53.2(14.8) Pain (WOMAC): 52.3(19.9) vs. 42.4(23.0) vs. 52.5(16.5) vs. 44.4(19.3) vs. 46.3(15.4) Stiffness (WOMAC): 53.4(24.1) vs. 58.6(21.1) vs. 58.4(24.7) vs. 51.2(24.4) vs. 62.8(18.2) Physical Function (WOMAC): 52.9(17.9) vs. 49.5(19.5) vs. 49.8(19.7) vs. 48.3(20.2) vs. 50.5(17.4) Pain (VAS): 61.2(16.8) vs. 64.0(12.7) vs. 66.4(11.3) vs. 59.2(13.3) vs. 57.6(9.0)	Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, higher scores indicate greater pain, stiffness or functional limitation) *no range for the scales provided Pain (VAS, range 0-100mm: higher scores indicate severity of pain)	2 and 4 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Pennix 2002 **FAST trial (substudy looking at baseline depressive symptoms)**	CES-D (Depressive Symptoms), average over time: A vs C: 2.12 vs 2.80, p<0.001 B vs C: 2.59 vs 2.80, p=0.27
Perlman 2012	A1 vs. A2 vs. A3 vs. A4 vs. B 2 months: Δ in mean Global (WOMAC): -17.4 (-25.3, -9.4) vs. -18.4 (-27.5, -9.2) vs. -24.0 (-32.1, -15.9) vs. -24.0 (-32.7, -15.3) vs. -6.3 (-12.8, 0.1) Δ in mean Pain (WOMAC): -15.1 (-23.4, -6.8) vs. -14.4 (-23.8, -5.1) vs. -27.2 (-36.3, -18.0) vs. -27.7 (-36.9, -18.6) vs. -5.6 (-13.1, 1.9) Δ in mean Stiffness (WOMAC): -19.0 (-30.4, -7.6) vs. -23.4 (-34.5, -12.3) vs. -23.7 (-34.6, -12.7) vs. -22.3 (-32.9, -11.6) vs. -6.7 (-15.7, 2.2) Δ in mean Physical Function (WOMAC): -18.0 (-25.5, -10.4) vs. -17.2 (-26.9, -7.6) vs. -21.2 (-29.3, -13.1) vs. -22.0 (-31.6, -12.5) vs. -6.6 (-12.2, -0.9) Δ in mean Pain (VAS): -14.2 (-25.0, -3.4) vs. -26.1 (-36.8, -15.3) vs. -39.8 (-48.1, -31.4) vs. -31.2 (-39.4, -22.9) vs. -9.8 (-18.6, -1.1) 4 months: Δ in mean Global (WOMAC): -14.3 (95%CI -22.9 to -5.7) vs. -7.0 (95%CI -15.6 to 1.6) vs. -14.2 (95%CI -23.4 to -5.0) vs. -15.1 (95%CI -25.1 to -5.1) vs. -6.0 (95%CI -12.6 to 0.5) Δ in mean Pain (WOMAC): -12.2 (95%CI -22.4 to -2.0) vs. -3.9 (95%CI -12.7 to 4.9) vs. -13.7 (95%CI -23.4 to -4.0) vs. -14.2 (95%CI -24.5 to -3.8) vs. -7.5 (95%CI -16.0 to 1.1) Δ in mean Stiffness (WOMAC): -15.4 (95%CI -26.4 to -4.5) vs. -9.6 (95%CI -20.6 to 1.3) vs. -16.9 (95%CI -28.5 to -5.2) vs. -16.8 (95%CI -29.7 to -3.9) vs. -6.4 (95%CI -13.2 to 0.4) Δ in mean Physical Function (WOMAC): -15.3 (95%CI -24.5 to 26.1) -7.4 (95%CI -14.8 to 0) -12.1 (95%CI -22.0 to -2.1) -14.4 (95%CI -23.4 to -5.4) -4.2 (95%CI -11.1 to 2.7) Δ in mean Pain (VAS): -14.4 (95%CI -25.9, -2.8) -14.0 (95%CI -24.7 to -3.3) -18.5 (95%CI -29.0 to -8.1) -22.8 (95%CI -35.5 to -10.1) -11.5 (95%CI -21.0 to -2.0)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Pennix 2002 **FAST trial (substudy looking at baseline depressive symptoms)**	NR
Perlman 2012	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Pennix 2002 **FAST trial (substudy looking at baseline depressive symptoms)**	NR	NR
Perlman 2012	NR	No adverse effects related to the intervention were seen during the course of the study.

Author, Year	Funding Source	Quality	Comments
Pennix 2002 **FAST trial (substudy looking at baseline depressive symptoms)**	Grant P60AG10484-01 from the National Institute on Aging	Fair	Secondary analysis/outcome of original trial (Ettinger 1997) The Fitness Arthritis and Seniors Trial (FAST)
Perlman 2012	"The publication was made possible by grant number R01 AT004623 from the National Center for Complementary and Alternative Medicine (NCCAM) at the National Institutes of Health. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript."	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Poole 2007	UK Number of centers: 5 reflexologists, 4 therapists Outpatient GP surgeries or local health center	Age 18-65 years Benign chronic LBP: an unresolved episode of LBP >12 weeks duration Exclude: Pregnancy Significant co-existing major medical illness Diagnosed with significant co-existing psychiatric disorder In litigation Previous use of reflexology Contraindication to reflexology, including recent surgery and circulatory disorders of the lower limbs	Randomized: 243 Analyzed: 156 (6 months) Attrition: 36% (87/243)
Quilty 2003	UK, 1 community setting	Inclusion: chronic knee pain and radiographic evidence of predominant PFJ involvement. Exclusion: Advanced tibiofemoral joint changes, hip disease, previous major knee surgery, fractures involving the knee joint or rheumatoid arthritis.	Randomized: 87 Treated: 82 Analyzed: 82 Attrition: 6% (5/87)

Author, Year	Intervention, Comparator
Poole 2007	A: Respondent therapy (progressive muscle relaxation) (n=54): Guided progressive muscle relaxation treatment instructing the participant to tense then relax successive groups of muscles, focusing attention on the differential experience of each state. Groups of 1-4 participants. 6 treatments, approximately 1 hour duration, over 6-8 weeks. B.Reflexology (n=57): Morrell technique, application of firm but gentle compression to points of the feet thought to correspond to other parts of the body. 6 treatments, approximately 1 hour duration, over 6-8 weeks. C.Usual care (n=45): Treatments per patient's physician (General Practitioner). Treatments included prescription medication, over the counter medication, physiotherapy, massage, acupuncture, herbal remedies, TENS, pain management program, and no treatment (reported by participants at end of the study).
Quilty 2003	A. Physiotherapy (n=40) 9 sessions over a 10 week period lasting half an hour each carried out in a community setting. Patellar taping, 7 exercises (tailored to each patient), posture correction, and footwear advice. All exercises were to be pain-free and performed 10 times each, 5 times a day. B. Control (n=43): At the baseline visit all patients had a half-hour discussion with the physiotherapist concerning diagnosis, prognosis, footwear, weight reduction, and activity. General exercise was encouraged but no specific quadriceps exercises were advised

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Poole 2007	A vs. C Age: 46 vs. 47 Female: 65% vs. 51% Duration of pain (months): 128 vs. 115 Previous use of CAM: 55% vs. 53%	SF-36 domains (0-100) Oswestry Disability Index (ODI): (0-100%; higher percentage=greater impairment) Beck Depression Inventory (BDI) (0-63, higher score=more depressive symptoms) Pain (0-100 VAS)	4.5 months
Quilty 2003	A vs B Age: 69 vs 67 years BMI: 30 vs 30 WOMAC Function: 27.4 (12.2) vs 27.8 (10.1) VAS pain: 51.0 (29.3) vs 53.4 (25.9)	Overall pain in the most painful knee (Scale 0-100 mm Visual Analog Scale) Western Ontario and McMaster University OAindex (WOMAC) function sub-score (Scale 0-68)	2.5 and 10.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Poole 2007	A vs. C <u>Baseline</u> ODI (0-100): 33.2 (19.8) vs. 36.6 (17.7) Beck Depression Inventory (0-63): 13.5 (11.5) vs. 14.4 (9.8) Pain (0-100 VAS): 40.7 (28.6) vs. 40.6 (26.7) SF-36 physical functioning (0-100): 56.7 (29.1) vs. 45.4 (27.7) SF-36 social functioning (0-100): 61.9 (30.4) vs. 58.2 (29.7) SF-36 physical role limitations (0-100): 36.1 (42.1) vs. 29.1 (39.8) SF-36 emotional role limitations (0-100): 58.0 (46.2) vs. 58.1 (46.0) SF-36 pain (0-100): 43.8 (23.3) vs. 37.5 (20.3) SF-36 mental health (0-100): 61.3 (21.6) vs. 60.2 (18.4) SF-36 energy/vitality (0-100): 41.1 (22.3) vs. 39.7 (23.2) SF-36 general health perception (0-100): 52.1 (24.7) vs. 55.0 (23.1) <u>4.5 months</u> ODI (0-100): 31.3 (21.1) vs. 32.9 (17.6) Beck Depression Inventory (0-63):12.6 (10.9) vs. 12.8 (9.2) Pain (0-100 VAS): 41.3 (28.5) vs. 42.7 (28.4) SF-36 physical functioning (0-100): 57.3 (31.8) vs. 52.2 (29.5) SF-36 social functioning (0-100): 66.7 (31.6) vs. 61.5 (30.8) SF-36 physical role limitations (0-100): 53.2 (45.1) vs. 37.8 (42.5) SF-36 emotional role limitations (0-100): 63.0 (43.8) vs. 62.0 (44.0) SF-36 pain (0-100): 48.8 (25.9) vs. 44.4 (28.5) SF-36 mental health (0-100): 64.4 (20.7) vs. 67.7 (18.5) SF-36 energy/vitality (0-100): 44.8 (21.3) vs. 48.3 (21.8) SF-36 general health perception (0-100): 52.4 (22.8) vs. 55.0 (24.1)
Quilty 2003	A vs B <u>2.5 months post-treatment</u> WOMAC function: 26.5 (13.2) vs 27.5 (10.7); Adjusted MD* -0.6 (95% CI -3.7, 2.4), p=0.68 VAS Pain: 42.8 (25.1) vs 50.5 (25.6); Adjusted MD* -6.4 (95% CI -15.3, 2.4), p=0.16 <u>10.5 months post-treatment</u> WOMAC function: 29.7 (11.2) vs 28.3 (11.3); Adjusted MD* 1.7 (95% CI -1.8, 5.2), p=0.34 VAS Pain: 48.1 (25.7) vs 54.1 (22.5); Adjusted MD* -4.9 (95% CI -13.6, 3.8), p=0.27 *Analysis of covariance (ANCOVA) with baseline measures as covariates to account for any random baseline variability between the groups

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Poole 2007	NR
Quilty 2003	NA

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Poole 2007	NR	A vs. C Withdrawal prior to treatment: 4% (3/85) vs. 5% (4/79) Withdrawal at 18 weeks: 36% (31/85) vs. 43% (34/79) Withdrawal due to AEs: NR Serious AEs: NR Nonserious AEs: NR
Quilty 2003	NA	A vs B Withdrawals 2% (1/43) vs 0% (0/44) "There were no major side effects associated with the treatment, but 7 (16%) patients in the physiotherapy group experienced mild and short-lived skin reactions associated with prolonged use of the zinc oxide patellar tape"

Author, Year	Funding Source	Quality	Comments
Poole 2007	NR	Poor	Group B had Reflexology (Massage) intervention. Didn't enter those results here - abstracted in the massage excel. Only entered for Relaxation vs. Usual Care
Quilty 2003	NHS Research and Development programme (Physical and Complex Disabilities PCD/A1/123).	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Quinn 2008	UK Number of centers: 1 Outpatient	Diagnosed with non-specific LBP Any treatment for LBP stabilized for 3 months Reflexology naive Exclude: Involvement in other research projects within 3 months	Randomized: 15 Treated: 15 Analyzed: 15

Author, Year	Intervention, Comparator
Quinn 2008	A: Reflexology: Pressure massage stimulation of numerous specific reflex points on the feet associated with the vertebrae of the spine and surrounding musculature (n=7) B: Sham reflexology: Simple foot massage with stimulation of reflex points, avoiding vertebrae of the spine and surrounding musculature. (n=8) Both groups received 40 minute weekly sessions for 6 weeks

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Quinn 2008	Age (median): 42 vs. 45 Female: 86% vs. 50% Pain visual analogue scale: 4.7 vs. 3.4 RDQ: 5 vs. 7.5 McGill pain scale: 24 vs. 19	Primary outcomes: Pain Visual Analogue Scale: 10cm scale, higher number = worse pain Secondary outcomes: RDQ: total score 0-24, higher number=worse function McGill Pain questionnaire: total score 0-77, higher number=worse pain SF-36 health survey: total score 0-100, higher number=better health quality of life	1.5 and 3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Quinn 2008	A vs. B, median (IQR) <u>Baseline</u> RDQ: 5 (4 to 8.6) vs. 7.5 (3 to 9.3) Pain (0-10 VAS): 4.7 (3.5 to 6.6) vs. 3.4 (3.0 to 4.2) McGill Pain Questionnaire (0-77): 24 (22.5 to 28) vs. 19 (12.8 to 21.8) <u>1.5 months</u> RDQ: 4 (3 to 4.5) vs. 4.5 (1 to 7) Pain (0-10 VAS): 2.1 (1.5 to 4.9) vs. 4.1 (2.7 to 5.1) McGill Pain Questionnaire (0-77): 11 (6 to 17) vs. 6.5 (5 to 13) <u>3 months</u> RDQ: 4 (2 to 5) vs. 3.5 (1.8 to 4.8) VAS: 2.2 (1.6 to 3.2) vs. 3.2 (2.6 to 4.6) McGill Pain Questionnaire (0-77): 6 (4 to 13) vs. 7.5 (3.8 to 9.8)

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Quinn 2008	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Quinn 2008	NR	Adverse Events: None reported Withdrawals: None

Author, Year	Funding Source	Quality	Comments
Quinn 2008	NR	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Redondo 2004	Spain 1 center Tertiary care hospital	Females with FM fulfilling ACR criteria Exclude: Serious concomitant diseases	Randomized: 40 Treated: 40 Analyzed: 31 Attrition: 23% (9/40)

Author, Year	Intervention, Comparator
Redondo 2004	A.Cognitive Behavior Therapy (n=21): One 2.5 hour session per week for 8 weeks. Sessions were designed to reduce distorted pain dimensions, to cope with chronic pain, and to increase self-efficacy. Techniques included giving information about chronic pain, giving information about FM, teaching relaxation techniques, and teaching coping strategies for chronic pain. Rate of compliance with sessions was mean = 72%. B.Exercise (n=19): Five 45 minute sessions of PE per week for 8 weeks. Each week consisted of 1 sessions of aquatic exercises, 2 sessions of flexibility and endurance exercises, and 2 sessions of cardiovascular fitness exercises. At the end of the 8 week program, patients received instructions to maintain daily physical exercises at home. Rate of compliance with sessions was mean = 84%. All subjects: Offered pharmacologic treatment of anti-inflammatory doses of ibuprofen or diclofenac, 25 mg of amitriptyline a day, amd acetaminophen. Patients were free to modify medication based on their clinical response

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Redondo 2004	A vs B* Female: 100% vs 100% FIQ†: 52.0 (12.0) vs 52.0 (11.4) FIQ pain: 7.3 (2.3) vs 6.8 (1.7) FIQ depression: 5.2 (3.0) vs 5.3 (3.3) FIQ anxiety: 6.4 (3.4) vs 6.3 (3.3) Beck Anxiety Inventory: 24.1 (12.3) vs 22.1 (11.8) Beck Depression Inventory: 19.2 (12.0) vs 16.8 (13.4) SF-36 physical functioning: 41.9 (22.3) vs 47.1 (15.0) SF-36 physical role: 16.7 (26.6) vs 18.4 (24.8) SF-36 bodily pain: 23.3 (15.7) vs 28.5 (9.9) SF-36 general health: 25.7 (14.8) vs 39.0 (17.4) SF-36 vitality: 32.1 (16.7) vs 31.3 (17.3) SF-36 social functioning: 55.3 (25.8) vs 67.1 (26.7) SF-36 emotional role: 45.0 (46.2) vs 64.9 (40.8) SF-36 mental health: 43.7 (21.8) vs 49.9 (24.5) SF-36 health change: 4.2 (0.7) vs 4.0 (1.0)	FIQ (0-80, higher score=higher disability); FIQ pain (0-10, higher score=greater pain); FIQ depression (0-10, higher score=greater depression); FIQ anxiety (0-10, higher score=greater anxiety); Beck Anxiety Inventory (0 63, higher score=higher anxiety); Beck Depression Inventory (0-63, higher scores=higher depression) SF-36 subscales (0-100, higher score=higher quality of health); SF-36 health change (0-5, higher score=more negative health change)	6 and 12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Redondo 2004	

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Redondo 2004	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Redondo 2004	A vs B <u>6 months</u> FIQ: 47.4 (15.4) vs 48.0 (17.3), (MD -0.6, 95% CI -12.6 to 11.4) p=0.92 FIQ pain: 5.9 (2.6) vs 6.9 (2.4), (MD -1.0, 95% CI -2.8 to 0.8) p=0.28 FIQ depression: 5.2 (3.5) vs 5.3 (3.2), (MD -0.1, 95% CI -2.6 to 2.4) p=0.93 FIQ anxiety: 6.0 (3.1) vs 5.8 (3.5), (MD 0.2, 95% CI -2.2 to 2.6) p=0.87 Beck Anxiety Inventory: 25.2 (10.0) vs 22.1 (12.3), (MD 3.1, 95% CI -5.1 to 11.3) p=0.45 Beck Depression Inventory: 17.1 (12.2) vs 15.0 (11.4), (MD 2.1, 95% CI -6.6 to 10.8) p=0.63 SF-36 physical functioning: 52.2 (18.4) vs 43.9 (21.5), (MD 8.3, 95% CI -6.4 to 23.0) p=0.26 SF-36 physical role: 22.4 (35.2) vs 18.3 (33.7), (MD 4.1, 95% CI -21.2 to 29.4) p=0.74 SF-36 bodily pain: 31.4 (20.1) vs 32.9 (19.6), (MD -1.5, 95% CI -16.1 to 13.1) p=0.84 SF-36 general health: 35.5 (14.7) vs 37.6 (21.0), (MD -2.1, 95% CI -15.3 to 11.1) p=0.75 SF-36 vitality: 38.9 (18.0) vs 32.6 (17.9), (MD 6.3, 95% CI -6.9 to 19.5) p=0.34 SF-36 social functioning: 66.4 (30.9) vs 66.9 (26.1), (MD -0.5, 95% CI -21.6 to 20.6) p=0.96 SF-36 emotional role: 68.4 (40.8) vs 66.0 (42.6), (MD 2.4, 95% CI -28.2 to 33.0) p=0.87 SF-36 mental health: 48.9 (20.9) vs 51.8 (23.6), (MD -2.9, 95% CI -19.3 to 13.5) p=0.72 SF-36 health change: NR <u>12 months</u> FIQ: 47.8 (14.7) vs 47.7 (14.1), (MD 0.1, 95% CI -10.5 to 10.7) p=0.98 FIQ pain: 6.3 (2.3) vs 6.6 (2.0), (MD -0.3, 95% CI -2.0 to 1.3) p=0.70 FIQ depression: 5.4 (3.4) vs 4.9 (3.5), (MD 0.5, 95% CI -2.0 to 3.0) p=0.69 FIQ anxiety: 6.0 (3.0) vs 5.8 (3.2), (MD 0.2, 95% CI -2.1 to 2.5) p=0.86 Beck Anxiety Inventory: 20.0 (9.0) vs 20.0 (11.2), (MD 0.0, 95% CI -7.4 to 7.4) p=1.00 Beck Depression Inventory: 13.0 (8.0) vs 13.6 (11.7), (MD -0.6, 95% CI -7.9 to 6.7) p=0.87 SF-36 physical functioning: 38.9 (24.0) vs 41.6 (21.7), (MD -2.7, 95% CI -19.5 to 14.1) p=0.75 SF-36 physical role: 26.1 (30.3) vs 31.0 (32.3), (MD -4.9, 95% CI -27.9 to 18.1) p=0.67 SF-36 bodily pain: 33.8 (30.7) vs 34.3 (24.2), (MD -0.5, 95% CI -20.9 to 19.9) p=0.96 SF-36 general health: 39.7 (20.6) vs 35.7 (15.3), (MD 4.0, 95% CI -9.4 to 17.4) p=0.55 SF-36 vitality: 38.4 (14.1) vs 34.5 (16.6), (MD 3.9, 95% CI -7.4 to 15.2) p=0.49 SF-36 social functioning: 60.7 (23.0) vs 57.2 (32.8), (MD 3.5, 95% CI -17.2 to 24.2) p=0.73 SF-36 emotional role: 66.7 (41.3) vs 58.7 (42.1), (MD 8.0, 95% CI -19.2 to 35.2) p=0.55 SF-36 mental health: 56.5 (27.4) vs 53.8 (31.8), (MD 2.7, 95% CI -19.1 to 24.5) p=0.80 SF-36 health change: 3.3 (1.2) vs 3.9 (1.0), (MD -0.6, 95% CI -1.4 to 0.2) p=0.14	NR

Author, Year	Funding Source	Quality	Comments
Redondo 2004		Poor	*Authors state that baseline characteristics were measured but no demographics were actually reported in the study †Individual subscales were also reported but only pain, anxiety, and depression were abstracted separately MDs and p values calculated. Baseline values of outcome measures may be different enough to warrant adjusted analysis to be done

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Rejeski 2002 ADAPT Trial (same trial as Messier 2004; reports quality of life outcomes)	United States 1 center University	Aged 60 or older, BMI greater or equal to 28, knee pain on most days of the month, sedentary lifestyle with less than 20 minutes of formal exercise once a week for the past 6 months, self-reported difficulty in at least one of the following activities due to knee pain: 0.25 mile walk, climbing stairs, bending, stopping, kneeling, shopping, housecleaning, radiographic evidence of tibio-femoral osteoarthritis, willingness to undergo testing and intervention procedures Exclude: Serious medical condition preventing safe participation in an exercise program, Mini-Mental score less than 24, inability to complete 18 month study, inability to walk without a cane or assistive device, participation in another research study, greater than or equal to 14 alcoholic drinks per week, inability to complete protocol	Randomized: 158 Treated: NR Analyzed: 158 Attrition:
Roche 2007/2011	France, inpatient rehabilitation center	Inclusion Criteria: Eligibility for patients with nonspecific chronic LBP for at least 3 months, age 18 to 50 years, on sick leave or at risk of work disability, presently engaged in a nonlimited work contract, and having given informed consent. Exclusion Criteria: Exclusion for LBP of specific origin (malignant, traumatic, infectious, or inflammatory LBP, acute sciatica, spondylolisthesis), recent spinal surgery (< 4 months), cardiac or respiratory insufficiency (detected by stress tests), neurologic impairment, a psychiatric disorder precluding group therapy, and receiving disability pensions.	Randomized: 86 Treated: 131 Analyzed: 113 Attrition: 14.4% (19/132)

Author, Year	Intervention, Comparator
Rejeski 2002 ADAPT Trial (same trial as Messier 2004; reports quality of life outcomes)	A.Exercise (n=80): Three 1 hour sessions per week done at the study facility for 4 months. After 4 months, participants who wanted to do a home-based program had the option to undergo a 2 month transition phase alternating between facility and home sessions, after which they carried out the program at home. Sessions consisted of 15 minutes of aerobic exercises, 15 minutes of resistance-training, an additional 15 minutes of aerobic exercises, and a 15 minute cool down phase. B.Control (n=78): 1 hour sessions monthly for three months consisting of presentations on osteoarthritis, obesity, and exercise and a question and answer session. Monthly phone contact was maintained for months 4-6 and bimonthly phone contact was maintained for months 7-18. During phone calls, researchers gathered information on pain, medication, illnesses, and hospitalizations. On phone calls, participants were also able to ask questions and voice concerns.
Roche 2007/2011	A: Multidisciplinary intensive functional restoration Program (n=68): Patients in groups of 6-8 were exposed to an exercise program with a physiotherapist including warm-up, stretching, flexibility training, aerobic exercises, and strengthening (with occupational therapist), muscular endurance and coordination exercises, and balneotherapy sessions. Patients also received psychologist provided counseling. 5 days/week for 5 weeks (25 total), 6 hours per day B. Individualized exercise therapy (n=64): Active exercise directed by physiotherapist including flexibility, stretching, strengthening, proprioception exercises, endurance training. Home exercise program including jogging, swimming, stretching. 3 sessions/week for 5 weeks (15 total), 1 hour each

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Rejeski 2002 ADAPT Trial (same trial as Messier 2004; reports quality of life outcomes)	A vs B Age: 68 vs 69 Female: 74% vs 67% Cardiovascular disease: 16% vs 15% Diabetes: 11% vs 9% SF-36 physical component score, mean (SE): 34.5 (1.1) vs 33.6 (1.0) SF-36 mental component score, mean (SE): 54.3 (1.0) vs 52.7 (1.3)	SF-36 physical component score (0-100, higher score=higher quality of life); SF-36 mental component score (0-100, higher score=higher quality of life)	6 and 18 months
Roche 2007/2011	A vs B Mean Age, years: 41 vs. 39 Female, %: 32.4 vs. 37.5 Race: NR History of spinal surgery, %: 23.5 vs. 18.8, p<0.05 Mean duration of symptoms: NR No. of sick-leave days in the 2 yr. before treatment: 185 (149) vs. 180(135) Pain (0-10 VAS): 4.7 (2.1) vs. 4.5 (2.1) Dallas Pain Questionnaire daily activities (0-100): 51.8 (SD not reported) vs 51 (23.3) Dallas Pain Questionnaire work and leisure (0-100): 51.9 (SD not reported) vs. 58 (27.7) Dallas Pain Questionnaire anxiety/depression (0-100): 36.7 (SD not reported) vs. 30.9 (23.5) Dallas Pain Questionnaire social interaction (0-100): 30.7 vs. 27.4 (SD not reported)	Primary Dallas Pain Questionnaire, 4 subscales (0-100, higher scores are more unfavorable) Pain (0-10 VAS) % return to work % working full-time days of sick leave Anxiety/Depression Dallas Pain Questionnaire (DPQ-Anxiety/Depression)	10.75 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Rejeski 2002 ADAPT Trial (same trial as Messier 2004; reports quality of life outcomes)	A vs B SF-36 physical component score, mean (SE): 37.1 (1.3) vs 34.4 (1.1) SF-36 physical component score, adjusted mean (SE): 37.6 (0.9) vs 35.3 (0.8) SF-36 mental component score, mean (SE): 52.9 (1.3) vs 53.5 (1.2) SF-36 mental component score, adjusted mean (SE): 54.1 (0.8) vs 53.7 (0.8) Results were an average of 6 and 18 month followup data
Roche 2007/2011	NR

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Rejeski 2002 ADAPT Trial (same trial as Messier 2004; reports quality of life outcomes)	
Roche 2007/2011	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Rejeski 2002 ADAPT Trial (same trial as Messier 2004; reports quality of life outcomes)		NR
Roche 2007/2011	A vs. B, mean (SD) Baseline Pain (0-10 VAS): 4.7 (2.1) vs. 4.5 (2.1) Dallas Pain Questionnaire daily activities (0-100): 51.8 (SD not reported) vs 51 (23.3) Dallas Pain Questionnaire work and leisure (0-100): 51.9 (SD not reported) vs. 58 (27.7) Dallas Pain Questionnaire anxiety/depression (0-100): 36.7 (SD not reported) vs. 30.9 (23.5) Dallas Pain Questionnaire social interaction (0-100): 30.7 vs. 27.4 (SD not reported) 10.75 months No. of Sick-leave days: 37.3 (67.8) vs. 72.0 (109.9), difference -34.7 (95% CI -68.00 to -1.41) Working: 81.6% (52/64) vs. 82.8% (56/68) Pain (0-10 VAS): 2.9 (2.4) vs. 3.5 (2.3), difference -0.6 (95% CI -1.49 to 0.29) Dallas Pain Questionnaire daily activities (0-100): 31.4 (22.9) vs. 39.1 (21.9), difference -7.7 (95% CI -16.15 to 0.75) Dallas Pain Questionnaire work and leisure (0-100): 29.8 (25.2) vs. 39.6 (24.4), difference -9.8 (95% CI -19.15 to -0.45) Dallas Pain Questionnaire anxiety/depression (0-100): 21.9 (23.6) vs. 25.5 (24.1), difference -3.6 (95% CI -12.56 to 5.36) Dallas Pain Questionnaire social interaction (0-100): 15.5 (20.9) vs. 24.7 (25.6), difference -9.2 (95% CI -17.87 to -0.53)	NR

Author, Year	Funding Source	Quality	Comments
Rejeski 2002 ADAPT Trial (same trial as Messier 2004; reports quality of life outcomes)	Grants AG14131 and 5P60 AG10484 from the National Institute on Aging and Grant M01-RR00211 from the General Clinical Research Center	Fair	A diet group (n=73) and a diet+exercise group (n=68) were also included in the study but data was not abstracted *Number randomized was given and percent of participants that completed the study, but back calculations using percents differed (were higher) from N's given in baseline characteristics table. Unclear where additional patients were lost Analyses were conducted using SAS PROC MIXED, a procedure that used all of the available followup information collected at the 6- and 18-month assessments. This procedure provides maximum-likelihood estimates allowing for missing data. The method enables missing data to be dependent on baseline and other observed data and provides unbiased estimates making a missing at random assumption. --> Implications for # analyzed? Adjusted mean information: "Analyses for group differences were adjusted for the prerandomized levels of the baseline value of the outcome beng analyzed, age, and gender"
Roche 2007/2011	"institutional funds"	Fair	Differences at followup calculated

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Rosedale 2014	Canada Number of centers unclear Outpatient	Knee pain for longer than 4 months and a radiologically confirmed diagnosis of knee OA. Exclude: Unable to attend exercise physiotherapy 2 to 3 times per week for 2 weeks, neurological conditions affecting lower extremities	Randomized: 180 Treated: 158 Analyzed: 124 Attrition: 31% (56/180)
Rudolfsson 2014	Sweden Outpatient setting 2008	Swedish-speaking women, age range 25–65 years, with chronic (>3 months) non-specific neck pain, disability, measured as >9 normalized points of the first 19 items in the Disability Arm Shoulder Hand (DASH) questionnaire Excluded: onset or worsening of neck pain associated with trauma; psychiatric, rheumatic, neurological, inflammatory, endocrine or connective tissue disease; fibromyalgia; cancer; stroke; cardiac infarction or diabetes type I; surgery or fracture to the back, neck, or shoulder in the last 3 years or shoulder luxation in the last year; strenuous exercise >3 times/week during the last 6 months.	Randomized: 108 Treated: 101 Analyzed: 85 Attrition: 21% (23/108)
Sahin 2010	Turkey	Chronic soft tissue neck pain ≥3 months;, 18-65 years of age; >3 in 0-10 VAS pain scale; failed physical therapy, medical therapy or collar for one month; no previous acupuncture therapy. Excluded: radicular pain, neurological deficits and disk herniation; lumbar pain ≥3 months with VAS >5; radiological evidence of narrowing of cervical neural foramen and facet osteoarthritis; fracture; congenital neck deformities; spondylolysis or spondylolisthesis; trauma, vertebral collapse, infection, malignancy, systemic disease, thoracic outlet syndrome, temporomandibular joint dysfunction, spinal cord surgery, psychotic disorder, pregnancy, previous use of antineoplastic and immunosuppressive medications, bleeding diathesis, physical or medical or manual therapy within a week before study initiation.	Randomized: 31 Treated: 31 Analyzed: 29 Attrition: 6% (2/31)

Author, Year	Intervention, Comparator
Rosedale 2014	A.Exercise (n=120): Program was based on the exercise-based treatment program Mechanical Diagnosis and Therapy (MDT). Subjects were categorized as MDT derangement, meaning a direction of knee movement performed repeatedly had a positive and lasting effect on symptoms, or to MDT nonresponder, accounting for subjects that did not have a lasting positive change from the repeated movements. The MDT derangement group was given end-range exercises in the direction they had responded to, to be performed 10 times every 2 to 3 hours. The MDT nonresponder group was given exercises to strengthen quadriceps and aerobic exercises. All subjects in the exercise group attended 4 to 6 physiotherapy sessions, 2 to 3 assessment sessions lasting up to 1 hour and the rest followup sessions lasting 20 minutes, over a 2 week period. B.Waiting list (n=60): Subjects were followed up in the orthopedic department at the surgeon's discretion and continued receiving their usual care.
Rudolfsson 2014	A.Massage (n=28) (classical) for the upper body including the back, neck and shoulders. Care was taken not to massage the affected body regions too forcefully. B.Neck coordination exercise (n=28) performed with a newly developed training device designed to improve the fine movement control of the cervical spine. The device, strapped to the head, consists of a plate with 5 exchangeable surfaces that allow for progression of task difficulty (decreasing rolling resistance). The exercise task, performed in sitting, was to control the movement of a metal ball on the plate. Visual feedback was provided via mirror. Training consisted of a basic training program and a progression program with 12 levels of increasing training dose, task variability and difficulty. C.Strength training (n=29) with isometric and dynamic exercises targeting the neck and shoulder regions. Three exercises were isometric (15 repetitions) and 3 dynamic (2 sets of 15 repetitions). Progressive resistance was given as strength increased during the sessions. Both intensity and the extent of training were considered adequate to attain strength gains. All 3 interventions consisted of 22 individually supervised single treatment sessions, 30 min each, distributed over 11 weeks
Sahin 2010	A.Electro-acupuncture (n=13) 3 sessions per week, each lasting for 30 minutes, 10 sessions in total. Local and distant acupuncture points used: (BL10), BL60, LI4, TE5, GB20, GB21 and GV14. Electric needle stimulation for 30 minutes at low frequency (I -4Hz), pulse width of 200|is, interrupted currents with high intensity. Deqi perception obtained. B.Sham acupuncture (n=16) 3 sessions in a week, each lasting for 30 minutes, with 10 sessions in total. The sham acupuncture was similar to needle placement in group A, but needles were inserted into points 1-2 cm away from meridian points in group A. Electrical stimulation was administered as in group A until the patient perceived the current, after which it was switched off

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Rosedale 2014	A vs B Age: 66 vs 64 Female: 56% vs 60% Median comorbidities: 3 vs 3 KOOS function: 56 (17) vs 51 (18) KOOS function in sport and recreation: 22 (21) vs 20 (19) KOOS pain: 51 (17) vs 46 (17) P4 pain scale: 21 (10) vs 23 (8) KOOS knee symptoms: 50 (17) vs 48 (21) KOOS quality of life: 28 (17) vs 27 (19)	KOOS function subscale (0-100, higher score=higher function); KOOS function in sport and recreation subscale (0-100, higher score=higher function); KOOS pain subscale (0-100, higher score=lower pain); P4 pain scale (0-40, higher score=higher pain); KOOS knee symptoms subscale (0-100, higher score=fewer symptoms); KOOS quality of life subscale (0-100, higher score=higher quality of life)	2.5 months
Rudolfsson 2014	A vs B vs C Age: 51 vs 52 vs 51 years Female: 100% vs 100% vs 100% Weight (kg): 73 vs 74 vs 74 Height (cm): 167 vs 164 vs 165 Pain duration: 120 vs 123 vs 84 months (median) Pain NRS (0-10), 5 vs 6 vs 6 (median) NDI: 26 vs 29 vs 31 SF-36 PCS: 43 vs 39 vs 39 (median) SF-36 MCS: 49 vs 52 vs 47 (median)	Pain NRS (scale 0-10, higher score worse pain)	6 months
Sahin 2010	A vs B Age: 39 vs 35 years Female: 100% vs 81% Not married: 23% vs 25% University graduate: 54% vs 94% BMI: 23.9 vs 24.6 Pain with motion (0-10): 7.38 (1.61) vs 6.19 (1.60) Pain at rest: 4.00 (3.03) vs 5.25 (1.95)	Neck pain at rest and with motion in the last week (scale 0-10, higher score worse pain) Short-Form 36 (SF-36) (scale 0-100, higher score=better QoL)	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Rosedale 2014	A vs B KOOS function: 61 (17) vs 52 (16), (Adj MD 5, 95% CI 1 to 9) KOOS function in sport and recreation: 31 (23) vs 24 (19), (Adj MD 6, 95% CI 0 to 11) KOOS pain: 56 (17) vs 46 (16), (Adj MD 7, 95% CI 3 to 11) P4 pain scale: 24 (8) vs 21 (10), (Adj MD -2, 95% CI -4 to 1) KOOS knee symptoms: 56 (17) vs 52 (19), (Adj MD 2, 95% CI -2 to 6) KOOS quality of life: 34 (19) vs 32 (19), (Adj MD 1, 95% CI -3 to 6)
Rudolfsson 2014	
Sahin 2010	A vs B 3 month outcomes Pain with motion: 4.50 (2.48) vs 5.38 (2.29), MD -0.88 (95% CI -2.70 to 0.94), p=0.330 Pain at rest: 4.00 (2.97) vs 3.54 (3.13), MD 0.46 (95% CI -1.88 to 2.80), p=0.690

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Rosedale 2014	
Rudolfsson 2014	
Sahin 2010	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Rosedale 2014		NR
Rudolfsson 2014	A vs B 6-month outcomes Pain NRS: 4.0 (2.1) vs 3.8 (1.7), MD 0.2 (95% CI -0.82 to 1.22), p=0.697 A vs C: Pain NRS: No data given at 6 month, however, authors state no difference among A, B or C.	A vs B vs C Increased headache and neck pain throughout intervention period: 0 vs 1 vs 0 Increased transient symptoms in the neck or headache on 1-4 occasions: 0 vs 10 vs 0
Sahin 2010		NR

Author, Year	Funding Source	Quality	Comments
Rosedale 2014	The International MDT Research Foundation	Fair	Effect sizes were reported at Cohens d
Rudolfsson 2014	Alfta Research Foundation**,** grants from the Swedish Council for Working Life and Social Research (2006-1162) and Länsförsäkringar Forskning och Framtid (51-1010/06).	Fair	Purpose was to evaluate neck coordinating exercise (treatment B) vs. strengthening ("best available treatment" C) vs. sham (massage, A).
Sahin 2010	NR	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Sanudo 2010	Spain Recruited from physician practices and FM support groups	Women who met ACR 1990 criteria for FM Exclusion: inflammatory rheumatic disease, severe psychiatric illness, respiratory or cardiovascular disease that prevents physical exertion, receiving psychological or physical therapy	Randomized: 64 Analyzed: 55 Attrition: 14% (9/64)
Sanudo 2012	Spain Recruited from physician practices and FM support groups	Women who met ACR 1990 criteria for FM Exclusion: inflammatory rheumatic disease, severe psychiatric illness, respiratory or cardiovascular disease	Randomized: 41 Analyzed: 15 Attrition: 63% (26/41)
Sanudo 2015	Spain Recruited from FM support groups	Inclusion: women with FM Exclusion: pulmonary, cardiovascular, severe psychiatric, or inflammatory rheumatic disease; attended psychological or physical therapy or received exercise training in past year	Randomized: 32 Analyzed: 28 Attrition: 13% (4/32) (4 control subjects "excluded from analysis by removal of outliers")

Author, Year	Intervention, Comparator
Sanudo 2010	A.Supervised aerobic exercise (n=18): 2 sessions/week for 24 weeks of 45-60 minutes. Each session included warm-up, 15-20 minutes of steady-state aerobic exercise, 15 minutes of interval training that included aerobic dance and jogging, and 5-10 minutes of cool down. B.Supervised aerobic, muscle strengthening, and flexibility exercises (n=17): twice-weekly sessions for 24 weeks of aerobic and resistance exercise with warmup, 10-15 minutes of aerobic exercise, 15-20 minutes of muscle strengthening exercise, and 10 minutes of flexibility exercises. C.Usual care control (n=20): medical treatment for FM and continued normal daily activities, which did not include aerobic exercise.
Sanudo 2012	A.Exercise (n=13): Twice-weekly 45- to 60-minute sessions of exercise (10-minute warmup, 10-15 minutes aerobic exercise, 15-20 minutes muscle strengthening exercise, 10 minutes flexibility exercises) for 6 months. B.Usual care (n=12): usual medical care and normal daily activities, which did not include structured exercise. Subjects alternated between 6 months of training and 6 months with no exercise intervention (asked not to participate in any structured exercise program) for 30 months.
Sanudo 2015	A.Aerobic exercise (n=16): two sessions per week of 45-60 minutes, for 24 weeks. Each session included 10 minutes warmup, 15-20 minutes steady state exercise at 60-65% of predicted maximum heart rate, 15 minutes of interval training at 75-80% of predicted maximum heart rate, and 5- 10 minutes cool down. B.Usual care control (n=12): normal activities, which did not include structured exercise.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Sanudo 2010	A vs C Age: 55.9 (1.6) vs 56.6 (1.9) FIQ: 60.9 (3.4) vs 60.5 (3.8) 6-minute walk test: 512.2 (15.9) vs 488.7 (16.9) BDI: 28 (4) vs 31 (3) SF-36 total: 36.1 (2.9) vs 37.7 (3.3) B vs C Age: 55.9 (1.7) vs 56.6 (1.9) FIQ: 62.2 (4.2) vs 60.5 (3.8) 6-minute walk test: 535.0 (16.2) vs 488.7 (16.9) BDI: 25 (3) vs 31 (3) SF-36 total: 39.1 (3.9) vs 37.7 (3.3)	FIQ (0-100; higher scores=more severe symptoms and disability) 6-minute walk test: higher scores=greater distance Beck Depression Inventory (BDI; 0-63, higher scores=greater depression) SF-36 (0-100, higher scores=better health-related quality of life)	Immediately post-intervention (24 weeks)
Sanudo 2012	A vs B Female: 100% vs 100% Pain duration NR FIQ: 58.6 (12.2) vs 55.6 (12.5) SF-36: 41.4 (14.7) vs 33.5 (11.7) BDI: 19.9 (7.6) vs 20.4 (7.7)	FIQ (0-80 without job-related items; higher scores = more negative impact) Beck Depression Inventory (BDI; 0-63, higher scores = greater depression) SF-36 (0-100, higher scores=better outcomes)	Immediately post 6-month intervention and at the beginning and end of two more 6-month exercise programs -
Sanudo 2015	A vs B Age: 55 vs 58 years Female: 100% vs 100% Race NR Pain VAS: 7.4 vs 7.2 Anxiety: 6.9 vs 6.4 Depression: 6.5 vs 7.1 Sleep disturbance: 7.5 vs 8.4	Pain VAS (0-10 scale, higher scores=greater pain) Anxiety VAS (0-10, higher scores=greater anxiety) Depression VAS (0-10, higher scores=greater depression) Sleep VAS (0-10, higher scores=worse sleep)	Immediately post-intervention (24 weeks from baseline)

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Sanudo 2010	A vs C, mean improvement from baseline FIQ: -8.8 (14) vs. NR; p < 0.05 BDI: -8.5 (8) vs. NR; p < 0.01 SF-36 total: 8.9 (10) vs.NR; p < 0.05 B vs C, mean improvement from baseline FIQ: -8.8 (12) vs. NR; p < 0.01 BDI: -6.4 (4) vs. NR; p < 0.01 SF-36 total: 8.4 (11) vs. NR; p < 0.01
Sanudo 2012	A vs B 6 months (n = 18 vs. 19): FIQ: 48.5 (9.4) vs 55.4 (12.6), p<0.0005; MD -6.92 (95% CI -14.35, 0.51), p =0.07 SF-36: 49.5 (17.0) vs 37.9 (11.0), p=0.13; MD 4.68 (95% CI .096 to 21.104), p = 0.02 BDI: 14.7 (7.4) vs 16.6 (6.4), p=0.18; MD -1.9 (95% CI -6.5, 2.7), p = 0.41 18 months (n = 15 vs. 15): FIQ: 45.6 (7.3) vs 51.3 (15.1), p NR SF-36: 51.8 (14.7) vs 41.3 (11.9), p NR BDI: 14.3 (6.4) vs 14.2 (8.2), p NR 30 months (n = 13 vs. 12) FIQ: 38.5 (11.3) vs 49.5 (10.2), p NR; MD -11.0 (95% CI -19.93 to -2.07), p =0.02 SF-36: 60.5 (12.7) vs 42.0 (16.1), p NR; MD 18.5 (95% CI 8.79 to 28.21), p = 0.0005 BDI: 9.7 (3.8) vs 17.9 (8.4), p NR; MD -8.2 (95% CI -12.594 to -3.806), p = 0.0006
Sanudo 2015	A vs B Mean (SE) Pain VAS: 6.7 (2.2) vs 7.0 (1.7), ns (p NR); MD -0.3 (95% CI -6.347 to 5.747), p=0.92 Anxiety VAS: 5.7 (3.3) vs 7.5 (2.5), p < 0.05; MD -1.8 (95% CI -10.827 to 7.227), p=0.69 Depression VAS: 5.6 (3.4) vs 6.7 (2.2), ns (p NR); MD -1.1 (95% CI -10.094 to 7.894), p=0.80 Sleep disturbance VAS: 7.2 (2.8) vs 8.6 (1.9), ns (p NR); MD -1.4 (95% CI -8.876 to 6.076), p=0.70

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Sanudo 2010	
Sanudo 2012	
Sanudo 2015	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Sanudo 2010		Adverse events: NR Withdrawals: A vs C: 18% (4/22) vs 5% (1/21) B vs C: 19% (4/21) vs 5% (1/21)
Sanudo 2012		Adverse events: NR Withdrawals: A vs B: 14% (3/21) vs 5% (1/20) at first 6-month assessment; 38% (8/21) vs 40% (8/20) at final assessment
Sanudo 2015		Adverse events: NR Withdrawals: 0

Author, Year	Funding Source	Quality	Comments
Sanudo 2010	University of Seville	Fair	Effect sizes are shown in a figure, but difficult to estimate exact values.
Sanudo 2012	NR	Poor	No significant differences between A and B after 6 months on any outcome *Data analysis after the initial exercise intervention (6 mos) was conducted using analysis of covariance, with the baseline scores of each outcome measure used as a covariate and Bonferroni correction for multiple testing used throughout. Analysis revealed that there was a significant improvement for the Exercise group over the Control group in FIQ scores, (F[1, 34] = 20.618, P G 0.0005, G2 = 0.377) at the 6-mo time point
Sanudo 2015	NR	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Saper 2017	US Number of centers 8 Outpatient	Age 18-64 Nonspecific low back pain Duration at least 12 weeks Average pain intensity in previous week of 4 or greater on a 0-10 numerical rating scale Exclude: Specific causes of low back pain	Randomized: 320 Treated: 307 Analyzed at 26 weeks: 251 Analyzed at 52 weeks: 258
Saral 2016	Turkey 1 center Rehabilitation department	Inclusion: female, FM diagnosis based on 1990 ACR criteria, aged 25-60 years old, followed up for ≥6 months after FM diagnosis, pain intensity ≥5 on 10 cm VAS, presence of ≥5 five years of primary school education Exclusion: previous diagnosis of an endocrine, neuromuscular, infectious, or inflammatory disease, presence of hepatic or renal disease, malignancy, history of severe trauma, advanced psychiatric diseases, serious physical comorbidities, and pregnancy	Randomized: 66 Analyzed: 59 Attrition: 11% (7/66)
Schimmel 2009	Netherlands Number of centers 1	Patients with LBP for at least 1 year and one or more non-surgical treatment. Patients with previous surgical treatment and radicular leg pain.	Randomized: 60 Treated: 60 Analyzed: 60 Attrition: 7% (4/60)

Author, Year	Intervention, Comparator
Saper 2017	A:Hatha yoga (n=127): 12 weekly 75-minute Hatha yoga sessions including relaxation and meditation exercises, yoga breathing, and yoga philosophy, yoga poses, and relaxation. Thirty minutes of daily home practice encouraged. Aids used to accommodate various physical abilities. After 12 weeks patients randomized to weekly drop-in yoga classes (A1, maintenance) or home practice only (A2) B: Exercise (n=129): 15 60 minute appointments over 12 weeks, including supervised and individualized stabilization and aerobic exercise; patients with high fear avoidance scores received the Back Book and reinforcement in psychologically informed principles. Patients given instructions and supplies for home practice. After 12 weeks patients randomized to 5 booster sessions at 4, 6, 8, 10, and 12 months (B1, maintenance) or home practice only (B2) C: Education (n=64): Back Pain Helpbook, newsletter and 5 minute check-in call every 3 weeks. After 12 weeks, brief check-in call every 6 weeks
Saral 2016	A. Long-term interdisciplinary group (n=22): Patients had 1 full day session of a scientific and interactive educational program and 1 full day session of an exercise education program. Patients had instructions to peform strengthening and stretchingexercises 3 days a week for 20-30 minutes, as well as relaxation techniques twice a day for 5 days a week. Subjects also had a 3 hour session of CBT per week for 10 weeks. B. Short-term interdisciplinary group (n=22): Over 2 full days, patients participated in education, exercise, and CBT. Patients had instructions to peform strengthening and stretchingexercises 3 days a week for 20-30 minutes, as well as relaxation techniques twice a day for 5 days a week. Subjects had two 3 hours CBT sessions. C. Control group (n=22): Patients continued current medical treatments, normal daily living, and current physical activity levels
Schimmel 2009	A.Intermittent traction (n=31): Intermittent differential dynamics therapy: 20 sessions, 6 weeks, 25-30 minutes, traction force 50% of body weight. B.Sham (n=29): Similar treatment but at <10% body weight

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Saper 2017	A vs. B vs. C Age: 46 vs. 46 vs. 44 Female: 57% vs. 70% vs. 66% Race: 20% vs. 16% vs. 17% Pain (0-10 NRS): 7.1 vs. 7.2 vs. 7.0 Modified RDQ (0-23): 13.9 vs. 15.6 vs. 15.0 SF-36 physical component: 36.2 vs. 35.2 vs. 36.6 SF-36 mental component: 43.4 vs. 41.4 vs. 42.3 Opioid use in past week: 22% vs. 18% vs. 19%	Primary outcomes: Modified RDQ (0-23) Pain (0-10 NRS) Medication use in previous week (yes/no) Global improvement (7 point scale from extremely worsened to extremely improved) Patient satisfaction (5 point scale from very dissatisfied to very satisfied) SF-36 (0-100)	3.5, 6.5, and 9 months
Saral 2016	A vs B vs C Age, years: 38 vs 43 vs 44 Female: 100% vs 100% vs 100% Symptom duration, months: 69 vs 113 vs 88 FIQ: 71.6 (14.2) vs 67.7 (12.0) vs 65.5 (13.2) Pain VAS: 8.2 (0.9) vs 7.6 (0.8) vs 7.5 (0.9) BDI: 23.4 (11.0) vs 20.7 (6.6) vs 21.4 (10.4) SF-36 PCS: 32.8 (7.9) vs 36.5 (8.7) vs 36.0 (7.2) SF-36 MCS: 30.4 (11.7) vs 33.2 (8.9) vs 36.1 (9.8) Sleep VAS: 7.2 (2.8) vs 5.2 (2.8) vs 5.8 (2.7)	FIQ (0-100, higher score=greater impact of FM); pain VAS (0-10, higher score=higher pain severity); BDI (0-63, higher score=higher severity of depression); SF-36 PCS (0-100, higher score=higher quality of life); SF-36 MCS (0-100, higher score=higher quality of life); sleep VAS (0-10, higher score=lower quality of sleep)	6 months* 4 months based on intervention group
Schimmel 2009	A vs. B Age (mean): 42 vs. 46 years Female: 39% vs. 52% Race: NR Use of pain medication: 48% vs. 51% Previous surgery: 100% vs. 100% VAS low back pain (mean): 61 vs. 53 ODI (mean): 36 vs. 33 Total score SF-36 (mean): 52 vs. 53 VAS right leg pain (mean): 37 vs. 33 VAS left leg pain (mean): 27 vs.31 Tampa score (mean): 39 vs. 38	100-mm VAS (unbearable pain intensity was recorded as 100, and 0 indicated no pain at all) Oswestry Disability Index (ODI, effect of LBP on daily function in ten domains) Quality of life, Short-Form 36 (SF-36, assesses general quality of life in nine subscales)	2 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)	
Saper 2017	A vs. C <u>Baseline, mean (SD)</u> Modified RDQ (0-23): 13.9 (5.60) vs. 15.0 (5.0) Pain (0-10 NRS): 7.1 (1.5) vs. 7.0 (1.4) A1 vs. A2 vs. C <u>3.5 months, mean (SE)</u> Modified RDQ (0-23): 10.1 (0.77) vs. 9.5 (0.77) vs. 11.6 (0.75) Pain (0-10 NRS): 4.3 (0.32) vs. 4.6 (0.32) vs. 5.5 (0.31) <u>6.5 months, mean (SE)</u> Modified RDQ (0-23): 9.8 (0.81) vs. 8.4 (0.81) vs. 11.7 (0.78) Pain (0-10 NRS): 4.3 (0.34) vs. 4.4 (0.34) vs. 5.5 (0.33) <u>9 months, mean (SE)</u> Modified RDQ (0-23): 9.2 (0.88) vs. 8.9 (0.88) vs. 11.1 (0.85) Pain (0-10 NRS): 4.3 (0.36) vs. 4.4 (0.35) vs. 5.2 (0.34)	
Saral 2016	A vs C 6 months* FIQ: 53.9 (19.3) vs 65.5 (11.5), p=0.011 (MD -11.60, 95% CI -21.91 to -1.29) Percent change from baseline in FIQ: -22.1% vs 3.2% Pain VAS: 5.1 (2.4) vs 7.6 (1.4), p<0.001 (MD -2.50, 95% CI -3.78 to -1.22) Percent change from baseline in pain VAS: -38.3% vs 1.5% BDI: 16.6 (9.6) vs 18.7 (9.5), p NR (MD -2.10, 95% CI -8.22 to 4.02) Percent change from baseline in BDI: -12.3% vs 0.2% SF-36 PCS: 39.9 (7.5) vs 34.3 (8.1), p=0.007 (MD 5.60, 95% CI 0.61 to 10.59) Percent change from baseline in SF-36 PCS: 27.3% vs -2.2% SF-36 MCS: 40.7 (12.3) vs 37.6 (10.0), p NR (MD 3.10, 95% CI -4.12 to 10.32) Percent change from baseline in SF-36 MCS: 60.0% vs 12.7% Sleep VAS: 3.0 (2.8) vs 4.9 (3.0), p NR (MD -1.90, 95% CI -3.76 to -0.04) Percent change from baseline in sleep VAS: -45.0% vs 52.3%	B vs C 6 months* FIQ:54.5 (14.2) vs 65.5 (11.5), p=0.015 (MD -11.00, 95% CI -19.50 to -2.49) Percent change from baseline in FIQ: -18.9% vs 3.2% Pain VAS: 5.8 (1.0) vs 7.6 (1.4), p<0.001 (MD -1.8, 95% CI -2.60 to -1.00) Percent change from baseline in pain VAS: -22.8% vs 1.5% BDI: 15.0 (10.2) vs 18.7 (9.5), p NR (MD -3.70, 95% CI -10.19 to 2.79) Percent change from baseline in BDI: -24.9% vs 0.2% SF-36 PCS: 39.6 (8.1) vs 34.3 (8.1), p=0.212 (MD 5.30, 95% CI -0.03 to 10.63) Percent change from baseline in SF-36 PCS: 13.4% vs -2.2% SF-36 MCS: 40.2 (10.0) vs 37.6 (10.0), p NR (MD 2.60, 95% CI -3.98 to 9.18) Percent change from baseline in SF-36 MCS: 28.7% vs 12.7% Sleep VAS: 3.1 (2.5) vs 4.9 (3.0), p NR (MD -1.80, 95% CI -3.62 to 0.02) Percent change from baseline in sleep VAS: 33.7% vs 52.3%
Schimmel 2009	A vs. B, mean (SD) <u>Baseline</u> Pain (0-100 VAS): 61 (24.6) vs. 53 (26.4) ODI (0-100)): 36 (15.7) vs. 33 (16.8) SF-36, total (0-100): 52 vs. 53 <u>8 weeks</u> Pain (0-100 VAS): 32 (26.8) vs. 36 (27.1); p=0.70 ODI: 25 vs. 23 (SD not reported) SF-36, total: 66 vs. 65 (SD not reported)	

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Saper 2017	NR
Saral 2016	
Schimmel 2009	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Saper 2017	A vs. B <u>Baseline, mean (SD)</u> Modified RDQ (0-23): 13.9 (5.60) vs. 15.6 (5.10) Pain (0-10 NRS): 7.1 (1.5) vs. 7.2 (1.5) A1 vs. A2 vs. B1 vs. B2 <u>3.5 months, mean (SE)</u> Modified RDQ (0-23): 10.1 (0.77) vs. 9.5 (0.77) vs. 10.4 (0.84) vs. 10.1 (0.83) Pain (0-10 NRS): 4.3 (0.32) vs. 4.6 (0.32) vs. 4.7 (0.35) vs. 4.8 (0.34) <u>6.5 months, mean (SE)</u> Modified RDQ (0-23): 9.8 (0.81) vs. 8.4 (0.81) vs. 10.0 (0.88) vs. 9.6 (0.87) Pain (0-10 NRS): 4.3 (0.34) vs. 4.4 (0.34) vs. 5.1 (0.37) vs. 4.6 (0.37) <u>9 months, mean (SE)</u> Modified RDQ (0-23): 9.2 (0.88) vs. 8.9 (0.88) vs. 8.9 (0.96) vs. 9.4 (0.94) Pain (0-10 NRS): 4.3 (0.36) vs. 4.4 (0.35) vs. 4.0 (0.39) vs. 4.1 (0.37)	A vs. B vs. C Withdrawals due to AE: NR Any possibly or definitely related adverse event: 7.1% (9/127) vs. 10.9% (14/.129) vs. 1.6% (1/64) Serious possibly related adverse event: 0.8% (1/127) vs. 0% (0/129) vs. 0% 0/64); the 1 serious adverse events was a case of cellulitis
Saral 2016		The patients in the intervention groups reported no harms or adverse events regarding CBT and/or exercise training except for occasional mild increases in pain after some exercise sessions. Further details NR.
Schimmel 2009	NR	NR

Author, Year	Funding Source	Quality	Comments
Saper 2017	National Center for Complementary and Integrative Health of the National Institutes of Health	Fair	
Saral 2016	"No grant or industry support was received for this study"		*Short term interdisciplinary group and control group were followed up at 6 months from end up intervention, long term interdisciplinary group was followed up at 4 months from end of intervention
Schimmel 2009	NR	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Schmidt 2011	Germany, single-site	Inclusion Criteria: Women aged 18-70 diagnosed with fibromyalgia according to American College of Rheumatology criteria, along with German language competency. Exclusion Criteria: Any life-threatening diseases, evidence of suppressed immune functioning, or participation in other clinical trials.	Randomized: 177 Treated: 168 Analyzed (ITT): 168 Completers: 137 Attrition: 5% (9/177)

Author, Year	Intervention, Comparator
Schmidt 2011	A. Mindfulness-based Stress Reduction [MBSR] (n=53) 8-week group-based program with one 2.5 hour session/week and one 7 hour all-day session covering training in specific exercises and topics of mindfulness practices. Participants were asked to complete daily practices of 45-60 minutes each B.Active-control Intervention (n=56) Controlled for nonspecific aspects of the MBSR program with similar meeting structure and format to MBSR treatment arm. Equivalent levels of social support and weekly topical education was provided along with Jacobson Progressive Muscle Relaxation training and fibromyalgia-specific gentle stretching exercises. Participants were asked to complete daily homework assignments with the same duration as MBSR group. C.Waitlist (n=59) Received no active treatment but were offered either intervention at the conclusion of the followup period.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Schmidt 2011	A vs. B vs. C Age (SD): 53 vs. 52 vs. 52 years Female: 100% (all female study) Race: NR Mean duration of chronicity: 14.5 vs. 15.6 vs. 12.8 years Fibromyalgia Impact Questionnaire (FIQ): 5.84 (1.37) vs. 5.50 (1.68) vs. 5.65 (1.86); Avs.B: MD 0.34 (95%CI -0.24 to 0.92) p=0.251; Avs.C: MD 0.19 (95%CI -0.43 to 0.81) p=0.543 Pain Perception Scale (PPS) Affective: 35.47(9.38) vs. 31.96(9.02) vs. 34.78(7.66); Avs.B: MD 3.51 (95%CI 0.02 to 7.00) p=0.049; Avs.C: MD 0.69 (95%CI -2.50 to 3.88) p=0.669 Pain Perception Scale (PPS) Sensory: 22.35(6.12) vs. 22.85(6.58) vs. 22.64(5.65); Avs.B: MD -0.50 (95%CI -2.92 to 1.92) p=0.683; Avs.C: MD -0.29 (95%CI -2.49 to 1.91) p=0.795 Center for Epidemiological Studies Depression Inventory (CES-D): 25.19(9.60) vs. 22.92(10.27) vs. 25.43(9.26); Avs.B: MD 2.27 (95%CI -1.51 to 6.05) p=0.237; Avs.C: MD -0.24 (95%CI -3.77 to 3.29) p=0.893 State-Trait-Anxiety-Inventory (STAI): 51.60(9.18) vs. 49.8(10.91) vs. 48.68(10.68); Avs.B: MD 1.80 (95%CI -2.04 to 5.64) p=0.355; Avs.C: MD 2.92 (95%CI -0.83 to 6.67) p=0.126 Pittsburgh Sleep Quality Index (PSQI): 11.31(3.45) vs. 11.37(4.24) vs. 11.12(4.36); Avs.B: MD 0.26 (95%CI -1.21 to 1.73) p=0.727; Avs.C: MD 0.19 (95%CI -1.29 to 1.67) p=0.80 Freigburg Mindfulness Inventory: 36.38(6.10) vs. 35.86(7.81) vs. 36.67(6.64); Avs.B: MD 0.52 (95%CI -2.15 to 3.19) p=0.700; Avs.C: MD -0.29 (95%CI -2.69 to 2.11) p=0.811 Giessen Complaint Questionnaire (GCQ): 48.43(13.53) vs. 47.02(14.65) vs. 48.36(14.79); Avs.B: MD 1.41 (95%CI -3.95 to 6.77) p=0.603; Avs.C: MD 0.07 (95%CI -5.26 to 5.40) p=0.979 HRQoL (PLC): 11.69(2.94) vs. 11.75(3.27) vs. 11.67 (3.18); Avs.B: MD -0.06 (95%CI -1.24 to 1.12) p=0.920; Avs.C: MD 0.02 (95%CI -1.13 to 1.17) p=0.973	Primary: Fibromyalgia Impact Questionnaire (FIQ) Pain Perception Scale (PPS) Secondary: Center for Epidemiological Studies Depression Inventory (CES-D, >23 indicates clinically relevant depression) State-Trait Anxiety Inventory Trait Subscale (STAI, range 20-80: higher scores indicate higher anxiety levels) Pittsburgh Sleep Quality Index (PSQI, range 0-21: higher scores indicate worse sleep) Giessen Complaint Questionnaire (GCQ) Quality of Life Profile for the Chronically Ill (PLC)	2 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Schmidt 2011	A vs B <u>2 months</u> Proportion of Patients who saw MCID (>14% improvement) in FIQ scores: 30%(16/53) vs. 25%(14/56); RR 1.21 (95% CI 0.79 to 1.82) p=0.396 Fibromyalgia Impact Questionnaire (FIQ): 5.23(2.00) vs. 5.33(1.90); MD -0.10 (95%CI -0.84 to 0.64) p=0.789 Pain Perception Scale (PPS) Affective: 30.79(9.20) vs. 32.17(8.76); MD -1.38 (95%CI -4.79 to 2.03) p=0.424 Pain Perception Scale (PPS) Sensory: 21.16(5.42) vs. 21.87(5.40); MD -0.71 (95%CI -2.77 to 1.34) p=0.494 Proportion of Patients who saw Clinically Relevant Improvement (reduction below score of 23) in CES-D scores: 28% (15/53) vs. 23%(30/56); RR 0.53 (95% CI 0.54 to 1.12) p=0.165 Center for Epidemiological Studies Depression Inventory (CES-D): 21.70 (9.93) vs. 22.55(10.13); MD -0.85 (95%CI -4.66 to 2.96) p=0.659 State-Trait-Anxiety-Inventory Trait Subscale (STAI):): 47.86(9.12) vs. 48.44(10.94); MD -0.58 (95%CI -4.42 to 3.26) p=0.765 Proportion of Patients who dropped below PSQI score of 5 (<5 considered to indicate good sleep): 17%(9/53) vs. 7%(4/56); RR 2.38 (95% CI 0.85 to 2.34) p=0.180 Pittsburgh Sleep Quality Index (PSQI, 0-21): 10.01(3.60) vs. 10.25(4.09); MD -0.24 (95%CI -1.71 to 1.23) p=0.746 Freigburg Mindfulness Inventory: 37.66(5.15) vs. 35.14(7.61); MD 2.52 (95%CI 0.04 to 5.00) p=0.047 Giessen Complaint Questionnaire (GCQ): 42.63(12.20) vs. 43.91(15.10); MD -1.28 (95%CI -6.51 to 3.95) p=0.629 HRQoL (PLC): 12.83(3.06) vs. 12.16(3.61); MD 0.67 (95%CI -0.60 to 1.94) p=0.299 A vs C <u>2 months</u> Proportion of Patients who saw MCID (>14% improvement) in FIQ scores: 30%(16/53) vs. 22%(13/59); RR 1.37 (95% CI 0.83 to 1.94) p=0.275 Fibromyalgia Impact Questionnaire (FIQ): 5.23(2.00) vs. 5.29(1.66); MD -0.06 (95%CI -0.75 to 0.63) p=0.863 Pain Perception Scale (PPS) Affective: 30.79(9.20) vs. 32.38(9.07); MD -1.59 (95%CI -5.01 to 1.83) p=0.360 Pain Perception Scale (PPS) Sensory: 21.16(5.42) vs. 21.44(5.34); MD -0.28 (95%CI -2.30 to 1.74) p=0.784 Proportion of Patients who saw Clinically Relevant Improvement (reduction below score of 23) in CES-D scores: 28% (15/53) vs.19% (11/59); RR 1.52 (95% CI 0.85 to 2.04) p=0.220 Center for Epidemiological Studies Depression Inventory (CES-D): 21.70 (9.93) vs. 24.00(9.61); MD -2.3 (95%CI -5.96 to 1.36) p=0.216 State-Trait-Anxiety-Inventory Trait Subscale(STAI): 47.86(9.12) vs. 49.18(10.47); MD -1.32 (95%CI -5.02 to 2.38) p=0.481 Proportion of Patients who dropped below PSQI score of 5 (<5 considered to indicate good sleep): 17%(9/53) vs. 10%(6/59); RR 1.67 (95% CI 0.80 to 2.14) p=0.280 Pittsburgh Sleep Quality Index (PSQI, 0-21): 10.01(3.60) vs. 10.37(4.06); MD -0.36 (95%CI -1.80 to 1.08) p=0.622 Freigburg Mindfulness Inventory: 37.66(5.15) vs. 36.13(7.27); MD 1.53 (95%CI -0.85 to 3.91) p=0.206 Giessen Complaint Questionnaire (GCQ): 42.63(12.20) vs. 45.29(15.04); MD -2.66 (95%CI -7.82 to 2.50) p=0.310 HRQoL (PLC): 12.83(3.06) vs. 12.29(3.28); MD 0.54 (95% CI -0.65 to 1.73) p=0.371

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Schmidt 2011	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Schmidt 2011	NR	NR

Author, Year	Funding Source	Quality	Comments
Schmidt 2011	This study was supported by the Samueli Institute, Alexandria, VA., and by the Manfred Köhnlechner Stiftung, Munich, Germany.	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Seferiadis 2015	Sweden 1 center Hospital	Whiplash injury of WAD grades I, II, or III* for a minimum of 1 year Exclude: Comorbidity that would increase possibility of harm from intervention and/or measurement of outcomes	Randomized: 113 Treated: 109 Analyzed: 93 Attrition: 18% (20/113)

Author, Year	Intervention, Comparator
Seferiadis 2015	A.Basic body awareness therapy (n=57): 1.5 hour sessions twice a week for 10 weeks. Sessions consisted of exercises based on activities of daily living, meditation, and Tai Chi inspired exercises aiming to improve posture and increase efficient movement patterns B.Exercise (n=56): 1.5 hour sessions twice a week for 10 weeks. Sessions consisted of 45 minutes of muscle strengthening, 15 minutes of stretching, and 20 minutes of progressive muscle relaxation

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Seferiadis 2015	A vs B Age: 47 vs 49 Female: 66% vs 77% Duration of symptoms (years): 10 vs 9 WAS classification: 1: 0% vs 2% 2: 23% vs 28% 3: 77% vs 70% Neck Disability Index: 20 (8.9) vs 18.8 (7.6) SF-36 physical functioning: 67.5 (21.3) vs 69.7 (17.5) SF-36 role-physical: 33.9 (39.4) vs 24.5 (39.2) SF-36 bodily pain: 34.3 (19.7) vs 35.2 (18.2) SF-36 general health: 54.7 (22.5) vs 48.7 (18.7) SF-36 vitality: 39.5 (23.9) vs 35.1 (22) SF-36 social functioning: 60 (27) vs 59.4 (27.2) SF-36 role-emotional: 55.4 (41.8) vs 51.7 (44.5) SF-36 mental health: 65.9 (21.8) vs 62.7 (24)	Neck Disability Index (0-50, higher scores=higher disability) SF-36 (0-100, higher score=higher quality of life)	3 months

Author, Year	**Results - Subquestion a** (vs. sham, no treatment, waitlist, attention control)
Seferiadis 2015	

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Seferiadis 2015	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Seferiadis 2015	A vs. B <u>3 months</u> Neck Disability Index: MD -2 (95% CI -3.5 to -0.5) vs. MD -1 (95% CI -2.5 to 0.4) SF-36 physical functioning: MD 7.1 (95% CI 3.7 to 11.4) vs. MD 0.5 (95% CI -3.2 to 4.1) SF-36 role-physical: MD 17.5 (95% CI 5.9 to 29) vs. MD 19 (95% CI 9.3 to 28.6) SF-36 bodily pain: MD 12.2 (95% CI 6.9 to 17.6) vs. MD 4.9 (95% CI -0.1 to 9.8) SF-36 general health: MD 7.5 (95% CI 2.4 to 12.6) vs. MD 4.5 (95% CI -0.1 to 9) SF-36 vitality: MD 7.3 (95% CI 1 to 13.6) vs. MD 5.6 (95% CI -0.5 to 11.6) SF-36 social functioning: MD 13.3 (95% CI 6.6-19.9) vs. MD 3.5 (95% CI -3 to 9.9) SF-36 role-emotional: MD 9.3 (95% CI-2.3 to 21) vs. MD 4 (95% CI -8.3 to 16.4) SF-36 mental health: MD 2.8 (95% CI -2 to 7.6) vs. MD 1.2 (95% CI -3.6 to 5.9)	A vs B No serious adverse effects Non-serious adverse effects: Any: 14/53 vs 21/52 (RR 0.65, 95% CI 0.37 to 1.14) Increased pain: 18% (10/57) vs 32% (18/56), (RR 0.6, 95% CI 0.3 to 1.1) Fatigue: 4% (2/57) vs 0% (0/56) Increased headache: 2% (1/57) vs 0% (0/56) Training soreness: 2% (1/57) vs 0% (0/56) Back pain: 0% (0/57) vs 2% (1/56) Hip pain: 0% (0/57) vs 2% (1/56) Nausea: 0% (0/57) vs 2% (1/56)

Author, Year	Funding Source	Quality	Comments
Seferiadis 2015	Grants from The Health and Medical Care Committee of the Region Vastra Gotaland (VGFOUREG-11419, VGFOUREG-24191, VGFOUREG-5525) and grants from the Research and development council of the county Sodra Alvsborg (VGFOUSA-162631, VGFOUSA-38041, VGFOUSA-43901, VGFOUSA-87931)	Fair	*WAD grades made using Quebec classification Outcomes not included: Tampa Scale of Kinesiophobia (pain-related fear of movement), pain intensity Likert scale 0-5 (NR in text), pain frequency Likert scale 0-5 (NR in text), Body Awareness Scale, ROM Outcomes reported as mean change *within* groups

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Segal 2015	United States, multi-site, outpatient clinic	Inclusion Criteria: Men and women age 60 and older with symptomatic knee osteoarthritis and mobility disability. Exclusion Criteria: Exclusion of those with conditions other than knee OA which could affect walking (e.g. amputation, severe back pain, severe peripheral vascular or heart disease and neurological or developmental disease including multiple sclerosis, Parkinson disease, myositis, rickets, or lower limb musculoskeletal surgery in the previous 6 months). Additionally, patients were excluded if they had undergone corticosteroid injection either into a peripheral joint or into the spine in the previous 3 months, or who anticipated inability to return for followup were excluded. Other exclusion criteria were: medical conditions that may preclude safe participation in the study protocol, including but not limited to acute or terminal illness or unstable cardiovascular condition (e.g., New York Heart Association class III or IV congestive heart failure, clinically significant aortic stenosis, history of cardiac arrest, use of a cardiac defibrillator, uncontrolled angina); report of medical conditions that may impair ability to participate including but not limited to pulmonary disease requiring the use of supplemental oxygen; inability or unwillingness to comply with the study protocol or be randomized; inability to obtain written clearance for participation in the study by a physician; concurrent participation in another observational or interventional research study; current consumption of more than 14 alcoholic drinks per week; and/or judgment of the principal investigator that participation would endanger the safety of an individual.	Randomized: 58 Treated: 54 Analyzed: 3 months= 77.6% (45/58) 9 months= 72.4% (42/58) Attrition: 27.5% (16/58)

Author, Year	Intervention, Comparator
Segal 2015	A.Gait Training (n=24) Gait training sessions composed of guided strategies to optimize knee movements during treadmill walking, computerized motion analysis with visual biofeedback. Additionally, on the basis of evaluation of strength, flexibility, trunk and lower limb range of motion and gait at the baseline visit, a physical therapist instructed the participants in individualized home programs. No. of Sessions: Twice weekly for 12 weeks (24 total) Length of Sessions: 45 minutes each B.Usual Care (n=18) Usual care for knee osteoarthritis and were not asked to make changes in their lifestyle (e.g., annual visit to their physician, use of pain medications, knee surgery and/or physical therapy). Participants were asked to record twice weekly for 3 months in an Arthritis Foundation symptom diary and once a week for the remaining 9 months of the study.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Segal 2015	A vs B Age: 70 vs. 69 years Female: 76% vs. 53% Race: NR Mean Duration of Chronicity: NR LLFDI basic lower limb function score: 65.8 (9.2) vs. 63.5 (6.1) KOOS Pain: 62.7 (10.8) vs. 59.8 (13.1) KOOS Symptoms: 60.1 (16.8) vs. 63.0 (13.6)	Late Life Function and Disability Instrument LLFDI: Basic Lower Limb Function scores (LLFDI, range) Knee Injury Osteoarthritis Outcome Score Pain (KOOS, range 0-100: higher scores represent severity of pain) Knee Injury Osteoarthritis Outcome Score Symptoms (KOOS, range 0-100: higher scores represent severity of symptoms)	3 and 9 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Segal 2015	A vs. B 3 months *Between group difference in change score compared with baseline* LLFDI basic lower limb function score: 2.3 (95%CI -1.8 to 6.3) p=0.265 KOOS Pain: 3.7 (95%CI -4.7 to 12.1) p=0.384 KOOS Symptoms: 6.2 (95%CI -2.9 to 15.4) p=0.175 9 months *Between group difference in change score compared with baseline* LLFDI basic lower limb function score: 1.0 (95%CI -7.4 to 9.4) p=0.809 KOOS Pain: 7.2 (95%CI -2.0 to 16.5) p=0.120 KOOS Symptoms: 6.0 (95%CI -6.2 to 18.2) p=0.327

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Segal 2015	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Segal 2015	NR	None reported.

Author, Year	Funding Source	Quality	Comments
Segal 2015	Supported by a Paul B. Beeson Career Development Award in Aging Research (K23AG030945). "The investigators retained full independence in the conduct of this research. No conflicts of interest have been reported by the authors or by any individuals in control of the content of this article"	Fair at 3 months Poor at 9 months	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Senna 2011	Egypt Number of centers: 1 Hospital	Patients 20 to 60 years old with chronic (>=6 months) nonspecific LBP Exclude: “red flags” for a serious spinal condition, structural deformity, spondylolisthesis, spinal stenosis, ankylosing spondylitis, osteoporosis, prior surgery to the lumbar spine or buttock, obvious psychiatric disorders, referred pain to the back, widespread pain (e.g. , fibromyalgia), obese patients, current pregnancy, patients older than 60 years or younger than 20 years, and patients who had previous experience with SMT	Randomized: 93 Treated: 93 Analyzed: 60 Attrition: 35% (33/93)
Sephton 2007 see Cash 2015			

Author, Year	Intervention, Comparator
Senna 2011	A: Spinal Manipulation (SMT) (n=27): High velocity thrust, 12 sessions over 1 month B: SMT (n=27): High velocity thrust, 12 sessions over 1 month C: Sham manipulation (n=40): Manually applied forces of diminished magnitude, aimed purposely to avoid treatable areas of the spine and to provide minimal likelihood of therapeutic effect, 12 sessions over 1 month
Sephton 2007 see Cash 2015	

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Senna 2011	A vs. B vs. C Mean age: 40 vs. 42 vs. 42 years Female: 27% vs. 24% vs. 24% Race: Not reported Pain (0-100 VAS): 42 vs. 43 vs. 41 ODI (0-100): 39 vs. 40 vs. 38 SF-36, total (0-100): 28 vs. 19 vs. 27	Oswestry Disability Index (0-100) Pain intensity (0-100 VAS) SF-36 (scale 0-100 for each subscale; higher score=less disability)	3, 6, and 9 months (based on completion of initial treatment phase)
Sephton 2007 see Cash 2015			

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Senna 2011	A vs B mean (SE) <u>Baseline</u> ODI (0-100): 38.7 (3.05) vs. 39.6 (2.62) vs. 38.1 (2.44) Pain (0-100 VAS): 41.8 (3.31) vs. 42.8 (2.83) vs. 41.2 (2.64) SF-36, total (0-100): 27.8 (1.62) vs. 28.2 (1.39) vs. 27.5 (1.30) <u>3 months</u> ODI (0-100): 29.8 (2.11) vs. 23.1 (1.62) vs. 33.5 (2.13) Pain (0-100 VAS): 35.2 (1.28) vs. 25.9 (1.23) vs. 35.2 (1.25) SF-36, total (0-100): 29.2 (1.62) vs. 32.8 (1.40) vs. 26.4 (1.31) <u>6 months</u> ODI (0-100): 32.2 (2.13) vs. 22.4 (1.64) vs. 35.3 (2.11) Pain (0-100 VAS): 35.5 (2.13) vs. 25.4 (1.66) vs. 36.8 (1.40) SF-36, total (0-100): 27.8 (1.63) vs. 33.1 (1.41) vs. 26.1 (1.31) <u>9 months</u> ODI (0-100): 34.9 (2.36) vs. 20.6 (1.53) vs. 37.4 (2.20) Pain (0-100 VAS): 38.5 (2.45) vs. 23.5 (1.59) vs. 38.3 (2.12) SF-36, total (0-100): 27.6 (1.62) vs. 33.70 (1.41) vs. 25.9 (1.27)
Sephton 2007 see Cash 2015	

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Senna 2011	NR
Sephton 2007 see Cash 2015	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Senna 2011	NR	No SAEs, most common complaint, local tenderness and tiredness.
Sephton 2007 see Cash 2015		

Author, Year	Funding Source	Quality	Comments
Senna 2011	None	Poor	
Sephton 2007 see Cash 2015			

Author, Year	Country Number of Centers and Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Sencan 2004	Turkey, Setting NR	Inclusion: Patients with FM diagnosis based on ACR 1990 criteria, aged 18-50, with no other pharmacological treatment or co morbid disease which was an inclusion criteria stated in the study. Exclusion: Patients with tumoral, infectious, metabolic, cardiovascular, endocrine diseases, as well as those with drug dependency were excluded from the study.	Randomized: 67 Analyzed: 60 Attrition: 22.4% (15/67)

Author, Year	Intervention, Comparator
Sencan 2004	A. Exercise group (n=14): three 40-minute aerobic exercise sessions per week for 6 weeks. Additionally, all patients were instructed to take paracetamol as a rescue medication throughout the study. B. Paroxetine (n=18): subjects given 20/mg paroxetine/day for 6 weeks. Additionally, all patients were instructed to take paracetamol as a rescue medication throughout the study. C. SHAM TENS (n=20): Subjects were given placebo TENS with electrodes applied to two most painful tender points for 20 minutes, 3 times/week for 6 weeks. Additionally, all patients were instructed to take paracetamol as a rescue medication throughout the study.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Sencan 2004	A vs B vs. C Age, years: 35.4(9.6) vs. 35.6(9.4) vs. 35.5(7.8) Female: 100% vs. 100% BMI (kg/height-m2): 24.14(3.73) vs. 24.25 (4.31) vs. 24.60(2.64) Duration of symptoms, years: 4.68 (4.18) vs. 6.53 (5.63) vs. 5.10 (4.68) VAS: 6.85(1.23) vs. 6.62(1.42) vs. 7.70(1.72) cm BDI: 16.20 (4.88) vs 20.80 (5.25) vs. 18.50 (5.31) Analgesic Consumption: 9.65(2.2) vs. 7.10(1.65) vs. 8.10(1.75)	Visual Analogue Scale (VAS 0-10cm, higher scores = higher pain) Beck Depression Inventory (BDI 0-63; higher scores=greater depression) Analgesic Consumption (mean daily analgesic consumption)	6 months

Author, Year	Results - Subquestion a (vs. Sham, no treatment, waitlist, attention control)
Sencan 2004	A vs C 6 months VAS: 4.75(1.21) vs. 5.01(1.91); MD -0.26 (95%CI -1.46 to 0.94) p=0.660 BDI: 9.95(2.81) vs. 15.15(3.21); MD -5.2 (95%CI -7.41 to -2.99) p<0.001 Analgesic Consumption: 1.15(0.21) vs. 4.35(1.11); MD -3.17 (95%CI -3.79 to -2.55) p<0.001

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Sencan 2004	A vs. B 6 months VAS:4.75(1.21) vs. 5.84(2.11); MD -1.09 (95%CI -2.37 to 0.19) p=0.092 BDI: 9.95(2.81) vs. 10.12(2.64); MD -0.17 (95%CI -2.09 to 1.75) p=0.858 Analgesic Consumption: 1.15(0.21) vs. 2.40(0.19); MD -1.25 (95%CI -1.39 to -1.11) p<0.001

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawls
Sencan 2004		A vs B vs. C Exclusions: 7/67* Withdrawals: 30% (6/20) vs 10% (2/20) vs. NR Adverse Events: NR *Seven patients due to transportation difficulties or drug intolerance were dropped from the study and the study group consisted of 60 patients

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Sherman 2009	USA Group Health 2004	Age 20-64 years of age, primary care for neck pain ≥3 months. Excluded: neck pain likely due to a non-mechanical cause (e.g., metastatic cancer, fractured vertebrae, spinal stenosis); 2) complex neck pain or neck pain potentially inappropriate for massage (cervical radiculopathy, prior neck surgery, litigation for neck pain, motor vehicle accident within past three months); unstable serious medical or psychiatric conditions or dementia; minimal neck pain (rating <3 on 0-10 point bothersomeness scale) or neck pain lasting <12 weeks; receiving other treatments for neck pain apart from medications; used massage for neck pain within the last year; or could not speak or understand English.	Randomized: 64 Treated: 64 Analyzed: 58 Attrition: 9% (6/64)
Sherman 2005	US Number of centers unclear Outpatient	Age 20-64 Primary care visit for back pain 3 to 15 months prior to the study Exclude: Complicated back pain (sciatica, previous back surgery, or spinal stenosis); Potentially attributable underlying diseases or conditions Minimal pain (<3 on 0-10 "bothersomeness" scale); Receiving other pack pain treatments or had participated in yoga or exercise training for back pain in the past year; Those with a possible disincentive to improve (workers; compensation or litigation); Unstable medical or severe psychiatric conditions or dementia	Randomized: 101 Treated: 99 Analyzed at 6 weeks: 92 Analyzed at 12 weeks: 96 Analyzed at 26 weeks: 95 Attrition at 26 weeks: 6% (6/101)

Author, Year	Intervention, Comparator
Sherman 2009	A.Massage (n=30), Swedish and clinical techniques and self-care recommendations; 10 massage treatments over a 10-week period (exact number based on participant's clinical progress as determined by the licensed massage therapist and member of CAM practitioners, based on their findings and the comments of the participant.) B.Self-care book (n=28) providing information on potential causes of neck pain, neck-related headaches, whiplash, recommended strengthening exercises, body mechanics and posture, conventional treatment, complementary therapies for neck pain, and first aid for intermittent flare-ups. No additional instruction about using the book was provided.
Sherman 2005	A: Yoga (n=36): 12 weekly 75-minute Viniyoga classes (median attended=9). Each class included a question-and-answer period, an initial and final breathing exercise, 5 to 12 postures, and a guided deep relaxation. Postures were selected from 17 viniyoga postures. Each session had a specific focus: strength-building, flexibility, and large-muscle movement; asymmetric poses; strengthening the hip muscles; lateral bending; integration; and customizing a personal practice. Participants were asked to practice daily at home and were given handouts that described home practices, and auditory compact discs to guide them through the sequence of postures with the appropriate mental focus. B: Exercise (n=35): 12 weekly 75 minute classes (median attended=8) designed by a physical therapist to be different from what most participants would have probably experienced in previous physical therapy sessions. Each class included educational talk, feedback from the previous week, simple warm-ups to increase heart rate, repetitions of a series of 7 aerobic exercises and 10 strengthening exercises that emphasized leg, hip, abdominal and back muscles. Repetitions of each exercise increased from 8 to 30 in increments of 2 over the course of the 12-week series. The strengthening exercises were followed by 12 stretches for the same muscle group. Each stretch was held for 30 seconds. Classes ended with a short, unguided period of deep, slow breathing. C: Attention control (self-care education) (n=30): Participants were mailed a copy of *The Back Pain Helpbook.* The book emphasized such self-care strategies as adoption of a comprehensive fitness and strength program, appropriate lifestyle modification, and guidelines for managing flare-ups. The study did not provide any instructions for using the book, many of the chapters concluded with specific action items.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Sherman 2009	A vs B Age: 47 vs 46 years Female: 69% vs 69% Attended some college: 81% vs 81% White: 87% vs 81% Married: 78% vs 59% Income >$35,000: 74% vs 83% Smoker: 9% vs 6% Pain lasted > 1 year: 81% vs 81% Symptom bothersome: 4.8 (2.3) vs 4.9 (1.8) NDI: 14.2 (5.0) vs 14.2 (4.7) SF-36 PCS: 46.0 (5.6) vs 44.1 (8.0) SF-36 MCS: 51.9 (7.0) vs 53.1 (7.6)	NDI: (scale 0-50, higher score greater disability) Bothersome numerical rating scale (scale, 0-10, higher score=greater bothersome) Short-Form 36 (SF-36) (scale 0-100, higher score=better QoL) Medication use	2.5 and 6.5 months
Sherman 2005	A vs. B vs. C Age: 44 vs. 42 vs. 45 Female: 69% vs. 63% vs. 67% Race: 83% vs. 85% vs. 70% white Pain lasting >1 year: 75% vs. 57% vs. 70% SF-36, physical: 44 vs. 43 vs. 43 SF-36, mental health: 53 vs. 54 vs. 53 RDQ: 8.1 vs. 9.0 vs. 8.0 Exercise in past week (mean hours): 3 vs. 3 vs. 3 Medication use for back pain in past week: 58% vs. 57% vs. 50%	Primary outcomes: Modified RDQ (0-23, higher score=more disability)) Bothersomeness: (scale 0-10, higher score=more bothersome) Secondary outcomes: General health status: SF-36 Degree of restricted activity (3 questions) Medication use	3.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Sherman 2009	A vs B 2.5 months, mean difference (95% CI) NDI, mean difference: -2.3 (95% CI -4.7 to 0.15), p= .066 NDI, % ≥5 points: 39% vs 14%, RR 2.7 (95% CI 0.99 to 7.5), p=0.052 Bothersome score: -1.2 (95% CI -2.5 to 0.1), p=0.081 Bothersome improvement ≥30%: 55% vs 25%, RR 2.1 (95% CI 1.04 to 4.2), p=0.038 SF-36 PCS: 52.8 (CI, 53.0 to 53.7) vs 53.3 (CI, 52.4 to 54.2), p=0.982 SF-36 MCS: 45.9 (CI, 46.0 to 46.8) vs 45.3 (CI, 44.2 to 46.4), p=0.444 6.5 months NDI, mean difference: -1.9 (95% CI -4.4 to 0.63), p=0.14 NDI, % ≥5 points: 57% vs 31%, RR 1.8 (95% CI 0.97 to 3.5), p=0.061 Bothersome score: -0.14 (95% CI -1.5 to 1.2), p=0.84 Bothersome improvement ≥30%: 43% vs 39%, RR 1.1 (95% CI 0.6 to 2.0), p=0.80 SF-36 PCS and MCS: data not given, no statistical difference Medication use: No change in group A, 14% increase in group B
Sherman 2005	A vs. C, mean <u>Baseline</u> Modified RDQ (0-23): 8.1 (SD 4.5) vs. 8.0 (SD 4.0) Bothersomeness (0-10): 5.4 (SD 1.5) vs. 5.4 (SD 1.9) <u>14 weeks</u> Modified RDQ (0-23): 3 vs. 7 (estimated from graph), adjusted difference -3.6 (95% CI -5.4 to -1.8),* Reduction in RDQ ≥50%: 69% vs. 30%, RR 2.3 (95% CI 1.3 to 4.2) Bothersomeness (0-10): 1.8 vs. 4.1 (estimated from graph), adjusted difference -2.2 (95% CI -3.2 to -1.2)* SF-36: No significant differences, data not provided Medication use: 21% vs. 59%, RR 0.35 (95% CI 0.15 to 0.73) *Adjusted for baseline scores

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Sherman 2009	
Sherman 2005	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Sherman 2009		No moderate or severe adverse experiences reported Mild adverse experiences: Discomfort or pain during one or more massages, n=5 Increased soreness after treatment, n=3 Nausea after each treatment n=1
Sherman 2005	A vs. B, mean <u>Baseline</u> Modified RDQ (0-23): 8.1 (SD 4.5) vs. 9.0 (SD 4.1) Bothersomeness: 5.4 (SD 1.5) vs. 5.7 (SD 1.9) <u>14 weeks</u> Modified RDQ (0-23): 3 vs. 5 (estimated from graph), adjusted difference -1.5 (-3.2 to 0.2)* Reduction in RDQ score ≥50%:69% vs. 50%, RR 1.4 (95% CI 0.91 to 2.1) Bothersomeness: 1.8 vs. 3.3 (estimated from graph), adjusted difference -1.4 (95% CI -2.5 to -0.2)* SF-36: No significant differences, data not provided Medication use: 21% vs. 50%, RR 0.41 (95% CI 0.20 to 0.87) *Adjusted for baseline scores	Adverse events NR Withdrawals due to adverse events NR

Author, Year	Funding Source	Quality	Comments
Sherman 2009	National Center for Complementary and Alternative Medicine Grant Number R21 AT 001584	Fair	
Sherman 2005	Grant funds: National Center for Complementary and Alternative Medicine and the National Institute for Arthritis and Musculoskeletal and Skin Diseases.	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Sherman 2011	US Number of centers 6 Outpatient	Age 20-64 ICD-9 diagnosis indicative of non-specific low back pain Chronic low back pain persisting for at least 3 months Pain bothersomeness rating of ≥3 (0-10 scale) Exclude: Back pain attributed to a specific cause, Complex back pain Minimally painful at time of screening Medical condition for which yoga or exercise were contraindicated Major depression	Randomized: 229 Treated: 228 Analyzed at 6 weeks: 208 Analyzed at 12 weeks: 206 Analyzed at 26 weeks: 208 Attrition at 26 weeks: 9% (21/229)
Somers 2012	United States,	Inclusion Criteria: Participants were included if they: 1) reported knee pain on most days of the month for at least the prior 6 months; 2) were over the age of 18 years; 3) were overweight or obese (body mass index [BMI] P25 and 642); 4) met the American College of Rheumatology criteria for OA and had radiographic evidence of OA affecting one or both knees (knee X-rays were graded by an experienced reader) on the basis of the Kellgren-Lawrence grading system (0–4; [28]); 5) had no other major weight bearing joint affected by OA; 6) OA of the knee(s) was considered the medical condition that contributed most to limitations in their daily function as assessed by the health care provider; and 7) were able to read and speak English. Exclusion Criteria: Participants were excluded if they: 1) had a significant medical condition that increased their risk of a significant adverse health event during physical activity (e.g., myocardial infarction in the previous 6 months, abnormal blood pressure response to exercise, etc.); 2) had another known organic disease that would contraindicate safe participation in the study (e.g., cancer); 3) had a non-OA inflammatory arthropathy or another arthritic disorder (e.g., rheumatoid arthritis); 4) used oral corticosteroids regularly; or 5) were participating in a regular exercise or weight loss program.	Randomized: 111 Treated: 89 Analyzed: 111 Attrition: post-treatment - 12/60 vs. 10/51 6 month - 17/60 vs. 14/51 12 month - 21/60 vs. 14/51 Total - 31.5% (35/111)

Author, Year	Intervention, Comparator
Sherman 2011	A: Viniyoga (n=92): 12 weekly 75-minute Viniyoga classes (median attended=10). Each class included a question-and-answer period, an initial and final breathing exercise, 5 to 12 postures, and a guided deep relaxation. Postures were selected from 17 viniyoga postures. Each session had a specific focus: strength-building, flexibility, and large-muscle movement; asymmetric poses; strengthening the hip muscles; lateral bending; integration; and customizing a personal practice. Participants were asked to practice daily at home and were given handouts that described home practices, and auditory compact discs to guide them through the sequence of postures with the appropriate mental focus. B: Exercise (n=91): 12 weekly 75 minute classes (median attended=9) designed by a physical therapist to be different from what most participants would have probably experienced in previous physical therapy sessions. Each class included educational talk, feedback from the previous week, simple warm-ups to increase heart rate, repetitions of a series of 7 aerobic exercises and 10 strengthening exercises that emphasized leg, hip, abdominal and back muscles. Repetitions of each exercise increased from 8 to 30 in increments of 2 over the course of the 12-week series. The strengthening exercises were followed by 12 stretches for the same muscle group. Each stretch was held for 30 seconds. Classes ended with a short, unguided period of deep, slow breathing. C: Attention control (self-care education) (n=30): Participants were mailed a copy of *The Back Pain Helpbook.* The book emphasized such self-care strategies as adoption of a comprehensive fitness and strength program, appropriate lifestyle modification, and guidelines for managing flare-ups. The study did not provide any instructions for using the book, many of the chapters concluded with specific action items.
Somers 2012	A.Pain Coping Skills Training (PSCT) (n=60) PCST strategies and education were delivered in group session by clinical psychologists. PCST is designed to decrease maladaptive pain catastrophizing and enhance participants' ability to control and decrease pain by increasing use of adaptive coping strategies. No. of Treatments: weekly for 12 weeks then every other week for the remaining 12 weeks (18 total) Length of Treatments: 60 minutes each B.Usual Care (n=51) Participants assigned to this group continued to receive their routine care

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Sherman 2011	A vs. B vs. C Age: 47 vs. 49 vs. 50 Female: 67% vs. 63% vs. 60% Race: 87% vs. 84% vs. 96% white Pain lasting >1 year: 92% vs. 89% vs. 91% RDQ: 9.8 vs. 8.6 vs. 9.0 Bothersomeness score: 4.9 vs. 4.5 vs. 4.7 Back exercise in past week (mean hours): 0.4 vs. 0.3 vs. 0.5 Medication use for back pain in past week: 57% vs. 65% vs. 53%	Primary outcomes: Modified RDQ (scale 0-23, higher score=more disability) Bothersomeness: (scale 0-10, higher score=more bothersome) Secondary outcomes: Degree of restricted activity Global rating of improvement	3.5 months
Somers 2012	<u>A vs B</u> Age: 58 vs. 58 Female: 67% vs. 68% Race: 62% vs. 61% Mean Duration of Pain: NR Mean Physical Disability (AIMS): 1.6 (95%CI 1.3–1.8) vs. 1.6 (95%CI 1.2–1.9) Mean Function (WOMAC): 46.2 (95%CI 41.1–51.3) vs. 46.1 (95%CI 39.7–52.5) Mean Stiffness (WOMAC): 54.7 (95%CI 48.3–61.1) vs. 53.2 (95%C 46.0–60.7) Mean Pain (AIMS): 5.6 (95%CI 5.2–6.0) vs. 5.5 (95%CI 4.9–6.1) Mean Pain (WOMAC): 42.8 (95%CI 42.1–53.3) vs. 43.4 (95%CI 37.4–49.5) Mean Psychological (AIMS): 2.9 (95%CI 2.6–3.9) vs. 3.0 (95%CI 2.6–3.4)	<u>Primary</u> Arthritis Impact Measurement Scales (AIMS) Western Ontario and McMaster Osteoarthritis Index (WOMAC) Physical Disability (AIMS, range 0-10: higher scores indicating greater pain or disability) Function (WOMAC, range 0-100: higher scores indicating greater pain or disability) Stiffness (WOMAC, range 0-100: higher scores indicating greater pain or disability) Pain (AIMS, range 0-10: higher scores indicating greater pain or disability) Pain (WOMAC, range 0-100: higher scores indicating greater pain or disability) <u>Secondary</u> Psychological Disability (AIMS, range 0-10: higher scores indicating greater pain or disability)	6 and 12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Sherman 2011	A vs. C, mean <u>Baseline</u> Modified RDQ (0-23): 9.8 (SD 5.2) vs. 9.0 (SD 5.0) Bothersomeness (0-10): 4.9 (SD 1.9) vs. 4.7 (SD 2.5) <u>14 weeks</u> Modified RDQ (0-23): 4.49 (95% CI 3.51 to 5.48) vs. 5.73 (95% CI 4.33 to 7.12), adjusted difference -1.81 (95% CI -3.12 to -0.50) Reduction in RDQ score ≥50%: 60% vs. 31%, RR 1.90 (95% CI 1.21 to 2.99) Bothersomeness (0-10): 3.59 (95% CI 3.12 to 4.06) vs. 3.80 (95% CI 3.14 to 4.46) Reduction in bothersomeness score ≥50%: 22% vs. 11%, RR 2.13 (95% CI 0.96 to 4.73) LBP better, much better, or completely gone: 51% vs. 20%, RR 2.57, 95% CI 1.39 to 4.78) Estimates adjusted for baseline RDQ and bothersomeness, sex, age, body mass index, days of lower back pain in the last 6 months, pain traveling down the leg, and employment-related exertion
Somers 2012	<u>A vs. B vs. C</u> <u>Post-treatment Average (6-12 months)</u> Mean Physical Disability (AIMS): 1.5 (95%CI1.3–1.6) vs. 1.5 (95%CI 1.3–1.6) vs. 1.4 (95%CI 1.2–1.6) Mean Function (WOMAC): 35.2 (95%CI 31.8–38.6) vs. 36.0 (95%CI 32.6–39.3) vs. 37.5 (95%CI 33.9–41.2) Mean Stiffness (WOMAC): 44.5 (95%CI 39.7–49.2) vs. 45.7 (95%CI 41.2–50.2) vs. 46.4 (95%CI 41.3–51.3) Mean Pain (AIMS): 4.4 (95%CI 4.1–4.8) vs. 4.7 (95%CI 4.3–5.1) vs. 4.7 (95%CI 4.3–5.1) Mean Pain (WOMAC): 34.5 (95%CI 30.8–38.2) vs. 35.5 (95%CI 31.9–39.0) vs. 38.0 (95%CI 34.1–41.8) Mean Psychological (AIMS): 2.6 (95%CI 2.4–2.8) vs. 2.5 (95%CI 2.2–2.7) vs. 2.5 (95%CI 2.3–2.8)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Sherman 2011	NR
Somers 2012	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Sherman 2011	A vs. B <u>Baseline</u> Modified RDQ (0-23): 9.8 (SD 5.2) vs. 8.6 (4.0) Bothersomeness (0-10): 4.9 (SD 1.9) vs. 4.5 (1.9) <u>14 weeks</u> Modified RDQ (0-23): 4.49 (95% CI 3.51 to 5.48) vs. 4.26 (95% CI 3.30 to 5.22), adjusted difference -0.35 (95% CI -1.52 to 0.83) Reduction in RDQ score ≥50%: 60% vs. 51%, RR 1.17 (95% CI 0.88 to 1.54) Bothersomeness (0-10): 3.59 (95 %CI 3.12 to 4.06) vs. 3.34 (95% CI 2.86 to 3.81) Reduction in bothersomeness score ≥50%: 22% vs. 29%, RR 0.78 (95% CI 0.47 to 1.31) LBP better, much better, or completely gone: 51% vs. 51%, RR 1.00 (95% CI 0.75 to 1.34) Estimates adjusted for baseline RDQ and bothersomeness, sex, age, body mass index, days of lower back pain in the last 6 months, pain traveling down the leg, and employment-related exertion	A vs. B vs. C Withdrawals due to AE: NR Mild or moderate adverse experience: 15% (13/87) vs. 17% (13/75) vs. NR
Somers 2012	NR	None reported.

Author, Year	Funding Source	Quality	Comments
Sherman 2011	Center for Complementary and Alternative Medicine	Fair	
Somers 2012	This publication was made possible by grant number P01 AR50245 from the National Institutes of Health.	Poor	*The PCST+BWM data will not be abstracted as per our protocol.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Soriano 1998	Argentina Number of centers: NR Unclear	Patients older than 60 years, with chronic low back pain for more than 3 months. Exclude: Patients with suspicion of cancer, osteomyelitis, gout, Paget's or collagen disease, symptoms of neurological deficit in lower limbs, or use of corticoids within 30 days.	Randomized: 85 Treated: 71 Analyzed: 71 Attrition: 16% (14/85)
Stewart 2007	Australia 2 physiotherapy clinics	Presented for medical care of a whiplash-associated disorder grades I–III ≤ 1 month after accident, at least ‘‘mildly’’ disabled with respect to pre-injury status and have had significant pain or disability as indicated by a score of at least 20% on any primary outcome measures. Duration of symptoms, 3-12 months. Exclude: Previous neck surgery, known or suspected serious pathology, nerve root compromise, contraindication to exercise (ACSM, 1995) severe or greater depressive symptoms as measured by the Depression Anxiety Stress Scale (DASS), no neck radiograph obtained since the accident and current physiotherapy neck treatment, poor English comprehension.	Randomized: 134 Treated: 134 Analyzed: 125 Attrition: 7% (9/134)

Author, Year	Intervention, Comparator
Soriano 1998	A: GaAS laser (n=38): Wavelength 904 nm, pulse frequency 10,000 Hz, pulse width 200 nsec, peak power 20W, average power 40mW, administered at dose of 4 J/cm2 per point to pain areas, 5 sessions a week for 2 weeks B. Sham laser (n=33)
Stewart 2007	A.Exercise plus advice (n=62): 6 weeks of 1 hour graded exercise program based on behavioral theory and supervised by a physiotherapist, 12 sessions total to include aerobic exercise, stretches, functional activities, activities to build speed, endurance and coordination, and trunk and limb strengthening exercises, individualized home exercise program. B.Advice alone (n=63): Standardized education, reassurance and encouragement to resume light activity, given in 1 consultation and 2 followup phone contacts.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Soriano 1998	A vs B Age: 63 vs. 64 years Female: 58% vs. 52% Pain score (1 to 10): 7.9 vs. 8.1 Osteopenia: 32% vs. 30% Osteophytes: 63% vs. 66% Narrowing of disc space: 34% vs. 33% Spondylolisthesis Grade I: 5% vs. 3%	Pain score (percentage of relief: 0-29% = poor, 30-59% = average, 60 -89% = good, 90-100% = excellent)	Intermediate term 6 months
Stewart 2007	A vs B Age: 44 vs. 43 years Female: 73% vs. 62% Pain duration: 9.5 vs. 8.6 months Pain intensity: 5.2 (2.0) vs 5.3 (2.0) Bothersomeness: 6.8 (2.4) vs 7.1 (2.3) Patient Specific Functional Scale (PSFS): 3.9 (1..7) vs 4.1 (1.6) NDI: 18.2 (6.3) vs. 19.7 (6.9) SF-36 physical: 36.4 (9.9) vs. 36.8 (8.6) SF-36 mental: 49.0 (11.0) vs 48.0 (11.4) Global Perceived Effect (GPE): 0.6 (2.4) vs 0.3 (2.4)	Pain intensity (box scale 0-10, higher score worse pain) Bothersomeness (scale 0-10) PSFS: average of 3 scores, all out of 10 (0 unable to perform activity,10 able to perform activity at pre-injury level) NDI: (scale 0-50, higher score greater disability) SF-36 physical and mental summary scores (scale 0-100 for each) GPE (scale -5 to 5, -5 vastly worse, 0 unchanged, 5 completely recovered) Adverse events	1.5 months, 12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Soriano 1998	A vs. B <u>6 months</u> No pain: 44.7% vs. 15%; p<0.01 Pain recurrence in subgroup of patients with a good or excellent response at end of treatment: 35 % vs. 70%; p=NR
Stewart 2007	A vs B <u>1.5 months</u> Pain severity (0-10): 3.2 (2.2) vs. 4.3 (2.5), p=0.005 Bothersomeness (0-10): 3.6 (2.6) vs 4.8 (2.9), p=0.019 PSFS (0-10): 6.4 (2.1) vs 5.6 (2.0), p=0.006 NDI (0-50): 12.0 (6.8) vs 15.7 (7.9), p=0.004 SF 36 physical: 42.1 (8.9) vs 38.9 (9.3), MD in change score, 3.6 (95% CI 1.23 to 5.97) p=0.003 SF 36 mental (0-100): 51.4 (9.7) vs 46.4 (12.9), MD in change score 4.00 (95% CI 1.24 to 6.77) p=0.005 GPE (-5 to 5): 2.5 (1.8) vs 1.5 (2.5), p=0.006 <u>12 months</u> Pain severity: 3.5 (2.3) vs. 3.8 (2.7), p=0.590 Bothersomeness 4.1 (2.5) vs 4.0 (3.0), p=0.480 PSFS: 6.6 (1.9) vs 6.0 (2.4), p=0.100 NDI: 12.1 (7.5) vs 15.5 (9.9), p=0.080 SF 36 physical: 42.3 (9.8) vs 38.9 (9.3), MD change score 3.80 (95% CI 1.30 to 6.30) p=0.003 SF 36 mental: 48.4 (11.4) vs 46.1 (12.4), p=0.330 GPE: 2.3 (2.0) vs 1.9 (2.3), p=0.480

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Soriano 1998	NR
Stewart 2007	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Soriano 1998	NR	None (no cutaneous, ophthalmologic or systemic side effects reported).
Stewart 2007		AEs: none requiring referral to medical practitioner At 6 weeks subjects were asked if they suffered any AEs. 13 (20%) in the advice plus exercise group answered 'yes', main complaint was muscle pain with exercise (3), knee pain (2) and lumbar spine pain (2). 12 subjects (18%) in the advice group answered 'yes', main complaint was muscle pain (4) increase in headaches (2) and ongoing pain (2).

Author, Year	Funding Source	Quality	Comments
Soriano 1998	Poor	Poor	Duration of f/u corrected. NW
Stewart 2007	NSW Motor Accidents Authority and National Health and Medical Research Council of Australia	Fair	During the intervention period, 10 (15%) in the exercise plus advice group and 15 (23%) in the advice only group reported seeking additional treatment to include physiotherapy, massage therapy, gym program, chiropractic treatment, Pilates classes, & work conditioning

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Strand 2001	Norway	Inclusion Criteria: Patients on >8 weeks sick leave with low back pain Exclusion Criteria: Pregnant, substance abuse, and illness conditions such as progressive nervous system disease, serious cardiac disease, and acute infection.	Randomized: 117 Treated: 117 Analyzed: 117 Attrition: 0% (0/117)
Stukstette 2013	The Netherlands 3 centers Outpatient	ACR criteria for hand OA, hand OA was the most or second most important problem, AUSCAN score ≥9 Exclude: Not willing to participate in a group treatment program	Randomized: 151 Treated: 150 Analyzed: 147 Attrition: 3% (4/151)

Author, Year	Intervention, Comparator
Strand 2001	A: Multidisciplinary rehabilitation (n=81): Physical training (strengthening, body awareness, aerobic fitness, relaxation), education, and cognitive behavioral training (coping, responsibility for prescriptions, focus away from pain) and a workplace intervention. 5 days/week for 4 weeks, 6 hours/day B: Usual Care (n=36): Usual care in community, did not follow a predefined treatment course. Most had physiotherapy (76%; and most had more than 24 treatments) and 32% had alternative interventions (not further specified); 14% did not receive physiotherapy or alternative treatments
Stukstette 2013	A.Multidisciplinary treatment program (n=75): 4 group based occupational therapy sessions 2.5-3 hours duration consisting of self-management techniques, ergonomic principles, daily home exercises, splint (optional) B.Waiting list (n=72): Details NR All patients: 30 minute explanation of written information about OA

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Strand 2001	A vs. B Age: 45 vs. 42 Female: 59% vs. 64% Race: NR BMI, kg/m2: 25.5 (3.9) vs. 25.6 (4.4) Duration of symptoms (years): 10 (10) vs. 9 (7) Disability Rating Index (0-100): 55.6(13.4) vs. 58.3 (12.4) Norwegian Pain Questionnaire (0-106): 39.4(21.8) vs. 43.4(23.7) Pain (0-100 VAS)): 48.3(19.6) vs. 53.0(21.4)	Primary: Disability Rating Index (0-100, higher scores indicate worse disability) Norwegian Pain Questionnaire (0-106) Pain (0-100 VAS) Work (% return to work)	11 months
Stukstette 2013	A vs B Age: 60 vs 58 Female: 18% vs 16% Mean duration of diagnosis (yrs): 4 (6) vs 4 (7) % taking Opioids: 3% vs 4% AUSCAN function: 21.0 (6.9) vs 21.8 (6.3) Patient global assessment: 49.5 (25.1) vs 51.3 (24.8) AUSCAN pain: 10.4 (3.4) vs 10.2 (3.3) SF-36 physical score: 39.5 (7.3) vs 39.4 (6.9) SF-36 mental score: 49.7 (9.0) vs 50.7 (10.0)	AUSCAN function (0-36, higher score=greater disability): patient global assessment of disease activity (0-10, higher score=greater disease activity): OARSI OMERACT (responder vs nonresponder): AUSCAN pain (0-20, higher score=higher pain): SF-36 (0-100, higher score=higher quality of life)	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Strand 2001	A vs. B, mean (SD) Baseline Disability Rating Index (0-100): 55.6 (13.4) vs. 58.3 (12.4) Norwegian Pain Questionnaire (0-106): 39.4 (21.8) vs. 43.4 (23.7) Pain (0-100 VAS)): 48.3 (19.6) vs. 53.0 (21.4) A (work, n=38) vs. A (not work, n=43) vs. B (work, n=21) vs. B (not work, n=15), mean change from baseline 11 months, Disability Rating Index (0-100): -27.3 (95% CI -34 to -21) vs. -3.3 (95 % CI -10 to 14) vs. -16.4 (95% CI -26 to -7.3) vs. 0.2 (95% CI -14 to 14), difference -3.8 (95% CI -13.9 to 6.3) Norwegian Pain Questionnaire (0-106): -17.6 (95 % CI -26 to -9.5) vs. -8.2 (95% CI -16 to -0.4) vs. -27.1 (95% CI -38 to -16) vs. -15.5 (95 % CI -31 to 0.2), difference 5.3 (95%CI -4.9 to 15.6) Pain (0-100 VAS): -21.1 (95% CI -31 to -11) vs. -2.3 (95% CI -9.4 to 4.8) vs. -23.1 (95% CI -37 to 9.2) vs. 7.1 (95% CI -7.7 to 22), difference -1.0 (95% CI -11.7 to 9.6) Working: 47% (38/81) vs. 58% (21/36). difference -11% (95% CI -8 to 30)
Stukstette 2013	A vs B 3 months AUSCAN function: 18.6 (7.3) vs 18.8 (6.4) (Adj MD 0.49, 95% CI -0.09 to 0.37) Patient global assessment: 60.4 (20.6) vs 66.0 (20.6) (Adj MD -5.21, 95% CI -11.43, 1.01) OARSI OMERACT responders: 33% vs 37% (OR 0.82, 95% CI 0.42 to 1.61) AUSCAN pain: 9.4 (2.8) vs 9.0 (3.7) (Adj MD 0.40, 95% CI, -0.5 to 1.3) SF-36 physical score: 39.8 (6.7) vs 39.9 (6.7) (Adj MD -0.14, 95% CI -1.62 to 1.35) SF-36 mental score: 50.3 (9.4) vs 51.6 (9.8) (Adj MD 0.27, 95% CI -2.13 to 2.67)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Strand 2001	NR
Stukstette 2013	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Strand 2001	NR	NR
Stukstette 2013		Swollen hand and wrist and increased pain after second treatment session (n=1)* (authors did not report which group this patients was randomized to)

Author, Year	Funding Source	Quality	Comments
Strand 2001	"Professional Organizational funds were received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript"	Poor	Differences at followup were calculated
Stukstette 2013	Dutch Arthritis Association	Fair	*Patient was rediagnosed with psoriatic arthritis Outcomes not reported: Escola Paulista de Medicina range of motion scale, Kapandji index, JAMAR hand dynamometer, Pain Coping Inventory, General Self-Efficacy Scale, Chronic Pain Self-Efficacy Scale

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Suarez-Almazo 2010	US, Texas. Conducted through Baylor and MD Anderson with 6 acupuncturists, unclear number of "sites"	Inclusion Criteria: 50 years or older, radiographic knee OA using ACR criteria, pain in the knee in the preceding 2 weeks 3/10 on VAS, no prior acupuncture, stable NSAIDs and analgesics in the previous month, 4) if receiving glucosamine, a stable dose for the past 2 months, and no intraarticular knee injections in the previous 2 months. Exclusion criteria: non stated other than inc criteria	Randomized: 560 Treated: 527 Analyzed: 494 Attrition: 11.8% (66/560) at 12 weeks
Sullivan 1998	United States Number of centers unclear 1 hospital, multiple GP clinics	Over 40 years old, diagnosis of chronic, stable, primary OA in one or both knees, knee pain occurring during weight-bearing activities for ≥4 months, radiographic evidence of primary OA of one or both knees, use of NSAIDs ≥2 days per week Exclude: Serious medical conditions that were contraindications for exercise, asymptomatic primary OA of one or both knees, dementia, involvement in any program of regular exercise or study protocol	Randomized: 102 Treated: 102 Analyzed: 52 Attrition: 49% (50/102)

Author, Year	Intervention, Comparator
Suarez-Almazo 2010	A.Electroacupuncture (n=153): Traditional Chinese Medicine points on the basis of clinical practice; TENS equipment emitted a dense disperse wave impulse at 50Hz, dispersing at 15 Hz, 20 cycles/minute. Voltage was increased slowly from 5V to 60V until maximal tolerance was achieved. Patients rested for 20 minutes with continuing TENS. B.Sham (n=302): instead of a dense disperse wave, a 40Hz adjustable wave was used. Voltage was increased until the patient could feel it and then immediately turned off. Patients rested for 20 minutes with the needles retained, but without TENS stimulation; sham points were outside the relevant meridians; depth of needle placement was shallower than true electroacupuncture; Both groups received 20 minute treatments 2/week for 6 weeks, with 12 sessions in total C. Waitlist control (n=72) Note: this was a nested trial with acupuncture group randomized to high or low expectations and sham randomized to high or low expectations.
Sullivan 1998	A.Exercise (n=52): 3 group sessions of 10-15 subjects per week were done for 8 weeks. Sessions were structured as a hospital-based supervised fitness walking and supportive patient education program. Sessions consisted of stretching and strengthening exercises, expert speakers, group discussions, instructions in safe walking techniques, and up to 30 minutes of walking. At the end of the 8 week treatment period, subjects were encouraged to continue walking and given guidelines for managing individualized programs of fitness walking. B.Usual care (n=50): Subjects continued to receive the standard routine medical care they had been receiving prior to enrollment in the study. Subjects were interviewed weekly during the 8 week treatment period about their functional and daily activities.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Suarez-Almazo 2010	A vs B vs. C Age: 64.5 vs. 64.5 vs. 64.1 years Sex (n, % female): 101 (66%) vs. 195 (65%) vs. 42 (58.3%) Race (% white): 107 (70%) vs. 204 (68%) vs. 47 (65.3%) Duration of symptoms: 9.2 vs. 8.6 vs. 11.5 years WOMAC function: 42.9 (19.0) vs. 44.6 (18.1) vs. 40.1 (16.5) J-MAP: 4.4 (1.3) vs. 4.4 (1.3) vs. 4.3 (1.2) WOMAC pain: 44.5 (18.4) vs. 45.0 (18.2) vs. 44.1 (15.2) VAS pain: 58.3 (22.3) vs. 57.4 (23.5) vs. 54.6 (21.3) SF-12 PCS: 35.0 (9.9) vs. 33.5 (8.7) vs. 35.3 (8.4) SF-12 MCS: 52.3 (9.4) vs. 53.4 (9.3) vs. 53.7 (10.7)	WOMAC function subscale (scale unclear) Joint-Specific Multidimensional Assessment of Pain (J-MAP, range 1-7; higher scores=more pain) WOMAC pain subscale (0-100; higher scores=greater pain) Average knee pain (VAS, 0-10; higher scores=greater pain) SF-12 PCS (scale 0-100; higher scores=better health) SF-12 MCS (scale 0-100; higher scores=better health)	1.5 months
Sullivan 1998	A vs B Age: 71 vs 68 Female: 77% vs 90% AIMS physical activity subscale: 6.3 (2.2) vs 6.4 (2.5) AIMS arthritis impact subscale: 4.6 (2.1) vs 4.5 (2.5) AIMS pain subscale: 4.9 (2.1) vs 5.5 (2.4) Pain VAS: 4.1 (2.6) vs 6.3 (3.2) AIMS general health perception subscale: NR	AIMS physical activity subscale (0-10, higher score=higher disability); AIMS arthritis impact subscale (0-10, higher score=higher impact); AIMS pain subscale (0-10, higher score=higher pain); pain VAS (0-10, higher score=higher pain); AIMS general health perception subscale (0-10, higher score=worse health)	10 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Suarez-Almazo 2010	A vs. B <u>1.5 months</u> WOMAC Function subscale: 31.2 (17.9) vs. 32.1 (18.3); MD -0.9 (95% CI -4.4, 2.6), p=0.62 J-MAP: 3.3 (1.4) vs. 3.4 (1.5); MD -0.1 (95% CI -0.39, 0.19), p=0.49 WOMAC Pain subscale: 30.8 (17.9) vs. 31.0 (19.1); MD -0.2 (95% CI -3.8, 3.4), p=0.91 VAS Pain: 36.2 (28.5) vs. 36.7 (29.0); MD -0.5 (95% CI -6.1, 5.1), p=0.86 SF-12 PCS: 39.5 (9.7) vs. 38.7 (10.1); MD 0.8 (95% CI -1.1, 2.7) SF-12 MCS: 54.1 (8.2) vs. 53.2 (8.9); MD 0.9 (95% CI -0.8, 2.6) A vs. C <u>1.5 months</u> WOMAC Function subscale: 31.2 (17.9) vs. 41.7 (18.0); MD -10.5 (95% CI -15.6, -5.5); p=0.0001 J-MAP: 3.3 (1.4) vs. 4.2 (1.3); MD -0.9 (95% CI -1.3, -0.5), p=0.0001 WOMAC Pain subscale: 30.8 (17.9) vs. 42.4 (16.8); MD -11.6 (95% CI -16.5, -6.7), p=0.0001 VAS Pain: 36.2 (28.5) vs. 53.2 (24.3); MD -17.0 (95% CI -24.7, -9.3), p=0.0001 SF-12 PCS: 39.5 (9.7) vs. 35.8 (8.9); MD 3.7 (95% CI 1.0, 6.4), p=0.001 SF-12 MCS: 54.1 (8.2) vs. 51.6 (9.8); MD 2.5 (95% CI 0.04, 5.0), p=0.046
Sullivan 1998	A vs B AIMS physical activity subscale: 6.1 (3.0) vs 6.2 (2.8), (MD -0.1, 95% CI -1.7 to 1.5) p=0.89 AIMS arthritis impact subscale: 3.3 (2.6) vs 3.8 (2.1), (MD -0.5, 95% CI -1.8 to 0.8) p=0.41 AIMS pain subscale: 4.6 (2.4) vs 5.5 (2.1), (MD -0.9, 95% CI -2.2 to 0.4) p=0.15 Pain VAS: 5.0 (2.8) vs 5.4 (3.1), (MD -0.4, 95% CI -2.0 to 1.2) p=0.60 AIMS general health perception subscale: 3.7 (2.8) vs 3.3 (1.9), (MD 0.4, 95% CI -1.0 to 1.8) p=0.52

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Suarez-Almazo 2010	
Sullivan 1998	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Suarez-Almazo 2010		AEs only reported for acupuncture groups *Exacerbation of knee pain:* TCA: 7.2% (11/153) Sham: 4.9% (15/302) RR 1.4 (95% CI 0.7, 3.1), p=0.34 *Bruising at the needle site:* TCA: 5.8% (9/153) Sham 4.6% (14/302) RR 1.3 (95% CI 0.6, 2.9) *Muscle cramps:* TCA: 0.7% (1/153) Sham: 0.7% (2/302) RR 0.99 (95% CI 0.1, 10.8) *Headache:* TCA: 0.7% (1/153) Sham: 0% (0/302) RR not calculable *Infection at the needle site:* TCA: 0.7% (1/153) Sham: 0% (0/302) RR not calculable
Sullivan 1998		NR

Author, Year	Funding Source	Quality	Comments
Suarez-Almazo 2010	NIAMS, AHRQ	Good - sham Fair - waitlist	Also reported the following but not abstracted: Satisfaction with Knee Procedure (SKIP, range 1-5), Timed Up and Go Test (TUG), Range of Motion (ROM). Mean age and duration of knee pain for A vs. B were calculated using weighted means
Sullivan 1998	National Institute of Arthritis and Musculoskeletal and Skin Diseases, and the Arthritis Foundation	Poor	MDs and 95% CIs calculated by AAI, p values given by study

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Tak 2005	The Netherlands Number of centers unclear Outpatient	55 years or older, clinical diagnosis of OA, and living independently Exclude: On waiting list for hip replacement, hip replacement within previous year, inability to safely use fitness equipment, serious depression or dementia, regular physical therapy treatment	Randomized: 109 Treated: 94 Analyzed: 94 Attrition: 14% (15/109)
Tascioglu 2004	Turkey, university hospital	Inclusion Criteria: Patients who had idiopathic knee OA according to American College of Rheumatology criteria were recruited for the study. All patients had Grade II to III bilateral knee OA confirmed radiologically according to the Kellgren-Lawrence grading system. Exclusion Criteria: Exclusion for Kellgren-Lawrence Grade I and IV radiological changes, knee joint disease other than OA, OA of the hip joint, osteoarthritic involvement of the foot joints, serious concomitant systemic diseases, intra-articular fluid effusion, previous physical therapy and intra-articular corticosteroid or hyaluronic acid injections during the last six months.	Randomized: 60 Treated: NR Analyzed: NR Attrition: NR

Author, Year	Intervention, Comparator
Tak 2005	A.Exercise (n=45): Eight 1 hour weekly group sessions of strength training, information on a home exercise program, ergonomic advice, and dietary advice B.Standard of care (n=49): Subject-initiated contact with their own GP
Tascioglu 2004	A.Active Laser 3 joule (n=20) Participants were exposed to Low Level Laser Therapy (LLLT) to affected painful points. No. of Treatments: 1/day, 5 days/week for 2 week (10 treatments total) No. of Treatment Points: 5 painful points, two minute irradiation per point (10 minutes total) Total Dose: 15 joule, 3 joule per point (150 joule total) Power Output: 50 mW, continuous Wavelength: 830 nm Laser Beam Diameter: 1 mm Device: Endolaser 476, Enraf Nonius, Netherlands B.Active Laser 1.5 joule (n=20) Participants were exposed to Low Level Laser Therapy (LLLT) to affected painful points. No. of Treatments: 1/day, 5 days/week for 2 week (10 treatments total) No. of Treatment Points: 5 painful points, one minute irradiation per point (5 minutes total) Total Dose: 7.5 joule, 1.5 joule per point (75 joule total) Power Output: 50 mW, continuous Wavelength: 830 nm Laser Beam Diameter: 1 mm Device: Endolaser 476, Enraf Nonius, Netherlands C.Placebo Laser (n=20) Identical treatment parameters except the device was rigged to appear operational but output energy

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Tak 2005	A vs B Age: 68 vs 69 Female: 64% vs 71% General health: Moderate/bad: 40% vs 45% Good/very good: 60% vs 53% No. of chronic conditions: 2.6 (1.8) vs 2.7 (1.9) HHS: 71.1 (12.9) vs 71.0 (13.3) GARS: 22.8 (5.4) vs 25.3 (5.7) SIP-136 physical: 7.2 (9.2) vs 7.6 (8.3) Pain VAS: 3.8 (2.1) vs 4.2 (2.2) HHS pain subscale: 27.9 (8.1) vs 28.8 (9.0) QoL VAS: 7.0 (4.3) vs 5.6 (2.3) HRQoL: 28.2 (3.1) vs 27.3 (2.4)	HHS (0-100, higher score=higher function); GARS (18-72, higher score=higher disability); SIP-136 physical (0-100, higher score=higher disability); pain VAS (0-10, higher score=higher pain); HHS pain subscale (0-44, higher score=less pain); QoL VAS (0-10, higher score=higher QoL); HRQoL (7-39, higher score=higher QoL)	3 months
Tascioglu 2004	A vs. B vs. C Age: 63 vs. 60 vs. 64 Female: 70% vs. 75% vs. 65% Race: NR Mean Duration of Chronicity: 7.92(5.12) vs. 6.36(4.21) vs. 7.05(6.53) Mean Function (WOMAC): 36.60 (7.09) vs. 37.96 (9.67) vs. 39.46 (12.56) Mean Stiffness (WOMAC): 4.12 (3.01) vs. 4.64 (1.89) vs. 4.45 (2.51); Mean Pain (WOMAC): 10.28 (3.56) vs. 11.60 (4.81) vs. 9.56 (3.88) Mean Pain at Rest (VAS): 39.08 (14.86) vs. 41.55 (16.65) vs. 37.92 (11.00) Mean Pain at Movement (VAS): 68.00 (15.45) vs. 65.72 (18.68) vs. 63.88 (16.07)	WOMAC total (0-96: higher score=worse disability) WOMAC function (0-68; higher score=worse function) WOMAC Stiffness (0-8; higher score=worse stiffness) WOMAC pain (0-20, higher score=greater pain) Pain at Rest (VAS, 0-100; higher score=greater pain) Pain at Activation (VAS, 0-100; higher score=greater pain)	6 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Tak 2005	A vs B <u>3 months</u> HHS: 75.4 (14.6) vs 71.1 (15.1), (MD 4.3, 95% CI -2.2 to 10.8) p=0.081 GARS: 23.7 (5.4) vs 26.3 (6.3), (MD -2.6, 95% CI -6.0 to 0.8) p=0.447 SIP-136 physical: 5.1 (4.7) vs 8.4 (8.4), (MD -3.3, 95% CI -5.3 to -1.3) p=0.041 Pain VAS: 3.5 (2.1) vs 5.1 (2.3), (MD -1.6, 95% CI -2.6 to -0.6) p=0.019 HHS pain subscale: 29.6 (10.4) vs 26.9 (9.8), (MD -0.9, 95% CI -4.7 to 2.9) p=0.047 QoL VAS: 5.0 (1.5) vs 4.2 (1.5), (MD 1.4, 95% CI -0.2 to 3.0) p=0.204 HRQoL: 28.6 (3.6) vs 27.3 (2.7), (MD 0.9, 95% CI -0.4 to 2.2) p=0.262
Tascioglu 2004	<u>A vs. B vs. C</u> <u>6 months</u> Function (WOMAC): 34.84 (8.86) (31.04–37.96) vs. 38.52 (10.49) (35.47–41.93) vs. 38.66 (9.65) (34.47–42.83); AvsC: MD -3.82 (95%CI -9.75 to 2.11) p=0.200; BvsC: MD -0.14 (95% CI -6.59 to 6.31). Stiffness (WOMAC): 3.92 (1.80) (3.08–4.82) vs. 4.48 (1.56) (3.91–4.99) vs. 4.23 (2.05) (3.39–5.11); AvsC: MD -0.31 (95%CI -1.55 to 0.93) p=0.614 Pain (WOMAC): 10.44 (3.03) (9.00–11.80) vs. 11.28 (2.41) (9.00–11.79) vs. 9.86 (3.56) (9.03–10.77); AvsC: MD 0.58 (95%CI -1.54 to 2.70) p=0.582 Pain at Rest (VAS): 38.68 (14.87) (32.49–43.81) vs. 40.02 (9.11) (35.19–45.01) vs. 38.94 (15.05) (34.79–43.01); AvsC: MD -0.26 (95%CI -9.84 to 9.32) p=0.957; BvsC: MD 0.11 (95% CI -0.69 to 0.91) Pain at Activation (VAS): 66.84 (13.54) (61.41–72.19) vs. 61.84 (12.90) (56.76–66.94) vs. 62.04 (16.66) (54.77–69.33); AvsC: MD 4.8 (95%CI -4.92 to 14.52) p=0.324; BvsC: MD -0.02 (95% CI -0.98 to 0.94)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Tak 2005	
Tascioglu 2004	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Tak 2005		NR
Tascioglu 2004	NR	NR

Author, Year	Funding Source	Quality	Comments
Tak 2005	Grant from The Netherlands Health Research and Development Council	Poor	Outcomes not reported: 20 m walk with turn halfway, Timed Up and Go test, ascending and descending stairs, and reaching for toes P values differ from values calculated in t test analysis but were reported as given by the author. Authors t test analysis was described as follows "Contrasts were used to analyze time-group interaction effects for differences between baseline versus post-test and baseline versus followup. Because the program was expected to have a significant positive effect in the experimental group, one-sided tests of significance were used." Mean differences calculated by AAI. No substantial differences between baseline measurements were noted
Tascioglu 2004	None reported.	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Tavafian 2008	Iran, single site, research center	Inclusion Criteria: Age 18 years and over, chronic LBP (persisting for 90 days or more). Exclusion Criteria: Back surgery within 2 years, having complaint restricted to sacroiliac joint, cervical or thoracic regions and congenital spine diseases.	Randomized: 102 Treated: 102 Analyzed: 74 Attrition: 27.5% (28/102)
Tavola 1992	Italy, single site, outpatient headache center	Inclusion criteria: Diagnosis of muscle-tensive and tension-type headache, frequency of headache episodes greater than once a week having a mean intensity not less than 'moderate,' abstaining from other therapies previously undertaken (except for non-narcotic analgesics). Exclusion Criteria: organic pathology	Randomized: 30 Treated: 30 Analyzed: 30 Attrition: 0%

Author, Year	Intervention, Comparator
Tavafian 2008	A: Multidisciplinary program + medications (n=37): The back school program was a multidimensional and interdisciplinary educational regime designed based on patients' characteristics, lifestyle and subsequent ability to cope; led by a rheumatologist. Included education in anatomy, physiology, pathology of low back pain, self-care, health behaviors, biomechanics, lifestyle factors, and prevention. Additionally they were accompanied by psychologist in coping skills, anger management, relaxation, and by a physiotherapist in stretching, strengthening, posture, and functional movement advice (HEP). 5 sessions over 4 days, duration of sessions not reported; patient also received medications as described below B: Oral medication only (n=37): Acetaminophen, NSAID and chlordiazepoxide, given under the supervision of the rheumatologist
Tavola 1992	A: Acupuncture (n=15) No. of treatments: 1 treatment per week for 8 weeks Type of needle: stainless steel, 0.3 mm diameter Acupoints: placements made according to traditional Chinese medicine criteria on an individual basis No. of needles: 6-10 No. of insertions per needle: NR Insertion depth: 10-20mm Time length of treatment: 20 minutes B: Sham (n=15) No. of treatments: 1 treatment per week for 8 weeks No. of needles: 6-10 Acupoints: same regions, but not in specific acupoints Insertion depth: 2-4mm Time length of treatment: 20 minutes

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Tavafian 2008	A vs B Age, year: 43 vs. 45 Female, %: 100 vs. 100 Race: NR Duration of symptoms (months): 8.90 vs. 9.24 SF-36 Physical component summary (0-100): 41.18 (17.07) vs. 42.29 (21.63) SF-36 Mental component summary (0-100): 47.52 (28.77) vs. 47.68 (23.38)	Secondary SF-36 Physical component summary (0-100) SF-36 Mental component summary (0-100)	3, 6, and 12 months
Tavola 1992	A vs. B Age: 33 vs. 33 years Female: 87% vs. 87% Disease duration: 8 vs. 8 years Mean frequency of headache attacks per month: 18 vs. 17 Prior preventative treatments: NR Medication overuse: NR Mean analgesic use: 12 vs. 12 units/month Mean headache index (HI): 4.3 (3.9) vs. 4.5 (3.4) Mean duration of attacks: 3.3 (1.5) vs. 4.4 (3.2)	Responders, 33% and 50% thresholds (proportion of patients with ≥33% or ≥50% improvement over baseline on Headache Index Headache index (intensity X duration X frequency/30) Pain intensity (sum of the intensity of the attacks in a month/number of attacks) Duration of headache attacks (sum of the hours of headache in a month/number of attacks) Analgesic consumption (sum of the drugs taken per month)	1, 6 and 12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Tavafian 2008	A vs. B, mean (SD) <u>Baseline</u> SF-36 Physical component summary (0-100): 41.2 (17.1) vs. 42.3 (21.6) SF-36 Mental component summary (0-100): 47.5 (28.8) vs. 47.7 (23.3) <u>3 months</u> SF-36 Physical component summary (0-100): 76.7 (17.3) vs. 51.2 (28.1), difference 25.5 (95% CI 14.69 to 36.31) SF-36 Mental component summary (0-100): 80.4 (22.8) vs. 57.4 (29.5), difference 23.0 (95% CI 10.78 to 35.22) <u>6 months</u> SF-36 Physical component summary (0-100): 66.6 (27.5) vs. 51.2 (28.8), difference 15.4 (95% CI 2.35 to 28.45) SF-36 Mental component summary (0-100): 66.9 (29.9) vs. 57.9 (25.5), difference 9.0 (95% CI -3.88 to 21.88) <u>12 months</u> SF-36 Physical component summary (0-100): 64.7 (36.3) vs. 51.1 (28.3), difference 13.6 (95%CI -1.48 to 28.68) SF-36 Mental component summary (0-100): 65.1 (27.2) vs. 60.2 (26.6), difference 4.9 (95%CI -7.57 to 17.37)
Tavola 1992	<u>1 month</u> Responders, ≥33% improvement in Headache Index: 86.7% (13/15) vs. 60.0% (9/15), p=0.125; RR 1.44 (95% CI 0.91 to 2.28) Responders, ≥50% improvement in Headache Index: 53.3% (8/15) vs. 46.7% (7/15), p=1; RR 1.14 (95% CI 0.56 to 2.35) Headache index, mean (SEM)*: 2.4 (1.4) vs. 3.0 (2.3); MD -0.60 (95% CI -6.12 to 4.92), p=0.83 Mean decrease in Headache index from baseline: 58.3% vs. 27.8% Mean decrease in headache attack frequency from baseline: 44.3% vs. 21.4% Mean decrease in analgesic consumption from baseline: 57.7% vs. 21.7% <u>6 months</u> Headache index, mean (SEM)*: 2.2 (1.6) vs. 3.1 (2.6); MD -0.90 (95% CI -7.15 to 5.35), p=0.77 <u>12 months</u> Responders, ≥33% improvement in Headache Index: 53.3% (8/15) vs. 46.7% (7/15), p=1; RR 1.14 (95% CI 0.56 to 2.35) Responders, ≥50% improvement in Headache Index: 40.0% (6/15) vs. 26.7% (4/15), p=0.7; RR 1.50 (95% CI 0.53 to 4.26) Headache index, mean (SEM)*: 3.2 (2.1) vs. 3.7 (2.2); MD -0.50 (95% CI -6.73 to 5.73), p=0.87 *means and SEMs estimated from graph

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Tavafian 2008	
Tavola 1992	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Tavafian 2008	NR	No adverse events or side effects were reported from subjects in either intervention group. Withdrawals: 2% (1/50) vs. 2% (1/52)
Tavola 1992		NR

Author, Year	Funding Source	Quality	Comments
Tavafian 2008	Health Resources and Services Administration (HRSA) for their financial support (Grant # R18 AH 10001), National Chiropractic Mutual Insurance Company, and many chiropractic physicians for their generous donations.	Poor	The study reported all baseline and outcome values as mean (standard error). MD was obtained with a SD calculated with the following equation [SD = SEM * sqrt(n)]. Differences calculated by Spectrum, but studies appear to report SD not SE
Tavola 1992	NR	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Teirlinck 2016	The Netherlands General practitioners Number of centers unclear	45 years or older, non-traumatic hip pain fulfilling ACR clinical criteria for hip OA diagnosis Exclude: Exercise therapy in the past 3 months, hip pain score <3 on 11-point NRS, score of <2 on Algofunctional Index, hip surgery or on waiting list, disabling co-morbidity, mentally incapable of participation	Randomized: 203 Treated: 203 Analyzed: 189 Attrition: 7% (14/203)
Thamsborg 2005	Denmark, single-site, outpatient	Inclusion Criteria: Patients older than 45 years with painful knee osteoarthritis of the femorotibial compartment (fulfilling criteria of the American College of Rheumatology) Exclusion Criteria: Inflammatory joint disease, acromegaly, Charcot's arthropathy, haemochromatosis, Wilson's disease, ochronosis, terminal illnesses/malignancies, pregnancy or lack of contraception use in women of childbearing age, and use of pacemaker or any implanted electrical device. Additionally, participants were excluded if they were unable to understand/fill out the questionnaires, had received intra-articular glucocorticoid or hyaluronic acid injection 1 month prior to study entry, or had hip and/or lumbar spine OA with referred pain to the study knee.	Randomized: 90 Treated: 83 Analyzed: 83 Attrition: 7.7% (7/90)

Author, Year	Intervention, Comparator
Teirlinck 2016	A.Exercise+usual care (n=101): Maximum of 12 sessions over 3 months with each session 30 minutes long. Sessions consisted of information on lifestyle adaptations, possible walking aids, appropriate postural loading of joints, and (in)appropriate pain behavior. Exercises performed during the session focused on strengthening, increasing flexibility, and improving endurance. Three booster sessions occurred at 2, 4, and 6 months after the initial 3 month treatment period. B.Usual care (n=102): Routine care provided by GP, which could include education, counselling, prescription of pain medication, additional diagnostic tests, or referral to an orthopedic surgeon. Referral to a physical therapist was discouraged but not restricted All patients: Received brochure with information about hip OA
Thamsborg 2005	A.Pulsed Electromagnetic Fields (PEMF) (n=42) Two sets of two adjacent coils were placed on the medial and lateral regions of the study knee, with the interspace between the coils being at the level of the koin line. The coils were placed on an insulating bandage of 3-5 mm thickness that could No. of Treatments: daily treatment 5 days per week for 6 weeks (30 total Length of Treatments: 2 hours each Device: ±50V in 50Hz pulses changing voltage in 3 ms intervals. B.Sham Electromagnetic Field (n=41) Patients in the control group were subjected to a noneffective placebo electromagnetic field. No. of Treatments: daily treatment 5 days per week for 6 weeks (30 total Length of Treatments: 2 hours each

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Teirlinck 2016	A vs B Age: 64 vs 67 Females: 62% vs 55% High blood pressure: 37% vs 44% Heart disease: 17% vs 16% Lung disease: 8% vs 9% Diabetes: 10% vs 16% Knee OA: 29% vs 31% Hand OA: 29% vs 31% Rheumatoid arthritis: 1% vs 5% Duration of symptoms, median (IQR): 365 (810) vs 365 (819) Pain medication used daily in past 3 months: 21% vs 31% HOOS function: 35.4 (18.0) vs 32.2 (17.5) HOOS pain: 37.6 (16.1) vs 38.9 (15.7) ICOAP constant pain: 5.4 (3.5) vs 5.8 (3.8) ICOAP intermittent pain: 8.0 (3.9) vs 8.4 (4.3) ICOAP total pain: 30.4 (15.8) vs 32.2 (7.5) EuroQol 5D-3L: 0.79 (0.12) vs 0.75 (0.16)	HOOS function (0 to 100, higher score=higher function); HOOS pain (0 to 100, higher score=lower pain); ICOAP constant pain (0-20, higher score=higher pain); ICOAP intermittent pain (higher score=higher pain); ICOAP total pain (0-100, higher score=higher pain); EuroQol 5D-3L (-0.329-1.0, higher score=higher quality of life)	3, 6, and 9 months
Thamsborg 2005	A vs B Age: 60 vs. 60 Female: 47.6% vs. 61% Race: NR Mean Duration of Chronicity (years): 7.5 (5.2) vs. 7.9 (7.7) Analgesics Medication use: 55% (23/42) vs. 61% (25/41) Activities of Daily Living (WOMAC): 43.83 (1.93) vs. 46.49 (2.21) Stiffness (WOMAC): 5.74(0.29) vs. 5.85(0.28) Pain (WOMAC): 13.15(0.57) vs. 14.49(0.54)	Primary Western Ontario and McMaster Osteoarthritis Index (WOMAC, higher scores indicate severity of pain, stiffness and dysfunction) Activities of Daily Living (WOMAC, range 0-85) Joint Pain (WOMAC, range 0-25) Stiffness (WOMAC, range 0-10)	1.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Teirlinck 2016	A vs B <u>3 months:</u> HOOS function: 30.8 (21.9) , 35.3 (20.7), (Adj MD -2.4, 95% CI -6.7 to 1.9) p=0.27 HOOS pain: 34.4 (19.7) vs 37.2 (18.0), (Adj MD -2.2, 95% CI -6.2 to 1.7) p=0.27 ICOAP constant pain: 4.0 (4.2) vs 5.3 (4.3), (Adj MD -0.9, 95% CI -1.9 to 0.1) p=0.09 ICOAP intermittent pain: 7.0 (4.6) vs 7.9 (4.6), (Adj MD -0.6, 95% CI -1.7 to 0.6) p=0.33 ICOAP total pain: 24,9 (19.1) vs 29.8 (19.3), (Adj MD -3.3, 95% CI -8.0 to 1.4) p=0.16 EuroQol 5D-3L: 0.77 (0.19) vs 0.76 (0.17), (Adj MD -0.01, 95% CI -0.06 to 0.04) p=0.73 <u>9 months</u> HOOS function: 26.8 (21.2) vs 34.2 (21.4), (Adj MD -3.0, 95% CI -6.7 to 0.2) p=0.06 HOOS pain: 31.6 (19.5) vs 34.6 (19.3), (Adj MD -1.6, 95% CI -6.2 to 3.0) p=0.49 ICOAP constant pain: 3.6 (3.8) vs 4.7 (4.3), (Adj MD -0.7, 95% CI -1.7 to 0.4) p=0.23 ICOAP intermittent pain: 6.1 (4.1) vs 7.2 (4.9), (Adj MD -0.6, 95% CI -1.8 to 0.6) p=0.35 ICOAP total pain: 22.2 (17.1) vs 27.0 (19.8), (Adj MD -2.8, 95% CI -7.6 to 2.0) p=0.25 EuroQol 5D-3L: 0.78 (0.20) vs 0.78 (0.15), (Adj MD -0.01, 95% CI -0.06 to 0.04) p=0.69 Total hip replacements: 6 vs 9
Thamsborg 2005	<u>A vs. B</u> <u>1.5 months</u> Activities of Daily Living (WOMAC): 37.89(2.14) vs. 41.37(2.27); MD -3.48 (95%CI -4.44 to -2.51) p=0.0001 Stiffness (WOMAC): 4.81(0.32) vs. 5.15(0.30); MD -0.34(95%CI -0.48 to -0.20) p=0.0001 Joint Pain (WOMAC): 11.40(0.57) vs. 12.24(0.63); MD -0.84 (95%CI -1.10 to -0.58) p=0.0001

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Teirlinck 2016	
Thamsborg 2005	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Teirlinck 2016		No serious adverse events reported
Thamsborg 2005	NR	12 in the experimental group reported either throbbing sensation, warming sensations or aggravation of pain vs. 6 in the control

Author, Year	Funding Source	Quality	Comments
Teirlinck 2016	Netherlands Organization for Health Research and Development, grant from the Dutch Arthritis Foundation	Fair	Outcomes not reported: Recovery on 0-6 Likert Scale, timed up and go test
Thamsborg 2005	Funding support from IMK Almene Fond and Københavns Amts Erhvervskontor.	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Thieme 2006	Unclear 10 centers Outpatient	Married females with a diagnosis of FM fulfilling ACR criteria. Pain for at least 6 months and spouses willing to participate. Exclude: Inflammatory rheumatologic diseases, concurrent major disease	Randomized: 125 Treated: 125 Analyzed: 125 Attrition: 20% (25/125)

Author, Year	Intervention, Comparator
Thieme 2006	A.Operant behavior therapy (n=43): 2 hour sessions weekly for 15 weeks, with spouses attending the 1st, 5th, 9th, and 13th sessions. Sessions consisted of structured time-contingent exercises aiming to change observable pain behaviors. Treatment also consisted of reduction of medication, increase of activity, reduction of interference of pain with activities, reduction of pain behaviors, and training in assertive pain incompatible behaviors. 40/43 completed treatment. B.Cognitive behavior therapy (n=42): 2 hour sessions weekly for 15 weeks. Sessions focused on changing patients' thinking and involved problem-solving, stress and pain coping strategies, and relaxation exercises that were performed during and between sessions. 40/42 completed treatment. C.Attention placebo (n=40): 2 hour sessions weekly for 15 weeks. Sessions consisted of general discussions centered on the medical and psychosocial problems of FM. 20/40 completed treatment. All patients: Received general medical advice and a rheumatological assessment including a blood chemistry analysis, neurological examination, and an evaluation of trigger points.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Thieme 2006	A vs B vs C Age: 43 vs 49 vs 47 Female: 100% vs 100% vs 100% Duration of symptoms, years: 9.0 vs 9.1 vs 8.7 Number of physician visits: 36.9 (15.2) vs 30.6 (16.2) vs 34.3 (16.3) Occupational status: Working: 40% vs 45% vs 50% Unemployed: 37% vs 38% vs 30% Worker's compensation: 7% vs 5% vs 8% Retired: 16% vs 10% vs 8% Student: 0% vs 2% vs 5% FIQ physical impairment: 4.8 (2.2) vs 4.4 (2.1) vs 4.2 (2.1) WHYMPI pain intensity:4.2 (1.0) vs 4.2 (0.8) vs 3.8 (1.0) WHYMPI affective distress: 3.2 (1.4) vs 3.2 (1.0) vs 3.5 (1.3) WHYMPI solicitous spouse behavior: 4.0 (0.8) vs 3.3 (1.6) vs 3.2 (1.3) PRSS pain coping: 3.0 (1.0) vs 3.3 (0.6) vs 2.9 (0.7) PRSS pain catastrophizing: 2.5 (1.2) vs 2.3 (0.9) vs 2.4 (1.0)	FIQ physical impairment (0-10, higher score=higher disability); pain intensity VAS (0-10, higher score=higher pain) WHYMPI pain intensity (0-6, higher score=higher pain); WHYMPI affective distress (0-6, higher score=higher distress); WHYMPI solicitous spouse behavior (0-6, higher score=lower spouse response); PRSS pain coping (0-5, higher score=higher coping ability); PRSS pain catastrophizing (0-5, higher score=higher catastrophizing)	6 and 12 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Thieme 2006	A vs C <u>6 months</u> FIQ physical impairment: 3.9 (2.1) vs 4.8 (2.6), (MD -0.9, 95% CI -2.1 to 0.3) p=0.15 WHYMPI pain intensity: 3.8 (0.9) vs 4.1 (1.1), (MD -0.3, 95% CI -0.8 to 0.2) p=0.26 WHYMPI affective distress: 3.1 (1.2) vs 4.0 (1.4), (MD -0.9, 95% CI -1.6 to -0.2) p=0.012 WHYMPI solicitous spouse behavior: 3.2 (1.4) vs 4.0 (1.2), (MD -0.8, 95% CI -1.5 to -0.1) p=0.033 PRSS pain coping: 3.4 (0.8) vs 2.7 (0.7), (MD 0.7, 95% CI 0.3 to 1.1) p=0.0015 PRSS pain catastrophizing: 1.7 (1.0) vs 2.6 (0.9), (MD -0.9, 95% CI -1.1 to -0.4) p=0.0012 Number of physician visits: NR <u>12 months</u> FIQ physical impairment: 2.6 (1.6) vs 5.2 (2.5). (MD -2.6, 95% CI -3.7 to -1.5) p<0.0001 WHYMPI pain intensity: 3.1 (1.4) vs 4.1 (1.5), (MD -1.0, 95% CI -1.8 to -0.2) p=0.014 WHYMPI affective distress: 2.9 (1.2) vs 4.2 (1.4), (MD -1.3, 95% CI -2.0 to -0.6) p=0.0004 WHYMPI solicitous spouse behavior: 2.8 (1.3) vs 4.1 (1.2), (MD -1.3, 95% CI -2.0 to -0.6) p=0.0004 PRSS pain coping: 3.5 (1.1) vs 2.3 (1.0), (MD 1.2, 95% CI 0.6 to 1.8) p=0.0001 PRSS pain catastrophizing: 1.7 (1.2) vs 2.8 (1.1), (MD -1.1, 95% CI -1.7 to -0.5) p=0.0011 Number of physician visits: 16.4 (18.3) vs 47.7 (20.0), (MD -31.3, 95% CI -41.6 to -21.0) p<0.0001 B vs C <u>6 months</u> FIQ physical impairment: 3.0 (2.4) vs 4.8 (2.6); MD -1.8 (95% CI -2.899 to -0.701), p=0.0016 WHYMPI pain intensity: 3.7 (0.9) vs 4.1 (1.1); MD -0.4 (95% CI -0.841 to 0.041), p=0.07 WHYMPI affective distress: 2.6 (1.1) vs 4.0 (1.4); MD -1.4 (95% CI -1.952 to -0.848), p<0.0001 <u>12 months</u> FIQ physical impairment: 3.4 (2.3) vs 5.2 (2.5); MD -1.8 (95% CI -2.855 to -0.745), p=0.001 WHYMPI pain intensity: 3.2 (1.4) vs 4.1 (1.5); MD -0.9 (95% CI -1.537 to -0.263), p=0.006 WHYMPI affective distress: 2.6 (1.2) vs 4.2 (1.4); MD -1.6 (95% CI -2.172 to -1.028), p <0.0001

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Thieme 2006	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Thieme 2006		Withdrawals: 3/43 in A due to depression/lack of motivation 2/42 in B due to depression 20/40 in C due to worsening of symptoms

Author, Year	Funding Source	Quality	Comments
Thieme 2006	Grants from the Deutsche Forshungsgemeinschaft to KT (Th 899-1/2 and 899 2/2) and HF (FL 156/26, Clinical Research Unit 107 'Learning, plasticity and pain'), the Max-Planck Aware for International Cooperation to HF, and the National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases to DCT (AR44724 and AR 47298	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Thomas 2002	UK 2 centers General practitioner	Aged 45 or over with knee pain on most days in the previous month Exclude: Total knee replacement, lower limb amputation, permanent cardiac pacemaker, no knee pain within the past week	Randomized: 786 Treated: NR Analyzed: 600 Attrition: 24% (186/786)
Thomas 2006	UK Number of centers: 21 Setting: Outpatient (private acupuncture clinics and general practices)	Age 18-65 years Non-specific LBP for 4-52 weeks General practitioner assessment as suitable for primary care management Exclude Current acupuncture treatment Possible spinal disease (such as carcinoma) Severe or progressive motor weakness Prolapsed central disc Past spinal surgery Bleeding disorders (such as hemophilia) Pending litigation	Randomized: 241 Analyzed: - 3 months: 217 - 12 months: 215 - 24 months: 182 Attrition: 24% (59/241)

Author, Year	Intervention, Comparator
Thomas 2002	A.Exercise (n=470): Two year, self paced program that started with four 30 minute visits in the first two months followed by visits every six months. The program was designed to maintain and improve strength of muscles around the knee, range of motion at the knee joint, and locomotor function. 121 of the 470 patients also received attention control which consisted of monthly phone calls by a study researcher that sought to monitor symptoms and offer simple advice on knee pain management. 114 of the 470 patients received the attention control and a placebo tablet in addition to the exercise program. The remaining 235 participate in the exercise program only.* B.Control (n=316): 160 subjects received attention control consisted of monthly phone calls by a study researcher that sought to monitor symptoms and offer simple advice on knee pain management. 78 subjects took a placebo tablet. 78 patients had no contact with the researchers between assessment visits.*
Thomas 2006	A. Acupuncture (n=147): Up to 10 individualized traditional acupuncture treatment sessions over 3 months. Acupuncturists had ≥3 years of experience. Content and number of treatments were determined by the acupuncturist according to patients' needs. Disposable acupuncture needles were used. The patients remained under the care of their general practitioner. B: Usual care (n=68): NHS treatment according to the patient's general practitioner's assessment of need.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Thomas 2002	A vs B Age: 62 vs 62 Female: 63% vs 66% WOMAC pain score: 7.15 vs 7.35	WOMAC physical function (0-68, higher score=higher disability); WOMAC pain (0-20, higher score=higher pain); HADS depression (0-21, higher score=higher depression); HADS anxiety (0-21, higher score=higher anxiety); SF-36 (0-100, higher score=higher quality of life)	6, 12, 18, and 24 months*
Thomas 2006	A vs. B Age: 42 vs. 44 Female: 62% vs. 58% Weeks with back pain: 17.1 vs. 16.7 Baseline SF-36 physical functioning score: 55.5 vs. 60.0 Baseline SF-36 bodily pain score: 30.8 vs. 30.4 Baseline ODI: 33.7 vs. 31.4 Baseline SF-MPQ present pain index: 2.64 vs. 2.70 Number of previous episodes of LBP - None: 16% vs. 16% - 1-5: 36% vs. 29% - >5: 48% vs. 55% Presence of leg pain: 67% vs. 59% Work status - Full-time: 52% vs. 56% - Part-time: 25% vs. 28% - Housewife, retired, or student: 14% vs. 15% - Permanently unable to work due to LBP: 7% vs. 0% - Permanently unable to work due to other health reason: 2% vs. 1% Drugs for LBP in past 4 weeks: 88% vs. 90% Major health problems in addition to back pain: 28% vs. 31% Ever used private acupuncture for any reason: 13% vs. 9%	SF-36 bodily pain subscale (0-100, 100=no pain) Oswestry Disability Index (0-100, 0=no disability) SF-McGill Pain Questionnaire Present Pain Index (0-5, 0=no pain) Presence LBP or leg pain in the past 12 months Medication use for LBP in the past 4 weeks	9 months, 21 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Thomas 2002	A (exercise) vs B (no exercise) 6 months WOMAC physical function, mean difference (95% CI): NR WOMAC pain, mean difference (95% CI): -0.6 (-1.0 to -0.2), p=0.003 HADS: NR SF-36: NR 24 months WOMAC physical function, mean difference (95% CI): -2.6 (-4.1 to -1.1), p=0.001 WOMAC pain: -0.82 (-1.3 to -0.3), p=0.001 HADS: NR (NS) SF-36: NR (NS)
Thomas 2006	A vs. B Baseline SF-36 bodily pain (0-100): 30.8 (16.2) vs. 30.4 (18.0) Oswestry Disability Index (0-100): 33.7 (15.4) vs. 31.4 (14.2) McGill Present Pain Index (0-5): 2.64 (1.0) vs. 2.70 (1.0) 9 months SF-36 bodily pain (0-100): 64.0 (25.6) vs. 58.3 (22.2), adjusted difference 5.6 (95% CI -0.2 to 11.4) Oswestry Disability Index (0-100): 20.6 (19.3) vs. 19.6 (15.4), adjusted difference -0.5 (-5.1 to 4.2) McGill Present Pain Index (0-5): 1.43 (1.1) vs. 1.53 (0.9), adjusted difference -0.1 (-0.4 to 0.3) 21 months SF-36 bodily pain (0-100): 67.8 (24.1) vs. 59.5 (23.4), adjusted difference 8.0 (2.8 to 13.2) Oswestry Disability Index (0-100): 18.3 (16.5) vs. 21.0 (14.2), adjusted difference -3.4 (-7.8 to 1.0) McGill Present Pain Index (0-5): 1.42 (1.1) vs. 1.71 (1.1), adjusted difference -0.2 (-0.6 to 0.1) LBP or leg pain in the past 12 months: 82% vs. 92%, difference10% (-20 to 2) Used medication for LBP in the past 4 weeks: 40% vs. 59%, difference -19% (-35 to -3), p=0.03 Differences adjusted for baseline SF-36 bodily pain score and clustering by acupuncturist

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Thomas 2002	
Thomas 2006	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Thomas 2002		NR
Thomas 2006	NR	A vs. B Withdrawals: 11% (17/160) vs. 1% (1/81) Withdrawals due to AEs: 3% (4/160) vs. 0% Serious AEs: None were reported Nonserious AEs: 23% (30/133) vs. 0%

Author, Year	Funding Source	Quality	Comments
Thomas 2002	Department of Health	Poor	Thomas 2005 is a cost analysis of study in Thomas 2002 *Original study design was a factorial study with the groups exercise therapy, monthly phone contact, exercise therapy+monthly phone contact, and no intervention. Subjects in the combined exercise+phone and the no intervention groups were further randomized to receive or not receive a placebo pill. Authors found no statistical differences between groups that did/did not receive tablet and decided to merge these subgroups. Authors also decided to report results in only two groups, comparing subjects who had done the exercise program to subjects that had not done the exercise program. The attention control and no intervention group seemed similar that the method of reporting the results was accepted. *All followup periods occurred during two year treatment period
Thomas 2006	Funded by the UK NHS Executive health technology programme; treatment costs of the acupuncture funded by York Health Authority.	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Thorstensson 2005	Sweden Number of centers unclear 1 hospital, numerous GPs	Aged 35-65, diagnosis of radiographic osteoarthritis of Kellgren and Lawrence grade III or more Exclude: Inflammatory joint disease, anterior cruciate ligament injury, injury to the menisci, hip symptoms more aggravating than knee symptoms, knee replacement surgery within 6 months after study initiation, co-morbidities not allowing exercise	Randomized: 65 Treated: 61 Analyzed: 46 Attrition: 29%
Tilbrook 2011	UK Number of centers unclear Outpatient/nonmedical setting	Age 18-65 Visit for low back pain in prior 18 months RDQ score ≥4 Musculoskeletal pain bounded by the lowest ribs and gluteal folds Exclude: Performed yoga in past 6 months Could not get off floor unassisted Pregnant Life-threatening comorbid conditions Prior spinal surgery severe psychiatric problems or alcohol dependency Indications of serious spinal neurologic abnormality	Randomized: 313 Treated: 299 Analyzed at 12 months: 272 Attrition: 13% (41/313)

Author, Year	Intervention, Comparator
Thorstensson 2005	A.Exercise (n=30): 1 hour group exercise sessions of 2 to 9 participants, twice a week for 6 weeks. Sessions consisted of weight-bearing exercises to increase postural control and to increase endurance and strength in the lower extremity. Patients were given daily exercises to perform at home. B.Control group (n=31): Subjects were told not to make any lifestyle changes. Subjects met with the physical therapist at baseline, at 6 weeks, and at 6 months
Tilbrook 2011	A: Iyengar yoga (n=156): Twelve weekly 75-minute classes. Participants were given student manual, a mat, and a relaxation CD. Home practice sheets were distributed at 4 intervals over the 12 weeks. Yoga was taught by two trained teachers. The program included foundational elements of yoga adapted appropriately for low back pain, including asana, pranayama, relaxation techniques, mental focus and philosophy. Classes consisted of an introduction to the weekly theme; pain-relieving or settling in relaxing poses; a program of seated, standing, prone and supine poses; educative postural advice; and 5 to 15 minutes relaxation. Poses targeted stiff, weak and uneducated areas of the whole body, with the intention of improving mobility, strength and posture and reducing pain. Participants were encouraged to practice 30 minutes daily or at least 2 times per week, and to use the CD. B: Attention control (self-care education): *The Back Book* back pain education booklet and usual care (n=157)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Thorstensson 2005	A vs B Age: 55 vs 57 Female: 50% vs 52% KOOS pain: 60 (18) vs 64 (19) KOOS ADL: 69 (18) vs 71 (21) KOOS symptoms: 63 (20) vs 66 (18) KOOS sports and recreation: 34 (31) vs 37 (29) KOOS QOL: 40 (15) vs 46 (21) SF-36 physical component score, mean (95% CI): 42.5 (24.4 to 57.5) vs 43.8 (24.2 to 57.3) SF-36 mental component score, mean (95% CI): 55.6 (40.2 to 66.2) vs 56.3 (37.0 to 67.0)	KOOS pain (0-100, higher score=lower disability); KOOS ADL (0-100, higher score=lower disability); KOOS symptoms (0-100, higher score=lower disability); KOOS sports and recreation(0-100, higher score=lower disability); KOOS QOL (0-100, higher score=lower disability); SF-36 physical component score (0-100, higher score=higher quality of life); SF-36 mental component score (0-100, higher score=higher quality of life)	5 months
Tilbrook 2011	A vs. B Age: 46 vs. 46 Female: 68% vs. 73% Race: NR Duration of back pain (median months): 96 vs. 72 Medication use: 57% vs. 55%	RDQ (0-24) SF-12 (0-100) Aberdeen Back Pain Scale (0-100)	3 and 6 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Thorstensson 2005	A vs B KOOS pain, mean Δ (95% CI): 3.1 (-1.9 to 8.2) vs -1.1 (-6.6 to 4.4), p=0.32 KOOS ADL, mean Δ (95% CI): 0.9 (-3.8 to 5.6) vs -1.9 (-7.7 to 3.9), p=0.61 KOOS symptoms, mean Δ (95% CI): 1.0 (-3.8 to 5.8) vs -3.4 (-8.8 to 1.9), p=0.31 KOOS sports and recreation, mean Δ (95% CI): 0.5 (-10.1 to 11.2) vs -8.3 (-19.5 to 2.8), p=0.32 KOOS QOL, mean Δ (95% CI): 5.1 (-0.7 to 11.0) vs -2.3 (-9.5 to 4.9), p=0.02 SF-36 physical component score, mean Δ (95% CI): 3.0 (-5.9 to 16.3) vs -0.7 (-14.8 to 9.8), p=0.09 SF-36 mental component score, mean Δ (95% CI): 0.7 (-18.1 to 13.2) vs -0.7 (-16.8 to 12.8), p=0.40
Tilbrook 2011	A vs. B <u>Baseline, mean (SD)</u> RDQ (0-24): 7.84 (3.96) vs. 7.75 (4.72) Aberdeen Back Pain Scale (0-100): 25.36 (10.59) vs. 26.69 (10.87) SF-12 PCS (0-100): 44.41 (9.13) vs. 44.04 (9.45) SF-12 MCS (0-100): 45.04 (10.90) vs. 45.02 (10.66) <u>3 months (mean difference in change from baseline [95% CI])</u> RDQ: -1.48 (-2.62 to -0.33) Aberdeen Back Pain Scale (0 to 100): -1.74 (-4.32 to 0.84) SF-12 PCS: 1.24 (-0.83 to 3.33) SF-12 MCS: 2.02 (-0.34 to 4.37) <u>6 months (mean difference in change from baseline [95% CI])</u> RDQ: -1.57 (-2.71 to -0.42) Aberdeen Back Pain Scale: -0.73 (-3.30 to 1.84) SF-12 PCS: 0.80 (-1.28 to 2.87) SF-12 MCS: 0.42 (-1.92 to 2.77)

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Thorstensson 2005	
Tilbrook 2011	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Thorstensson 2005		A vs B Increased knee pain: 3% (1/30) vs 0% (0/31)
Tilbrook 2011	NR	A vs. B Withdrawal due to AE: NR Adverse events: 8% (12/156) vs. 1% (2/157), RR 6.04 (95% CI 1.37 to 26.54)

Author, Year	Funding Source	Quality	Comments
Thorstensson 2005	Grants from the Vardal Foundation, The Swedish Rheumatism Association in Stockholm and Gothenburg, The Swedish Research Council, The Department of Research and Development at Spenshult Hospital for Rheumatic Diseases	Fair	Patients not treated were erroneously randomized
Tilbrook 2011	Grant funds: Arthritis Research UK	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Tomas-Carus 2008 2009	Spain 1 site Recruited by advertisements in newsletters of local FM association	Inclusion: FM diagnosis by ACR 1990 criteria Exclusion: history of severe trauma, frequent migraines, peripheral nerve entrapment, inflammatory rheumatic disease, severe psychiatric illness; other disease that prevents physical loading; pregnancy; attendance at another psychological or physical therapy or regular physical exercise with more than one exercise session of 30 minutes per week during a 2-week period in last 5 years.	Randomized: 33 Analyzed: 30 Attrition: 9% (3/33)
Trock 1994	USA 3 treatment centers in two States	≥35 years of age; pain and stiffness of ≥1 year duration; radiographs with evidence of disk space narrowing with osteophyte formation and/or subchondral sclerosis in ≥1 locations; or osteophyte formation and subchondral sclerosis of facet joints. Excluded: Changed therapeutic regimen within 1 month before evaluation; possible pregnancy; women of childbearing age not willing to use contraception; unstable medical illness or cardiac pacemaker.	Randomized: NR Treated: 81 Analyzed: 70 Attrition: 14% (11/81)* *Number at baseline used for denominator

Author, Year	Intervention, Comparator
Tomas-Carus 2008 2009	A.Exercise (n=15): Supervised training in a waist-high pool of warm water 3 times per week for 8 months. Each session was 1 hour and included 10 minutes warmup, 10 minutes of aerobic exercise at 60-65% of maximal hart rate, 20 minutes of overall mobility and lower limb strength exercises using water resistance and upper limb strength exercises without water resistance, another 10 minutes of aerobic exercise, and 10 minutes cooldown. Heart rate was monitored using a pulse meter. Two subjects who failed to attend at least 95% of treatment sessions for personal reasons were excluded from analysis. The rate of compliance with therapy sessions was 93 (standard deviation 2) times out of a maximum of 96 sessions. B.Control (n=15): For 8 months, participants continued their normal activities, which did not include exercise similar to that in A. One subject who failed to attend for measurements for personal reasons was excluded from analysis.
Trock 1994	A.Extremely low frequency pulsed electromagnetic fields (n=38), <2 A with 120 V; applied with stepwise energy characteristics as follows: 5 Hz, 0-15 gauss for 10 minutes; 10 Hz, 15-25 gauss for 10 minutes; and 12 Hz, 15-25 gauss for 10 minutes. Maximum number of pulses/burst was 20. B.Sham (n=32). Same setup but no electromagnetic field generated. Treatments were given for 30 minute periods, 3-5 times per week for 18 treatments.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Tomas-Carus 2008 2009	A vs B Age: 51 vs 51 Female: 100% vs 100% Symptom duration, years: 20.1 vs 19.4 FIQ Total: 6.1 (1.2) vs 6.3 (1.3) FIQ Physical Function: 3.0 (1.5) vs 3.7 (1.5) FIQ Pain: 5.6 (1.9) vs 6.4 (2.3) FIQ Anxiety: 6.5 (2.7) vs 5.7 (2.5) FIQ Depression: 5.4 (2.6) vs 6.0 (2.1) STAI State Anxiety: 45.1 (9.9) vs 41.9 (8.0) Additional measures reported in Tomas-Carus 2009: SF-36 Physical Function: 43.4 (14.2) vs 32.8 (19.8) SF-36 Bodily Pain: 28.7 (13.4) vs 20.8 (19.2) SF-36 Mental Health: 45.5 (18.5) vs 51.2 (26.2)	FIQ total score (0-10, higher scores=greater impairment) FIQ Physical Function (0-10, higher scores=greater impact) FIQ Pain (0-10, higher scores=greater impact) FIQ Anxiety (0-10, higher scores=greater impact) FIQ Depression (0-10, higher scores=greater impact) State-Trait Anxiety Inventory (STAI) (20-80; higher scores=greater anxiety) Additional measures reported in Tomas-Carus 2009: SF-36 Physical Function (0-100, higher scores=better outcomes) SF-36 Bodily Pain (0-100, higher scores=better outcomes) SF-36 Mental Health (0-100, higher scores=better outcomes)	Immediately after 8 months of exercise
Trock 1994	A vs B Age: 61 vs 67 years Female: 71% vs 67% Weight (lb): 161 vs 162 Duration of symptoms: 7 vs 8 years Pain (0-100): 72.02 (18.45) vs 62.3 (24.16) ADL difficulty 11.94 (5.63) vs 11.5 (5.27)	Pain (VAS, 0-100, higher score worse pain) ADL difficulty (scale, 0-24, higher score worse disability) Patient assessment of improvement (scale, 0-100, higher score greater the improvement)	1 month

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Tomas-Carus 2008 2009	A vs B <u>8 months</u> FIQ Total: 5.2 (1.6) vs 6.5 (1.0), p=0.017; MD 45.5 (95% CI 44.502 to 46.498), p <0.0001 FIQ Physical Function: 2.4 (1.7) vs 3.7 (2.0), p = 0.047; MD -1.3 (95% CI -2.688 to 0.088), p = 0.07 FIQ Pain: 5.3 (1.4) vs 6.6 (1.8), p = 0.04; MD -1.3 (95% CI -2.506 to -0.094), p=0.04 FIQ Anxiety: 4.7 (2.7) vs 6.6 (2.1), p = 0.037; MD -1.9 (95% CI -3.709 to -0.091), p=0.04 FIQ Depression: 4.0 (3.3) vs 6.1 (1.7), p = 0.03; MD -2.1 (95% CI -4.063 to -0.137), p=0.04 STAI State Anxiety: 37.5 (8.0) vs 44.4 (8.9), p = 0.035; MD -6.9 (95% CI -13.229 to -0.571), p = 0.03 Additional measures reported in Tomas-Carus 2009: SF-36 Physical Function: 54.1 (19.8) vs 36.6 (17.8), p=0.017; MD 17.5 (95% CI 3.418 to 31.582), p=0.02 SF-36 Bodily Pain: 51.7 (13.1) vs 27.1 (20.9), p = 0.001; MD 24.6 (95% CI 11.554 to 37.646), p=0.0006 SF-36 Mental Health: 67.3 (21.4) vs 49 (20.8), p=0.025; MD 18.3 (95% CI 2.516 to 34.084), p=0.02
Trock 1994	A vs B <u>1 month outcomes:</u> Pain (0-100): 25.87 (30.22) vs 14.66 (29.39), MD 11.21 (95%CI -3.08 to 25.50) p=0.122 ADL difficulty: 3.78 (7.35) vs 2.14 (5.57), p=NS Patients' assessment of improvement: 41.18 (35.88) vs 40.00 (32.27), p=ns

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Tomas-Carus 2008 2009	
Trock 1994	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Tomas-Carus 2008 2009		A vs B Withdrawals: 2/ 17 (12%) vs 0/16 Adverse events: NR
Trock 1994		NR

Author, Year	Funding Source	Quality	Comments
Tomas-Carus 2008 2009	Regional government of Extremadura, Spain, and the Health Department.	Poor	
Trock 1994	NR	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Turner 1990	US Number of centers: Unclear Outpatient	20-65 years old Currently married or cohabitating Exclude Current infectious medical disorder Cardiovascular disease Spine fracture or dislocation Spondylolisthesis Spine instability Ankylosing spondylitis Rheumatoid arthritis or connective tissue disease History of cancer Surgery in previous year Nonspine limitation of lower extremity function Leg pain with sciatic tension signs	Randomized: 49 Analyzed: 31 at 6 months, 33 at 12 months Attrition: 37% (18/49) at 6 months, 33% (16/49) at 12 months
UK BEAM Trial Team 2004	United Kingdom Number of centers: 14 181 general practices clinics	Patients 18 and 65 years old, with LBP and a Roland disability score of 4 or more, who experienced pain every day for 28 days before randomization or for 21 out of the 28 days before randomization and 21 out of the 28 days before that and agreed to 3 months of treatment. Exclude: Patients older than 65, or those with a possibility of serious spinal disorder, only pain below the knee, previous spinal surgery, Roland disability score of 3 or less	Randomized: 1,334 Treated: 1,334 Analyzed: 1,334* Attrition: 16% (1128/1334) *ITT

Author, Year	Intervention, Comparator
Turner 1990	A.Behavioral therapy (n=25): 2-hour group sessions every week for 8 weeks, with spouses attending 5 sessions. Concepts of pain behaviors, well behaviors, and the role of social reinforcers in maintaining pain behaviors were taught, and couples received communication training. Individual patients set behavioral goals in areas affected by pain. Treatment included group discussion, role playing, and feedback with social reinforcement. B.Exercise (n=24): 2-hour sessions every week for 8 weeks. The exercise program aimed at increasing aerobic fitness through fast-walking/slow jogging. Sessions consisted of discussion of progress and problems, instruction on stretching. Subjects engaged in aerobic exercise 5 times a week on their own using a quota system. C.Interdisciplinary - Behavioral plus Exercise (n=24): Subjects received the behavioral therapy intervention followed by the exercise intervention in each session, for 8 weeks. Protocols were identical to the ones given to the individual intervention groups (A & B, respectively). Spouses attended 5 behavioral therapy sessions but did not participate in the exercise intervention. D.Waitlist (n=23): Patients waited 8 weeks after initial assessment thern were randomized to one of the 3 treatments (A, B, or C).
UK BEAM Trial Team 2004	A: Manipulation (n=353) UK chiropractic, osteopathic, and physiotherapy techniques including at least 1 high velocity thrusts, 8 treatments, 20 minute sessions, 12 weeks B: General practice care (n=338) C: Exercise (n=310) group classes incorporating cognitive behavioral principles, 8 classes, 60 minute sessions for 4-8 plus a “refresher” class at 12 weeks (n=310) D: Manipulation and exercise combined (n=333), 12 weeks

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Turner 1990	Overall Age: 44 Female: 48% (46/96) Duration of symptoms: 12.9 years Previous back surgery: 10% (10/96) Employment: - Full or part time: 73% Receiving financial compensation for pain: 8% Involved or anticipating litigation related to pain 11% *no significant differences on any measure* A vs. B vs. C vs. D Baseline scores Sickness Impact Profile: 7.9 vs. 8.4 vs. 8.5 vs. 6.2 MPQ Pain Rating Index: 21.0 vs. 19.4 vs. 25.5 vs. 21.2 Pain Behavior Observation Method: 4.4 vs. 4.3 vs. 3.5 vs. 3.0 Pain Behavior Checklist: 42.3 vs. 43.5 vs. 44.0 vs. 39.1 CES-D: 10.4 vs. 12.0 vs. 12.4 vs. 10.5 *no significant differences on any measure*	Sickness Impact Profile (SIP, 0-100, higher score=higher disability) McGill Pain Questionnaire Pain Rating Index (0-78, higher score=more pain) Center for Epidemiologic Studies - Depression Scale (CES-D, 0-60, higher score=more depressive symptoms)	6 and 12 months
UK BEAM Trial Team 2004	A vs. B vs. C. vs. D Age: 42 vs. 42 vs. 44 vs. 43 years Female: 63% vs. 53% vs. 55% vs. 57% White: 97% vs. 95% vs. 96% vs. 92% RDQ (0-24): 8.9 vs. 9.0 vs. 9.2 vs. 8.9-9.1 SF-36 Physical component score: 41 vs. 41 vs. 40 vs. 41 SF-36 Mental component score: 45-46 vs. 47 vs. 45 vs. 46	RDQ (0-24) Modified Von Korff disability scale(0-100, 0=best) Modified Von Korff pain (0-100, 0=best) SF-36 Physical component score (mean=50, SD=10, 100=best) SF-36 Mental component score (mean=50, SD=10, 100=best)	9 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Turner 1990	NR
UK BEAM Trial Team 2004	A (private manipulation) and A (NHS manipulation) vs. B, mean (SD) <u>Baseline</u> RDQ (0-24): 8.9 (4.0) and 8.9 (4.0) vs. 9.0 (3.9) Von Korff Disability (0-100): 46.9 (22.0) and 46.6 (22.7) vs. 44.9 (21.0) Von Korff Pain (0-100): 61.4 (19.0) and 61.6 (19.0) vs. 60.5 (17.6) SF-36 Physical component score (0-100): 41.1 (6.4) and 40.8 (6.6) vs. 41.0 (6.4) SF-36 Mental component score (0-100): 45.0 (10.0) and 45.8 (9.7) vs. 46.6 (10.4) A vs. B, mean (SE) <u>9 months</u> RDQ (0-24): 5.15 (0.29) vs. 6.16 (0.31), adjusted difference -1.01 (95% CI -1.81 to -0.22) Von Korff Disability (0-100): 29.85 (1.50) vs. 35.50 (1.60), adjusted difference -5.65 (95% CI -9.72 to -1.57) Von Korff Pain (0-100): 41.68 (1.58) vs. 47.56 (1.69), adjusted difference -5.87 (95% CI -10.17 to -1.58) SF-36 Physical component score (0-100): 44.18 (0.55) vs. 42.50 (0.60), adjusted difference 1.68 (95% CI 0.18 to 3.19) SF-36 Mental component score (0-100): 48.09 (0.69) vs. 46.41 (0.75), adjusted difference 1.68 (95% CI -0.21 to 3.57) Differences estimated by ANCOVA adjusted for center and baseline score

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Turner 1990	NR
UK BEAM Trial Team 2004	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Turner 1990	C vs. B <u>Baseline</u> McGill Pain Questionnaire Pain Rating Index (0-78): 25.5 (12.4) vs. 19.4 (10.6) Sickness Impact Profile (0-100): 8.5 (4.6) vs. 8.4 (8.2) Center for Epidemiologic Studies-Depression Scale (0-60): 12.4 (7.3) vs. 12.0 (7.7) <u>6 months</u> McGill Pain Questionnaire Pain Rating Index (0-78): 13.3 (9.2) vs. 15.7 (9.2) Sickness Impact Profile (0-100): 4.5 (4.7) vs. 6.3 (10.1) Center for Epidemiologic Studies-Depression Scale (0-60): 8.3 (7.9) vs. 9.3 (8.3) <u>12 months</u> McGill Pain Questionnaire Pain Rating Index (0-78): 18.2 (13.3) vs. 14.9 (7.9) Sickness Impact Profile (0-100): 4.8 (3.4) vs. 4.7 (7.9) Center for Epidemiologic Studies-Depression Scale (0-60): 10.0 (7.6) vs. 9.3 (7.7)	C vs. B Withdrawal at 6 months: 42% (10/24) vs. 29% (7/24) Withdrawal at 12 months: 42% (10/24) vs. 33% (8/24) Withdrawal due to AEs: NR Serious AEs: NR Nonserious AEs: NR
UK BEAM Trial Team 2004	A (private manipulation) and A (NHS manipulation) vs. B, mean (SE) <u>Baseline</u> RDQ (0-24): 8.9 (4.0) and 8.9 (4.0) vs. 9.2 (4.3) Von Korff Disability (0-100): 46.9 (22.0) and 46.6 (22.7) vs. 47.7 (22.6) Von Korff Pain (0-100): 61.4 (19.0) and 61.6 (19.0) vs. 60.8 (17.6) SF-36 Physical component score (0-100): 41.1 (6.4) and 40.8 (6.6) vs. 40.5 (6.7) SF-36 Mental component score (0-100): 45.0 (10.0) and 45.8 (9.7) vs. 45.4 (10.8) A vs. C, mean (SE) <u>9 months</u> RDQ (0-24): 5.15 (0.29) vs. 5.74 (0.31) Von Korff Disability (0-100): 29.85 (1.50) vs. 29.73 (1.68) Von Korff Pain (0-100): 41.68 (1.58) vs. 41.54 (1.84) SF-36 Physical component score (0-100): 44.18 (0.55) vs. 44.39 (0.63) SF-36 Mental component score (0-100): 48.09 (0.69) vs. 46.77 (0.81)	No serious adverse events occurred.

Author, Year	Funding Source	Quality	Comments
Turner 1990	Grants from the National Institute of Neurological and Communicative Disorders and Stroke (2 R01 NS 19619 and P01 NS 16329)	Poor	Unclear if SIP scored on a 0-100 scale or alternative scale
UK BEAM Trial Team 2004	UK Medical Research Council (MRC)	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
van der Roer 2008	The Netherlands Number of centers: 49 Setting: Primary care physiotherapist practices	18-65 years old New episode of non-specific LBP lasting >12 weeks Inability to resume daily activities in the last 3 weeks Health insurance through one specific insurance company Exclude Specific LBP General practitioner advice not to perform physically straining activities Pregnancy Pelvic girdle pain Legal involvement related to either LBP or work disability	Randomized: 114 Analyzed: 114 intention-to-treat; 67 per-protocol Attrition: 0% intention-to-treat; 41% (47/114) per-protocol
van Eijk-Hustings 2013	Netherlands Outpatient rheumatology clinics of 3 medical centers	Inclusion: FM diagnosis based on ACR 1990 criteria, literate, age 18-65 years Exclusion: Patients randomized to A were excluded after randomization if they were pregnant, involved in work disability litigation, used non-pharmacologic treatments such as psychological or physical treatments, had alcohol or drug abuse, or used walking devices	Randomized: 203 (108 in A, 47 in B, and 48 in C) Treated: 67 in A, 19 in B Analyzed: 203 (A, B, and C) Attrition: 0/203

Author, Year	Intervention, Comparator
van der Roer 2008	A.Interdisciplinary (n=60): Exercise therapy, back school, and behavioral principles delivered over 10 individual sessions and 20 group sessions. Individual sessions covered treatment information, assessing baseline functional capacity, goal setting, signing treatment contract, and evaluating treatment goals. Group sessions involved training in operant behavioral principles, based on baseline functional capacity. B.Usual care physiotherapy (n=54): Patients received individual treatment following the Low Back Pain Guideline of the Royal Dutch College for Physiotherapy. The number of treatment sessions at the physiotherapist's discretion.
van Eijk-Hustings 2013	A.Multidisciplinary intervention (n=108): one-year outpatient program involving 12-week course for three half-days per week, with two therapy sessions of 1.5 hours duration per day (multidisciplinary team offered program of sociotherapy, graded-activity physiotherapy, psychotherapy, and creative arts therapy), followed by 5 meetings over the next 9 months and up to 7 individual therapy sessions with one of the therapists. 60/108 started treatment and 60/108 randomized attended >70% of sessions. B.Aerobic exercise (n=47): two group sessions per week for 12 weeks led by a physiotherapist (10-minute warmup, 30 minute aerobic exercise, then 15-minute resistance training to strengthen muscles, then 5-minute cooldown). Subjects were given a videodisc with exercises to do at home and advised to perform these once a week. 19/47 randomized started treatment and 8/47 randomized completed >70% of sessions. C.Usual care (n=48): indvidualized FM education and lifestyle advice within 1-2 consultations, plus care as usual

Author, Year	Study Participants	Outcome Measures	Duration of Followup
van der Roer 2008	A vs. B Age: 42 vs. 42 Female: 55% vs. 48% Ethnic background: - Dutch: 48% vs. 35% - European immigrant: 5% vs. 4% - Non-European immigrant: 47% vs. 61% Duration of current episode, weeks: 53.9 vs. 47.2 Paid work (% yes): 70% vs. 57%	Roland Morris Disability Questionnaire (RDQ, 0-24, higher scores indicate worse health) Pain (0-10 NRS) Global Perceived Effect (GPE, 6-point scale from "much worse" to "completely recovered") Direct health care costs (12 months)	4 and 10 months
van Eijk-Hustings 2013	A vs. B vs C: Age: 42 for those who started treatment and 41 for those who did not start treatment (group A) vs. 44 for those who started treatment and 39 for those who did not start treatment (group B) vs 43 (group C) Female: 94% for those who started treatment and 93% for those who did not start treatment (group A) vs. 100% (group B) vs 98% (group C) Duration of FM symptoms (years): 7.1 for those who started treatment and 6.1 for those who did not start treatment (group A) vs. 6.2 for those who started treatment and 7.3 for those who did not start treatment (group B) vs 7.1 (group C) FIQ physical function: 4.2 (SE 0.2) vs 3.6 (SE 0.2) vs 3.4 (SE 0.3) FIQ total: 64.5 (SE 1.4) vs 60.0 (SE 2.1) vs 55.4 (SE 2.3) FIQ Pain: 6.3 (SE 0.2) vs 6.2 (SE 0.3) vs 5.5 (SE0.3) FIQ Depression: 5.2 (SE 0.3) vs 4.8 (SE 0.3) vs 4.2 (SE 0.4) FIQ Anxiety:5.9 (SE 0.3) vs 4.9 (SE 0.3) vs 4.8 (SE 0.4) EQ-5D: 0.36 (SE 0.03) vs. 0.41 (SE 0.05) vs 0.51 (SE 0.04)	FIQ total (0-100; higher scores=more negative impact) and subscales (0-10, higher is worse) FIQ pain (0-10, higher scores=greater pain) FIQ Depression (0-10, higher scores=greater depression) FIQ Anxiety: (0-10, higher scores=greater anxiety) EQ-5D (-0.59 to 1.00, with higher scores= better health)	18 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
van der Roer 2008	A vs. B, mean <u>Baseline</u> RDQ (0-24): 11.6 vs. 12.1 Pain (0-10 NRS): 6.2 vs. 5.9 <u>4 months</u> RDQ (0-24): 7.4 vs. 7.7, adjusted difference 0.13 (95% CI -2.24 to 2.50) Pain (0-10 NRS): 4.1 vs. 4.8 , adjusted difference -0.97 (95% CI -1.88 to -0.06) Global Perceived Effect positive (%): 38.2% vs. 39.8%, OR 0.93 (95% CI 0.36 to 2.43) <u>10 months</u> RDQ (0-24): 6.7 vs. 7.1, adjusted difference 0.06 (-2.22 to 2.34) Pain (0-10 VAS): 3.9 vs. 4.6, adjusted difference -1.02 (-2.14 to 0.09) Global Perceived Effect positive (%): 45.0% vs. 32.3%, OR 1.71 (95% CI 0.67 to 4.38 Direct health care costs: 1003 vs. 527 Euros, mean difference 233 Euros (95% CI €-2185 to 2764) Differences adjusted for baseline values and work status using multilevel model-based mean scores; pain intensity also adjusted for work status
van Eijk-Hustings 2013	A vs C <u>18 months:</u> FIQ physical function: 3.6 (SE 0.2) vs 3.9 (SE 0.3), ES 0.12 (-0.22 to 0.46) FIQ: 50.9 (SE 2.0) vs 56.2 (SE 2.9), ES (95% CI) = 0.25 (-0.09 to 0.59) FIQ pain: 5.3 (SE 0.2) vs 5.3 (SE 0.3), ES (95% CI) = -0.01 (-0.35 to 0.34) FIQ Depression: 3.9 (SE 0.3) vs 4.2 (SE 0.4), ES (95% CI) = 0.10 (-0.24 to 0.44) FIQ Anxiety: 4.7 (SE 0.3) vs 4.8 (SE 0.4), ES (95% CI) = 0.03 (-0.31 to 0.37) EQ-5D: 0.55 (SE 0.03) vs 0.51 (SE 0.05), ES (95% CI)= 0.12 (-0.22 to 0.46) B vs C <u>18 months:</u> FIQ physical function: 3.6 (SE 0.4) vs 3.9 (SE 0.3), ES (95% CI)=0.11 (-0.29 to 0.52) FIQ: 52.0 (3.2) vs 56.2 (2.9), ES (95% CI) = 0.22 (-0.20 to 0.61) FIQ pain: 5.2 (0.37) vs 5.3 (0.3), ES (95% CI) = 0.05 (-0.36 to 0.44) FIQ Depression: 5.0 (0.5) vs 4.2 (0.4), ES (95% CI) = 0.09 (-0.31 to 0.49) FIQ Anxiety: 5.0 (0.5) vs 4.8 (0.4), ES (95% CI) = -0.06 (-0.46 to 0.34) EQ-5D: 0.54 (0.05) vs 0.51 (0.05), ES (95% CI)= 0.10 (-0.31 to 0.50)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
van der Roer 2008	NR
van Eijk-Hustings 2013	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
van der Roer 2008	NR	A vs. B Lost to followup: 2% (1/60) vs. 4% (2/54) Discontinued therapy: 20% (12/60) vs. 24% (15/54) Withdrawal due to AEs: NR Serious AEs: None reported Nonserious AEs: NR
van Eijk-Hustings 2013	A vs B <u>18 months:</u> FIQ physical function: 3.6 (SE 0.2) vs 3.6 (SE 0.4); MD 0 (95% CI -0.79 to 0.79), p=1.0 FIQ: 50.9 (SE 2.0) vs. 52.0 (SE 3.2); MD -1.1 (95% CI -8.40 to 6.20), p=0.77 FIQ pain: 5.3 (SE 0.2) vs. 5.2 (SE 0.4); MD 0.10 (95% CI -0.69 to 0.89), p=0.80 FIQ Depression: 3.9 (SE 0.3) vs. 5.0 (SE 0.5), MD -1.1 (95% CI -2.21 to 0.01) p=0.052 FIQ Anxiety: 4.7 (SE 0.3) vs. 5.0 (SE 0.5); MD -0.3 (95% CI -1.41 to 0.81) EQ-5D: 0.6 (SE 0.03) vs. 0.5 (0.05); MD 0.10 (95% CI -0.01 to 0.21), p=0.077	Adverse events: NR Withdrawals: 0

Author, Year	Funding Source	Quality	Comments
van der Roer 2008	The Netherlands Organisation for Health Research and Development (ZONMW) grant number: 945-03-023.	Fair	Means adjusted for baseline values and ethnic background (and work status - for pain intensity and PSEQ).
van Eijk-Hustings 2013	Maastricht University Medical Centre and Care Renewal Grants of medical insurance companies in the region	Fair	ES and p-values reported in article only for interventions vs UC; MD and p values calculated for A vs. B

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
van Santen 2002	The Netherlands 2 centers Outpatient	Female patients aged 18-60 years old, clinical diagnosis of FM according to 1990 ACR criteria, living within 30 km of the clinical centers Exclude: Known comorbidity, localized myalgia, pregnancy, on waiting list for elective surgery	Randomized: 143 Treated: 129 Analyzed: 118 Attrition: 17% (25/143)
Vas 2006	Spain Single Primary Attention Healthcare Center, 2002-2004	Outpatients ≥17 years with symptomatic uncomplicated neck pain of >3 months' duration, a motion-related neck pain intensity ≥30 on a visual analogue scale (0-100 mm), no treatment during the week preceding study onset. Excluded: Previous treatment with acupuncture; pain < 30 mm on VAS (0-100 mm); neck pain classed as neuropathologic, infectious, inflammatory, neoplasic, endocrine, metabolic or visceral; cervical fracture or trauma; previous spinal surgery, non-specific fever, severe psychiatric illness, severe disorder of overall health state, infectious feverish disease, severe or generalized dermatopathy, malignant tumor; incompatibility with the medication described in the protocol; occupation-related lawsuit arising from neck pain; pregnancy; prior recommendation for treatment with antineoplastic drugs, corticosteroids, immunosuppressor drugs or opioids; inability or unwillingness to follow instructions	Randomized: 123 Treated: 115 Analyzed: 85 Attrition:31% (38/123)

Author, Year	Intervention, Comparator
van Santen 2002	A.Fitness training (n=47): Group sessions of 15-17 patients for 60 minutes twice a week for 24 weeks consisting of aerobic exercises, stretching, general flexibility and balance exercises, and isometric muscle strengthening. Subjects were encouraged to attend an additional third, unsupervised, 60 minute session weekly and subjects were encouraged to use the sauna or swimming pool after all sessions. 79% (37/47) of the subjects who completed the fitness program attended more than 67% of the training sessions. B.Biofeedback (n=43): Individual 30 minute sessions of electromyographic biofeedback and progressive muscle relaxation trianing 2 times per week for 8 weeks. The progressive muscle relaxation technique was taught, with the biofeedback apparatus used as a tonometer to measure the change in tension of the musculus frontalis. Subjects were encourage to practice techniques twice daily at home during the 8 weeks of treatment and for 16 weeks afterwards. 88% (38/43) of the subjects who completed the biofeedback program attended more than 67% of the biofeedback sessions C.Usual care (n=28): Subjects continued with usual care at the outpatient rheumatology department (analgesics NSAIDs, or tricyclic antidepressants, if appropraite) but their general physicians were informed that aerobic exercises and relaxation should not be prescribed or encouraged Subjects within each intervention group were randomized to receive an additional education program aimed at compliance with exercise or biofeedback training. The program consisted of 6 sessions 90 minutes in length spread over 24 weeks and included information on FM, general health education, self-management, relapse prevention principles, and the importance of the intervention the subjects were randomized to.
Vas 2006	A.Bilateral needle acupuncture (n=45) at locations depending on perceived origin of pain, muscle/myofascial or arthritic: Muscle/myofascial; GB 20, GB 21, LR 3, LI 4, GB 34, Shenmen, Neck, Liver, Muscle Relaxation, Occiput, Thalamus Arthritic: BL 10, GV 14, SI 3, BL 62, Shenmen, Neck, Kidney, Muscle Relaxation, Occiput, Thalamus, Kidney Extra acupuncture for pain lateral to neck or anxiety or dizziness: (GB 39, extra Yintang, GV 20 or SP 6) B.Sham TENS treatment (n=40) with patient in prone position for 30 minutes, electrodes over GB 21 bilateral, and TENS unit in front of patient with flashing diode simulating visible and audible stimulus. 5 sessions, applied over 3 weeks (2 each of the first and second weeks and 1 in the third). Both groups were provided with rescue medication (21 tablets of diclophenac, 50 mg)

Author, Year	Study Participants	Outcome Measures	Duration of Followup
van Santen 2002	A vs B vs C Age: 46 vs 44 vs 43 Female: 100% vs 100% vs 100% Duration of symptoms: 9.7 vs 10.1 vs 15.4 years SIP physical score: 11.3 (7.7) vs 11.4 (11.2) vs 9.8 (9.3) AIMS: 1.9 (2.1) vs 3.1 (2.1) vs 5.4 (2.0) Pain VAS: 66.8 (15.3) vs 59.1 (18.5) vs 62.4 (20.5) SCL-90-R Global Severity Index: 182.4 (48.0) vs 176.5 (40.5) vs 183.9 (51.3) SIP total score: 14.4 (7.8) vs 14.0 (9.4) vs 11.4 (9.4) SIP psychosocial score: 16.3 (11.8) vs 15.8 (11.8) vs 18.1 (13.9) Patient global assessment: 2.8 (0.7) vs 2.9 (0.8) vs 3.0 (0.8)	SIP physical score (0-100, higher score=higher impact Arthritis Impact Measurement Scale (Dutch AIMS; 0-10, higher score=higher impact) Pain VAS (0-100, higher score=higher pain) SCL-90-R Global Severity Index (higher score=more severe psychological distress) SIP total score (0-100, higher score=higher health-related dysfunction) SIP psychosocial score (0-100, higher score=higher psychosocial dysfunction) Patient global assessment (1-5, higher score=higher general sense of well-being)	Immediately post-intervention (treatment of 6 months)
Vas 2006	A vs B Age: 46 vs 47 years Female: 75% vs 89% Intensive physical work: 31% vs 21% Pain duration: 47 vs 43 months Pain VAS with motion (0-100): 68.7 (14.3) vs 72.3 (15.4) NPQ (0-100): 52.7 (14.0) vs 56.5 (13.2) SF-36 PCS (0-100): 36.7 (9.7) vs 37.6 (7.9) SF-36 MCS (0-100): 38.7 (13.0) vs 34.0 (11.4)	Pain intensity with movement (scale 0-100, higher score worse pain) Northwick Park Neck pain Questionnaire (NPNQ) (scale: 0-100%, higher percentage the greater the disability) Short-Form 36 (SF-36) (scale 0-100, higher score=better QoL) Rescue medication use (scale none, occasional, prescribed dose, above prescribed dose)	6 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
van Santen 2002	A vs C <u>6 months (mean change score (95% CI)):</u> SIP physical score: -1.7 (-3.7 to 0.3) vs -0.6 (-2.9 to 1.7) AIMS: 0.1 (-0.6 to 0.8) vs 0.8 (-1.8 to -0.2) Pain VAS: -5.5 (-10.9 to -0.1) vs 1.3 (-4.5 to 7.1) SCL-90-R Global Severity Index: -6.8 (-20.1 to 6.5) vs -8.1 (-19.8 to 3.6) SIP total score: -1.9 (-3.9 to 0.1) vs -1.4 (-3.4 to 0.6) SIP psychosocial score: -3.2 (-6.2 to 0.2) vs -3.5 (-7.0 to 0.0) Patient global assessment: 0.5 (0.2 to 0.8) vs 0.5 (0.2 to 0.8) B vs C <u>6 months (mean change score (95% CI)):</u> SIP physical score: -1.6 (-3.4 to 0.2) vs -0.6 (-2.9 to 1.7) Pain VAS: -0.6 (-6.5 to 5.3) vs 1.3 (-4.5 to 7.1) SCL-90-R Global Severity Index: Data NR AIMS: 0.4 (-0.1 to 0.9) vs 0.8 (-1.8 to -0.2) SIP total score: -2.3 (-4.3 to -0.3) vs -1.4 (-3.4 to 0.6) SIP psychosocial score: -3.7 (-4.9 to -2.5) vs -3.5 (-7.0 to 0.0) Patient global assessment: 0.3 (0.0 to 0.6) vs 0.5 (0.2 to 0.8)
Vas 2006	A vs B <u>6 months</u> (mean difference from baseline) Pain VAS with motion (0-100): 41.1 (26.9) vs 26.8 (25.9), MD 14.4 (95% CI 2.9 to 25.8), p=0.014 SF-36 PCS: (0-100): 9.3 (11.0) vs 5.3 (8.0), p=0.054 SF-36 MCS: (0-100): 8.0 (13.5) vs 5.2 (14.1), p=0.351 Rescue med (none or occasional): 87% (39/45) vs 68% (27/40), p=0.041

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
van Santen 2002	
Vas 2006	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
van Santen 2002	B vs A <u>6 months (mean change score (95% CI)):</u> SIP physical score: -1.6 (-3.4 to 0.2) vs -1.7 (-3.7 to 0.3) Pain VAS: -0.6 (-6.5 to 5.3) vs -5.5 (-10.9 to -0.1) SCL-90-R Global Severity Index: Data NR AIMS: 0.4 (-0.1 to 0.9) vs 0.1 (-0.6 to 0.8) SIP total score: -2.3 (-4.3 to -0.3) vs -1.9 (-3.9 to 0.1) SIP psychosocial score: -3.7 (-4.9 to -2.5) vs -3.2 (-6.2 to 0.2) Patient global assessment: 0.3 (0.0 to 0.6) vs 0.5 (0.2 to 0.8)	NR
Vas 2006		A vs B Any adverse event: n=4 vs n=2 Swelling of the hand: n=1 vs n=0 Bruising: n=1 vs n=0 Pain of the ear: n=1 vs n=0 Ulcer of the ear: n=1 vs n=0 Cephalea: n=0 vs n=1 Aggravation of symptoms: n=0 vs n=1

Author, Year	Funding Source	Quality	Comments
van Santen 2002	Dutch Arthritis Foundation	Poor	Authors only provided mean change scores as results at followup. P-values were not reported for comparisons of A vs C. No intervention led to statistically significant or clinically relevant improvement on any outcome measure. Outcomes not reported: Total myalgic score, fatigue VAS, amount of additional therapy, Wmax, Borg scale
Vas 2006	Consejeria de Salud de la Junta de Andalucia (File No. 52/02) in 2002, and partially by the IRYSS network (File No. G03/202)	Fair	Patients considered treatments similarly "credible" as measured by the credibility score after first treatment.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Vas 2016	Spain, multicenter, primary care	Inclusion Criteria: Patients included were over 17 years old, were diagnosed with fibromyalgia according toe American College of Rheumatology criteria, had not received acupuncture before and were referred by their general practitioner. Exclusion Criteria: Participants were excluded if they had chronic pain in relation to any process other than fibromyalgia, were using anticoagulants or opiates, were pregnant or a nursing mother, or were involved in occupational litigation for reasons involving fibromyalgia.	Randomized: 164 Treated: NR Analyzed: Attrition: Post-treatment: 3.0% (5/164) 3.75 months: 5.4% (9/164) 9.75 months: 6.7% (11/164)
Verkaik 2014	Netherlands 1 center Type of center unclear	FM diagnosis fulfilling 1990 ACR criteria of 6 years of less, ability to travel and sit for 1.5 hours, and sufficient hearing Exclude: Presence of psychiatric illness	Randomized: 70 Treated: 65 Analyzed: 53 Attrition: 24% (17/70)

Author, Year	Intervention, Comparator
Vas 2016	A.Acupuncture (n=80) Patients received acupuncture according to principles of Traditional Chinese Medicine from a trained medical expert. Patients also received pharmacological treatment as prescribed by GP. No. of Treatments: 1 session per week for 9 weeks (9 total) Length of Treatments: 20 min each Acupoints: NR No. of Needles: NR B.Sham Acupuncture (n=82) Treatment and evaluation time were identical in both groups. The sham group received an acupuncture simulation on the dorsal and lumbar regions, in which guide tubes for the same type of needle as used in the real acupuncture group were applied to the body surface, but after removal of the needles. Patients also received pharmacological treatment as prescribed by GP.
Verkaik 2014	A.Guided imagery (n=33): Two 1.5 hour group sessions of 6-12 subjects. The first sessions consisted of group discussion, the theoretical background of guided imagery, and instructions to practice at least one exercise daily for 4 weeks. Each exercise was a CD and contained relaxation techniques, music, positive imagery, and pain management techniques. The second group session took place after the 4 weeks and consisted of a group discussion. B.Attention control (n=37): Two 1.5 hour group sessions of 6-12 subjects held 4 weeks apart. Group sessions were a group discussion and did not contain any information or training on guided imagery.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Vas 2016	A vs. B Age (SD): 52.3 vs. 53.2 Female: 100% vs. 100% Race: 98.8% vs. 98.8% Spanish nationality Mean duration of chronicity: 5.89 vs. 5.76 Fibromyalgia Impact Questionnaire (FIQ): 71.7(11.0) vs. 70.1 (14.2) Pain Intensity (VAS): 79.3(11.0) vs. 75.8(13.3) HDRS: 16.3(7.0) vs. 16.6(6.7) Short Form 12 Physical Component: 28.5 (8.3) vs. 31.0(8.4) Short Form 12 Mental Component: 32.8(11.1) vs. 34.1(10.4)	Fibromyalgia Impact Questionnaire (FIQ, range 0-100: higher scores indicate severity of symptoms) Pain Intensity (VAS, range: 0-100; higher score=greater pain) Hamilton Depression Rating Scale (HDRS, range NR: higher scores indicate severity of depression) Short Form 12 Physical Component (SF-12, range 0-100: higher scores indicate optimal health status) Short Form 12 Mental Component (SF-12, range 0-100: higher scores indicate optimal health status)	3.75 and 9.75 months
Verkaik 2014	A vs B Age: 47 vs 48 Female: 100% vs 97% Employment: Unemployed: 35% vs 30% < 16 hours weekly: 9% vs 28% Between 16 and 32 hours weekly: 44% vs 30% Between 33 and 40 hours weekly: 9% vs 9% > 40 hours weekly: 0% vs 3% Years since diagnosis: 0-1: 53% vs 37% 2-4: 38% vs 48% 5-6: 9% vs 12% FIQ: 53.7 (2.7) vs 56.4 (2.0) Pain VAS, mean (95% CI): 5.9 (5.3 to 6.3) vs 5.8 (5.0 to 6.6)	FIQ (0-100, higher score=lower function); pain VAS (0-10, higher score=higher pain)	1.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Vas 2016	A vs. B <u>3.75 months</u> Mean relative change Fibromyalgia Impact Questionnaire (FIQ): −25.0 (−29.8 to −20.2) vs. −11.2 (−16.9 to −5.5) p<0.001 Mean relative change Short Form 12 Physical Component: 37.0 (27.8 to 46.3) vs. 15.5 (7.8 to 23.3) p=0.001 Mean relative change Pain Intensity (VAS, range: 0-100mm): -23.6 (−28.8 to −18.5) vs. −16.6 (−22.7 to −10.5) p=0.047 Mean relative change Short Form 12 Mental Component: 30.6 (19.7 to 41.5) vs. 13.9 (5.4 to 22.5) p=0.011 Mean relative change HDRS: NR <u>9.75 months</u> Mean relative change Fibromyalgia Impact Questionnaire (FIQ): −22.2 (−26.4 to −18.0) vs. −4.9 (−10.2 to 0.5) p<0.001 Mean relative change Short Form 12 Physical Component: 35.0 (25.1 to 45.0) vs. 11.2 (2.6 to 19.7) p<0.001 Mean relative change Pain Intensity (VAS, range: 0-100mm): −19.9 (−24.6 to −15.1) vs. −6.2 (−11.2 to −1.2) p<0.001 Mean relative change HDRS: −19.1 (−34.2 to −3.9) vs. −5.9 (−16.6 to 4.8) p=0.011 Mean relative change Short Form 12 Mental Component: 23.0 (13.7 to 32.4) vs. 9.4 (1.9 to 16.9) p=0.013
Verkaik 2014	A vs B FIQ: 54.2 (2.6) vs 53.0 (2.5), (MD 1.2, 95% CI -0.2 to 2.6) p=0.09 Pain VAS: NR*

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Vas 2016	NR
Verkaik 2014	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Vas 2016	NR	No serious adverse events 2.6% of sessions led to aggravation of fibromyalgia symptoms 0.5% led to headache. In real acupuncture group pain, bruising and vagal symptoms presented after 4.7% of sessions.
Verkaik 2014		NR

Author, Year	Funding Source	Quality	Comments
Vas 2016	This paper presents independent research funded by the Spanish Ministry of Health and Consumer Affairs (Carlos III Health Institute, project number PI10/00675) and by the Andalusian Public Health System (project number PI0436/09). The funding agencies had no influence on the design of the study, the analysis, or the writing of the paper.	Good	
Verkaik 2014	Fonds NutsOhra	Poor	*Study only reported pain VAS values for days 1 to 26 of the study period (intervention lasted 4 weeks) MD and p value calculated

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Viljanen 2003	Finland 5 centers Occupational healthcare centers (outpatient)	Females aged 30-60 years old with chronic non-specific neck pain for ≥ 3 months Exclude: Cancer, major trauma, rheumatic disease, neural entrapment, or major rehabilitation within previous 3 months	Randomized: 393 Treated: 357 Analyzed: 340 Attrition: 13% (53/393)

Author, Year	Intervention, Comparator
Viljanen 2003	A.Exercise (dynamic muscle training) (n=135): exercises performed with 1-3 kg dumbbells to activate large muscle groups in the neck and shoulder region performed in 30 minute sessions 3 times per week for 12 weeks. 1 week of reinforcement training was done 6 months after randomization B.Relaxation training (n=128): various techniques based on progressive relaxation method, autogenic training, functional relaxation, and systematic desensitization to teach participants correct activation and relaxation of muscles used in daily activities. Trainings were done in 30 minute sessions 3 times per week for 12 weeks. 1 week of reinforcement training was done 6 months after randomization. C.No intervention (n=130): patients were instructed not to change their usual activities during the 12 months of followup

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Viljanen 2003	A vs B vs C Age: 45 vs 43 vs 44 years Female: 100% Performing physical activity ≥3x/week: 44% vs. 34% vs. 41% Duration of office work: 23 vs. 20 vs. 21 years Sedentary work >6 hours/day: 76% vs. 75% vs. 73% Computer work >6 hours/day: 33% vs. 39% vs. 35% Absent from work due to neck pain: 12% vs. 12% vs. 12% Pain duration: 11 vs 11 vs 10 years Neck disability scale (0-80) 29 (15.4) vs 29 (14.3) vs 26 (13.8) Pain VAS: 4.8 (2.3) vs 4.8 (2.3) vs 4.1 (2.2) Depression index: 16 (4.4) vs 16 (4.9) vs 16 (4.6)	Neck disability scale (0-80, higher score=higher disability); pain VAS (0-10, higher score=higher pain); depression index (10-40, higher score=more depression)	3 and 9 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Viljanen 2003	A vs C <u>3 months</u> Neck disability scale: (0-80): 15 (15.4) vs 14 (13.8); Adj MD -0.1 (95% CI -3.1, 2.9) Pain VAS: 2.9 (2.8) vs 2.9 (2.8); Adj MD 0.4 (95% CI -0.3, 1.0) <u>9 months</u> Neck disability scale: 19 (15.5) vs 17 (13.7); Adj MD -0.1 (95% CI -3.0 to 2.9) Pain VAS: 3.1 (2.5) vs 3.2 (2.5); Adj MD 0.5 (95% CI -0.1 to 1.0) B vs C <u>3 months</u> Neck disability scale: 15 (14.5) vs 14 (13.8); Adj MD 0.1 (95% CI -2.9, 3.2) Pain VAS: 3.0 (2.7) vs 2.9 (2.8); Adj MD 0.2 (95% CI -0.4, 0.8) <u>9 months</u> Neck disability scale: 19 (14.7) vs 17 (13.7); Adj MD 0.2 (95% CI -2.8, 3.1) Pain VAS: 3.3 (2.6) vs 3.2 (2.5); Adj MD 0.2 (95% CI -0.3, 0.8)

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Viljanen 2003	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Viljanen 2003	B vs A <u>3 months</u> Neck disability scale: 15 (14.5) vs 15 (15.4); Adj MD 0.2 (95% CI -2.8, 3.2) Pain VAS: 3.0 (2.7) vs 2.9 (2.8); Adj MD -0.2 (95% CI -0.8, 0.4) <u>9 months</u> Neck disability scale: 19 (14.7) vs 19 (15.5); Adj MD 0.2 (95% CI -2.7, 3.2) Pain VAS: 3.3 (2.6) vs 3.1 (2.5); Adj MD -0.2 (95% CI -0.8, 0.3)	NR

Author, Year	Funding Source	Quality	Comments
Viljanen 2003	Finish work environment fund (project No 96243)	Fair	Results were reported comparing exercise (A) to control (C] and separately relaxation training (B) to control (C]. Outcomes not reported: subjective work ability, sick leave owing to neck pain, cervical ROM, self reported recovery Neck disability scale as reported by these authors is not the validated NDI measure; it is comprised of 8 questions, each rated on a 0-10 VAS. While the authors refer to this as a neck disability index, we use the term neck disability scale to avoid confusion with the validated NDI.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Von Korff 2005	USA Number of centers unclear Outpatient	Primary care back pain patients Age 25-64 Endorsing ≥7 activity limitations on the RDQ Exclude: Patients being considered for back surgery Currently being managed by a physical therapist or psychologist for back pain	Randomized: 240 Treated: 228 Analyzed: 207 Attrition: 14% (33/240)

Author, Year	Intervention, Comparator
Von Korff 2005	A.Interdisciplinary intervention (n=119): 4 in-person visits over approximately 5 weeks: Visit 1. Psychologist visit (90 minutes), included developing an action plan. Visit 2. Physical therapy visit 7-10 days after visit 1 (60 minutes), included mechanical examination, stretches and exercises relevant to the action plan. Visit 3. Physical therapy visit approximately 10 days after visit 2 (30 minutes) focused on action plan and exercises relevant to the action plan Visit 4. Psychologist visit (30 minutes) 2 weeks after visit 3 to review progress. Patients also received *The Back Pain Helpbook* and a 40-minute back pain self-care video. B.Usual care (n=121), variable across patients but often included pain medication, infrequent primary care visits and physical therapy.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Von Korff 2005	A vs. B Age (mean): 50 vs. 50 years Female: 65% vs. 60% Race: White: 84% vs. 83% >90 back pain days in 6 months: 66% vs. 56% Chronic Pain Grade: Low pain intensity, Grade I: 15% vs. 24% High pain with low activity limitations, Grade II: 18% vs. 22% Moderate activity limitations, Grade III: 23% vs. 25% Severe activity limitations, Grade IV: 44% vs. 29%	Modified Roland Morris Disability Qu questionnaire (modified RDQ, 0-23, higher number=worse function) Pain (0-10 NRS) SF-36 Mental Health (0-100, higher number=better quality of life) SF-36 Social Functioning (0-100) Missed 30+ days from usual activities in prior 3 months (yes/no) On disability or workers compensation (yes/no) Unable to work (yes/no)	4.5, 10.5, and 22.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Von Korff 2005	A vs. B , mean (SD) <u>Baseline</u> Modified RDQ (0-23): 12.3 (5.5) vs. 11.4 (5.7) On disability or workers compensation: 4.4% vs. 3.3% Unable to work: 8.7% vs. 5.0% Missed 30+ days from usual activities in 3 months: 33.9% vs. 24.8% Pain (0-10 NRS): 5.7 (1.8) vs. 5.8 (1.8) SF-36 Social Functioning: 66.7 (26.7) vs. 70.4 (27.0) SF-36 Mental Health: 67.0 (18.3) vs. 68.9 (16.9) <u>4.5 months</u> Modified RDQ (0-23): 9.2 (6.6) vs. 10.1 (6.4), p=0.0003 >1/3 reduction in RDQ: 42.2% vs. 23.7%, adjusted OR 3.5, p=0.0007 On disability or workers compensation: 4.6% vs 4.6%, p=0.45 Unable to work: 9.1% vs. 4.6%, p=0.37 Missed 30+ days from usual activities in 3 months: 9.1 % vs. 15.7%, p=0.02 Pain (0-10 NRS): 4.2 (2.0) vs. 4.7 (2.2), p=0.007 SF-36 Social Functioning (0-100):74.4 (27.1) vs. 73.6 (27.8), p=0.26 SF-36 Mental Health (0-100): 70.3 (19.9) vs. 69.5 (19.1), p=0.23 <u>10.5 months</u> Modified RDQ (0-23): 8.4 (7.0) vs. 9.1 (6.3), p=0.0063 >1/3 reduction in RDQ: 44.6% vs. 22.7%, adjusted OR 2.1, p=0.03 On disability or workers compensation: 7.1% vs. 3.1%, p=0.53 Unable to work: 10.1% vs. 5.1%, p=0.28 Missed 30+ days from usual activities in 3 months: 4.3% vs. 6.5%, p=0.28 Pain (0-10 NRS): 4.0 (2.3) vs. 4.7 (2.1), p=0.004 SF-36 Social Functioning (0-100):75.8 (28.3) vs. 74.4 (24.0), p=0.18 SF-36 Mental Health (0-100): 70.9 (19.9) vs. 71.1 (18.4), p=0.42 <u>22.5 months</u> Modified RDQ (0-23): 8.1 (6.5) vs. 9.1 (7.2), p=0.0078 >1/3 reduction in RDQ: 49.4% vs. 37.0%, adjusted OR 1.8, p=0.08 Disability or workers compensation: 6.4% vs. 5.4%, p=0.67 Unable to work: 4.3% vs. 6.5%, p=0.28 Missed 30+ days from usual activities in 3 months:8.5% vs. 14.3%, p=0.04 Pain (0-10 NRS): 4.3 (2.1) vs. 4.6 (2.5), p=0.115 SF-36 Social Functioning (0-100): 76.7 (25.2) vs. 76.3 (25.8), p=0.28 SF-36 Mental Health (0-100): 71.0 (18.2) vs. 72.4 (18.3), p=0.98

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Von Korff 2005	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Von Korff 2005	NR	Withdrawals NR AEs NR

Author, Year	Funding Source	Quality	Comments
Von Korff 2005	NIH grant	Fair	p-values adjusted for baseline value of the outcome variable, number of pain days and graded chronic pain (Results - Subquestion a)

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Waling 2002	Sweden Various work places in the city of Umea, number not reported	Work related pain (pain related to work situation with such intensity that working required extra effort) in the trapezius muscle, tenderness at palpation, and limited motion of the cervical spine Exclude: Diseases of other origin	Randomized: 126* Treated: 103 Analyzed: 6 months: 87 Attrition: 31% (39/126) 14 months: 83 Attrition: 34% (43/126) 3 years: 101 Attrition: 20% (25/126) *Randomization of clusters formed by selecting a time that best fit participants' schedule

Author, Year	Intervention, Comparator
Waling 2002	A.Strength training (n=29): 3 times per week for 10 weeks, 1 hour per session, of physiotherapist supervised strength training of neck and shoulder muscles with loads of 10 to 12 maximal voluntary contractions, 3 sets. B.Endurance training (n=28): 3 times per week for 10 weeks, 1 hour per session, of physiotherapist supervised endurance training using arm-cycling and arm exercises with rubber band resistance, 30 repetition maximum. C.Coordination training (n=25): 3 times per week for 10 weeks, 1 hour per session, of physiotherapist supervised body awareness training focusing on balance and postural stability similar to Tai Chi Chuan. D.Reference group (n=21): 1 time per week for 10 weeks, 2 hours per session of occupational nurse led stress management.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Waling 2002	A vs B vs C vs D Age: 38 vs 39 vs 38 vs 39 years Female: 100% all groups Pain duration: 6.3 vs 6.5 vs 6.6 vs 7.7 years Pain at present (0-100): 26 (21) vs 28 (20 vs 33 (21) vs 37 (24) Pain in general (0-100): 39 (18) vs 40 (21) vs 41 (17) vs 43 (19) Pain at worst (0-100): 74 (16) vs 70 (17) vs 77 (13) vs 75 (21)	Pain at present (VAS scale 0-100, higher score worse pain) Pain in general (VAS scale 0-100, higher score worse pain) Pain at worst (VAS scale 0-100, higher score worse pain) Frequent neck-shoulder pain (% with pain several times/week or more)	6 months, 14 months 36 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Waling 2002	A vs B vs C vs D <u>6 months</u> Frequent pain: 76% vs 91% vs 78 % vs 73%, p=0.50 <u>14 months</u> Frequent pain: 70% vs 80% vs 91 % vs 56%, p=0.13 <u>36 months</u> Pain at present: 31 (27) vs 22 (26) vs 27 (27) vs 16 (19), p=0.073 Pain in general: 32 (22) vs 29 (19) vs 29 (21) vs 20 (18), p=0.249 Pain at worst: 61 (27) vs 58 (27) vs 57 (28) vs 58 (29), p=0.902 Frequent pain: 47% vs 50% vs 58% vs 39%, p=0.66

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Waling 2002	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Waling 2002		NR

Author, Year	Funding Source	Quality	Comments
Waling 2002	The Swedish Council for Work Life Research, Dnr 94-0315 and 97-0940	Poor	6.6 month f/u pain results were estimated from figures, but were judged unreliable as baseline and 3 year values differed from those given in table 3.

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Wang 2009	United States, hospital, single-site	Inclusion Criteria: Patients age ≥55 years, body mass index (BMI) ≤40 kg/m2, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale score (visual analog version) >40 (range 0–500), and fulfillment of the American College of Rheumatology criteria for knee OA with radiographic Kellgren/Lawrence scale knee OA grade 2 . Exclusion Criteria: Exclusion of individuals who had prior Tai Chi training or similar types of alternative medicine like Qi Gong or yoga; individuals with serious medical conditions, limiting their ability for full participation as determined by primary care physicians; individuals with intraarticular steroid injections in the previous 3 months, or reconstructive surgery on the affected knee and any intraarticular hyaluronate injections in the previous 6 months; and individuals unable to pass the Mini-Mental examination (score <24).	Randomized: 40 Treated: 40 Analyzed: 40 (ITT) Attrition: 0% (0/40)

Author, Year	Intervention, Comparator
Wang 2009	A.Tai Chi (n=20) Subjects in the tai chi group attended group tai chi classes where they learned 10 forms from the classic Yang style Tai Chi. They were also instructed to practice Tai Chi at least 20 minutes per day at home with a Tai Chi DVD. Home practice continued after group sessions ended until the 48 week followup. No. of Treatments: 2/week for 12 weeks (24 total) Length of Treatments: 60 min/session B.Attention Control (n=20) Subjects in the attention control group attended group classes where they received nutritional and medical information paired with 20 minutes of stretching. Additionally, participants were instructed to practice at least 20 minute sof stretching exercises per day at home. No. of Treatments: 2/week for 12 weeks (24 total) Length of Treatments: 60 min/session

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Wang 2009	A vs B Age: 63 vs. 68 Female: 80% vs. 70% Race: NR Mean Duration of Chronicity: 9.7(7.0) vs. 9.7(8.3) years Pain (WOMAC): 209.3(58.5) vs. 220.4(101.0) Stiffness (WOMAC): 105.7(37.3) vs. 120.7(50.4) Physical Function (WOMAC): 707.6(246.9) vs. 827(258.8) Patient VAS: 4.2(2.1) vs. 4.8(2.0) Physician VAS: 4.8(1.7) vs. 5.8(2.2) SF-36 PCS: 37.5(8.5) vs. 32.0(8.8) SF-36 MCS: 51.4(12.2) vs. 50.8(12.6) CES-D: 13.6 (11.7) vs. 9.3(9.2)	Primary: Western Ontario and McMaster Osteoarthritis Index Overall (WOMAC VAS, range 0-2,400mm: higher scores represent more pain, stiffness and disability) Pain (WOMAC, range 0-500) Stiffness (WOMAC, range 0-200) Physical Function (WOMAC, range 0-1,700) Patient Assessed Pain Global (VAS, range 0-10 cm: higher scores indicate severity of pain) Physician-Assessed Pain(VAS, range 0-10 cm: higher scores indicate severity of pain) Secondary: Center for Epidemiologic Studies Depression Scale (CES-D; score range 0–60, where 0 no dysphoria) Short Form 36 Physical Component Summary Score (SF-36 range 0–100, higher scores indicate improved state) Short Form 36 Mental Component Summary Score (SF-36 range 0–100, higher scores indicate improved state)	3 and 9 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Wang 2009	A vs. B 3 months mean Δ in Pain (WOMAC): -131.55 (95%CI -177.41 to -85.69) vs. -64.60 (95%CI -110.46 to -18.74); MD -66.95 (95%CI -131.81 to -2.09) p=0.050 mean Δ in Stiffness (WOMAC): -65.00 (95%CI -86.31 to -43.69) vs. -50.20 (95%CI -71.51 to -28.89); MD -14.80 (95%CI -44.94 to 15.34) p=0.300 mean Δ in Physical Function (WOMAC): -440.50 (95%CI -574.41 to -306.59) vs. -257.30 (95%CI -391.21 to -123.39); MD -183.20 (95%CI 372.58 to 6.18) p=0.060 mean Δ in Patient Assessed Pain (VAS): -2.36 (95%CI -3.53 to -1.18) 1.71 (2.89, 0.53) 0.65 (2.31, 1.02) 0.4 mean Δ in Physician Assessed Pain (VAS): -2.59 (95%CI -3.33 to -1.86) vs. -2.06 (95%CI -2.80 to -1.32); MD -0.53 (95%CI -1.58, 0.51) p=0.300 mean Δ in SF-36 PCS: 10.80 (95%CI 7.31 to 14.29)vs. 6.29 (95%CI 2.80 to 9.77); MD 4.51 (95%CI -0.42 to 9.45) p=0.080 mean Δ in SF-36 MCS: 4.39 (95%CI -0.11 to 8.89) vs. 4.50 (95%CI 0.00 to 9.00); MD -0.11 (95%CI -6.47 to 6.25) p=1.00 mean Δ in CES-D: -6.40 (95%CI -9.88 to -2.92) vs. -1.10 (95%CI -4.58 to 2.38); MD -5.30 (95%CI -10.23 to -0.37) p=0.040 9 months mean Δ in Pain (WOMAC): -115.35 (95%CI -161.21 to -69.49) vs. -69.20 (95%CI -115.06 to -23.34); MD -46.15 (95%CI -111.01 to 18.71) p=0.200 mean Δ in Stiffness (WOMAC): -64.15 (95%CI -85.46 to -42.84) vs. -60.50 (95%CI -81.81 to -39.19); MD -3.65 (95%CI -33.79 to 26.49) p=0.800 mean Δ in Physical Function (WOMAC): -405.85 (95%CI -539.76 to -271.94) vs. -300.55 (95%CI -434.46 to -166.64); MD -105.30 (95%CI 294.68 to -84.08) p=0.300 mean Δ in Patient Assessed Pain (VAS): -1.65 (95%CI -2.83 to -0.48) vs. -1.70 (95%CI -2.87 to -0.52); MD 0.04(95%CI -1.62 to 1.70) p=1.000 mean Δ in Physician-Assessed Pain (VAS): -2.53 (95%CI -3.27 to -1.80) vs. -1.50 (-2.25 to -0.75); MD -1.03 (95%CI -2.09 to 0.02) p=0.060 mean Δ in SF-36 PCS (range 0–100): 10.41 (95%CI 6.92 to 13.90) vs. 4.10 (95%CI 0.61 to 7.58); MD 6.32 (95%CI 1.38 to 11.25) p=0.010 mean Δ in SF-36 MCS (range 0–100): 5.80 (95%CI 1.31 to 10.30) vs. 1.04 (95%CI -3.46 to 5.53); MD 4.77 (95%CI -1.59, 11.13) p=0.100 mean Δ in CES-D (range 0–60): -7.25 (95%CI -10.73 to -3.77) vs. 1.65 (95%CI -1.83 to 5.13); MD -8.90 (95%CI -13.83 to -3.97) p=0.001

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Wang 2009	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Wang 2009	NR	No severe adverse events were observed.

Author, Year	Funding Source	Quality	Comments
Wang 2009	Supported by the National Center for Complementary and Alternative Medicine of the NIH (grant R21AT002161).	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Wang 2010	United States 1 center Hospital	Aged 21 or older, diagnosis of FM fulfilling 1990 ACR criteria Exclude: Participation in tai chi training in the previous 6 months, serious medical conditions that would limit participation, diagnosis of medical conditions known to contribute to FM symptoms, positive pregnancy test or plans to become pregnant during study period, a Mini-Mental State Examination score less than or equal to 24.	Randomized: 66 Treated: NR Analyzed: 59 Attrition: 11% (7/66)
Weng 2009	Taiwan Number of centers unclear Setting type NR	Bilateral, moderate knee OA (Altman Grade II) Exclude: Patients with hip joint OA or any hip problems with range of motion limitations	Randomized: 132 Treated: 132 Analyzed: 103 Attrition: 22% (29/132)

Author, Year	Intervention, Comparator
Wang 2010	A.Tai chi (n=33): 60 minutes sessions twice a week for 12 weeks. Sessions consisted of lessons covering 10 forms of the classic Yang style of tai chi. Subjects were instructed to practice tai chi at home for at least 20 minutes a day and encouraged to maintain tai chi practice, using an instructional DVD, during the followup period. B.Control group (n=33): 60 minutes sessions twice a week for 12 weeks. Each session consisted of a 40 minute lesson on a topic relating to FM followed by 20 minutes of supervised stretching of the upper body, trunk, and lower body. Subjects were instructed to practice stretching at home for 20 minutes a day. All subjects: Continued taking regular medications and encouraged to continue their routine activities during the 12-week intervention. Subjects were asked to not take part in any new or additional exercise programs
Weng 2009	A.Isokinetic exercise (n=33): 3 sessions a week for 8 weeks. Sessions consisted of sets of concentric and eccentric contractions at varying angular velocities and start and stop angles. B.No intervention (n=33): Warm-up cycling for 10 minutes All patients: Hot packs for 10 minutes and passive range of motion exercises

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Wang 2010	A vs B Age: 50 vs 51 Female: 85% vs 88% Duration of symptoms, years: 11.8 vs 10.0 Medication use: Analgesics: 88% vs 73% Antidepressants: 51% vs 45% Anticonvulsants: 27% vs 15% Muscle relaxants: 27% vs 12% Benzadiazepines: 15% vs 9% Comorbidities: Heart disease: 0% vs 0% Hypertension: 36% vs 18% Diabetes: 18% vs 3% FIQ: 62.9 (15.5) vs 68.0 (11.0) Patient global assessment VAS: 5.8 (2.3) vs 6.3 (1.8) Physician global assessment VAS: 5.7 (1.9) vs 5.6 (2.4) CES-D: 22.6 (9.2) vs 27.8 (9.2) SF-36 physical component score: 28.5 (8.4) vs 28.0 (7.8) SF-36 mental component score: 42.6 (12.2) vs 37.8 (10.5) PSQI: 13.9 (3.1) vs 13.5 (3.7)	FIQ (0-100, higher score=more severe symptoms); patient global assessment VAS (0-10, higher score=higher pain); Physician global assessment VAS (0-10, higher score=higher pain); CES-D (0-60, higher scores=more severe depression); SF-36 physical component score (0-100, higher score=higher quality of life); SF-36 mental component score (0-100, higher score=higher quality of life); PSQI (0-21, higher scores=worse sleep quality)	3 months
Weng 2009	A vs B Age (mean of all patients randomized): 64 Female (mean of all patients randomized): 75% Duration of symptoms (mean of all patients randomized): 42.5 months Lequesne Index: 7.3 (2.5) vs 7.1 (1.8) Pain VAS: 4.7 (1.6) vs 4.5 (1.5)	Lequesne Index (0-24, higher score=higher severity); pain VAS (0-10, higher score=higher pain)	10 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Wang 2010	A vs B FIQ mean Δ from baseline (95% CI): -28.6 (-34.8 to -22.4) vs -10.2 (-16.4 to -4.0), (MD -18.3, 95% CI -27.1 to -9.6) p<0.001 Patient global assessment VAS mean Δ from baseline (95% CI): -2.4 (-3.1 to -1.7) vs -0.7 (-1.4 to 0.01), (MD -1.7, 95% CI -2.7 to -0.8) p=0.001 Physician global assessment VAS, Δ from baseline (95% CI): -0.5 (-1.2 to 0.1) vs (0.6) (0.03 to 1.2), (MD -1.1, 95% CI -2.0 to -0.2) p=0.02 CES-D, Δ from baseline (95% CI): -6.5 (-9.4 to -3.6) vs -2.4 (-5.3 to 0.5), (MD -4.1, 95% CI -8.2 to 0.1) p=0.05 SF-36 PCS, Δ from baseline (95% CI): 8.4 (5.6 to 11.3) vs 1.5 (-1.4 to 4.3), (MD 7.0, 95% CI 2.9 to 11.0) p=0.001 SF-36 MCS, Δ from baseline (95% CI): 8.5 (4.6 to 12.4) vs 1.2 (-2.7 to 5.0), (MD 7.3, 95% CI 1.9 to 12.8) p=0.009 PSQI, Δ from baseline (95% CI): -4.2 (-5.8 to -2.7) vs -1.2 (-2.7 to 0.4), (MD -3.0, 95% CI -5.2 to -0.9) p=0.007
Weng 2009	A vs B Lequesne Index: 6.3 (1.7) vs 7.3 (1.7) Pain VAS: 3.6 (1.6) vs 5.0 (1.4)

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Wang 2010	
Weng 2009	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Wang 2010		None
Weng 2009		A vs B Treatment related pain causing withdrawal: 9% (3/33) vs 0% (0/33) RR=inf, p=0.08

Author, Year	Funding Source	Quality	Comments
Wang 2010	Grant (R21AT003621) from the National Center for Complementary and Alternative Medicine of the National Institutes of Health, the American College of Rheumatology Research and Education Foundation Health Professional Investigator Award, and the Boston Claude D. Pepper Older Americans Independence Center Research Career Development Award	Fair	
Weng 2009		Poor	It looks like the study defined attrition as those that withdrew but did not include the patients that discontinued treatment due to pain or the patients that they lost contact with. Static stretching+isokinetic exercises (n=33) and PNF stretching+isokinetic exercises (n=30) groups were also included in the study but were not included in data abstraction because they were considered additive treatment

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
White 2004	United Kingdom Outpatient departments of a General and District Hospital, 199-2001	18 to 80 years of age, chronic mechanical neck pain, pain score >30 mm onVAS (0-100) for 5 of 7 pretreatment days. Excluded: pregnant patients, fracture or surgery to the neck, cervical congenital abnormality, uncontrolled LBP, contraindication to acetaminophen, systemic illness, ongoing neck-related litigation or disability claims, current or recent manual neck treatment or steroid use (oral or local injection).	Randomized: 135 Treated: 125 Analyzed: 124 Attrition:21% (29/135) Randomized: 135 Treated: 135 6 month Analyzed: 111 Attrition:18% (24/135) 12 month Analyzed: 107 Attrition: 21% (28/135)
Wicksell 2013 - see Jensen 2013			
Wigers 1996	Norway 2 center 1 outpatient, 1 patient association	Patients with generalized aching or stiffness involving 3 or more areas in at least 4 out of 15* well-defined tender points for a minimum of 3 months. Exclude: Patients with pain thought to be related to trauma	Randomized: 60 Treated: NR Analyzed: 44 Attrition: 27% (16/60)

Author, Year	Intervention, Comparator
White 2004	A.Unilateral or bilateral Western needle acupuncture (n=70) at locations depending on pain distribution and tenderness, using the following points: Primary local neck: GB 20, 21; GV 14; secondary local neck: SI 12, 13 14; BL 9, 10; ST 11; SI 15, 16; BL 11, 41, 15, 17; GB 29; TE 16, 17; GV 15, 16, 17; Primary distal points: LI 4, SI 3, GB 34, TE 5; secondary distal points: LI 11; SI 8; TE 10, 36, 39, 40; BL 60; extra Luozhen deqi obtained B.Sham electroacupuncture (n=65) with audio and visual signals and up to 8 electrodes placed over acupuncture points simultaneously, but no current through severed cables. Both groups treated 2x/week for 4 weeks for 20 minutes each session, acetaminophen only for pain.
Wicksell 2013 - see Jensen 2013	
Wigers 1996	A.Stress management (n=20): 90 minute group sessions of 10 patients done 2 times a week for 6 weeks followed by 1 session per week for the next 8 weeks. Sessions consisted of equal portions of presentations stress mechanisms and strategies for improving quality of life, group discussions on patients' experiences of stress and coping with pain, and relaxation training aimed at helping cope with stress and pain. B.Aerobic exercise (n=20): 45 minute group sessions of 10 patients done 3 times a week for 14 weeks. The exercise program involved the whole body and aimed to minimize eccentric muscle strain. Sessions consisted of training to music (further details not given) and aerobic games C.Treatment as usual (n=20): Subjects continued treatments they had been using at baseline.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
White 2004	A vs B Age: 54 vs 53 years Female: 66% vs 63% Pain score (0-100): 49.6 (12.3) vs 54.1 (14.6) NDI: 16.8 (6.3) vs 17.2 (6.1) SF-36 PCS: 36.8 (7.9) vs 36.3 (9.3) SF-36 MCS: 46.9 (10.4) vs 48.3 (9.9) Duration of symptoms: 4.8 vs 7.7 years	NDI: (scale 0-50, higher score greater disability) Pain intensity (scale, 0-10, higher score=greater pain) Short-Form 36 (SF-36) (scale 0-100, higher score=better QoL)	2, 6 and 12 months
Wicksell 2013 - see Jensen 2013			
Wigers 1996	A vs B vs C Age: 44 vs 43 vs 46 Female: 90% vs 90% vs 95% Duration of symptoms (years): 11 (10) vs 9 (5) vs 11 (9) Working status: Full time: 25% vs 20% vs 20% Part time: 25% vs 35% vs 10% Sick leave: 30% vs 25% vs 30% Disability pension: 15% vs 20% vs 30% Housewife or retired: 5% vs 0% vs 10% Pain VAS: 72 (18) vs 72 (19) vs 65 (17) Depression VAS: 44 (32) vs 34 (29) vs 40 (37)	Pain VAS (0-100, higher score=higher pain); depression VAS (0-100, higher score=higher depression); global subjective improvement (0-4, higher score=higher improvement)	48 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
White 2004	A vs B 2 months, n=59 vs 59 NDI: 11.0 (6.3) vs 12.7 (7.8), MD -1.7 (95% CI -4.3 to 0.9), p=0.195 Pain (0-100): 17.3 (17.0) vs 23.2 (20.7), MD -5.9 (95% CI -12.8 to 1.01), p=0.09 SF-36 physical: 42.5 (9.8) vs 43.8 (10.0), p=ns SF-36 mental: 52.5 (8.6) vs 50.3 (10.1), p=ns 6 months, n=56 vs 53 NDI: 9.9 (7.0) vs 10.6 (8.3), MD 0.7 (95% CI -3.61 to 2.21), p=0.634 Pain (0-100): 19.2 (24.2) vs 21.0 (24.4), MD -1.8 (95% CI -11.0 to 7.4), p=0.700 12 months, n=54 vs 53 NDI: 8.9 (6.6) vs 10.7 (9.1), MD -1.8 (95% CI -4.84 to 1.24), p=0.244 Pain (0-100): 20.9 (25.7) vs 24.36 (26.7), MD -3.46 (95% CI -13.5 to 6.6), p=496
Wicksell 2013 - see Jensen 2013	
Wigers 1996	A vs C 48 months Pain VAS: 70 (18) vs 69 (24), (MD 1, 95% CI -12.6 to 14.6) p=0.88 Depression VAS: 40 (28) vs 30 (31), (MD 10, 95% CI -8.9 to 28.9) p=0.29 Sleep VAS: 67 (25) vs 47 (32), (MD 20.0, 95% CI 1.6 to 38.4) p=0.03 Global subjective improvement: 47% (6/13) vs 12% (2/16), (RR 3.7, 95% CI 0.9 to 15.3) B vs C 48 months Pain VAS: 68 (24) vs 69 (24), (MD -1.0, 95% CI -16.3 to 14.4) p=0.90 Depression VAS: 32 (34) vs 30 (31), (MD 2.0, 95% CI -18.8 to 22.8) p=0.85 Sleep VAS: 56 (34) vs 47 (32), (MD 9.0, 95% CI -12.1 to 30.1) p=0.39 Global subjective improvement: 75% (11/15) vs 12% (2/16), (RR 5.9, 95% CI 1.5 to 22.2)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
White 2004	
Wicksell 2013 - see Jensen 2013	
Wigers 1996	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
White 2004		Bruise at site of L1-4: n=1 vs n=0 Discomfort during treatment: n=0 vs n=1 Dizziness after treatment: n=1 vs n=1 Euphoria after treatment: n=1 vs n=0 Faintness after treatment: n=2 vs n=1 Mild headache after each treatment: n=1 vs n=1 Nausea on several occasions after treatment: n=0 vs n=1 Slight swelling of hand: n=1 vs n=0 Tingling of thumb: n=0 vs n=1 Tiredness on several occasions after treatment: n=0 vs n=1 Uncomfortable cold feeling from electrodes: n=0 vs n=1
Wicksell 2013 - see Jensen 2013		
Wigers 1996	A vs B <u>48 months</u> Pain VAS: 70 (18) vs 68 (24), (MD 2, 95% CI -11.6 to 15.6) p=0.77 Depression VAS: 40 (28) vs 32 (34), (MD 8, 95% CI -11.9 to 27.9) p=0.42 Sleep VAS: 67 (25) vs 56 (34) Global subjective improvement: 47% (6/13) vs 75% (11/15), (RR 0.6, 95% CI 0.3 to 1.2) p=0.15	NR

Author, Year	Funding Source	Quality	Comments
White 2004	Henry Smiths Charity and the Hospital Savings Association	Fair	Similar credibility test suggest that 2 interventions had similar credibility before and after treatment period.
Wicksell 2013 - see Jensen 2013			
Wigers 1996	The Research Council of Norway (project number 101416/320) and the Norwegian Fibromyalgia Association	Poor - stress management vs. usual care and vs. exercise Fair - exercise vs. usual care	Authors cited two articles were used to determine inclusion/exclusion criteria, "Primary fibromyalgia (fibrositis): Clinical study of 50 patients with matched normal controls" (Yunus 1981) and "Nonarticular rheumatism and psychogenic musculoskeletal syndromes" (Smythe 1979). Smythe 1979 could not be accessed so inclusion/exclusion criteria was reported from Yunus 1981 Global subjective improvement was the percent of patients that gave a rating of feeling "better" or "much better" on a 5 step VRS ranging from 0=much worse to 4=much better. Outcome was reported as a percent; percent was used to back-calculate to determine n's which were used for RR calculation MDs and p values calculated using n=20 for both groups Per protocol results, apart from global subjective improvement, was not abstracted. For missing data in ITT analysis, the latest available recording was used

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Williams 2002	USA Recruited from registry of patients being followed in tertiary care rheumatology clinic specializing in FM	Inclusion: meet 1990 ACR criteria for FM, age 18+, in standard medical care at clinic for at least 6 months Exclusion: severe physical impairment that precluded receiving CBT, comorbid medical illnesses capable of causing worsening physical function status, malignancy in past 2 years, history of psychosis , current suicide risk or attempt in past 2 years, substance abuse in past 2 years	Randomized: 145 analyzed: 122 Attrition: 16% (23/145)
Williams 2005	US Number of centers unclear Outpatient	Non-specific LBP with symptoms for >3 months >18 years Ambulatory Exclude: LBP due to nerve root compression, disc prolapse, spinal stenosis, tumor, spinal infection, alkylosing spondylosis, spondylolisthesis, kyphosis, or structural scoliosis Presurgical candidates Were involved in litigation or compensation Body mass index >35 Major depression or substance abuse Practitioners of yoga	Randomized: 60 Treated: 60 Analyzed at 12-weeks: 44 Analyzed at 3 months: 42 Attrition: 18/60 (30%)

Author, Year	Intervention, Comparator
Williams 2002	A.Group CBT plus Usual Care (n= 62): 6 1-hour group sessions delivered in 4-week period by clinical psychologist and focused on improving functional status. Content included progressive muscle relaxation, imagery, activity pacing, pleasant activity scheduling, communication skills and assertiveness training, cognitive restructuring, stress management and problem-solving. Median number of sessions attended = 4 (range 2-6) B.Usual Care (n=60): Standard pharmacological management of symptoms (typically low-dose tricyclic antidepressant medication , analgesics, and/or antidepressants) plus suggestions to engage in aerobic fitness.
Williams 2005	A: Yoga (n=30): 16 weekly 1.5 hour Iyengar yoga classes. The classes consisted of 29 postures from the categories: supine, seated, standing, forward bending, trists and inversions. Initially, restorative poses were done to relieve pain and muscle tension. Then poses were introduced to lengthen muscles attached to the spine and pelvis, then standing poses to open the hips and groins and to teach how to use legs and arms to lengthen pelvic and spinal tissues. Twists and inversions were also included. Participants gradually progressed from simple poses to progressively more challenging poses. Participants were also encouraged to practice yoga at home for 30 minutes, 5 days per week. At the program end, participants were encouraged to continue yoga therapy at home and through community classes. B: Educational control (n=30) Both groups received 16 weekly newsletters on back care and two 1 hour lectures of occupational/physical therapy education.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Williams 2002	A + B Age, mean, years: 47.7 Females: 90% Race: White non-Hispanic 88%, black non-Hispanic 9%, Hispanic 2%, Asian American 1% Average years of education: 16 Married: 60% Compensation present or pending: 28% McGill Pain Questionnaire sensory pain score (mean, scale NR): 14.8 McGill Pain Questionnaire affective pain score (mean, scale NR): 4.6 SF-36 Physical Component Summary Score (mean, 0-100): 28.6	SF-36 Physical Component Summary Score (0-100, higher scores=better functioning) Short Form McGill Pain Questionnaire (MPQ) (scale NR, higher scores=greater pain)	12 months
Williams 2005	A vs. B Age: 49 vs. 48 Female: 65% vs. 70% White: 90% vs. 92% Length of LBP (years): 11.3 vs. 11.0 Medication use: 45% vs. 50% Complementary and Alternative Medicine Use: 35% vs. 25%	Pain Disability Index (7-70 scale, higher score indicates higher disability) Pain intensity, McGill Pain Questionnaire (0-10 VAS) Present Pain Index (0-5 rating of pain) Pain medication use	3 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Williams 2002	A vs B 12 months M (SD) NR Proportion of subjects who improved more than 12 points from baseline on McGill Pain Questionnaire sensory scale: 3.9% vs 7.2%, p >0.05 Proportion of subjects who improved more than 5 points from baseline on McGill Pain Questionnaire affective scale: 9.2% vs 8.7%, p >0.05 Proportion of subjects who improved more than 6.5 points from baseline on SF-36 Physical Component Summary Score: 25% vs 11.6%, OR=2.9, p <0.05; RR 2.2 (95% CI 0.98 to 4.99), p=0.047
Williams 2005	A vs. B, mean (SD) <u>Baseline</u> Pain intensity, McGill Pain Questionnaire (0-10 VAS): 2.3 (1.6) vs. 3.2 (2.3) Pain Disability Index (7-70): 14.3 (13.6) vs. 21.2 (20.5) Present Pain Index, McGill Pain Questionnaire (0-5): 1.4 (0.9) vs. 1.6 (1.1) <u>3 months</u> Pain Intensity, McGill Pain Questionnaire (0-10 VAS): 0.6 (1.1) vs. 2.0 (2.1), p=0.039* Pain Disability Index (7-70): 3.9 (5.3) vs. 12.7 (11.4), p=0.009* Present Pain Index (0-5): 0.5 (0.6) vs. 1.1 (0.9), p=0.013* Stopped or decreased medication use: 50% (15/30) vs. 33% (10/30), p=0.007 *p adjusted for baseline score of pain intensity, PDI, and PPI

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Williams 2002	
Williams 2005	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Williams 2002		A vs B Withdrawals 18% (14/76) vs 13% (9/68) Adverse events NR
Williams 2005	NR	NR

Author, Year	Funding Source	Quality	Comments
Williams 2002	NIH and DAMD	Poor	
Williams 2005	University funding	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Williams 2009	US Number of centers unclear Outpatient	Age 18-70 BMI <37 LBP with symptoms for >3months Oswestry Disability Index 10-60 Visual analogue score 3-8 cm Ability to get up and down from the floor without assistance Exclude: LBP due to spinal stenosis, abdominal or spine tumors, spinal infection, osteoporosis with vertebral fractures, anklyosing spondylitis, spondylolisthesis, structural kyphosis, radicular pain, failed back syndrome Presurgical spine candidates Fibromyalgia Abdominal hernia Major depression Substance abuse issues Currently involved in litigation or have open workers compensation case Practiced yoga 1x/week for ≥3 months within last year	Randomized: 90 Treated: 90 Analyzed: 90 Attrition: 90
Williamson 2007	UK, Single site, outpatient setting (Great Western Hospital)	Inclusion criteria: patients listed for TKR with 3+ months knee pain due to OA (not defined) Exclusion criteria: taking anticoagulants, intra articular steroid injection within 2 months, back pain with referred leg pain, ipsilateral hip OA, skin conditions around knee, RA or having had PT or acupuncture within last year	Randomized: 121 Treated: 118 (3 randomized but did not get acupuncture) Analyzed: 79 (but all 121 included in analysis) Attrition: 35% (42/121)

Author, Year	Intervention, Comparator
Williams 2009	A: Iyengar yoga (n=43): 24 weeks of twice-weekly, 90-minute classes led by certified Iyengar yoga instructor and two assistants. Participants were also directed to practice 30 minutes of yoga at home on nonclass days and were supplied with props, a DVD and an Iyengar instruction manual. B: Wait list control (n=47): Self-directed standard medical care. Wait listed controls were offered yoga classes 6 months after the conclusion of the study.1
Williamson 2007	A.Acupuncture (n=60): conducted by a physiotherapist in a group setting (6-10 patients); needles (1 inch, 0.25 gauge) inserted into 7 acupoints until de qi was achieved and left in place for 20 minutes; treatments were 1x/week for 6 weeks, with 6 sessions in total B.Physiotherapy (n=60): Groups of 6–10 patients, hourly, once a week for 6 weeks. Exercise circuit of static quadriceps contractions; inner range quadriceps contractions; straight leg raises; sit to stands, stair climbing; calf stretches; theraband resisted knee extensions; wobble board balance training; knee flexion/extension sitting on gym ball and free standing peddle revolutions. C.usual care (n=61): exercise and advice leaflet; told they were enrolled in the "home exercise group"

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Williams 2009	Age: 48 vs. 48 years Female: 74% vs. 79% White: 86% vs. 100% BMI: 25.8 vs. 27.4 Taking medications for LBP: 91% vs. 94% Months of current LBP: 47 vs. 78 Months since first LBP: 146 vs. 213, p=0.027	Oswestry Disability Index (0-100) Pain intensity (0-100) Beck Depression Inventory-Second Edition (0-63)	Intermediate term 6 months
Williamson 2007	A vs B vs. C Age: 72 vs. 70 vs. 70 years Female: 55% vs. 52% vs. 54% Caucasian: NR Duration of symptoms: NR WOMAC: 50.9 (15.7) vs. 50.2 (17.8) vs. 51.1 (16.4) OKS: 40.2 (7.7) vs. 39.3 (8.7) vs. 40.5 (8.6) Pain VAS: 7.3 (2.5) vs. 6.8 (2.6) vs. 6.9 (2.3) HAD Anxiety: 7.3 (4.3) vs. 7.5 (4.9) vs. 6.7 (3.6) HAD Depression: 7.1 (3.2) vs. 7.1 (3.9) vs. 7.43 (3.4)	WOMAC (scale unclear, higher score=greater disability) Oxford Knee Scale (OKS, 12-60; higher score=worse function) Secondary: Knee pain VAS (scale 0-10; higher score=greater pain) Hospital Anxiety and Depression score (HAD, 0-21; higher score=worse symptoms)	1.5 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Williams 2009	A vs. B, mean (standard error of the mean) <u>Baseline</u> Oswestry Disability Index (0-100): 25.2 (1.08) vs. 23.1 (1.58) Pain (0-100 VAS): 41.9 (2.44) vs. 41.2 (2.67) Beck Depression Inventory (0-63): 9.2 (0.92) vs. 8.3 (0.89) <u>6 months</u> Oswestry Disability Index: 19.3 (1.94) vs. 23.5 (1.80), p=0.001 Pain (0-100 VAS): 22.2 (3.96) vs. 38.3 (3.09), p=0.0009 Beck Depression Inventory (0-63): 4.6 (0.84) vs. 7.8 (1.00), p=0.0004
Williamson 2007	A vs. C <u>1.5 months</u> WOMAC: 48.4 (14.3) vs. 52.3 (16.6); MD -3.9 (95% CI -9.5 to 1.6) OKS: 38.1 (6.88) vs 40.8 (8.14); MD -2.6 (95% CI -5.4 to 0.1) Pain: 6.58 (2.29) vs. 7.24 (2.07); MD -0.66 (95% CI -1.45 to 0.12) HAD Anxiety: 6.88 (4.15) vs 6.54 (3.93); MD 0.34 (95% CI -1.11 to 1.8) HAD Depression: 6.72 (3.18) vs 7.13 (3.54); MD -0.41 (95% CI -1.63 to 0.8) B vs. C <u>1.5 months</u> WOMAC total: 49.4 (17.3) vs 52.3 (16.6); MD -3 (95% CI -9.08 to 3.13) OKS: 38.8 (8.71) vs 40.8 (8.14); MD -2 (95% CI -5.04 to 1.03) VAS Pain: 6.36 (2.6) vs 7.24 (2.07); MD -0.88 (-1.72, -0.04) HAD Anxiety: 7.08 (5.16) vs 6.54 (3.93); MD 0.54 (95% CI -1.11, 2.19) HAD Depression: 6.75 (3.84) vs 7.13 (3.54); MD -0.38 (95% CI -1.71, 0.95)

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Williams 2009	NR
Williamson 2007	

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Williams 2009	NR	Adverse events: 1 during 6-month followup Withdrawal due to AE: 0
Williamson 2007	A vs. B 1.5 months WOMAC: 48.4 (14.3) vs. 49.4 (17.3); MD -1.0 (95% CI -6.7 to 4.7) OKS: 38.1 (6.88) vs 38.8 (8.71); MD -0.7 (95% CI -3.5 to 2.1) Pain: 6.58 (2.29) vs. 6.36 (2.6); MD 0.22 (95% CI -0.67 to 1.11) HAD Anxiety: 6.88 (4.15) vs 7.08 (5.16); MD -0.20 (95% CI -1.89 to 1.49) HAD Depression: 6.72 (3.18) vs 6.75 (3.84); MD -0.03 (95% CI -1.30 to 1.24)	No AEs reported except "occasional minor bruising and bleeding in acupuncture group"

Author, Year	Funding Source	Quality	Comments
Williams 2009		Fair	
Williamson 2007	Research and Development Grant, The Great Western Hospital, Swindon, UK	Poor	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Witt 2005	Germany, Number of centers unclear	Inclusion criteria: 50–75 years old, OA based on ACR criteria, Kellgren-Lawrence grade 2+ radiographic findings, average pain intensity of ≥40 on a 100 mm VAS in prior 7 days Exclusion criteria: Knee pain due to inflammatory, malignant, or autoimmune disease; serious valgus-defective or varus-defective position; knee surgery or arthroscopy in the past year, chondroprotective or intra-articular injection in the past 4 months, systemic corticoid treatment or beginning of a new treatment for OAin the past 4 weeks, local antiphlogistic treatment, acupuncture treatment during the past 12 months, or PT or other treatments for osteoarthritis knee pain (with the exception of NSAIDs) during the previous 4 weeks, application for pension or disability benefits, serious acute or chronic organic disease or mental disorder, pregnancy or breastfeeding, and blood coagulation disorders or coagulation-inhibiting medication other than aspirin	Randomized: 226 Treated: 224 (2 randomized but did not complete baseline questionnaires or get acupuncture) Analyzed: 217 (224 included in ITT analysis using LOCF) Attrition: 4% (9/226)
Yildiz 2015	Turkey, outpatient clinic	Inclusion Criteria: Patients between 40 and 65 years of age who were diagnosed with bilateral stage 2 and 3 primary knee OA according to Kellgren–Lawrence criteria, were enrolled in the study. Exclusion Criteria: Patients with secondary knee OA; active synovitis; symptomatic hip, foot, and ankle disease; neurologic deficits in a lower extremity; recent knee trauma; history of intraarticular steroid and/or hyaluronate injection in the past 6 months; history of knee surgery or arthroscopy to the knee joint in the last year; and application of physical treatment to the knee in the last 3 months were excluded from the study.	Randomized: 90 Treated: 90 Analyzed: 90 Attrition: 0% (0/90)

Author, Year	Intervention, Comparator
Witt 2005	A. Acupuncture (n=149): semi-standardized; patients received at least 6 local and at least 2 distant Traditional Acupuncture points; needle length and diameter were at physcian's discretion; elicitation of de qi; needles stimulated manually at least once during each session B. Minimal acupuncture (n=75): superficial insertion of fine needles at non-acupuncture sites away from knee; manual stimulation of the needles and provocation of de qi were avoided Both groups underwent 12 sessions of 30 minutes duration, administered over 8 weeks; In both groups, for patients with bilateral OA, both knees were needled with at least 8 out of 10 proposed points (at least 16 needles total); for unilateral OA, the physician was able to choose unilateral or bilateral acupuncture. For unilateral acupuncture, the treatment had to be done with at least 8 needles
Yildiz 2015	A.Continuous Ultrasound (n=30) In addition to application of ultrasound therapy to affected leg(s), all patients were given a home exercise program and instructed to perform isometric exercises and strengthening exercises 3 times/day for 8 weeks. No. of Treatments: 5 days/week for 2 weeks (10 total) Length of Treatments: 5 minutes Area: anterior, medial and lateral areas of the knees Frequency: 1 MHz Intensity: 1.5 W/cm2 Device: 5-cm2 head (Enraf Nonius Sono plus 492) B.Pulsed Ultrasound (n=30) Identical treatment protocol except device was set to a pulsed output. Pulse Ratio: 1:5 C.Sham Ultrasound (n=30) Identical treatment protocol except the device's power switch was off.

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Witt 2005	A vs. B Age: 65 vs. 63 years Female: 70% vs. 65% Duration of symptoms: 9.1 vs. 9.9 years Bilateral OA: 74% vs. 77% Previous acupuncture treatment: 9% vs. 7% Physiotherapy in past 6 months: 15% vs. 9% Pharmacological intervention in past 6 months: 29% vs. 36% WOMAC: 50.8 (18.8) vs. 52.5 (18.6) PDI: 27.9 (14.2) vs. 27.8 (13.2) VAS pain: 64.9 (14.2) vs. 68.5 (14.4) SF-36 Physical health: 30.0 (7.4) vs. 29.2 (8.2) SF-36 Mental health: 51.8 (12.1) vs. 51.1 (11.6) ADS: 51.2 (10.0) vs. 51.3 (7.9)	WOMAC (scales unclear); Pain Disability Index, German version (PDI, 0-10, higher score=more severe disability related to pain); SF-36 (0-100, higher score=better QoL); Allgemeine Depressionsskala (ADS, Depression Scale, scale unclear) *for bilateral OA, the knee defined at baseline as most painful was the one assessed throughout entire study	4 and 10 months
Yildiz 2015	A vs. B vs. C Age: 56 vs. 55 vs. 58 Female: 83.3% vs. 80% vs. 86.6% Race: NR Mean Duration of Chronicity: 4.1 vs. 2.8 vs. 5.1 years Lequesne Index Score: 13.20(3.66) vs. 12.90(2.73) vs. 12.37(3.68) Pain on Movement (VAS) 8.97(1.45) vs. 8.60(1.61) vs. 8.93(1.44) Pain at Rest (VAS): NR Quality of Life (SF-36): NR Sleep (VAS): NR	Lequesne Function Index for Knee Osteoarthritis (range 0-24, higher score=greater dysfunction) Pain on Movement (VAS, 0-10) Pain at Rest (VAS, 0-10) SF-36 (0-100) Sleep (VAS, 0-10)	2 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Witt 2005	A vs. B <u>4 months</u> WOMAC Total: 30.4 (21.3) vs. 36.3 (22.3); MD -5.8 (95% CI -12.0, 0.3), p=0.063 WOMAC Physical Function: 30.4 (21.4) vs. 36.5 (23.2); MD -6.2 (95% CI -12.4, 0.1), p=0.053 PDI (Disability): 18.6 (13.0) vs. 22.8 (15.3); MD -4.2 (95% CI -8.3, -0.0), p=0.048 WOMAC Pain: 28.9 (22.7) vs. 33.8 (22.3); MD -4.8 (95% CI -11.2, 1.6), p=0.137 SF-36 Physical: 35.1 (8.8) vs. 33.0 (10.0); MD 2.1 (95% CI -0·5, 4.8), p=0.111 SF-36 Mental: 52.6 (11.5) vs. 51.7 (11.2); MD 0.9 (95% CI 2.3, 4.2), p=0.580 ADS (Depression): 48.2 (9.9) vs. 48.7 (9.3); MD -0·5 (95% CI -3.6, 2.5), p=0.730 <u>10 months</u> WOMAC Total: 32.7 (22.4) vs. 38.4 (22.6); MD -5.7 (95% CI -12.1, 0.7), p=0.080 WOMAC Physical Function: 33.0 (23.0) vs. 38.9 (23.8); MD -5.9 (95% CI -12.5, 0.7), p=0.081 PDI (Disability): 20.0 (14.0) vs. 23.6 (15.0); MD -3.6 (95% CI, -7.7, 0.5), p=0.089 WOMAC Pain: 30.0 (23.5) vs. 33.5 (21.3) ; MD -3.5 (95% CI -10.0, 3.0), p=0.285 SF-36 Physical: 35.0 (10.0) vs. 32.8 (9.5); MD 2.2 (95% CI -0.6, 5,1), p=0.120 SF-36 Mental: 52.9 (11.0) vs. 51.1 (11.7); MD 1.9 (95% CI -1.3, 5.1), p=0.254 ADS (Depression): 48.6 (10.2) vs. 49.8 (10.1); MD -1.2 (95% CI -4.3, 1.8), p=0.430
Yildiz 2015	<u>A vs. C</u> <u>2 months</u> Lequesne Index: 5.45(3.43) vs. 11.73(4.53) p<0.001; AvsC: MD -6.2 (95%CI -8.36 to -4.20) Pain on Movement (VAS): 3.90(2.54) vs. 7.20(2.66) p<0.001; AvsC: MD -3.3 (95%CI -4.64 to -1.96) Pain at Rest (VAS): NR Quality of Life (SF-36): NR Sleep (VAS): NR B vs. C <u>2 months</u> Lequesne Index: 6.02(3.14) vs. 11.73(4.53) p<0.001; BvsC: MD -5.71 (95%CI -7.72 to -3.70) Pain on Movement (VAS): 3.83(2.61) vs. 7.20(2.66) p<0.001; BvsC: MD -3.37 (95%CI -4.73 to -2.01) Pain at Rest (VAS): NR Quality of Life (SF-36): NR Sleep (VAS): NR

Author, Year	**Results - Subquestion b** (vs. Pharmacological therapy)
Witt 2005	
Yildiz 2015	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Witt 2005		A vs. B Serious adverse events: 2.1% (3/146) vs. 2.7% (2/73) (1 patient in group B died of myocardial infarction; all cases were admitted to the hospital and considered unrelated to the study condition or treatment) Minor side effects: 24 cases in 20/146 (14%) patients vs. 16 cases in 13/73 (18%) patients, p=0.410 Small haematoma or bleeding: 18 cases vs. 9 cases Other side-effects, such as needling pain: 6 cases vs.6 cases Local inflammation at the needling site: 0 cases vs. 1 case
Yildiz 2015	NR	"No study participant left the research project for any reason. No side effects or complications were observed during the treatment."

Author, Year	Funding Source	Quality	Comments
Witt 2005	Institute for Social Medicine, Epidemiology and Health Economics	Fair	This study had a third waitlist control arm that was excluded from this report because these patients received 12 sessions of acupuncture after the 8 weeks (immediately post-treatment) assessment; thus the only useable comparative data is immediately post-treatment which does not meet our inclusion criteria.
Yildiz 2015	NR	Fair	

Author, Year	Country Number of Centers Setting	Inclusion/Exclusion Criteria	Number Randomized, Analyzed Attrition
Yurtkuran 2007	Turkey, single outpatient clinic	Inclusion Criteria: 50 years or older knee pain average severity of 40 or more on 0-100 VAS for ≥1 month prior, Kellgren and Lawrence grade 2 and 3 KOA Exclusion: knee surgery, serious valgus or varus deformity or who had hormonal, metabolic, or systemic rheumatologic problems leading to secondary KOA, PT in last 6 months, oral analgesics in last 4 weeks	Randomized: 55 Treated: 55 Analyzed: 52 Attrition: 5% (3/55)
Zgierska 2016	US Number centers: 1 Outpatient	21 ≥ years old treated with long-term opioids for chronic LBP Exclude: prior experience with mindfulness meditation; inability to consent for or reliably participate in study activities; diagnoses of borderline personality, bipolar, or delusional disorders; or current pregnancy	Randomized: 35 Treated: 35 Analyzed: 35 Attrition: 0.02% (1/35)
Zhang 2013	Hong Kong 2006-2009	Adult with chronic mechanical neck pain for ≥3 months Excluded: prior neck surgery, neurological deficits, history of malignancy, congenital abnormality of the spine, systemic diseases, and treatment by acupuncture in the last 6 months.	Randomized: 206 Treated: 175 Analyzed: 160 Attrition: 22% (46/206)

Author, Year	Intervention, Comparator
Yurtkuran 2007	A. laser acupuncture (n=27): infrared 27 GaAs diyode laser instrument; output power of 4 mW, 10 mW/cm2 power density, 0.4 cm2 spot size, 120-sec treatment time and 0.48 J dose per session. The irradiation was pulsed (duration of 1 pulse was 200 nanosecond), and only one point was treated with contact application technique. Applied to the medial side of the knee to the acupuncture point (Sp9) on the sural nerve. B. sham laser acupuncture (n=25): performed in the same location and under the same conditions as the true laser acupuncture; patients could see a red light but the machine was turned off Both groups: 5 days per week for 2 weeks (total duration of therapy was 10 days) and 20 min per day; 10 sessions total. In addition, all patients received a home-based, standardized exercise program
Zgierska 2016	A. Mindfulness-based stress reduction (n=21): 8 weekly 2 hour group sessions (mediation-CBT, "Mindfulness for Chronic Pain), plus 30 minutes/day, 6 days/week of at home practice B. Usual care (n=14): includes pharmacotherapy, safety, and treatment progress monitoring, treatment agreements, and referral to specialty care, including physical therapy, and complementary therapies for pain and/or mental health
Zhang 2013	A. Electro-acupuncture (n=84) with needles placed into LI4, x2; SI3, x2; GB20,x2; GB21, x2; and Bailao and stimulated with electro-acupuncture machine for 45 minutes. Two additional points could be chosen from tender points or acupuncture points immediately near the tender points. B. Sham laser acupuncture (n=76) was delivered via a mock laser pen that only emitted a red light. Each point was treated for 2 minutes, with the pen at a distance of 0.5 to 1 cm from the skin. Treatment 3x/week for 3 weeks

Author, Year	Study Participants	Outcome Measures	Duration of Followup
Yurtkuran 2007	A vs B Age: 52 vs. 53 years Female: 96% vs. 96% Duration of symptoms: 62 vs. 67 months WOMAC: 66.53 (17.6) vs. 51.31 (18.9) VAS pain on movement: 6.47 (1.6) vs. 6.06 (2.2) NHP: 8.79 (3.8) vs. 8.06 (4.5)	WOMAC (scale unclear; higher score=worse disability) Knee Pain on movement (VAS, 0-100; higher score-worse pain) Nottingham Health Profile (NHP) QOL (0-38; higher score=worse quality of life)	3 months
Zgierska 2016	Overall Age: 51.8 years Female: 80% Race: NR Medication use for pain: 3 months ≥ Severe pain related disability (mean): 66.7 Moderate pain severity (mean): 5.8 Morphine equivalent dose: 148.3 mg/day A vs B ODI (0-100): 68.1 (9.3) vs. 64.5 (14.1)	Oswestry Disability Index (0-100) Brief Pain Inventory pain intensity (0-10)) Opioid dose (morphine-equivalent dose) mg/day, past 28 days	4.5 months
Zhang 2013	A vs B Age: 46 years (whole population) Female: 70% (whole population) Duration: 75 months (whole population) NPQ: 40.7 (CI, 38.6 to 42.9) vs 41.1 (CI, 38.7-43.5) Pain with motion (0-100), SF-36 PCS: 52.5 (CI, 51.5 to 53.4) vs 52.7 (CI, 51.9 to 53.6) SF-36 MCS: 43.8 (CI, 42.9 to 44.8) vs 43.7 (CI, 42.6 to 44.8)	Northwick Park Neck pain Questionnaire (NPQ) (scale: 0-100%, higher percentage the greater the disability) SF-36 physical and mental summary scores (0-100, higher score=better QoL)	3 and 6 months

Author, Year	Results - Subquestion a (vs. sham, no treatment, waitlist, attention control)
Yurtkuran 2007	A vs. B <u>3 months</u> WOMAC total: 62.4 (22.3) vs. 50.6 (23.6); MD 11.8 (95% CI -1.0, 24.6), p=0.07 WOMAC Physical Function: 44.24 (15.8) vs. 35.25 (16.6); MD 11.9 (95% CI 2.9, 20.9), p=0.01 WOMAC Pain: 13.47 (5.8) vs. 11.50 (6.0); MD 2.0 (95% CI -1.3, 5.3) VAS Pain on movement: 5.6 (2.4) vs. 4.8 (3.5); MD 0.8 (95% CI -0.9, 2.5), p=0.34 NHP: 7.58 (5.4) vs. 6.44 (6.3); MD 1.14 (95% CI -2.1, 4.4), p=0.49
Zgierska 2016	A vs. B <u>4.5 months, mean change from baseline</u> ODI: -5.0 (95% CI 9.7, 0.2) vs. 1.6 (95% CI -4.3, 7.4), mean difference in change from baseline -6.5 (95% CI -14.0, 1.0) Brief Pain Inventory pain intensity: -0.5 (95% CI -1.1, 0.02) vs. 0.5 (95% CI 0.2, 1.2), mean difference in change from baseline -1.03 (95% CI -1.9, -0.2) Opioid dose (mg morphine equivalents): -10.1 (95% CI -35.5, 15.2) vs. -0.2 (95% CI -31.4, 30.9)
Zhang 2013	A vs B 3 month outcomes (mean and 95% CI) NPQ: 32.9 (CI, 30.3 to 35.4) vs 33.3 (CI 30.1 to 36.5), p=0.664 Pain with motion: 46.6 (CI, 42.2 to 51.0) vs 45.1 (CI, 40.5 to 49.6), p=0.617 SF-36 PCS: 52.8 (CI, 53.0 to 53.7) vs 53.3 (CI, 52.4 to 54.2), p=0.982 SF-36 MCS: 45.9 (CI, 46.0 to 46.8) vs 45.3 (CI, 44.2 to 46.4), p=0.444 6 month outcomes (mean and 95% CI) NPQ: 33.59 (CI, 30.7 to 36.4) vs 34.3 (CI 31.1 to 37.6), p=0.808 Pain with motion: 46.8 (CI, 42.0 to 51.5) vs 43.6 (CI, 38.8 to 48.4), p=0.813 SF-36 PCS: 53.0 (CI, 52.0 to 53.9) vs 53.2 (52.3 to 54.0), p=0.559 SF-36 MCS: 45.4 (CI, 44.5 to 46.3) vs 44,4 (CI, 43.4 to 45.4), p=0.246

Author, Year	Results - Subquestion b (vs. Pharmacological therapy)
Yurtkuran 2007	NR
Zgierska 2016	NR
Zhang 2013	NR

Author, Year	Results - Subquestion c (vs. Exercise)	Adverse Events Including Withdrawals
Yurtkuran 2007	NR	No systemic or local side effects (e.g., erythema, burning, blood pressure, and heart rate elevation) were observed during the study
Zgierska 2016	NR	None
Zhang 2013	NR	Increased neck pain: n=1 vs 2 Headache: n=2 vs 1 Dizziness: n=1 vs 1 Bruise at acupoints : n=2 vs 0 Pain at acupoint after treatment: n=1 vs 0 Chest discomfort: n=1 vs 0 Itching palm : n=1 vs 1 Warm feeling at the back : n=1 vs 1 No severe adverse reaction noticed.

Author, Year	Funding Source	Quality	Comments
Yurtkuran 2007	Sponsored by University Research Committee	Fair	
Zgierska 2016	"K23AA017508 (NIH) National Institute on Alcohol Abuse and Alcoholism (NIAAA), and University of Wisconsin-Madison"	Poor	
Zhang 2013	Health and Health Services Research Fund, Food and Health Bureau, Hong Kong SAR Government (#04060191), School of Chinese Medicine of Hong Kong	Fair	Credibility test: Electroacupuncture perceived more credible than laser acupuncture, p<0.05 Blinding successful for patients and practitioners

|is= ; 3B= ; 5D-3L=3 level version of EQ-5D; ACR=American College of Rheumatology; ACSM=American College of Sports Medcine; ACT=Acceptance and Commitment Therapy; ADAPT=The Arthritis, Diet, and Activity Promotion Trial; Adj=adjusted; ADL=Activities of Daily Living; ADS=Allgemeine Depressionsskala; AE=adverse event; AHRQ=Agency for Healthcare Research and Quality; AIMS=Arthritis Impact Measurement Scales; ALBA= ; ALF-LUA= ; AM=antidepressant medications; ANOVA=analysis of variance; AP=Arnold Peter; AQoL=assessment of quality of life; AT= ; ATEP=active trunk exercise program; AUSCAN=Australian/Canadian Osteoarthritis Hand Index; B2=B2 acupuncture point; BDI=Beck Depression Inventory; BDI-II= Beck Depression Inventory-II; BL10=BL10 acupuncture point; BL11=BL11 acupuncture point; BL12 =BL12 acupuncture point; BL16=BL16 acupuncture point; BL60=BL60 acupuncture point; BL62=BL62 acupuncture point; BL65=BL65 acupuncture point; Blvd=boulevard; BMI=body mass index; C4=C4 acupuncture point; CA=California; CAM=complementary and alternative medicine; CAPES=Coordination for the Improvement of Higher Education Personnel; CBT=cognitive behavioral training; CD=compact disc; CDC=United States Centers of Disease Control and Prevention; CES-D=Center for Epidemiological Studies Depression Scale; CI=confidence interval; cm/CM=centimeters; COX-2=cyclooxygenase-2; CPEQ=Comprehensive Pain Evaluation Questionnaire; CPGS=Von Korff Chronic Pain Grade Score; CTTH= ; DAK= ; DAMD= ; DANICA= ; DASS=Depression Anxiety Stress Scale; DFI=discrimination function index; diff=difference; Dr=drive; DU14=DU14 acupuncture point; DVD=digital versatile disc; ELF=extremely low frequency; EQ-5D= ; ES= ; ESWT=extracorporeal shock wave therapy; EuroQol= ; EVO=Engineering Virtual Organization; Ex-HN15=Ex-HN15 acupuncture point; F= ; FAST=The Fitness Arthritis and Seniors Trial; FD=flexion-distraction; FFbH-R=Funktionsfragebogen Hannover-Rücken; FIHOA=Functional Index for Hand Osteoarthritis; FIQ=Fibromyalgia Impact Questionnaire; Fl=floor; FM=fibromyalgia; FSI=Fatigue Symptom Inventory; f/u=followup; FYSIOPRIM= ; G= ; G2= ; GaAIAs=infrared emitting diodes; GaAs=gallium arsenide; GARS=Gilliam Autism Rating Scale; GB8=GB8 acupuncture point; GB12=GB12 acupuncture point; GB14=GB14 acupuncture point; GB20=GB20 acupuncture point; GB21=GB21 acupuncture point; GB34=GB34 acupuncture point; GB39=GB39 acupuncture point; GB41=GB41 acupuncture point; GB42=GB42 acupuncture point; GCQ=Giessen Complaint Questionnaire;

GP=general practitioner; GPE=Global Perceived Effect; GRASS=gradient-recalled acquisition in a steady state; GSI=Global Severity Index; GV14=GV14 acupuncture point; GV20=GV20 acupuncture point; HA= ; HAD=Hospital Anxiety and Depression; HADS=Hospital Anxiety and Depression Scale; HAM-A=Hamilton Anxiety Rating Scale; HAM-D=Hamilton Rating Scale for Depression; HAQ= ; HARS=Hamilton Anxiety Rating Scale; HDI=Headache Disability Index; HDRS=Hamilton Depression Rating Scale; HEA=home exercise and advice; HEP= ; HFAQ=Hannover Functional Ability Questionnaire; HHS= ; HI=Headache Index; HIT-6=Headache Impact Test; HMO=health maintenance organization; HRQoL=Health-related quality of life; HRSA=Health Resources and Services Administration; HSS= ; HT-7=HT7 acupuncture point; Hz=hertz; ICCHD= ; ICOAP=The Intermittent and Constant Osteoarthritis Pain Questionnaire; ICT=intermittent cervical traction; IHS=International Headache Society; IL=Illinois; IMK= ; Inc=incorporated; inf= ; IQR=interquartile range; IRYSS=Investigación en Resultados y Servicios Sanitarios; ITT=intention to treat; J=joule; J-MAP=joint-specific multidimensional assessment of pain; LBP=low back pain; kHz=kilohertz; kJ=kilojoules; K/L=Kellgren and Lawrence radiographic severity; km=kilometers; KOA=knee osteoarthritis; KOOS=Knee Injury and Osteoarthritis Outcome Score; KPS=Knee Pain Scale; KQ6=key question 6; L1=L1 acupuncture point; L2=L2 acupuncture point; L5=L5 acupuncture point; L14=L14 acupuncture point; LBO=Low Back Outcome Scale; LBP=low back pain; LI4=LI4 acupuncture point; LI5=LI5 acupuncture point; LI15=LI15 acupuncture point; LIV-3=LIV3 acupuncture point; LLC=limited liability corporation; LLFDI=Late-Life Function & Disability Instrument; LLLT=Low Level Laser Therapy; LLLT=Low Level Laser Therapy; LOCF=last observation carried forward; LR-2=LR2 acupuncture point; LR3=LR3 acupuncture point; LU7=LU7 acupuncture point; m=meters; mm=millimeters; MANOVA=Multivariate Analysis of Variance; MBSR=Mindfulness-based Stress Reduction; MCD=Mean Duration of Chronicity; MCID=minimally clinically important difference; MCS=mental composite score; MD=Maryland; MDT=Mechanical Diagnosis and Therapy; METS=metabolic equivalents; mg=milligrams; MHz=MegaHertZ; MIDAS=Migraine Disability Assessment; mm=millimeters; MMSE=Mini-Mental Status Exam; mo/mos/MOS=months; MPI=Multidisciplinary Pain Inventory; MPQ=McGill Pain Questionnaire; ms= ; mT=massage therapy; mW=milliwatts; NCAAM=National Center for Complementary and Alternative Medicine; NCCAM=National Center for Complementary and Alternative Medicine at the Institutes of Health; NCSS= ; NDI=Neck Disability Index; Nd:YAG= ; NHP=Nottingham Health Profile; NHS= ; NIAMS=National Institute of Arthritis and Musculoskeletal and Skin Diseases; NIH= National Institutes of Health; nm= ; NPAD=Neck Pain and Disability Scale; NPNQ=Northwick Park Neck pain Questionnaire; NPQ =Northwick Park Neck pain Questionnaire; NPRS=Numerical Pain Rating Scale; NPS=Neuropathy Pain Scale; NR=not reported; NRS= ; ns/NS=not significant; NSAIDS=nonsteroidal anti-inflammatory drugs; NSCLBP=nonspecific low back pain; nsec=nanoseconds; NSW=New South Wales; NY=New York; O2=oxygen; OA=osteoarthritis; OARSI OMERACT=Osteoarthritis Research Society International ; ODI=Oswestry Disability Index; OKS=Oxford Knee Scale; OTC=over the counter; OTES=occipital transcutaneous electrical stimulation; P= ; P-6= ; PCS=physical composite score; PCD=Physical and Complex Disabilities; PCL=Quality of Life Profile for the Chronically Ill; PCS=physical composite score; PCST=pain coping skills training; PD= Power Density; PDI=Pain and Disability Index; PEMF=Pulsed Electromagnetic Fields; PES=pulsed electrical stimulation; PFJ= ; PGE=Perceived Global Effect; PHQ-8=Patient Health Questionnaire 8-item; PI= ; PM&R=Physical Medicine & Rehabilitation; PMR=progressive muscle relaxation; PNF=proprioceptive neuromuscular facilitation; PPT= ; PRSS=Pain-Related Self Statements Scale; PSCT=Pain Coping Skills Training; PSFS=Patient-Specific Functional Scale; PSQI=Pittsburgh Quality of Sleep Index Questionnaire; PSS=Perceived Stress Scale; PSW=Pulsed Short Wave; PT= ; QALY=quality adjusted life year; QoL=quality of life; RA= ; RAND-36=the Rand 36-Item Health Survey; RDQ=Roland Disability Questionnaire; READ= ; RiG= ; RMD=Roland Morris Disability; RMDQ=Modified Roland Disability Scale; ROM= range of motion; RR= ; S=south; S1=S1 acupuncture point; S3=S3 acupuncture point; S13=S13 acupuncture point; SAS PROC MIXED= ; SCL-90-R=Symptom Checklist 90; SD=standard deviation; SDQ=Stanford Sleep Disorders Questionnaire; SE=adjusted mean; SEM=standard error of the mean; SES=Schmerzempfindungsskala; SET=supervised exercise therapy; SF-12= ; SF-12v2=Short-Form 12v2; SI=small intestine acupuncture point; SI3=SI3 acupuncture point; SI4=SI4 acupuncture point; SI15=SI15 acupuncture point; SI9= SI9 acupuncture point; SI10=SI10 acupuncture point; SI11=SI11 acupuncture point; SI12=SI12 acupuncture point; SI14=SI14 acupuncture point; SIP=Sickness Impact Profile; SIP-136=136-item Sickness Impact Profile; SKFS=Saudi Knee Function Scale; SKIP=Satisfaction with Knee Procedure; SMT=spinal manipulation therapy; SP-6=SP6 acupuncture point; SP9=SP9 acupuncture point; SR=systematic review; SSQ=Stanford Sleep Questionnaire; St=street; ST-36=ST36 acupuncture point; ST41=ST41 acupuncture point; STAI=State-Trait Anxiety Inventory; STAI-S=State-Trait Anxiety Inventory State Scale; STPI=State-Trait Personality Inventory; SWD=short wave diathermy; TAMMEF=Therapeutic Application of Musically Modulated Electromagnetic Field; TCA=traditional Chinese acupuncture;

TCM=traditional Chinese medicine; TE5=TE5 acupuncture point; TE14=TE14 acupuncture point; TE15=TE15 acupuncture point; TE16=TE16 acupuncture point; TE17=TE17 acupuncture point; TENS=transcutaneous electrical nerve stimulation; TES=transcutaneous electrical stimulation; TKR=total knee replacement; TUG=Timed Up and Go Test; TW5=TW5 acupuncture point; TW8=TW8 acupuncture point; tx=treatment; UB2= UB2 acupuncture point; UB10=UB10 acupuncture point; UB60=UB60 acupuncture point; UK=United Kingdom; US=United States; USA=United States of America; UT=Utah; V= ; VAS=visual analogue scale; VGFOUREG= ; vs.=versus; VTR= ; VU= ; W=watts; WAD=whiplash-associated disorders; WHYMPI=West Haven-Yale Multidimensional Pain Inventory; wks= weeks; WL=waitlist; WOMAC=Western Ontario and McMaster Osteoarthritis Index; WPSI=Wahler Phsycial Symptoms Inventory; x2=twice; yrs=years; ZONMW=The Netherlands Organization for Health Research and Development.

Appendix E. Quality Assessment

Table E-1. Quality assessment of randomized controlled trials

See Appendix B. Included Studies for references.

Author, Year	Randomization	Concealed Treatment Allocation	Intention-to-Treat Analysis	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Compliance Acceptable in All Groups	Attrition Reported
Abbassi, 2012	No	No	Yes	Yes	No	No	Unclear	Yes	Yes
Abbott, 2013	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes
Ajimsha 2014	Unclear	Unclear	Yes	Yes	Yes	No	Yes	Yes	Yes
Al Rashoud 2014	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Unclear	No
Alda 2011	Yes	Yes	Yes	Yes	No	No	Yes (CBO) No (PRO)	Unclear	Yes
Alfano 2001	Yes	Unclear	No	Yes	Yes (magnetic field and sham groups) No (usual care group)	Yes	Yes (outcome assessor) No (data analyst)	Unclear	Yes
Altan 2005	Unclear	Unclear	Yes	No	Yes	Unclear	Yes	Yes	Yes
Altan 2009	Yes	Unclear	Yes	Yes	No	No	Yes (CBO) No (PRO)	Unclear	Yes
Amris 2014	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Andersen 2008	Unclear	Unclear	Yes	Unclear	No	No	No	No	No
Ang 2010	Unclear	Unclear	Unclear	Unclear	No	No	No	Unclear	Yes
Aslan Telci 2012	Unclear	Unclear	Unclear	No	No	No	No	Unclear	No
Assefi 2005	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Banth, 2015	Unclear	Unclear	Yes	Unclear	No	No	Yes	Unclear	Yes
Baptista 2012	Yes	Yes	Yes	No	No	No	No	Unclear	Yes
Basford, 1999	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Battisti 2004	Unclear	Unclear	Unclear	Unclear	No	No	No	Yes	No
Bendix, 1995, 1997,	Yes (minimization)	Yes (minimization)	Yes	Yes	No	No	Yes	Unclear	Yes
Bendix, 2000	Yes (minimization)	Yes (minimization)	Yes	Yes	No	No	Yes	Unclear	Yes
Bendix,1996, 1998	Yes (minimization)	Yes (minimization)	Yes	Yes	No	No	Yes	Unclear	Yes
Bennell, 2005	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Bennell, 2016	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Berman, 1999	Yes	Yes	Yes	Yes	No	No	Unclear	Unclear	Yes
Berman, 2004	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Beurskens, 1997	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Birch 1998	Unclear	Unclear	Unclear	No	Yes/No*	No	Yes/No*	Yes	Yes

Author, Year	Attrition Acceptable	Attrition Between Groups Acceptable	Timing of Outcome Assessment in All Groups Similar	Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Abbassi, 2012	Yes	Yes	Yes	Unclear	Yes	Poor
Abbott, 2013	Yes	Yes	Yes	Yes	Yes	Fair
Ajimsha 2014	Yes	Yes	Yes	Unclear	Yes	Fair
Al Rashoud 2014	Unclear	Unclear	Yes	No	Yes	Fair
Alda 2011	Yes	Yes	Yes	Yes	Unclear	Fair
Alfano 2001	No	Yes	Yes	Unclear	Yes	Fair (all comparisons)
Altan 2005	Yes	Yes	Yes	No	Yes	Fair
Altan 2009	Yes	Yes	Yes	Unclear	Yes	Fair
Amris 2014	Yes	Yes	Yes	Yes	Yes	Fair
Andersen 2008	Unclear	Unclear	Yes	Yes	Yes	Poor
Ang 2010	Yes	Yes	Yes	Yes	Unclear	Poor
Aslan Telci 2012	Unclear	Unclear	Yes	No	Yes	Poor
Assefi 2005	Yes	Yes	Yes	No	Yes	Good
Banth, 2015	No	Unclear	Yes	No	Unclear	Poor
Baptista 2012	Yes	Yes	Yes	Yes	Unclear	Fair
Basford, 1999	Yes	Yes	Yes	Unclear	Yes	Fair
Battisti 2004	Unclear	Unclear	Yes	No	Yes	Poor
Bendix, 1995, 1997, 1998	No (22% at 12 months)	Yes	Yes	Unclear	Yes	Fair
Bendix, 2000	No (22% at 12\0 months)	Yes	Yes	No	Unclear	Fair
Bendix,1996, 1998	Yes	No	Yes	No	Yes	Fair
Bennell, 2005	Yes	No	Yes	No	Yes	Fair
Bennell, 2016	Yes	Yes	Yes	Yes	Yes	Fair
Berman, 1999	Yes	Yes	Yes	No	Yes	Fair
Berman, 2004	No	Yes	Yes	No	Yes	Fair
Beurskens, 1997	No	Yes	Yes	Unclear	Yes	Fair
Birch 1998	Yes	Yes	Yes	No	No	Poor

Author, Year	Randomization	Concealed Treatment Allocation	Intention-to - Treat Analysis	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Compliance Acceptable in All Groups	Attrition Reported
Blanchard 1990	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	No	Unclear	Yes
Blodt, 2015	Yes	Yes	Yes	No	No	No	Unclear	No (~70%)	Yes
Boline 1995	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Bono 2015	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No
Bourgault 2015	Yes	Unclear	No	Yes	No	No	No	No	Yes
Brinkhaus 2006a	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Brismee 2007	Yes	Unclear	Yes	Yes	No	No	Yes/No (assessor blinded/ patient reported	Yes	Yes
Bronfort, 2011	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Brosseau, 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Brouwer 2006	Yes	Yes	Yes	Yes	No	No	No	No	Yes
Buckelew 1998	Unclear	Unclear	Unclear	No	No	No	Yes (CBO) No (PRO)	Unclear	Yes
Cakir 2014	Yes	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes
Carlsson 2001	Unclear	Unclear	Yes	Yes	Yes	No	Yes	Unclear	Unclear
Cash 2015/Sephton 2007	Yes	Unclear	Yes	Yes	No	No	Yes (CBO) No (PRO)	No	Yes
Castel 2012	Unclear	Unclear	Yes	Yes	No	No	No	Yes	Yes
Castel 2013	Yes	Unclear	Yes	Yes	No	No	No	Unclear	Yes
Castien 2011	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Castro-Sanchez	Yes	Unclear	Yes	Yes	No	No	No	Yes	Yes
Castro-Sanchez	Unclear	Unclear	Yes	Yes	No	No	No	Yes	Yes
Cedraschi 2004	Yes	Yes	No	Yes	No	No	No	No	Yes
Chen, 2014	Yes	Yes	Yes	Unclear	Unclear	No	Yes	Yes	No
Cherkin 2001	Yes	Unclear	Yes	Yes	No	No	Yes	Yes	Yes
Cherkin 2009	Unclear	Unclear	Yes	Yes	No	No	Yes	Yes	Yes
Cherkin, 2011	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Cherkin, 2016	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Chiu 2011	Yes	Yes	Yes	No*	No	No	No	Unclear	Yes
Cho 2013	Yes	Yes	Yes	Yes	Yes	No	Unclear	Unclear	Yes
Cho 2014	Yes	Yes	Yes	No	No	No	No	Yes	Yes
Chow 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Author, Year	Attrition Acceptable	Attrition Between Groups Acceptable	Timing of Outcome Assessment in All Groups Similar	Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Blanchard 1990	Yes	Yes - Relax only vs. AC/WL No - CBT/relax vs. AC/WL	Yes	No	Yes	Poor
Blodt, 2015	Yes	Yes	Yes	Yes	Yes	Fair
Boline 1995	Yes	No	Yes	No	Yes	Poor
Bono 2015	Unclear	Unclear	Yes	No	Yes	Poor
Bourgault 2015	No	No	Yes	Yes	Yes	Poor
Brinkhaus 2006a	Yes	Yes	Yes	Yes	Yes	Good
Brismee 2007	No	No	Yes	No	Yes	Poor
Bronfort, 2011	Yes	Yes	Yes	Unclear	Yes	Fair
Brosseau, 2005	Yes	Yes	Yes	No	Yes	Good
Brouwer 2006	No	No	Yes	No	Yes	Poor
Buckelew 1998	Yes	Yes	Yes	Unclear	Yes	Poor (all comparisons)
Cakir 2014	Yes	Yes	Yes	No	No	Fair
Carlsson 2001	Unclear	Unclear	Unclear	Unclear	Yes	Poor
Cash 2015/Sephton 2007	No	No	Yes	Yes	No	Poor
Castel 2012	No	Yes	Yes	Unclear	Unclear	Poor
Castel 2013	No	No	Yes	No	Unclear	Poor
Castien 2011	Yes	Yes	Yes	Yes	Yes	Fair
Castro-Sanchez	Yes	Yes	Yes	No	Yes	Fair
Castro-Sanchez	Yes	Yes	Yes	No	Yes	Poor
Cedraschi 2004	No	No	Yes	No	Unclear	Poor
Chen, 2014	Unclear	Unclear	Yes	No	Yes	Poor
Cherkin 2001	Yes	Yes	Yes	Unclear	Yes	Fair
Cherkin 2009	Yes	Yes	Yes	Yes	Yes	Fair
Cherkin 2011	Yes	Yes	Yes	Yes	Yes	Fair
Cherkin, 2016	No	Yes	Yes	Yes	Yes	Fair
Chiu 2011	No**	No**	Yes	No	Yes	Poor
Cho 2013	Yes	Yes	Yes	Yes	Yes	Fair
Cho 2014	Yes	Yes	Yes	Yes	Yes	Poor
Chow 2006	Yes	Yes	Yes	No	Yes	Good

Author, Year	Randomization	Concealed Treatment Allocation	Intention-to-Treat Analysis	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Compliance Acceptable in All Groups	Attrition Reported
Clarke-Jenssen	Yes	Yes	Yes	No	No	No	No	Yes	Yes
Costa 2009	Yes	Yes	Yes	Yes	No (not blinded to exercise)	No	Yes	Yes	Yes (figure 1)
Da Costa 2005	Yes	Yes	Yes	Yes	No	No	No	Unclear	Yes
Dias, 2003	Yes	Unclear	Unclear	Yes	No	No	Yes	Unclear	Yes
Dilek, 2013	Yes	Yes	Yes	Yes	No	No	Yes	Unclear	Yes
Djavid, 2007	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ebadi, 2012	Yes	Yes	Yes	Yes	Yes	No	Unclear	Yes	Yes
Ebneshahidi 2005	Unclear	Unclear	Yes	No	Yes	No	Yes	Yes	Yes
Edinger 2005	Unclear	Unclear	Unclear	Unclear	No	No	No	Yes	Yes
Ettinger 1997	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes
Falcao 2008	Yes	Unclear	Yes	Yes	No	No	No	Unclear	Yes
Fary 2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Ferreira, 2007	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Fontaine 2010/2011	Yes	No	Yes	Yes	No	No	Unclear	No	Yes
Fukuda 2011	Yes	Yes	Yes	Yes	Yes	No (control) Yes (placebo	No	Yes	Yes
Giannotti 2014	Yes	Unclear	Yes	Yes	No	No	No	Unclear	Yes
Gibson, 1985	Unclear	Unclear	Yes	No	Yes	Yes	Yes	Unclear	Yes
Giombini 2011	Yes	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes
Goldby 2006	Yes	Unclear	Yes	Yes	No	No	Yes	Unclear	Yes
Gowans 2001	Unclear	Unclear	Yes	No	No	No	No	No	Yes
Groessl 2017	Yes		Yes	Yes	No	No	No	No	Yes
Gudavalli, 2006	Yes	Yes	Yes	Yes	No	No	Yes	Unclear	Yes
Gur 2004	Yes	Unclear	Unclear	Yes	Yes	No	Unclear	Yes	Yes
Gusi 2006	Unclear	Unclear	Yes	Yes	No	No	No	Yes	Yes
Haake 2007	Yes	Yes	Yes	Yes	No	No	Unclear	Yes	Yes
Haas, 2014	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Harkapaa, 1989	Unclear	Unclear	Yes	Yes	No	No	No	Unclear	Yes
Hegedus 2009	Yes	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Unclear	Yes
Helminen 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes

Author, Year	Attrition Acceptable	Attrition Between Groups Acceptable	Timing of Outcome Assessment in All Groups Similar	Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Clarke-Jenssen	Yes	Yes	Yes	No	Unclear	Fair
Costa 2009	Yes	Yes	Yes	Yes	Yes	Fair
Da Costa 2005	No	Yes	Yes	No	Yes	Fair
Dias, 2003	Yes	Yes	Yes	No	Unclear	Poor
Dilek, 2013	Yes	Yes	Yes	No	Yes	Fair
Djavid, 2007	Yes	Yes	Yes	Unclear	Yes	Fair
Ebadi, 2012	Yes	No	Yes	Yes	Yes	Fair
Ebneshahidi 2005	Yes	Yes	Yes	No	Yes	Fair
Edinger 2005	No	No	Yes	No	Unclear	Poor
Ettinger 1997	Yes	Yes	Yes	No	Yes	Fair
Falcao 2008	Yes	Yes	Yes	No	Unclear	Fair
Fary 2011	Yes	Yes	Yes	Yes	Yes	Good
Ferreira, 2007	Yes	Yes	Yes	Yes	Yes	Fair
Fontaine 2010/2011	No	Yes	Yes	No	Unclear	Fair
Fukuda 2011	No	Yes	No	No	Yes	Poor
Giannotti 2014	No	No	Yes	Yes	Unclear	Poor
Gibson, 1985	No	No (21% with diathermy vs. 6% with	Yes	Unclear	Yes	Poor
Giombini 2011	Yes	Yes	Yes	No	Yes	Fair
Goldby 2006	Yes (>80% at 12 months)	No	Yes	Unclear	Yes	Fair
Gowans 2001	Yes	Yes	Yes	No	Unclear	Poor
Groessl 2017	No	Yes	Yes	Yes	Yes	Fair
Gudavalli, 2006	Yes	No	Yes	Unclear	Yes	Fair
Gur 2004	Yes	Yes	Yes	No	Yes	Fair
Gusi 2006	Yes	Yes	Yes	No	Unclear	Poor
Haake 2007	Yes	Yes	Yes	Yes	Yes	Fair
Haas, 2014	Yes	Yes	Yes	Yes	Yes	Fair
Harkapaa, 1989	Yes	Yes	Yes	No	Yes	Poor
Hegedus 2009	No	No	Yes	No	Yes	Poor
Helminen 2015	Yes	Yes	Yes	Yes	Yes	Fair

Author, Year	Randomization	Concealed Treatment Allocation	Intention-to-Treat Analysis	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Compliance Acceptable in All Groups	Attrition Reported
Hinman, 2014	Yes	Yes	Yes	Yes	Yes (vs. sham) No (vs. no treatment)	Yes (vs. sham) No (vs. no treatment)	Yes	Yes	Yes
Ho 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Hoeksma 2004	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Holroyd 1991	Unclear	Unclear	Unclear	Yes	No	No	Unclear	Yes	Yes
Holroyd 2001	Yes	Yes	Yes	Yes	Yes-medication components, No-for stress	Yes	Yes	Yes	Yes
Hondras, 2009	Yes	Unclear	Yes	Yes	No	No	Yes	Yes	Yes
Huang, 2003	Yes	Yes	Yes	Yes	Unclear	No	Unclear	Yes	Yes
Huang, 2005a Arth & Rheum	Yes	Yes	Yes	Yes	Unclear	No	Yes	Unclear	Yes
Huang, 2005b, Archives PM&R	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes
Jensen 2012/Wicksell 2013	Unclear	Yes	Unclear	Yes	No	No	No	Unclear	Yes
Johnson 2007	Yes	Yes (minimization)	Yes	Yes	No	No	No	No	Yes
Jousset, 2004	Unclear	Unclear	Yes	Yes	No	No	No	Unclear	Yes
Jubb, 2008	Yes	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes
Juhakoski 2011	Yes	Yes	Yes	Yes	No	No	No/Yes (primary outcomes were patient reported and patient's	Yes/No (1st year 86%, 2nd year 58%)	Yes
Kankaanpaa 1999	Unclear	Unclear	Yes	Yes	No	No	No	Unclear	Yes
Karst 2000	Unclear	Unclear	Unclear	No*	Yes	No	Yes	Yes	No
Kayiran 2010	Unclear	Unclear	Unclear	No	No	No	Yes (CBO) No (PRO)	Unclear	Yes
Kayo 2012	Yes	Yes	Yes	No	No	No	No	Unclear	Yes
Kerr 2003	Yes	Unclear	Yes	Yes	Unclear	No	Yes	No	Yes
King 2002	Yes	unclear	No	Unclear	No	No	No	No	Yes
Lamb 2010/2012	Yes	Yes	Yes	Yes	No	No	Unclear	No	Yes

Author, Year	Attrition Acceptable	Attrition Between Groups Acceptable	Timing of Outcome Assessment in All Groups Similar	Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Hinman, 2014	Yes	Yes	Yes	Yes	Yes	Good - vs. sham Fair - vs. no treatment
Ho 2017	Yes	Yes	No	Yes	Yes	Fair
Hoeksma 2004	Yes	Yes	Yes	Unclear	Yes	Fair
Holroyd 1991	Yes	No	Yes	No	Yes	Poor
Holroyd 2001	No	No	Yes	No	Yes	Poor
Hondras, 2009	Yes	No	Yes	Unclear	Yes	Fair
Huang, 2003	Yes	No	Yes	No	Yes	Poor
Huang, 2005a Arth & Rheum	Yes	Yes	Yes	No	Yes	Fair
Huang, 2005b, Archives PM&R	Yes	Yes	Yes	No	Yes	Fair
Jensen 2012/Wicksell 2013	No	Yes	Yes	No	Unclear	Fair
Johnson 2007	Yes	Yes	Yes	Yes	Yes	Fair
Jousset, 2004	Yes	Yes	Yes	No	Yes	Poor
Jubb, 2008	Yes	Yes	Yes	No	Yes	Fair
Juhakoski 2011	Yes	Yes	Yes	Yes	Yes	Fair
Kankaanpaa 1999	Yes	Yes	Yes	Unclear	Yes	Fair
Karst 2000	Unclear	Unclear	Yes	No	Yes	Poor
Kayiran 2010	Yes	Yes	Yes	Yes	Yes	Poor
Kayo 2012	No	Yes	Yes	Yes	Unclear	Fair
Kerr 2003	No	No	Yes	Unclear	Yes	Poor
King 2002	No	Unclear	Yes	No	Unclear	Poor
Lamb 2010/2012	Yes	Yes	Yes	Yes	Yes	Fair

Author, Year	Randomization	Concealed Treatment Allocation	Intention-to-Treat Analysis	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Compliance Acceptable in All Groups	Attrition Reported
Lambeek, 2010a	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Lansdown, 2009	Yes	Yes	Yes	Yes	No	No	Unclear	Yes	Yes
Lansinger 2007	Yes	Yes	Yes	Yes	No	No	No	Unclear*	Yes
Larsson 2015	Yes	Yes	Yes	Yes	No	No	Yes (CBO) No (PRO)	No	Yes
Lauche 2016	Yes	Yes	Yes	Yes	No	No	No	Yes/No*	Yes
Laufer 2005	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes
Li 2017	Yes	Yes	Yes	Yes	No	No	No	Unclear	Yes
Liang 2011	Yes	Yes	Unclear	Yes	Yes	No	Unclear	Yes	Yes
Licciardone, 2013	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes
Little 2008	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Lund, 2008	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Lynch 2012	Yes	Yes	Yes	Yes	No	No	No	Unclear	Yes
MacPherson 2015	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Mannerkorpi 2009	Yes	Yes	Yes	Yes	No	No	No	No	Yes
Martin 2006	Unclear	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Martin 2012	Yes	Unclear	Yes	Yes	No	No	No	No	Yes
Mazzuca 2004	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes
Messier, 2004	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes
Miyamoto 2013	Yes	Yes	Yes	No	No	No	No	Yes	Yes
Monticone, 2013	Yes	Yes	Yes	Yes	No	No	Yes	Unclear	Yes
Monticone, 2014	Yes	Yes	Yes	Yes	No	No	Yes	Unclear	Yes
Morone, 2009	Yes	Yes	Unclear	Yes	No	No	Yes	Unclear	Yes
Morone, 2016	Yes	Yes	Unclear	Yes	No	No	Yes	Unclear	Yes
Nambi 2014	Yes	Unclear	Yes	Yes	No	No	Unclear	Yes	Yes
Nassif 2011	Yes	Unclear	Yes	Yes	No	No	No	Unclear	Yes
Natour 2015	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Nicholas 1991 Behav	Unclear	Unclear	Yes	Yes	No	No	Unclear	Unclear	Yes
Nicholas 1992 Pain 1992;48:339–47	Unclear	Unclear	Yes	Yes	No	No	Unclear	Unclear	Yes
Osteras, 2014	Yes	Yes	Yes	No	No	No	Yes	No	Yes
Paolucci 2015	Yes	Unclear	Yes	Yes	No	No	No	Yes	Yes

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Lambeek, 2010a	Yes	Yes	Yes	Yes	Yes	Fair
Lansdown, 2009	No	No	Yes	No	Yes	Poor
Lansinger 2007	No	No	No	Unclear	No	Poor
Larsson 2015	No	Yes	Unclear	Unclear	Yes	Poor
Lauche 2016	Yes/No**	Yes/No**	Yes	Yes	Yes	Fair Tai chi vs wait list; PoorTai chi vs Ex, Ex vs waitlist
Laufer 2005	Yes	No (High PSWD 28%, Low PSWD	Yes	No	Yes	Poor
Li 2017	Yes	Yes	Yes	Unclear	Yes	Fair
Liang 2011	Yes	Yes	Yes	Yes	Yes	Fair
Licciardone, 2013	Yes	Yes	Yes	Yes	Yes	Good
Little 2008	Yes	Yes	Yes	Yes	Yes	Fair
Lund, 2008	Yes	Yes	Yes	No	Yes	Fair
Lynch 2012	Yes	No	Yes	Yes	Yes	Fair
MacPherson 2015	Yes	Yes	Yes	Yes	Yes	Fair
Mannerkorpi 2009	No	Yes	Yes	No	Yes	Fair
Martin 2006	Yes	Yes	Yes	Unclear	Yes	Good
Martin 2012	No	Yes	Yes	No	Yes	Poor
Mazzuca 2004	Yes	Yes	Yes	No	Yes	Fair
Messier, 2004	Yes	Yes	Yes	No	Yes	Fair
Miyamoto 2013	Yes	Yes	Yes	Yes	Yes	Fair
Monticone, 2013	Yes	Yes	Yes	Unclear	Yes	Fair
Monticone, 2014	Yes	Yes	Yes	Unclear	Yes	Fair
Morone, 2009	Yes	Yes	Yes	Unclear	Yes	Fair
Morone, 2016	Yes	Yes	Yes	Yes	Yes	Fair
Nambi 2014	Yes	Yes	Yes	Unclear	Unclear	Fair
Nassif 2011	No	No	Yes	Unclear	Unclear	Poor
Natour 2015	Yes	Yes	Yes	Unclear	Yes	Fair
Nicholas 1991 Behav	No	Unclear	Yes	No	Yes	Poor
Nicholas 1992 Pain 1992;48:339–47	Yes	Yes	Yes	No	Yes	Fair
Osteras, 2014	No	No	Yes	Yes	Yes	Poor
Paolucci 2015	Yes	Yes	Yes	No	Unclear	Fair

Author, Year	Randomization	Concealed Treatment Allocation	Intention-to-Treat Analysis	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Compliance Acceptable in All Groups	Attrition Reported
Pennix, 2001 (FAST)	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes
Pennix, 2002 (FAST)	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes
Pennix, 2002 (FAST)	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes
Perlman 2012	Yes	Yes	Yes	Unclear	No	No	No	Yes	Yes
Poole 2007	Yes (minimization)	Yes (minimization)	Yes	Yes	No	No	No	Unclear	Yes
Quilty, 2003	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Quinn 2008	Yes	Unclear	Yes	Yes	Yes	No	Unclear	Yes	Yes
Redondo 2004	Yes	Unclear	Yes	Yes	No	No	No	Yes	Yes
Rejeski, 2002	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes
Rejeski, 2002	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes
Roche, 2007/2011	Yes	Yes	Yes	Yes	No	No	No	Unclear	Yes
Rosedale, 2014	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes
Rudolfsson 2014	Yes	Unclear	Unclear	Yes	No	No	Yes/No*	Unclear	Yes
Sahin 2010	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes
Sanudo 2010	Yes	Unclear	Yes	Yes	No	No	No	Yes	Yes
Sanudo 2012	Unclear	Unclear	No	Yes	No	No	No	No	Yes
Sanudo 2015	Unclear	Unclear	Yes	Unclear	No	No	No	Unclear	Yes
Saper 2017	Yes	Unclear	Yes	Yes	No	No	Yes	No	Yes
Saral 2016	Yes	Unclear	Yes	Yes	No	No	No	Unclear	Yes
Schimmel, 2009	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Schmidt 2011	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Seferiadis 2015	Yes	Yes	Yes	Yes	No	No	Yes/No*	No	Yes
Segal 2015	Yes	Yes	Yes	Unclear	No	No	No	Yes	Yes
Senna, 2011	Unclear	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes
Sherman 2005	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Sherman 2009	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Sherman 2011	Yes	Yes	Yes	Yes	No	No	Yes	Ye	Yes
Somers 2012	Yes	Yes	Yes	Yes	No	No	Yes/No (data	No	Yes
Soriano, 1998	Unclear	Unclear	No	Yes	Yes	Yes	Unclear	No	Yes
Stewart 2007	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Strand, 2001	Unclear	Unclear	Yes	Yes	No	No	Yes	Unclear	Yes
Stukstette, 2013	Yes	Yes	Yes	Yes	No	No	Yes	Unclear	Yes
Suarez-Almazo, 2010	Yes	Yes	Yes	Yes	Yes - sham No - waitlist	Yes - sham	Yes	Unclear	Yes

Author, Year	Attrition Acceptable	Attrition Between Groups Acceptable	Timing of Outcome Assessment in All Groups Similar	Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Pennix, 2001 (FAST)	Yes	Yes	Yes	No	Yes	Fair
Pennix, 2002 (FAST)	Yes	Yes	Yes	No	Yes	Fair
Pennix, 2002 (FAST)	Yes	Yes	Yes	No	Yes	Fair
Perlman 2012	Yes	Yes	Yes	Yes	Yes	Fair
Poole 2007	No	No	Yes	No	Yes	Poor
Quilty, 2003	Yes	Yes	Yes	No	Yes	Fair
Quinn 2008	Yes	Yes	Yes	Unclear	Yes	Fair
Redondo 2004	No	Yes	Yes	No	Yes	Poor
Rejeski, 2002	Yes	Yes	Yes	No	Yes	Fair
Rejeski, 2002	Yes	Yes	Yes	No	Yes	Fair
Roche, 2007/2011	Yes	No	Yes	Unclear	Yes	Fair
Rosedale, 2014	No	Yes	Yes	Yes	Yes	Fair
Rudolfsson 2014	No	Yes	Yes	Yes	Unclear	Fair
Sahin 2010	Yes	No	Yes	No	No	Fair
Sanudo 2010	Yes	Yes	Yes	Yes	Yes	Fair
Sanudo 2012	No	Yes	Yes	No	Unclear	Poor
Sanudo 2015	Yes	No	Yes	No	Yes	Poor
Saper 2017	Yes	Yes	Yes	Yes	Yes	Fair
Saral 2016	Yes	Yes	Yes	Yes	Yes	Fair
Schimmel, 2009	Yes	Yes	Yes	Unclear	Yes	Fair
Schmidt 2011	Yes	Yes (vs. attention control)	Yes	No	Yes	Fair
Sencan 2004	Unclear(method not described)	Unclear	Unclear	Yes	No	No
Seferiadis 2015	Yes	Yes	Yes	Yes	No	Fair
Segal 2015	No	Yes (3 months) No (9 months)	Yes	Yes	Yes	Fair at 3 months Poor at 9
Sencan 2004	No	Unclear	Yes	No	Yes	Poor
Senna, 2011	No	No	Yes	Unclear	Yes	Poor
Sherman 2005	Yes	Yes	Yes	Yes	Yes	Fair
Sherman 2009	Yes	Yes	Yes	No	Yes	Fair
Sherman 2011	Yes	Yes	Yes	Yes	Yes	Fair
Somers 2012	No	No	Yes	No	Yes	Poor
Soriano, 1998	No	No	Unclear	Unclear	Unclear	Poor
Stewart 2007	Yes	Yes	Yes	Yes	Yes	Fair
Strand, 2001	Yes	Yes	Yes	No	Yes	Poor
Stukstette, 2013	Yes	Yes	Yes	Yes	Yes	Fair
Suarez-Almazo, 2010	Yes	Yes	Yes	No	Yes	Good - sham Fair - waitlist

Author, Year	Randomization	Concealed Treatment Allocation	Intention-to-Treat Analysis	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Compliance Acceptable in All Groups	Attrition Reported
Sullivan, 1998	Unclear	Unclear	Unclear	No	No	No	Yes	Unclear	Yes
Tak 2005	Yes	Unclear	Yes	Yes	No	No	No/Yes (primary outcomes were patient reported and patient's	No	Yes
Tascioglu 2004	Yes	Unclear	Unclear	Yes	Unclear	Yes	Yes	Unclear	No
Tavafian, 2008	Unclear	Unclear	Yes	Yes	No	No	No	Unclear	Yes
Tavola 1992	Unclear	Unclear	Unclear	Yes	Yes	No	Yes	Yes	Yes
Teirlinck 2016	Yes	Yes	Yes	Yes	No	No	No	Yes/No (Yes during 3 month treatment period; No for booster sessions during	Yes
Thamsborg 2005	Unclear	Unclear	Yes	Yes	Yes	No	Yes	Yes	Yes
Thieme 2006	No	Unclear	Yes	Unclear	No	No	No	No	Yes
Thomas 2006	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Thomas, 2002	Unclear	Unclear	Yes	Yes	Unclear	No	Yes	No	Yes
Thorstensson, 2005	Yes	Unclear	Unclear	Yes	No	No	Unclear	Yes	Yes
Tilbrook 2011	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Tomas-Carus 2008/ Tomas-Carus 2009	Unclear	Unclear	No	Unclear	No	No	No	Yes	Yes
Trock 1994	Yes	Yes	Unclear	No	Yes	No	Yes	Unclear	No
Turner 1990	Unclear	Unclear	Yes	Yes	No	No	No	Unclear	Yes
UK BEAM Trial Team, 2004	Yes	Yes	Yes	Yes	No	No	No	No	Yes
Van der Roer 2008	Yes	Yes	Yes	Yes	No	No	NO	Unclear	Yes
van Eijk-Hustings 2013	Yes	Yes	Yes	Yes	No	No	No	No	Yes
van Santen 2002	Unclear	Unclear	Yes	No	No	No	Yes (CBO) No (PRO)	Unclear	Yes
Vas 2006	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Vas 2016	Yes	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes

Author, Year	Attrition Acceptable	Attrition Between Groups Acceptable	Timing of Outcome Assessment in All Groups Similar	Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Sullivan, 1998	No	No	Yes	No	Yes	Poor
Tak 2005	No	Yes	Yes	Unclear	Yes	Poor
Tascioglu 2004	Unclear	Unclear	Yes	No	Yes	Poor
Tavafian, 2008	No	Yes	Yes	Unclear	Yes	Poor
Tavola 1992	Yes	Yes	Yes	No	Yes	Poor
Teirlinck 2016	Yes	Yes	Yes	Yes	Yes	Fair
Thamsborg 2005	Yes	Yes	Yes	Yes	Yes	Fair
Thieme 2006	Yes	No	Unclear	No	Yes	Poor
Thomas 2006	Yes	Yes	Yes	Yes	Yes	Fair
Thomas, 2002	No	Yes	Yes	No	Unclear	Poor
Thorstensson, 2005	Yes	Yes	Yes	Yes	Yes	Fair
Tilbrook 2011	Yes	Yes	Yes	Yes (see note at end of text)	Yes	Fair
Tomas-Carus 2008/Tomas-Carus 2009	Yes	Yes	Yes	No	Unclear	Poor
Trock 1994	Unclear	Unclear	Yes	No	Yes	Poor
Turner 1990	No	No	Yes	No	Yes	Poor
UK BEAM Trial Team, 2004	Yes	Yes	Yes	Yes	Yes	Fair
Van der Roer 2008	Yes	Yes	Yes	Yes	Yes	Fair
van Eijk-Hustings 2013	Yes	Yes	Yes	Yes	Unclear	Fair
van Santen 2002	Yes	No	Yes	Unclear	Yes	Poor (all comparisons)
Vas 2006	No	Yes	Yes	No	Unclear	Fair
Vas 2016	Yes	Yes	Yes	Yes	Yes	Good

Author, Year	Randomization	Concealed Treatment Allocation	Intention-to-Treat Analysis	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Compliance Acceptable in All Groups	Attrition Reported
Verkaik 2014	Yes	Unclear	Yes	Yes	No	No	No	Yes	Yes
Viljanen 2003	Yes	Yes	Yes	No*	No	No	No	No**	Yes
Von Korff, 2005	Unclear	Unclear	Yes	Yes	No	No	Yes	Yes	Yes
Waling 2002	Unclear	Unclear	Yes	No	No	No	No	Unclear	Yes
Wang 2009	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Wang 2010	Yes	Yes	Yes	No	No	No	Yes (CBO) No (PRO)	No	Yes
Weng, 2009	Yes	Yes	Yes	Unclear	Unclear	No	Yes	Yes	Yes
White 2004	Yes	Unclear	Yes	Yes	Yes	No	Yes	Yes	Yes
Wigers 1996	Yes	Unclear	Yes	Yes	No	No	No	Unclear	Yes
Williams 2002	Unclear	Unclear	Unclear	Unclear	No	No	No	Unclear	Yes
Williams 2005	Yes	Unclear	Yes	Yes	No	No	Yes	Yes	Yes
Williams 2009	Unclear	Unclear	Yes	Yes	No	No	Yes	Yes	Yes
Williamson, 2007	Yes	Yes	Yes	Yes	No	No	Yes	Unclear	Yes
Witt, 2005	Yes	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes
Yildiz 2015	Yes	Unclear	Unclear	No	Yes	Yes	Unclear	Unclear	Yes
Yurtkuran, 2007	Yes	Unclear	Yes	Yes	Yes	No	Yes	Unclear	Yes
Zgierska 2016	Yes	Yes	Yes	No	No	No	Unclear	No	Yes
Zhang 2013	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes

Author, Year	Attrition Acceptable	Attrition Between Groups Acceptable	Timing of Outcome Assessment in All Groups Similar	Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Verkaik 2014	No	Yes	Yes	Yes	Yes	Poor
Viljanen 2003	Yes	Yes	Yes	No	Yes	Fair
Von Korff, 2005	Yes	Yes	Yes	Unclear	Yes	Fair
Waling 2002	No	Yes	Yes	No	Yes	Poor
Wang 2009	Yes	Yes	Yes	Yes	Yes	Fair
Wang 2010	Yes	Yes	Yes	Yes	Yes	Fair
Weng, 2009	Yes	No	Yes	No	Yes	Poor
White 2004	No	Yes	Yes	No	Yes	Fair
Wigers 1996	No	No (stress management vs. usual care and vs. exercise) Yes (exercise vs. usual care)	Yes	Unclear	Yes	Poor (stress management vs. usual care and vs. exercise) Fair (exercise vs. usual care)
Williams 2002	Yes	Yes	Yes	No	Unclear	Poor
Williams 2005	No	No	Yes	Unclear	Yes	Fair
Williams 2009	Yes	No	Yes	Unclear	Yes	Fair
Williamson, 2007	No	No	Yes	No	Yes	Poor
Witt, 2005	Yes	Yes	Yes	Yes	Yes	Fair
Yildiz 2015	Yes	Yes	Yes	No	Yes	Fair
Yurtkuran, 2007	Yes	Yes	Yes	No	Yes	Fair
Zgierska 2016	Yes	Yes	Yes	Yes	Yes	Poor
Zhang 2013	No	Yes	Yes	No	Yes	Fair

Table E-2. Quality assessment of crossover trials

Author, year	Randomization	Concealed treatment allocation	Intention-to-treat analysis	Independent or blind assessment	Appropriate washout period for condition	Attrition reported	Attrition acceptable	Number completing period reported; Attrition b/w periods acceptable (<10%)
Paolucci 2016	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes - first period; No - second period	Yes

Author, year	Results from first phase reported separately	Accounting for missing data	Use of methods for within-subject variation, correlated data	Analysis of carryover effect	Is there a registered or published protocol	Avoidance of selective outcomes reporting	Risk of bias (Cochrane Back Group
Paolucci 2016	Yes	No	Yes	No	Yes	Yes	Poor

Appendix F. Exercise Categories

Table F-1. Exercise and related intervention categories

General category	Types included
Muscle Performance	• Resistance training (strength, power or endurance exercises) • Sling exercise • Aquatic therapy/exercise • Musculoskeletal rehabilitation • Pilates
Neuromuscular Re-Education	• Motor control exercises (MCE) • Trunk coordination/trunk strengthening • Stabilization exercises • Posture training
Mobility, Flexibility	• McKenzie/directional preference • Stretching • Lumbar flexion exercises • Other mobility or flexibility exercises
Cardiovascular/Aerobic	• Cardiovascular training • Aerobic training • Walking • Aquatic therapy/exercise if aerobic focused
Combined Exercise	• Intervention combining exercises from two or more of the above categories

Appendix G. Strength of Evidence

All outcomes were considered direct; therefore, the Directness domain is not shown on the strength of evidence tables.
See Appendix B. Included Studies for references.

Table G-1. Low back pain (KQ 1) strength of evidence

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
Exercise	*Exercise vs. usual care, attention control, or a placebo intervention*	Function *Short-term*	6 (N=553) Costa 2009 Goldby 2006 Kankaanpaa 1999 Miyamoto 2013 Nassif 2011 Natour 2014	Moderate	Inconsistent	Precise	Undetected	Low	Pooled SMD -0.31 (95% CI -0.58 to -0.04); I^2=57%
		Function Intermediate-term	3 (N=332) Costa 2009 Goldby 2006 Kankaanpaa 1999	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled SMD -0.15 (95% CI -0.48 to 0.18); I^2=51%
		Function Long-term	1 (N=124) Goldby 2006	Moderate	Unknown	Imprecise	Undetected	Low	Difference 0.0 (95% CI -11.4 to 11.4) on the 0 to 100 ODI
		Pain *Short-term*	6 (N=553) Costa 2009 Goldby 2006 Kankaanpaa 1999 Miyamoto 2013 Nassif 2011 Natour 2014	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.81 (95% CI -1.26 to -0.36) on a 0 to 10 scale; I^2=0%
		Pain *Intermediate-term*	3 (N=332) Costa 2009 Goldby 2006 Kankaanpaa 1999	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled difference -1.37 (95% CI -2.10 to -0.65) on a 0 to 10 scale; I^2=34%

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
		Pain Long-term	1 (N=124) Goldby 2006	Moderate	Unknown	Imprecise	Undetected	Low	Difference -1.55 on a 0 to 10 scale (95% CI -2.78 to -0.32)
		Harms	2 (N=240) Costa 2009 Miyamoto 2013	Moderate	Consistent	Imprecise	Undetected	Low	No evidence of increased risk of serious harms
Psychological Therapy	*Psychological therapy vs. usual care or attention control*	Function *Short-term*	3 (N=1,028) Cherkin 2016 Lamb 2010 Poole 2007	Moderate	Consistent	Precise	Undetected	Moderate	Pooled SMD -0.25 (95% CI -0.38 to -0.12); I^2=0%
		Function *Intermediate-term*	3 (N=1,163) Cherkin 2016 Johnson 2007 Lamb 2010	Moderate	Consistent	Precise	Undetected	Moderate	Pooled SMD -0.25 (95% CI -0.37 to -0.13); I^2=0%
		Function *Long-term*	3 (N=1,163) Cherkin 2017 Johnson 2007 Lamb 2010	Moderate	Consistent	Precise	Undetected	Moderate	Pooled SMD -0.27 (95% CI -0.39 to -0.15); I^2=0%
		Pain *Short-term*	3 (N=1,028) Cherkin 2016 Lamb 2010 Poole 2007	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.76 (95% CI -0.99 to -0.53) on a 0 to 10 scale; I^2=0%
		Pain *Intermediate-term*	3 (N=1,163) Cherkin 2016 Johnson 2007 Lamb 2010	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.71 (95% CI -0.94 to -0.48); I^2=0%
		Pain *Long-term*	3 (N=1,163) Cherkin 2017 Johnson 2007 Lamb 2010	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.53 (95% CI -0.78 to -0.27); I^2=0%

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
	Psychological therapy vs. exercise	Function *Intermediate- and long-term*	1 (N=49) Turner 1990	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from 1 poor-quality trial
		Pain *Intermediate- and long-term*	1 (N=49) Turner 1990	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from 1 poor-quality trial
		Harms	1 (N=701) Lamb 2010/2012	Moderate	Unknown	Imprecise	Undetected	Low	One trial reported no serious adverse events and withdrawal due to adverse events in <1% of patients randomized to psychological therapy
Physical Modalities	*Short-wave diathermy vs. sham diathermy*	Pain, function, harms	1 (N=68) Gibson, 1985	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor-quality trial
	Ultrasound vs. sham ultrasound	Function *Short-term*	2 (N=505) Ebadi 2012 Licciardone 2013	Moderate	Inconsistent	Precise	Undetected	Insufficient	Inconsistent effects on function in two trials
		Pain *Short-term*	2 (N=505) Ebadi 2012 Licciardone 2013	Moderate	Consistent	Precise	Undetected	Low	No effects on pain in two trials
		Harms	1 (N=455) Licciardone	Moderate	Consistent	Imprecise	Undetected	Low	Any adverse event: RR 1.03 (95% CI 0.49 to 2.13) Serious adverse event: RR 0.48 (95% CI 0.12 to 1.88)
	Low-level laser therapy vs. sham laser	Function *Short-term*	1 (N=56) Basford 1999	Moderate	Unknown	Precise	Undetected	Low	Difference -8.2 (95% CI -13.6 to -2.8) on the 0 to 100 ODI
		Pain *Short-term*	1 (N=56) Basford 1999	Moderate	Unknown	Imprecise	Undetected	Low	Difference -16.0 (95% CI -28.3 to -3.7) on a 0 to 100 scale
	Low-level laser therapy vs. exercise therapy	Function *Intermediate-term*	1 (N=35) Djavid 2007	Moderate	Unknown	Imprecise	Undetected	Low	Difference -4.4 (95% CI -11.4 to 2.5) on the ODI (0 to 100 scale)
		Pain *Intermediate-term*	1 (N=35) Djavid 2007	High	Unknown	Imprecise	Undetected	Low	Difference -0.9 (95% CI -2.5 to 0.7) on a 0 to 10 scale

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
		Harms	3 (N=162) Djavid 2007 Basford 1999 Soriano 1998	Moderate	Consistent	Imprecise	Undetected	Low	No adverse events were reported
Manual Therapies	*Massage vs. sham massage, usual care, or attention control*	Function *Short-term*	4 (N=642) Ajimsha 2014 Cherkin 2011 Poole 2007 Quinn 2008	Moderate	Consistent	Imprecise	Undetected	Moderate	Pooled SMD -0.30 (95% CI -0.46 to -0.14); I^2=0%
		Function *Intermediate-term*	3 (N=713) Cherkin 2001 Cherkin 2011 Little 2008	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled SMD -0.09 (95% CI -0.24 to 0.06); I^2=0%
		Pain *Short-term*	4 (N=642) Ajimsha 2014 Cherkin 2011 Poole 2007 Quinn 2008	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.52 (95% CI -0.81 to -0.23) on a 0 to 10 scale; I^2=0%
		Pain *Intermediate-term*	3 (N=713) Cherkin 2001 Cherkin 2011 Little 2008	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled difference -0.01 (95% CI -0.40 to 0.38); I^2=0%
	Massage vs. exercise	Function Intermediate-term	1 (N=144) Little 2008	Moderate	Unknown	Imprecise	Undetected	Low	Difference 1.2 (95% CI -1.47 to 3.87) on the 0 to 24 Roland Disability Questionnaire
		Pain *Intermediate-term*	1 (N=144) Little 2008	Moderate	Unknown	Imprecise	Undetected	Low	Difference 0.60 (95% CI -0.67 to 1.87) on the 0 to 10 Von Korff pain scale
	Massage vs. sham, usual care, attention control, or exercise	Harms	4 (N=787) Ajimsha 2014 Cherkin 2001 Cherkin 2011 Little 2008	Moderate	Consistent	Imprecise	Undetected	Low	Two trials reported no serious adverse events; in four trials the proportion of massage patients with increased pain ranged from <1% to 26%

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
	Traction vs. sham traction	Function *Short-term*	2 (N=211) Beurskens 1997 Schimmel 2009	Moderate	Consistent	Imprecise	Undetected	Low	Differences 2 points on the ODI and 0.7 points on the Roland Disability Questionnaire, p>0.05 in both trials
		Pain *Short-term*	2 (N=211) Beurskens 1997 Schimmel 2009	Moderate	Consistent	Imprecise	Undetected	Low	Differences -4 points in one trial and 4 points in one trial, p>0.05 in both trials
		Harms	No studies	--	--	--	--	--	No evidence
	Spinal manipulation vs. sham manipulation, usual care, attention control, or placebo intervention	Function *Short-term*	3 (N=734) Haas 2014 Hondras 2009 Senna 2011	Moderate	Inconsistent	Precise	Undetected	Low	Pooled SMD -0.34 (95% CI -0.63 to -0.05); I^2=61%
		Function *Intermediate-term*	3 (N=1,185) Haas 2014 Senna 2011 UK BEAM 2004	Moderate	Inconsistent	Precise	Undetected	Low	Pooled SMD -0.40 (95% CI -0.69 to -0.11); I^2=76%
		Pain *Short-term*	3 (N=569) Gibson 1985 Haas 2014 Senna 2011	High	Inconsistent	Imprecise	Undetected	Low	Pooled difference -0.20 (95% CI -0.66 to 0.26) on a 0 to 10 scale; I^2=58%
		Pain *Intermediate-term*	3 (N=1,185) Haas 2014 Senna 2011 UK BEAM 2004	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.64 (95% CI -0.92 to -0.36); I^2=0%
	Spinal manipulation vs. exercise	Function *Short-term*	3 (N=776) Bronfort 2011 Ferreira 2007 Gudavalli 2006	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled SMD 0.01 (95% CI -0.22 to 0.25); I^2=62%
		Function *Intermediate-term*	4 (N=1,467) Bronfort 2011 Ferreira 2007 Gudavalli 2006 UK BEAM 2004	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled SMD 0.02 (95% CI -0.13 to 0.18); I^2=48%

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
		Pain *Short-term*	3 (N=776) Bronfort 2011 Ferreira 2007 Gudavalli 2006	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled difference 0.31 (95% CI -0.30 to 0.92) on a 0 to 10 scale; I^2=60%
		Pain *Intermediate-term*	3 (N=1,232) Bronfort 2011 Ferreira 2007 UK BEAM 2004	Moderate	Consistent	Imprecise	Undetected	Low	Pooled difference 0.22 (95% CI -0.09 to 0.52); I^2=9.4%
		Harms	7 (N=2,201) Bronfort 2011 Ferreira 2007 Gudavalli 2006 Haas 2014 Hondras 2009 Senna 2011 UK BEAM 2004	Moderate	Consistent	Precise	Undetected	Moderate	No serious adverse events or withdrawals due to adverse events in 7 trials. Nonserious adverse events (primarily increased pain) reported in 3 trials
Mindfulness Practices	*Mindfulness-based stress reduction vs. usual care or attention control*	Function *Short-term*	4 (N=577) Cherkin 2016 Morone 2009 Morone 2016 Zgierska 2017	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled SMD -0.25 (95% CI -0.53 to 0.04); I^2=53%
		Function *Intermediate-term*	1 (N=225) Cherkin 2016	Moderate	Unknown	Imprecise	Undetected	Low	SMD -0.20 (95% CI -0.47 to 0.06)
		Function *Long-term*	1 (N=228) Cherkin 2017	Moderate	Unknown	Imprecise	Undetected	Low	SMD -0.20 (95% CI -0.47 to 0.06)
		Pain *Short-term*	4 (N=577) Cherkin 2016 Morone 2009 Morone 2016 Zgierska 2017	Moderate	Consistent[a]	Precise	Undetected	Moderate	Pooled difference -0.76 (95% CI -1.13 to -0.39) on a 0 to 10 scale; I^2=29%
		Pain *Intermediate-term*	1 (N=225) Cherkin 2016	Moderate	Unknown	Precise	Undetected	Low	Difference -0.75 (95% CI -1.17 to -0.33)

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
		Pain *Long-term*	1 (N=228) Cherkin 2017	Moderate	Unknown	Precise	Undetected	Low	Difference -0.32 (95% CI -0.92 to 0.28)
		Harms	4 (N=577) Cherkin 2016 Morone 2009 Morone 2016 Zgierska 2017	Moderate	Consistent	Imprecise	Undetected	Low	One trial reported temporarily increased pain in 29% of patients undergoing MBSR and three trials reported no adverse events
Mind-Body Practices	*Yoga vs. attention control or wait list*	Function *Short-term*	6 (N=922) Groessl 2017 Saper 2017 Sherman 2005 Sherman 2011 Tilbrook 2011 Williams 2009	Moderate	Consistent	Precise	Undetected	Moderate	Pooled SMD -0.50 (95% CI -0.72 to -0.29); I^2=54%
		Function *Intermediate-term*	3 (N=584) Saper 2017 Tilbrook 2011 Williams 2009	Moderate	Consistent	Imprecise	Undetected	Low	Pooled SMD -0.33 (95% CI -0.49 to -0.16); I^2=0%
		Pain *Short-term*	5 (N=770) Groessl 2017 Saper 2017 Sherman 2005 Sherman 2011 Williams 2005	Moderate	Consistent	Imprecise	Undetected	Low	Pooled difference -1.10 (95% CI -1.77 to -0.42) on a 0 to 10 scale; I^2=74%
		Pain *Intermediate-term*	2 (N=271) Saper 2017 Williams 2009	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -1.17 (95% CI -1.91 to -0.44); I^2=26%
	Yoga vs. exercise	Function *Short-term*	3 (N=369) Saper 2017 Sherman 2005 Sherman 2011	Moderate	Consistent	Imprecise	Undetected	Low	Pooled SMD -0.10 (95% CI -0.34 to 0.13); I^2=38%

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
		Function *Intermediate-term*	1 (N=181) Saper 2017	Moderate	Unknown	Imprecise	Undetected	Low	SMD -0.01 (95% CI -0.26 to 0.24)
		Pain *Short-term*	4 (N=429) Nambi 2014 Saper 2017 Sherman 2005 Sherman 2011	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled difference -0.89 (95% CI -1.99 to 0.21) on a 0 to 10 scale; I^2=92%
		Pain *Intermediate-term*	1 (N=181) Saper 2017	Moderate	Unknown	Imprecise	Undetected	Low	Difference 0.30 (95% CI -0.39 to 0.99)
		Harms	3 (N=616) Saper 2017 Sherman 2011 Tilbrook 2011	Moderate	Consistent	Imprecise	Undetected	Low	No difference in risk of any adverse event; one trial reported one serious adverse event (cellulitis)
	Qi Gong vs. exercise therapy	Function *Short-term*	1 (N=125) Blodt 2015	Moderate	Unknown	Imprecise	Undetected	Low	Difference 0.9 (95% CI -0.1 to 2.0) on the 0 to 24 Roland Disability Questionnaire
		Function *Intermediate-term*	1 (N=125) Blodt 2015	Moderate	Unknown	Precise	Undetected	Low	Difference 1.2 (95% CI 0.1 to 2.3) on the Roland Disability Questionnaire
		Pain *Short-term*	1 (N=125) Blodt 2015	Moderate	Unknown	Precise	Undetected	Low	Difference 7.7 (95% CI 0.7 to 14.7) on a 0 to 100 scale
		Pain *Intermediate-term*	1 (N=125) Blodt 2015	Moderate	Unknown	Imprecise	Undetected	Low	Difference 7.1 (95% CI -1.0 to 15.2) on a 0 to 100 scale
		Harms	1 (N=125) Blodt 2015	Moderate	Unknown	Imprecise	Undetected	Low	No difference in risk of adverse events
Acupuncture	*Acupuncture vs. sham acupuncture, usual care, attention control, or a*	Function *Short-term*	4 (N=1,672) Brinkhaus 2006a Cherkin 2009 Cho 2013 Haake 2007	Moderate	Inconsistent	Precise	Undetected	Low	Pooled SMD -0.22 (95% CI -0.35 to -0.08); I^2=44%

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
	placebo intervention	Function Interme-diate-term	3 (N=1,032) Brinkhaus 2006a Cherkin 2001 Cherkin 2009	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled SMD -0.08 (95% CI -0.36 to 0.20); I^2=75%
		Function Long-term	1 (N=215) Thomas 2006	Moderate	Unknown	Imprecise	Undetected	Low	Adjusted difference -3.4 (95% CI -7.8 to 1.0) on the 0 to 100 ODI
		Pain *Short-term*	5 (N=2,176) Brinkhaus 2006a Carlsson 2001 Cherkin 2009 Cho 2013 Haake 2007	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.55 (95% CI -0.86 to -0.24) on a 0 to 10 scale; I^2=30%
		Pain *Intermediate-term*	5 (N=812) Brinkhaus 2006a Carlsson 2001 Cherkin 2009 Cherkin 2009 Thomas 2006	Moderate	Consistent	Imprecise	Undetected	Low	Pooled difference -0.25 (95% CI -0.67 to 0.16) on a 0 to 10 scale; I^2=33%
		Pain *Long-term*	1 (N=215) Thomas 2006	Moderate	Unknown	Precise	Undetected	Low	Difference -0.83 (95% CI -1.51 to -0.15) on a 0 to 10 scale
		Harms	6 (N=2,525) Brinkhaus 2006a Cherkin 2001 Cherkin 2009 Cho 2013 Haake 2007 Thomas 2006	Moderate	Consistent	Imprecise	Undetected	Low	No evidence of increased risk of serious harms
Multi-disciplinary Rehabilitation	*Multi-disciplinary rehabilitation vs. usual care*	Function *Short-term*	4 (N=945) Bendix 1996 Harkapaa 1989 Lambeek 2010 von Korff 2005	Moderate	Inconsistent	Precise	Undetected	Low	Pooled SMD -0.31 (95% CI -0.57 to -0.05); I^2=70%

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
		Function *Intermediate-term*	4 (N=524) Abbassi 2012 Lambeek 2010 Strand 2001 von Korff 2005	Moderate	Inconsistent	Precise	Undetected	Low	Pooled SMD -0.37 (95% CI -0.64 to -0.10); I^2=50%
		Function *Long-term*	2 (N=346) Bendix 1996, von Korff 2005	Moderate	Consistent	Imprecise	Undetected	Low	Pooled SMD -0.04 (95% CI -0.31 to 0.24); I^2=35%
		Pain *Short-term*	4 (N=945) Bendix 1996 Harkapaa 1989 Lambeek 2010 von Korff 2005	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.51 (95% CI -0.89 to -0.13) on a 0 to 10 scale; I^2=23%
		Pain *Intermediate-term*	4 (N=524) Abbassi 2012 Lambeek 2010 Strand 2001 von Korff 2005	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.63 (95% CI -1.04 to -0.22); I^2=0%
		Pain *Long-term*	2 (N=346) Bendix 1996, von Korff 2005	Moderate	Consistent	Imprecise	Undetected	Low	Pooled difference -0.34 (95% CI -0.86 to 0.18); I^2=0%
	Multi-disciplinary rehabilitation vs. exercise	Function *Short-term*	6 (N=430) Bendix 1995 Jousset 2004 Monticone 2014 Nicholas 1991 Nicholas 1992 van der Roer 2008	Moderate	Consistent	Precise	Undetected	Moderate	Pooled SMD -0.28 (95% CI -0.54 to -0.01); I^2=39%
		Function *Intermediate-term*	5 (N=479) Bendix 2000 Nicholas 1991 Roche 2007/2011, Turner 1990 van der Roer 2008	Moderate	Consistent[b]	Precise	Undetected	Moderate	Pooled SMD -0.22 (95% CI -0.40 to -0.03); I^2=0%

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction, and Magnitude of Effect
		Function *Long-term*	2 (N=180) Bendix, 1995X Turner 1990	Moderate	Consistent[b]	Imprecise	Undetected	Low	Pooled SMD -0.06 (95% CI -0.36 to 0.25); I^2=0%
		Pain *Short-term*	6 (N=430) Bendix 1995 Jousset 2004 Monticone 2014 Nicholas 1991 Nicholas 1992 van der Roer 2008	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.75 (95% CI -1.18 to -0.31) on a 0 to 10 scale; I^2=0%
		Pain *Intermediate-term*	5 (N=479) Bendix 2000 Nicholas 1991 Roche 2007/2011, Turner 1990 van der Roer	Moderate	Consistent[b]	Precise	Undetected	Moderate	Pooled difference -0.55 (95% CI -0.95 to -0.15); I^2=0%
		Pain *Long-term*	2 (N=180) Bendix, 1995 Turner 1990	Moderate	Consistent[b]	Imprecise	Undetected	Low	Pooled difference 0.00 (95% CI -0.94 to 0.95); I^2=0%
		Harms	2 (N=94) Monticone 2014 Tavafian 2008	High	Consistent	Imprecise	Undetected	Insufficient	Insufficient data on harms from 2 trials, though no serious harms were reported

a Outlier trial excluded, Banth 2015
b Outlier trial excluded, Monticone 2013

Table G-2. Neck pain (KQ 2) strength of evidence

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
Exercise	*Exercise vs. attention control, no treatment or advice alone*	Function *Short-term*	3 (N=444) Stewart 2007 Lauche 2016 Viljanen 2003	Moderate	Inconsistent[a]	Imprecise	Undetected	Low	Pooled SMD, (3 trials) -0.23, 95% CI -0.61 to 0.15, I^2=72.6% Combination exercise only (2 trials), pooled SMD -0.44, 95% CI -0.76 to -0.09
		Function *Intermediate-term*	1 (N=230) Viljanen 2003	Moderate	Unknown	Imprecise	Undetected	Low	SMD 0.14, 95% CI -0.12, 0.40)
		Function *Long-term*	1 (N=125) Stewart 2007	Moderate	Unknown	Imprecise	Undetected	Low	SMD -0.38, 95% CI -0.74 to -0.03
		Pain *Short-term*	3 (N=444) Stewart 2007 Lauche 2016 Viljanen 2003	Moderate	Inconsistent[a]	Imprecise	Undetected	Low	Pooled difference -0.72, 95% CI -1.49 to 0.06, I^2=63.7% Combination exercise only (2 two trials), pooled difference -1.12, 95% CI -1.82 to -0.43
		Pain *Intermediate-term*	2 (N=353) Andersen 2008 Viljanen 2003	Moderate	Consistent	Precise	Undetected	Low	Pooled difference -0.26, 95% CI -0.70 to 0.19, I^2=0.0%
		Pain *Long-term*	3 (N=349) Stewart 2007 Andersen 2008 Waling 2002	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled difference 0.12, 95% CI -0.52 to 0.76, I^2=37.8%
		Harms	2 (N=201) Stewart 2007 Lauche 2016	High	Consistent	Imprecise	Undetected	Low	No evidence of increased risk of serious harms

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
	Exercise vs. pharmaco-logical therapy	Pain, Function, Harms *Short- and Intermediate-term*	1 (N=40) Aslan Telci 2012	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient data from 1 poor quality trial
Psychological Therapies	*Relaxation training vs. no intervention*	Function *Short-term*	1 (N=258) Viljanen 2003	Moderate	Unknown	Imprecise	Undetected	Low	Adjusted difference 0.1 (95% CI -2.9 to 3.2) on 0-80 scale
		Function *Intermediate-term*	1 (N=258) Viljanen 2003	Moderate	Unknown	Imprecise	Undetected	Low	Adjusted difference 0.2 (95% CI -2.8, 3.1) on 0-80 scale
		Pain *Short-term*	1 (N=258) Viljanen 2003	Moderate	Unknown	Imprecise	Undetected	Low	Adjusted difference 0.2 (95% CI -0.4 to 0.8) on 0-10 scale
		Pain *Intermediate-term*	1 (N=258) Viljanen 2003	Moderate	Unknown	Imprecise	Undetected	Low	Adjusted difference 0.2 (95% CI -0.3 to 0.8) on 0-10 scale
	Relaxation training vs. exercise	Function *Short-term*	1 (N=263) Viljanen 2003	Moderate	Unknown	Imprecise	Undetected	Low	Adjusted difference 0.2 (95% CI -2.8 to 3.2) on 0-80 scale
		Function *Intermediate-term*	1 (N=263) Viljanen 2003	Moderate	Unknown	Imprecise	Undetected	Low	Adjusted difference 0.2 (95% CI -2.7 to 3.2) on 0-80 scale
		Pain *Short-term*	1 (N=263) Viljanen 2003	Moderate	Unknown	Imprecise	Undetected	Low	Adjusted difference -0.2 (95% CI -0.8 to 0.4) on 0-10 scale
		Pain *Intermediate-term*	1 (N=263) Viljanen 2003	Moderate	Unknown	Imprecise	Undetected	Low	Adjusted difference -0.2 (95% CI -0.8 to 0.3) on 0-10 scale
	Relaxation training vs. no intervention or exercise	Harms							No evidence
Physical Modalities	*Traction vs. attention control*	Function, Pain, Harms *Short-term*	1 (N=79) Chiu 2011	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor-quality trial.
	Laser vs. sham intervention	Function *Short-term*	2 (N=144) Chow 2006 Gur 2004	Low	Consistent	Imprecise	Undetected	Moderate	Pooled difference -14.98, (95% CI -23.88 to -6.07) on a 0-100 scale: I^2=39%

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Pain *Short-term*	3 (N=192) Chow 2006 Gur 2004 Altan 2005	Low	Consistent[b]	Imprecise	Undetected	Moderate	Pooled difference -1.81, (95% CI -3.35 to -0.27) on a 0-10 scale: I^2=76%
		Harms	1 (N=90) Chow 2006	Low	Unknown	Imprecise	Undetected	Low	Adverse effects occurred with similar frequency in both groups. The most frequently reported adverse effects in the intervention group included mild (78%) or moderate (60%) increased neck pain, increased pain elsewhere (78%), mild headache (60%) and tiredness (24%).
	Electro-magnetic fields vs. sham intervention	Function, Pain, Harms *Short-term*	1 (N=70) Trock 1994	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor-quality trial.
Manual Therapies	*Massage vs. attention control*	Function *Short-term*	1 (N=58) Sherman 2009	Moderate	Unknown	Imprecise	Undetected	Low	Success (≥5 points) RR 2.7 (95% CI .99 to 7.5)
		Function *Intermediate-term*	1 (N=58) Sherman 2009	Moderate	Unknown	Imprecise	Undetected	Low	Success (≥5 points) RR 1.8 (95% CI .97 to 3.5)
	Massage vs. exercise	Pain *Intermediate-term*	1 (N=85) Rudolfsson 2014	Moderate	Unknown	Imprecise	Undetected	Low	MD 0.2 (95% CI -0.82 to 1.22) on the 0-10 NRS
	Massage vs. attention control or vs. exercise	Harms	2 (N=143) Sherman 2009 Rudolfsson 2014	Moderate	Unknown	Imprecise	Undetected	Low	No evidence of increased risk of serious harms
Mind-body Practices	*Alexander Technique plus usual care vs. usual care alone*	Function *Short-term*	1 (N=344) MacPherson 2015	Moderate	Unknown	Imprecise	Undetected	Low	Difference -5.56 (95% CI -8.33 to -2.78) on 0-100% scale
		Function *Intermediate-term*	1 (N=344) MacPherson 2015	Moderate	Unknown	Imprecise	Undetected	Low	Difference -3.92 (95% CI -6.87 to -0.97) on 0-100% scale

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Harms	1 (N=344) MacPherson 2015	Moderate	Unknown	Imprecise	Undetected	Low	No clear difference in the risk of any non-serious adverse event (e.g., pain and incapacity, knee injury, muscle spasm, and complications after surgery): RR 2.25 (95% CI 1.00 to 5.04) No serious treatment-related adverse events reported.
	Basic body awareness therapy vs. exercise	Function *Short-term*	1 (N=113) Seferiadis 2016	Moderate	Unknown	Imprecise	Undetected	Low	Difference between groups in mean change from baseline -1, p>0.05
		Function *Intermediate- and long-term*	1 (N=139) Lansinger 2007	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor-quality trial
		Pain *Intermediate- and long-term*	1 (N=139) Lansinger 2007	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor-quality trial
		Harms	1 (N=113) Seferiadis 2016	Moderate	Unknown	Imprecise	Undetected	Low	No serious adverse effects Any non-serious adverse effects: RR 0.65 (95% CI 0.37 to 1.14)
Acupuncture	Acupuncture vs. sham, placebo or usual care	Function *Short-term*	5 (N=959) White 2004 Liang 2011 Zhang 2013 MacPherson 2015 Ho 2017	Moderate	Inconsistent	Precise	Undetected	Low	Pooled SMD -0.40 (95% CI -0.64 to -0.17); I^2=67.7%
		Function *Intermediate-term*	3 (N=563) White 2004 Zhang 2013 MacPherson 2015	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled SMD -0.19 (95% CI -0.35 to -0.02); I^2=0%
		Function *Long- term*	1 (N=107) White 2004	Moderate	Unknown	Imprecise	Undetected	Low	Difference -1.8 (95% CI -4.84 to 1.24) on a 0-50 scale

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Pain *Short-term*	4 (N=490) Sahin 2010 White 2004 Liang 2011 Zhang 2013	Moderate	Inconsistent	Precise	Undetected	Low	Pooled difference -0.27 (95% CI -0.59 to 0.05) on a 0-10 scale; I^2=2%
		Pain *Intermediate-term*	3 (N=354) White 2004 Vas 2006 Zhang 2013	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled difference 0.45 (95% CI -0.34 to 1.25) on a 0-10 scale; I^2=59%
		Pain *Long- term*	1 (N=107) White 2004	Moderate	Unknown	Imprecise	Undetected	Low	Pooled difference -0.35 (95% CI -1.34 to 0.64) on a 0-10 scale
	Acupuncture vs. pharmaco-logical care	Function *Short-term*	1 (N=30) Cho 2014	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence due to study limitations, unknown consistency and imprecision from one poor-quality study
		Pain *Short-term*	2 (N=53) Birch 1998 Cho 2014	High	Consistent	Imprecise	Undetected	Insufficient	Insufficient evidence due to study limitations and imprecision from 2 poor quality studies
	Acupuncture vs. sham, placebo, usual care or pharmaco-logical care	Harms	5 (N=907) MacPherson 2015 Vas 2006 White 2004 Liang 2011 Zhang 2013	Moderate	Consistent	Precise	Undetected	Moderate	No serious treatment-related adverse events reported. Most common non-serious adverse effects included numbness/ discomfort, fainting and bruising.

CI = confidence interval; RCT = randomized controlled trial; RR = risk ratio; SMD = standardized mean difference.

a Outlier trial excluded, Li 2017b Heterogeneity is explained in part by the contribution of the good quality study; the others are fair.

Table G-3. Knee osteoarthritis (KQ 3) strength of evidence

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
Exercise	*Exercise vs. usual care, attention control, or no intervention*	Function *Short-term*	7 (N=641) Bennell 2005 Quilty 2003 Lund 2008 Williamson 2007 Rosedale 2014 Thorstensson 2005 Segal 2015	Moderate	Consistent	Precise	Undetected	Moderate	Pooled SMD -0.25 (95% CI -0.4 to -0.09, I^2=0%)
		Function *Intermediate-term*	9 (N=637) Sullivan 1998 Quilty 2003 Messier 2004 Huang 2005a Huang 2005 b Weng 2009 Huang 2003 Chen 2014 Segal 2015	Moderate	Inconsistent[a]	Precise	Undetected	Low	Pooled SMD -0.78 (95% CI -1.37 to -0.19, I^2=91.4%)
		Function *Long-term*	2 (N= 913) Messier 2004 Thomas 2002	High	Consistent	Precise	Undetected	Low	Pooled SMD -0.24 (95% CI -0.37 to -0.11 I^2=0%)
		Pain *Short-term*	7 (N=641) Bennell 2005 Quilty 2003 Lund 2008 Williamson 2007 Rosedale 2014 Thorstensson 2005 Segal 2015	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference on 0-10 scale: -0.44, (95% CI -0.82 to -0.05, I^2=35%)

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Pain *Intermediate-term*	9 (N=638) Sullivan 1998 Quilty 2003 Messier 2004 Huang 2005a Huang 2005b Weng 2009 Huang 2003 Chen 2014 Segal 2015	Moderate	Inconsistent	Precise	Undetected	Low	Pooled difference on a 0-10 scale: -1.61 (95% CI -2.51 to -0.72, I^2=91%)
		Pain *Long-term*	2 (N=914) Messier 2004 Thomas 2002	High	Consistent	Precise	Undetected	Low	Pooled difference on a 0-10 scale: -0.24 (95% CI -0.72 to 0.24, I^2=55%)
		Harms	7 (N=1004) Bennell 2005 Weng 2009 Huang 2003 Chen 2014 Thorstensson Ettinger 1997 Abbott 2013	Moderate	Consistent	Precise	Undetected	Moderate	One trial reported greater temporary, minor increases in pain in the exercise group versus a sham group; however, four trials found no difference in worsening of pain symptoms with exercise vs. comparators. One trial found no difference in falls or deaths.
Psychological Therapies	*CBT/pain coping skills training vs. usual care*	Function, Pain *Short-term to long-term*	2 (N=222) Helminen 2015 Somers 2012	Moderate	Consistent	Imprecise	Undetected	Low	No differences in one fair quality trial of CBT and one poor quality trial of pain coping skills training averaged over 6 to 12 months (intermediate to long term) and 1.5 to 10.5 months (short to intermediate term).
		Harms	2 (N=222) Helminen 2015 Somers 2012	Moderate	Consistent	Imprecise	Undetected	Low	No adverse events observed in two trials.

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
Psychological Therapies	*pain coping skills training vs. exercise*	Function *Short-term and intermediate term*	1 (N=149) Bennell 2016	Moderate	Unknown	Precise	Undetected	Low	No difference in WOMAC physical 0-68 Short-term: difference 2.0 (95% CI -2.4 to 6.4), p=0.37 Intermediate-term: MD 3.2 (95% CI -0.6 to 7.0), p=0.10
		Pain *Short-term and intermediate term*	1 (N=149) Bennell 2016	Moderate	Unknown	Precise	Undetected	Low	No difference in WOMAC pain 0-20) Short-term: difference -0.1 (95% CI -1.2 to 1.0) Intermediate-term: difference 0.4 (95% CI -0.8 to 1.6), p=0.49)
		Harms	1 (N=149) Bennell 2016	Moderate	Unknown	Precise	Undetected	Low	Knee pain was more common in the exercise group during treatment (31% versus 3%) and during short and intermediate term followup (10% versus 7%) as was overall body pain (15% versus 2%)
Physical Modalities	*Ultrasound vs. sham*	Function, *Short-term*	1 (N=90) Yildiz 2015	Moderate	Unknown	Imprecise	Undetected	Low	Continuous and pulsed ultrasound vs. sham, 0-24 scale, differences: -6.2 (95% CI -8.36 to -4.20) and -5.71 (95% CI -7.72 to -3.70)
		Function *Intermediate-term*	1 (N=60) Cakir 2014	Moderate	Unknown	Imprecise	Undetected	Low	Continuous and pulsed ultrasound vs. sham, 0-68 scale, differences: -2.9 (95% CI -9.19 to 3.39) and 1.6 (95% CI -3.01 to 6.22)
		Pain *Short-term*	1 (N=90) Yildiz 2015	Moderate	Unknown	Imprecise	Undetected	Low	Continuous and pulsed ultrasound vs. sham, 0-10 scale, differences -3.3 (95% CI -4.64 to -1.96) and -3.37, (95% CI -4.73 to -2.01)

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Pain *Intermediate-term*	1 (N=60) Cakir 2014	Moderate	Unknown	Imprecise	Undetected	Low	Continuous and pulsed ultrasound vs. sham, 0-20 scale, differences: -1.6 (95% CI -3.26 to 0.06) vs. 0.2 (95% CI -1.34 to 1.74); also no difference between groups for other pain measures.
		Harms	2 (N=150) Cakir 2014 Yildiz 2015	Moderate	Unknown	Imprecise	Undetected	Low	No adverse events reported during the two trials
	TENS vs. sham	Function *Intermediate-term*	1 (N=70) Fary 2011	Low	Unknown	Imprecise	Undetected	Low	Difference in mean change -1.9 (95% CI -9.7 to 5.9) on a 0-100 scale; Proportion of patients who achieved MCID (≥9.1) in WOMAC function: 38% vs 39%, RR 1.2 (95% CI 0.6 to 2.2)
		Pain *Intermediate-term*	1 (N=70) Fary 2011	Low	Unknown	Imprecise	Undetected	Low	Dfference in mean change 0.9 (95% CI -11.7 to 13.4) on 0-100 VAS and -5.6 (95% CI -14.9 to 3.6) on 0-100 WOMAC pain scale. Proportion of patients who achieved MCID (≥20) in pain VAS: 56% vs 44%, RR 1.3 (95% CI 0.8 to 2.0)
		Harms	1 (N=70) Fary 2011	Low	Unknown	Imprecise	Undetected	Low	No evidence of increased risk of serious harms; no differences between treatments for harms (RR 1.06, 95% CI 0.38 to 2.97)
	Low level laser therapy	Function *Short-term*	1 (N=49) Al Rashoud 2014	Moderate	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one small fair quality trial

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
	vs. sham laser	Function *Intermediate-term*	2 (N=109) Al Rashoud 2014 Tascioglu 2004	High	Inconsistent	Imprecise	Undetected	Insufficient	Insufficient evidence from one small fair trial and one poor quality trial
		Pain *Short-term*	2 (N=84) Al Rashoud, 2014 Hegedus 2009	High	Inconsistent	Precise	Undetected	Insufficient	Insufficient evidence from two small trials, one fair trial and one poor quality
		Pain *Intermediate-term*	2 (N=109) Al Rashoud, 2014 Tascioglu, 2004	High	Inconsistent	Precise	Undetected	Insufficient	Insufficient evidence from one small fair trial and one poor quality trial
		Harms	2 (N=109) Al Rashoud, 2014 Tascioglu, 2004	High	Consistent	Imprecise	Undetected	Insufficient	Data for harms was insufficient. No adverse events were reported.
	Microwave diathermy vs. sham	Function *Short-term*	1 (N=63) Giombini 2011	Moderate	Unknown	Imprecise	Undetected	Insufficient	There was insufficient evidence to determine short-term effects or harms from one small trial microwave diathermy
		Pain *Short-term*	1 (N=63) Giombini 2011	Moderate	Unknown	Imprecise	Undetected	Insufficient	There was insufficient evidence to determine short-term effects or harms from one small trial microwave diathermy; substantial imprecision noted
		Harms	1 (N=63) Giombini 2011	Moderate	Unknown	Imprecise	Undetected	Insufficient	Data for harms were insufficient. However, no serious adverse events occurred in either group. Two patients in the diathermy group reported transient aggravation of symptoms.
	Pulsed Short-wave	Function *Short-term*	1 (N=115) Laufer 2005	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor quality trial

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
	Diathermy vs. Sham	Function *Long-term*	1 (N=86) Fukuda 2011	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor quality trial
		Pain *Short-term*	1 (N=115) Laufer 2005	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor quality trial
		Pain *Long-term*	1 (N=86) Fukuda 2011	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor quality trial
		Harms	2 (N=201) Laufer 2005 Fukuda 2011	High	Unknown	Imprecise	Undetected	Insufficient	Data were insufficient for harms. No adverse events were reported by either trial.
	Electro-magnetic fields vs. sham	Function *Short-term*	2 (N=180) Battisti 2004 Thamsborg 2005	Moderate	Consistent	Imprecise	Undetected	Low	The fair quality trial: (WOMAC) activities of daily living subscale (0-85) mean difference -3.48 (95% CI -4.44 to -2.51)
		Pain *Short-term*	2 (N=180) Battisti 2004 Thamsborg 2005	Moderate	Consistent	Imprecise	Undetected	Low	The fair quality trial: WOMAC-pain subscale (0-25) versus sham, -0.84 (95% CI -1.10 to -0.58).
		Harms	1 (N=90) Thamsborg 2005	Moderate	Unknown	Imprecise	Undetected	Low	More patients who received real versus sham electromagnetic field therapy reported throbbing or warming sensations or aggravation of pain; however the difference was not significant (RR 1.95, 95% CI 0.81 to 4.71)
	Superficial heat vs. placebo	Pain *Short-term*	1 (N=52) Mazzuca 2004	Moderate	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one small, fair-quality trial
		Harms	1 (N=52) Mazzuca 2004	Moderate	Unknown	Imprecise	Undetected	Insufficient	Data was insufficient for harms; no adverse events were reported

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
	Brace vs. usual care	Function, Pain, Harms *Intermediate- and long-term*	1 (N=118) Brouwer 2006	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor quality trial
Manual Therapies	*Manipulation vs. usual care*	Function, Harms *Intermediate-term*	1 (N=58 knee OA) Abbott 2013	Moderate	Unknown	Unknown	Undetected	Insufficient	Insufficient evidence from one fair-quality trial; inadequate data to determine effect sizes or statistical significance
	Manipulation vs. exercise	Function, Harms *Intermediate-term*	1 (N=59 knee OA) Abbott 2013	Moderate	Unknown	Unknown	Undetected	Insufficient	Insufficient evidence from one fair-quality trial; inadequate data to determine effect sizes or statistical significance
	Massage vs. usual care	Function, Pain, Harms *Short-term*	1 (N=125) Perlman 2012	Moderate	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one fair-quality trial.
Mind-body Practices	*Tai Chi vs. attention control*	Function *Short-term*	2 (N=81) Brismee 2007 Wang 2009	High	Consistent	Imprecise	Undetected	Insufficient	Insufficient evidence from two small, unblinded trials; (one fair, one poor quality)
		Function *Intermediate-term*	1 (N=40) Wang 2009	Moderate	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from two small, unblinded trials (one fair, one poor quality)
		Pain *Short-term*	2 (N=81) Brismee 2007 Wang 2009	High	Consistent	Imprecise	Undetected	Insufficient	Insufficient evidence from two small, unblinded trials (one fair, one poor quality)
		Pain *Intermediate term*	1 (N=40) Wang 2009	Moderate	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from two small, unblinded trials (one fair, one poor quality)
		Harms	2 (N=81) Brismee 2007 Wang 2009	High	Consistent	Imprecise	Undetected	Insufficient	Insufficient evidence from two small, unblinded trials(one fair, one poor quality)

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
Acupuncture	*Acupuncture vs. usual care, no treatment, waitlist, or sham*	Function *Short-term*	4 (N=871) Jubb 2008 Suarez-Almazo 2010 Yurturan 2007 Witt 2005	Moderate	Inconsistent[b]	Precise	Undetected	Low	Pooled SMD -0.05, 95% CI -0.32 to 0.38)
		Function *Intermediate-term*	4 (N=767) Berman 2004 Lansdown 2009 Witt 2005 Hinman 2014	Moderate	Consistent	Precise	Undetected	Moderate	Pooled SMD[c] -0.15, 95% CI -0.31 to 0.02, I^2=0%
		Pain *Short-term*	6 (N=1065) Berman 1999 Jubb 2008 Suarez-Almazo 2010 Williamson 2007 Witt 2005 Yurturan 2007	Moderate	Inconsistent	Precise	Undetected	Low	Pooled SMD -0.27, 95% CI -0.56 to 0.02, I^2=75%
		Pain *Intermediate term*	4 (N=767) Lansdown 2009 Witt 2005 Hinman 2014 Berman 2004	Moderate	Consistent	Imprecise	Undetected	Moderate	Pooled SMD - 0.16, 95% CI -0.31 to -0.02, I^2=0%); Individually no trial reached statistical significance.

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Harms	9 (N=1796) Berman 2004 Berman 1999 Hinman 2014 Jubb 2008 Lansdown 2009 Suarez-Almazo 2010 Witt 2005 Williamson 2007 Yurtkuran 2007	Moderate	Consistent	Imprecise	Undetected	Moderate	There is no apparent difference in risk of serious adverse events between any form of acupuncture and the control group. Worsening of symptoms (7%-14%), mild bruising, swelling or pain at the acupuncture site (1%-18%) were most common; One case of infection at an electroacupuncture site was reported.
	Acupuncture vs. exercise	Function, Pain, Harms *Short-term*	1 (N =120) Williamson	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor-quality trial.

CI = confidence interval; OA: osteoarthritis; MCID = minimal clinically important difference; RCT = randomized controlled trial; RR = risk ratio; SMD = standardized mean difference; TENS = transcutaneous electrical stimulation; VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

a Outlier excluded, Dias 2003.

b Outlier excluded, Berman 1999.

c Estimate based on proximal likelihood methods. Results for all trials individually were not statistically significant.

Table G-4. Hip osteoarthritis (KQ 3) strength of evidence

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
Exercise	*Exercise vs. usual care*	Function *Short-term*	3 (N=377) Juhakoski 2011 Teirlinck 2016 Tak 2005	Moderate	Consistent	Precise	Undetected	Low	Pooled SMD -0.33, 95% CI -0.53 to -0.12, I^2=0%
		Function *Intermediate-term*	2 (N=307) Juhakoski 2011 Teirlinck 2016	Moderate	Consistent	Precise	Undetected	Low	Pooled SMD -0.28, 95% CI -0.50 to -0.05, I^2=0%
		Function *Long-term*	1 (N=118) Juhakoski 2011	Moderate	Unknown	Imprecise	Undetected	Insufficient	SMD -0.37, 95% CI -0.74 to -0.01
		Pain *Short-term*	3 (N=371) Juhakoski 2011 Teirlinck 2016 Tak 2005	Moderate	Inconsistent	Imprecise	Undetected	Low	Pooled SMD -0.34, 95% CI -0.63 to -0.04, I^2=48.2%
		Pain *Intermediate-term*	2 (N=307) Juhakoski 2011 Teirlinck 2016	Low	Inconsistent	Imprecise	Undetected	Low	Pooled SMD -0.37, 95% CI -0.37 to -0.08, I^2=0%
		Pain *Long-term*	1 (N=118) Juhakoski 2011	Moderate	Unknown	Imprecise	Undetected	Insufficient	SMD -0.25, 95% CI -0.62 to 0.11
		Harms	2 (N=170) Tak 2005 Abbott 2013[a]	High	Consistent	Imprecise	Undetected	Insufficient	Insufficient data from two trials although no serious harms were reported in two trials.
Manual Therapies	*Manipulation vs. usual care*	Function *Intermediate-term*	1 (N=47) Abbott 2013[a]	Moderate	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one fair quality trial. No effect size could be calculated.
		Harms	1 (N=47) Abbott 2013[a]	Moderate	Unknown	Imprecise	Undetected	Insufficient	No treatment-related serious adverse events were detected
	Manipulation vs. exercise	Function *Short-term*	1 (N=109) Hoeksma 2004	Moderate	Unknown	Imprecise	Undetected	Low	Adjusted difference 11.1 (95% CI 4.0 to 18.6) on 0-100 scale

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Function *Intermediate-term*	2 (N=155) Abbott 2013[a] Hoeksma 2004	Moderate	Consistent	Imprecise	Undetected	Low	Adjusted difference 9.7, 95% CI, 1.5 to 17.9 on 0-100 scale; no effect size could be calculated in the other trial but direction of effect was similar
		Pain *Short-term*	1 (N=109) Hoeksma	Moderate	Unknown	Precise	Undetected	Low	Adjusted differences -0.72 (95% CI -1.38 to -0.05) for pain at rest and -1.21 (95% CI -2.29 to -0.25) for pain walking on 0-10 scale
		Pain *Intermediate-term*	1 (N=109) Hoeksma	Moderate	Unknown	Imprecise	Undetected	Insufficient	Adjusted differences -0.70 (95% CI -2.03 to 0.59) for pain at rest and -1.27 (95% CI -2.40 to -0.19) for pain walking on 0-10 scale; impact on pain is unclear from different measures
		Harms	2 (N=155) Abbott 2013[a] Hoeksma 2004	Moderate	Consistent	Imprecise	Undetected	Low	No treatment-related serious adverse events were detected in one trial; similar rates of study withdrawal due to symptom aggravation were seen in the second trial (5% vs. 4%; RR 1.42, 95% CI 0.25 to 8.16)

CI = confidence interval; RCT = randomized controlled trial; RR = risk ratio; SMD = standardized mean difference.

[a]Authors did not provide data on the number of hip osteoarthritis patients for each intervention, only gave hip osteoarthritis population as a whole

Table G-5. Hand osteoarthritis (KQ 3) strength of evidence

Intervention	Comparator	Outcome	N RCTs (patients)	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
Exercise	*Exercise vs. usual care*	Function, Pain, Harms *Short-term*	1 (N=130) Osteras	High	Unknown	Precise	Undetected	Insufficient	Poor quality trial of exercise vs waitlist High attrition rate in exercise arm (29%).
Physical Modalities	*Low level laser therapy vs. sham intervention*	Function *Short-term*	1 (N=88) Brosseau	Low	Unknown	Imprecise	Undetected	Low	No differences observed in one good quality trial (difference 0.2, 95% CI -0.2 to 0.6).
		Pain *Short-term*	1 (N=88) Brosseau	Low	Unknown	Imprecise	Undetected	Low	No differences observed in one good quality trial (difference 0.1, 95% CI -0.3 to 0.5).
		Harms	1 (N=88) Brosseau	Low	Unknown	Imprecise	Undetected	Low	No serious adverse events identified in one good quality trial.
	Superficial heat (paraffin) vs. no treatment	Function, Pain, Harms *Short-term*	1 (N=56) Dilek	Moderate	Unknown	Imprecise	Possible	Insufficient	Insufficient evidence from one small trial
Multidisci-plinary Rehabilitation	*Multidisci-plinary rehabilitation vs. waitlist*	Function *Short-term*	1 (N=151) Stukstette	Moderate	Unknown	Precise	Undetected	Low	Adjusted difference 0.49 (95% CI -0.09 to 0.37); OASRI-OMERACT Responder: OR 0.82 (95% CI 0.42 to 1.61)
		Pain *Short-term*	1 (N=151) Stukstette	Moderate	Unknown	Precise	Undetected	Low	Adjusted difference 0.40 (95% CI -0.5 to 1.3)
		Harms	1 (N=151) Stukstette	Moderate	Unknown	Imprecise	Undetected	Insufficient	No serious adverse events identified.

CI = confidence interval; OASRI-OMERACT = Osteoarthritis Research Society International-Outcome Measures in Rheumatology; OR = odds ratio; RCT = randomized controlled trial.

Table G-6. Fibromyalgia (KQ 4) strength of evidence

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
Exercise	*Exercise vs. usual care, attention control, or a placebo intervention*	Function *Short-term*	7 (N=410) King 2002 Baptista 2012 Kayo 2012 Giannotti 2014 Paolucci 2015 Da Costa 2005 Altan 2009	Moderate	Inconsistent	Precise	Undetected	Low	Pooled difference, -7.61 on a 0 to 100 scale, 95% CI, -12.78 to - 2.43, I^2=59.9%)
		Function *Intermediate-term*	8 (N=461) Gowans 2001 Sanudo 2010 Mannerkofpi 2009 Fontaine 2011 Giannotti 2014 Da Costa 2005 Saunudo 2012 Tomas-Carus 2008	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference on 0-100 scale, -6.04 95% CI -9.05 to -3.03, I^2=0%
		Function *Long-term*	3 (N=178) Van Eijk-Hustings 2013 Fontaine 2011 Sanudo 2012	Moderate	Consistent	Precise	Undetected	Low	Pooled difference, on 0-100 scale, -4.33, 95% CI -10.18 to 1.52, I^2=0%)
		Pain *Short-term*	6 (N=337) Kayo 2012 Buckelew 1998 Gusi 2006 Giannotti 2014 Da Costa 2005 Altan 20009	Moderate	Consistent[a]	Precise	Undetected	Moderate	Pooled difference -0.89, 95% CI -1.32 to -0.46, I^2=0%

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Pain *Intermediate-term*	7 (N=327) Sanudo 2015 Fontaine 2011 Tomas-Carus 2008 Giannotti 2014 vanSanten 2002 Da Costa 2005 Sencan 2004	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -0.41, on a 0-10 scale, 95% CI -0.87 to 0.05, I^2=9.5%
		Pain *Long-term*	4 (N=241) Wiggers 1996 van Eijk-Hustings 2013 Buckelew 1998 Fontaine 2011	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference – 0.18, 95% CI -0.77 to 0.42, I^2=0%
		Harms	3 (N=132) Gusi 2006 Kayo 2012 Paolucci 2015	Moderate	Unknown	Imprecise	Undetected	Insufficient	Insufficient data on harms. Most trials of exercise did not report on adverse events at all. One trial reported one non-study-related adverse event. Two trials reported no adverse events
	Exercise vs. pharma-cologial therapy	Pain *Intermediate-term*	1 (N=32) Sencan 2004	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from one small, poor-quality trial

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
Psychological Therapies	*Psycho-logical therapy vs. usual care, waitlist, or attention control*	Function *Short-term*	CBT: 2 (N=97)Pooled Castel 2012 Jensen 2012 2 (N=96) for RR Ang 2010 Castel 2012 EMG Biofeedback: 1 (N=59) Buckelew 1998 Imagery: 1 (N=70) Verkaik 2014	Moderate	Inconsistent	Imprecise	Undetected	Low (CBT) Insufficient (biofeed-back, imagery)	Pooled mean difference -10.67, 95% CI -17 to -4.30 I^2=0%, 0-100 scale for CBT; More CBT recipients with clinically important improvement, 2 trials, RR 2.2 (0.5 to 9.3) and RR 2.8(1.3 to 6.1) No clear difference for guided imagery (1 poor quality trial) or EMG biofeedback (1 poor quality trial)
		Function *Intermediate-term*	CBT: 2 (N=176) Pooled Alda 2011 Castel 2012 1 (N=82) Thieme 2006 EMG Biofeedback: 1 (N =85) van Santen 2002	Moderate	Consistent[b]	Imprecise	Undetected	Low (CBT) Insufficient (biofeed-back)	Pooled mean difference -10.36, 95% CI -23.52 to 2.8, I^2=84.5%, 0-100 scale for CBT; individual trials showed significant effect favoring CBT with more CBT recipients with a clinically important improvement RR 2.9 (95% CI 1.4 to 6.3) in one trial; additional trial, difference on a 0-10 scale -1.8 (95% CI -2.90 to -0.70) Trial of biofeedback vs. usual care: unclear difference, mean changes -1.6 (95% CI -3.4 to 0.2) versus -0.6 (95% CI -2.9 to 1.7)

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Function *Long-term*	CBT: 2 (N=227) Williams 2002 Thieme 2006 EMG Biofeedback: 1 (N=59) Buckelew 1998	High	Inconsistent	Imprecise	Undetected	Insufficient	Insufficient data from three poor quality trials
		Pain *Short-term*	CBT: 3 (N=125) Ang 2010 Castel 2012 Jensen 2012 EMG Biofeedback: 1 (N=53) Buckelew 1998	High	Consistent	Precise	Undetected	Low (CBT) Insufficient (biofeed-back)	Pooled mean difference -0.78, 95% CI -1.30 to -0.17, 0-10 scale for CBT; No clear difference for EMG biofeedback (1 poor quality trial)
		Pain *Intermediate-term*	CBT: 2 (N=176) Alda 2011 Castel 2012 EMG Biofeedback: 1 (N=65) Van Santen 2002	Moderate	Consistent	Precise	Undetected	Low (CBT) Insufficient (biofeed-back)	Pooled mean difference -0.44, 95% CI -1.30 to 0.01, 0-10 scale for CBT; Mean difference -1.11, 95% CI -2.06 to -0.16 for EMG biofeedback (1 poor quality trial)
		Pain *Long-term*	CBT: 1 (N=40) Wiggers 1996 EMG Biofeedback: 1 (N=53) Buckelew 1998	High	Consistent	Precise	Undetected	Insufficient	Insufficient data from two poor quality trials

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Harms	2 (N = 195) Alda 2011 Thieme 2006	High	Unknown	Imprecise	Undetected	Insufficient	Data were insufficient; one poor quality trial described two withdrawals related to depression in the CBT arm and 20/40 for worsening of symptoms in the attention control arm.
	Psychological therapy vs. pharma-cological therapy	Function *Short-term*	CBT: 1 (N=60) Falco 2008 EEG Biofeedback 1 (N=40) Kayiran 2010	Moderate	Inconsistent	Imprecise	Undetected	Insufficient	Insufficient data from one fair and one poor quality trial
		Function *Intermediate-term*	1 (N=113) Alda 2011 (CBT)	Moderate	Unknown	Precise	Undetected	Low	Mean difference -4.0 on the 0-100 FIQ, 95% CI -7.7 to -0.27
		Pain *Short-term*	CBT: 1 (N=60) Falco 2008 EEG Biofeedback 1 (N=40) Kayiran 2010	Moderate	Inconsistent	Imprecise	Undetected	Insufficient	Insufficient data from one fair and one poor quality trial
		Pain *Intermediate-term*	1 (N=113) Alda 2011 (CBT)	Moderate	Unknown	Precise	Undetected	Low	Difference 0.2 on a 0-100 VAS, 95% CI -4.0 to 4.4
		Harms	1 (N=113) Alda 2011 (CBT)	Moderate	Unknown	Imprecise	Undetected	Low	Withdrawals due to adverse events, CBT vs. pregabalin: 0% vs. 5.5%; events included two digestive problems, and one dizziness
	Psychological therapy vs. exercise	Function *Short-term*	1 (N=51) Buckelew 1998 (EMG Biofeedback)	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one small, poor quality trial

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Function *Intermediate-term*	CBT: 1 (N=40) Redondo 2004 EMG Biofeedback: 1 (N=114) Van Santen 2002	High	Consistent	Imprecise	Undetected	Insufficient	Insufficient evidence from two poor quality trials
		Function Long-term	CBT: 1 (N=40) Redondo 2004 Relaxation 1 (n=130) Larsson 2015 EMG Biofeedback 1 (N=51) Buckelew 1998	High	Inconsistent	Imprecise	Undetected	Insufficient	Insufficient evidence from three poor quality trials; inconsistency in findings noted.
		Pain *Short-term*	1 (N=51) Buckelew (EMG Biofeedback)	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one small, poor quality trial
		Pain *Intermediate-term*	CBT: 1 (N=40) Redondo 2004 EMG Biofeedback: 1 (N=114) Van Santen 2002	High	Consistent	Imprecise	Undetected	Insufficient	Insufficient evidence two poor quality trials
		Pain *Long-term*	CBT: 2 (N=80) Redondo 2004 Wiggers 1996 Relaxation 1 (n=130) Larsson 2015 EMG Biofeedback 1 (N=51) Buckelew 1998	High	Consistent	Imprecise	Undetected	Insufficient	Insufficient evidence from four poor quality trials

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Harms	(N=170) Larsson 2015 Wiggers 1996	High	Consistent	Imprecise	Undetected	Insufficient	Data were insufficient for harms. In one trial no patient had an adverse event in relaxation group compared to five (7.5%) in the strengthening exercise group (increased pain, three of which withdrew). In the other trial, withdrawals due to adverse events were similar between groups and none of the events were related to treatment.
Physical Modalities	*Magnetic fields vs. usual care or sham*	Function and Pain *Short-term*	(N=33) Paolucci 2016 (cross-over trial)	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from one poor quality trial
		Function *Intermediate-term*	(N=119) Alfano 2001 (parallel trial)	Moderate	Unknown	Imprecise	Undetected	Low	Difference -5.0 (95% CI -14.1 to 4.1) vs. sham and -5.5 (95% CI -14.4 to 3.4) vs. usual care on the 0-80 scale FIQ
		Pain *Intermediate-term*	(N=119) Alfano 2001 (parallel trial)	Moderate	Unknown	Imprecise	Undetected	Low	Difference -0.6 (95% CI -1.9 to 0.7) vs. sham and -1.0 (95% CI -2.2 to 0.2) vs. usual care on a 0-10 NRS
		Harms	(N=119) Alfano 2001 (parallel trial)	Moderate	Unknown	Imprecise	Undetected	Low	No differences in adverse events between the functional and sham magnetic groups (data not reported); none of the events were deemed to be related to the treatments
Massage	*Massage/ myofascial release vs. sham*	Function *Intermediate-term*	1 (N=94) Castro-Sanchez 2011[a]	Moderate	Unknown	Imprecise	Undetected	Low	Mean 58.6 (SD 16.3) vs. 64.1 (SD 18.1) on the FIQ (0-100 scale), p=0.048

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Function *Long-term*	1 (N=94) Castro-Sanchez 2011[a]	Moderate	Unknown	Imprecise	Undetected	Low	Mean 62.8 (SD 20.1) vs. 65.0 (19.8) on the FIQ (0-100 scale), p=0.329
		Pain *Short-term*	1 (N=64) Castro-Sanchez 2011[b]	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one poor quality trial
		Pain *Intermediate-term*	2 (N=158) Castro-Sanchez 2011[a] Castro-Sanchez 2011[b]	Moderate	Inconsistent	Imprecise	Undetected	Insufficient	Insufficient evidence from one fair and one poor quality trial due to inconsistency in the estimates
		Pain *Long-term*	1 (N=94) Castro-Sanchez 2011[a]	Moderate	Unknown	Imprecise	Undetected	Low	MPQ sensory domain, mean 18.2 (SD 8.3) vs. 21.2 (7.9) on a 0-33 scale, p=0.038; MPQ evaluative domain, mean 23.2 (SD 7.6) vs. 26.7 (SD 6.9) on a 0-42 scale, p=0.036
		Harms	1 (N=94) Castro-Sanchez 2011[a]	Moderate	Inconsistent	Imprecise	Undetected	Insufficient	Data for harms were insufficient; however, no adverse effect occurred in one fair quality trial
Mindfulness Practices	*Mindfulness-based stress reduction vs. waitlist or attention control*	Function *Short-term*	2 (N=1258) Cash 2015 Schmidt 2011	Moderate	Consistent	Precise	Undetected	Moderate	No clear effect: difference 0 to 0.06 on a 0-10 scale
		Pain *Short-term*	2 (N=1258) Cash 2015 Schmidt 2011	Moderate	Consistent	Precise	Undetected	Moderate	No clear effect: difference 0.1 on a 0-100 VAS pain scale in one poor quality trial; difference -1.38 to -1.59 on the affective and -0.28 to -0.71 on the sensory dimension (scales not reported) of the Pain Perception Scale in one fair-quality trial

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Harms							No evidence
Mind-Body Therapies	*Tai Chi, Qigong vs. waitlist or attention control*	Function *Short-term*	(N=154) Lynch 2012 Wang 2010	Moderate	Consistent[b]	Precise	Undetected	Low	FIQ total score (0-100): Qigong, mean difference -7.5 (95% CI -13.3 to -1.68) Tai chi, mean difference -23.5 (95% CI -30 to -17) Heterogeneity may be explained by duration and intensity of intervention and control group
		Pain *Short-term*	(N=154) Lynch 2012 Wang 2010	Moderate	Consistent[b]	Precise	Undetected	Low	Pooled difference -1.54 (95% CI -2.67, -0.41) I^2=75%, scale 0-10
		Harms	(N=154) Lynch 2012 Wang 2010	Moderate	Inconsistent	Unprecise	Undetected	Insufficient	Data for harms were insufficient. One trial reported two adverse events judged to be possibly related to Qigong practice: an increase in shoulder pain and plantar fasciitis; neither participant withdrew from the study. In the trial of Tai chi, no adverse events were reported.
Acupuncture	*Acupuncture vs. sham*	Function *Short-term*	2 (N=211) Vas 2016 Martin 2006	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -8.63 (95% CI 12.12 to -5.13), I^2=0%, scale 0-100
		Function *Intermediate-term*	2 (N=211) Vas 2016 Martin 2006	Moderate	Consistent	Precise	Undetected	Moderate	Pooled difference -9.41 (95% CI -13.96 to -4.85), I^2=27.4%, scale 0-100
		Pain *Short-term*	3 (N=297) Assefi 2005 Martin 2006 Vas 2016	Moderate	Inconsistent	Precise	Undetected	Low	Pooled difference -0.13 (95% CI -1.06 to 0.79), I^2=72.0%, scale 0-10

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Pain *Intermediate-term*	3 (N=297) Assefi 2005 Martin 2006 Vas 2016	Moderate	Inconsistent	Precise	Undetected	Low	Pooled difference -0.53 (95% CI -1.15 to 0.09), I^2 = 45.5%, scale 0-10
		Harms	3 (N=297) Assefi 2005 Martin 2006 Vas 2016	Moderate	Consistent	Precise	Undetected	Moderate	Discomfort and bruising were the most common reported adverse events and were more common in the true acupuncture groups. Discomfort was substantially more common for acupuncture or sham needling (61%to 70%) compared with simulated acupuncture (29%). Vasovagal symptoms and aggravation of fibromyalgia symptoms were less common (4%, 2.5 of sessions)
Multidisciplinary Rehabilitation	*Multi-disciplinary rehabilitation vs. usual care or waitlist*	Function *Short-term*	3 (N=381) Castel 2013 Amris 2014 Saral 2016 ("long-term" intervention arm)[c]	Moderate	Consistent[d]	Precise	Undetected	Low	Pooled mean difference -6.52, 95% CI -12.84 to -0.21, I^2=76.2%, on 0-100 FIQ Proportion with clinically meaningful improvement in FIQ total score compared with usual care at short (OR 3.1, 95% CI 1.6 to 6.2)
		Function *Intermediate-term*	3 (N=394) Martin 2012 Castel 2013 Cedraschi 2004	High	Consistent	Precise	Undetected	Low	Pooled difference -7.84, 95% CI -11.43 to -4.25, I^2=18.2% Proportion with clinically meaningful improvement in FIQ total score compared with usual care at short (OR 3.1, 95% CI 1.5 to 6.4)

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Function *Long-term*	2 (N=311) Castel 2013 van Ejik-Hustings 2013	Moderate	Consistent	Precise	Undetected	Low	Pooled difference -8.42, 95% CI -13.76 to -3.08, I^2=24.9% Proportion with clinically meaningful improvement in FIQ total score compared with usual care at short (OR 8.8, 95% CI 2.5 to 30.9)
		Pain *Short-term*	2 (N=341) Castel 2013 Amris 2014	Moderate	Consistent[e]	Precise	Undetected	Low	Pooled difference on 0-10 scale -0.24, 95%CI -0.63 to 0.15, I^2=0%
		Pain *Intermediate-term*	3 (N=394) Martin 2012 Castel 2013 Cedraschi 2004	High	Consistent	Precise	Undetected	Low	Pooled difference -0.68, 95% CI -1.07 to -0.30, I^2=0%
		Pain *Long-term*	2 (N=311) Castel 2013 van Ejik-Hustings 2013	Moderate	Consistent	Precise	Undetected	Low	Pooled difference -0.25, 95% CI -0.68 to 0.17, I^2=0%
		Harms	1 (N=164) Cedraschi 2004	High	Unknown	Imprecise	Undetected	Insufficient	Data were insufficient for harms; however, one poor quality trial reported that 19% (16/84) in the multidisciplinary group withdrew (versus 0% for waiting list), two gave increased pain as the reason. Reasons for other withdrawals were not given and there was not systematic reporting of adverse events

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
	Multi-disciplinary rehabilitation vs. exercise	Function *Long-term*	1 (N=155) van Eijk-Hustings 2013	Moderate	Unknown	Precise	Undetected	Low	Difference -1.10 (95% CI -8.40 to 6.20) on a 0-100 scale
		Pain *Long-term*	1 (N=155) van Eijk-Hustings 2013	Moderate	Unknown	Precise	Undetected	Low	Difference 0.10 (95% CI -0.67 to 0.87) on a 0-10 scale
		Harms	1 (N=155) van Eijk-Hustings 2013	Moderate	Unknown	Imprecise	Undetected	Insufficient	Data were insufficient. Harms not reported

CBT = cognitive behavioral therapy; CI = confidence interval; EMG = electromyography; FIQ = Fibromyalgia Impact Questionnaire; MD = mean difference; MPQ = McGill Pain Questionnaire; NDI = Neck Disability Index; PSFS = Patient Specific Functional Scale; RCT = randomized controlled trial; RR = risk ratio; SD = standard deviation; VAS = visual analog scale.

[a] Outlier excluded, Baptista 2012.

[b] Effect estimates go in the same direction even though magnitude of effect may differ

[c] The "long-term" multidisciplinary arm (2 days of education and exercise followed by 10 weeks of CBT) was determined to be most consistent with interventions employed by the other trials and was included in the pooled estimates; results for the "short-term" group (2 days of education, exercise and CBT programs) were similar to those of the "long-term" group and are detailed in Table 42 of the full report.

[d] I^2 >40% but not downgraded for inconsistency because direction of effect consistent across >75% of trials or heterogeneity explainable in subgroup/stratified/sensitivity analyses.

[e] Outlier excluded, Saral 2016.

Table G-7. Chronic tension headache (KQ 5) strength of evidence

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
Psychological Therapies	*CBT vs. waitlist, attention control, or placebo*	Function *Short- and intermediate term*	1 (N=60) Holroyd 2001	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from one small poor quality trial
		Pain *Short-term*	2 (N=105) Holroyd 2001 Blanchard 1990	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from two small poor quality trials
		Pain *Intermediate-term*	1 (N=60) Holroyd 2001	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from one small poor quality trial
		Harms	1 (N=60) Holroyd 2001	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from one small poor quality trial. The risk of withdrawal due to adverse events did not differ between CBT plus placebo and placebo alone (2% vs. 6%).
	Relaxation vs. waitlist of attention control	Pain, Harms *Short-term*	1 (N=55) Blanchard 1990	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from one small poor quality trial
	CBT vs. amitriptyline	Function *Short- and intermediate term*	1 (N=60) Holroyd 2001	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from one small poor quality trial
		Pain *Short-term*	2 (N=96) Holroyd 2001 Holroyd 1991	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from two small poor quality trials
		Pain *Intermediate-term*	1 (N=60) Holroyd 2001	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from one small poor quality trial

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Harms	2 (N=96) Holroyd 2001 Holroyd 1991	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from two small poor quality trial. Lower risk of "at least mild" adverse events in the CBT group (0% vs. 59%) in one poor quality trial; similar risk of withdrawal due to adverse events (2% in each group).
Physical Modalities	Occipital transcutaneous electrical stimulation vs. sham	Function, Pain, *Short-term*	1 (N=83) Bono 2015	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from one small poor quality trial
		Harms	1 (N=83) Bono 2015	High	Unknown	Precise	Undetected	Insufficient	Data for harms were insufficient; however, no adverse events occurred in either the real or the sham OTES group
Manual Therapies	Spinal manipulation vs. usual care	Function *Short-term*	1 (N=75) Castien 2011	Moderate	Unknown	Precise	Undetected	Low	Difference -5.0 (95% CI -9.02 to -1.16) on the Headache Impact Test (scale 36-78); Difference -10.1 (95% CI -19.5 to -0.64) on the Headache Disability Inventory (scale 0-100)
		Pain *Short-term*	1 (N=75) Castien 2011	Moderate	Unknown	Precise	Undetected	Low	Difference -1.4 on a 0-10 NRS scale, 95% CI -2.69 to -0.16
		Harms	1 (N=75) Castien 2011	Moderate	Unknown	Precise	Undetected	Low	No adverse events occurred in either group.
	Spinal manipulation vs. amitriptyline	Pain *Short-term*	1 (N=126) Boline 1995	High	Unknown	Precise	Undetected	Insufficient	Insufficient evidence from one poor quality trial

Intervention	Comparator	Outcome	Number of RCTs (patients) Author Year	Study Limitations	Consistency	Precision	Reporting Bias	Strength of Evidence	Findings, Direction and Magnitude of Effect
		Harms	1 (N=126) Boline 1995	High	Unknown	Precise	Undetected	Low	Fewer adverse events with manipulation versus amitriptyline (RR 0.05, 95% CI 0.02 to 0.16), though the risk of withdrawal due to adverse events was not significantly different (RR 0.16, 95% CI 0.02 to 1.33). Common complaints were neck stiffness in the manipulation group and dry mouth, dizziness, and weight gain in the medication group
Acupuncture	Traditional Chinese needle acupuncture vs. sham	Pain *Short-term*	2 (N=69) Karst 2000 Tavola 1992	High	Consistent	Imprecise	Undetected	Insufficient	Insufficient evidence from two small, poor quality trials
		Pain *Intermediate- and long-term*	1 (N=30) Tavola 1992	High	Unknown	Imprecise	Undetected	Insufficient	Insufficient evidence from one small, poor quality trial
		Harms							No evidence
	Laser acupuncture vs. sham laser	Pain *Short-term*	1 (N=50) Ebneshahidi 2005	Moderate	Unknown	Precise	Undetected	Low	Median difference -2, IQR 6.3, on a 0-10 VAS scale for pain intensity median difference -8, IQR 21.5, for number of headache days per month
		Harms	1 (N=50) Ebneshahidi 2005	Moderate	Unknown	Precise	Undetected	Low	No adverse events occurred in either group.

CBT = cognitive behavioral therapy; CI = confidence interval; IQR = interquartile range; NRS = numerical rating scale; RCT = randomized controlled trial; RR = risk ratio; VAS = visual analog scale

Appendix H. Definitions for Magnitude of Effects

Table H-1. Definitions for magnitude of effects, based on mean between-group differences

Outcome	Slight/Small Magnitude of Effect	Moderate Magnitude of Effect	Large/Substantial Magnitude of Effect
Pain	5–10 points on a 0-to 100-point VAS or the equivalent	>10–20 points on a 0-to 100-point VAS or the equivalent	>20 points on a 0-to 100-point VAS or the equivalent
	0.5–1.0 points on a 0-to 10-point numerical rating scale or the equivalent	>1–2 points on a 0-to 10-point numerical rating scale or the equivalent	>2 points on a 0-to 10-point numerical rating scale or the equivalent
Function	5–10 points on the ODI	>10–20 points on the ODI	>20 points on the ODI
	1–2 points on the RDQ	>2–5 points on the RDQ	>5 points on the RDQ
	1-2 points on Lequesne Index	>2-5 points on the Lequesne Index	5 points on the Lequesne Index
	5–10 points on the WOMAC	>10–20 points on the WOMAC	>20 points on the WOMAC
	5–10 points on the KOOS	>10–20 points on the KOOS	>20 points on the KOOS
	5-10 points on the NPQ	>10–20 points on the NPQ	>20 points on the NPQ
	5-10 points on the FIQ Total Score	>10–20 points on the FIQ Total Score	>20 points on the FIQ Total Score
	7.5-10 points on the NDI	>10-20 on the NDI	>20 points on the NDI
	1.3 – 2.2 on the PSFS	23.3 -2.6 on the PSFS	>2.6 on the PSFS
Pain or Function	0.2–0.5 SMD	>0.5–0.8 SMD	>0.8 SMD

ODI = Oswestry Disability Index; RDQ = Roland Morris Disability Questionnaire; SMD = standardized mean difference; VAS = visual analogue scale; WOMAC = Western Ontario and Mc Master Universities Osteoarthritis index; KOOS=Knee Injury and Osteoarthritis Outcome Score; NDI = neck disability index; NPQ = Northwick Park Questionnaire; PSFS = Patient-Specific Functional Scale; FIQ = Fibromyalgia Impact Questionnaire