Effective Health Care Program

Comparative Effectiveness Review
Number 169

Noninvasive Treatments for Low Back Pain

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Number 169

Noninvasive Treatments for Low Back Pain

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officer 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 $10,000 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 $10,000 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 Treatments for Low Back Pain

Structured Abstract

Objectives. Low back pain is common, and many pharmacological and nonpharmacological therapies are available. This review examines the evidence on the comparative benefits and harms of noninvasive treatments for low back pain.

Data sources. A prior systematic review (searches through October 2008), electronic databases (Ovid MEDLINE® and the Cochrane Libraries, January 2008 to April 2015), reference lists, and clinical trials registries.

Review methods. Using predefined criteria, we selected systematic reviews of randomized trials of pharmacological treatments (acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], opioids, skeletal muscle relaxants, benzodiazepines, antidepressants, antiseizure medications, and systemic corticosteroids) and nonpharmacological treatments (psychological therapies, multidisciplinary rehabilitation, spinal manipulation, acupuncture, massage, exercise and related therapies, and various physical modalities) for nonradicular or radicular low back pain that addressed effectiveness or harms versus placebo, no treatment, usual care, a sham therapy, an inactive therapy, or another active therapy. We also included randomized trials that were not in systematic reviews. The quality of included studies was assessed, data were extracted, and results were summarized qualitatively based on the totality of the evidence.

Results. Of the 2,545 citations identified at the title and abstract level, a total of 156 publications were included. Most trials enrolled patients with pain symptoms of at least moderate intensity (e.g., >5 on a 0- to 10-point numeric rating scale for pain). Across interventions, pain intensity was the most commonly reported outcome, followed by back-specific function. When present, observed benefits for pain were generally in the small (5 to 10 points on a 0- to 100-point visual analog scale or 0.5 to 1.0 points on a 0- to 10-point numeric rating scale) to moderate (10 to 20 points) range. Effects on function were generally smaller than effects on pain; in some cases, there were positive effects on pain but no effects on function, and fewer studies measured function than pain. Benefits were mostly measured at short-term followup. For acute low back pain, evidence suggested that NSAIDs (strength of evidence [SOE]: low to moderate), skeletal muscle relaxants (SOE: moderate), opioids (SOE: low), exercise (SOE: low), and superficial heat (SOE: moderate) are more effective than placebo, no intervention, or usual care, and that acetaminophen (SOE: low) and systemic corticosteroids (SOE: low) are no more effective than placebo. For chronic low back pain, effective therapies versus placebo, sham, no treatment, usual care, or wait list are NSAIDs, opioids, tramadol, duloxetine, multidisciplinary rehabilitation, acupuncture, and exercise (SOE: moderate) and benzodiazepines, psychological therapies, massage, yoga, tai chi, and low-level laser therapy (SOE: low); spinal manipulation was as effective as other active interventions (SOE: moderate). Few trials evaluated the effectiveness of treatments for radicular low back pain, but the available evidence found that benzodiazepines, corticosteroids, traction, and spinal manipulation were not effective or were associated with small effects (SOE: low). Relatively few trials directly compared the effectiveness of different medications or different nonpharmacological therapies, or compared pharmacological versus nonpharmacological therapies, and they generally found no clear differences in effects.

Pharmacological therapies were associated with increased risk of adverse events versus placebo (SOE: low to moderate). Trials were not designed or powered to detect serious harms from pharmacological therapies. Although rates appeared to be low and there was not an increased risk of serious harms versus placebo, this does not rule out significant risk from some treatments. For nonpharmacological therapies, assessment of harms was suboptimal, but serious harms appeared to be rare (SOE: low).

Conclusions. A number of pharmacological and nonpharmacological noninvasive treatments for low back pain are associated with small to moderate, primarily short-term effects on pain versus placebo, sham, wait list, or no treatment. Effects on function were generally smaller than effects on pain. More research is needed to understand optimal selection of treatments, effective combinations and sequencing of treatments, effectiveness of treatments for radicular low back pain, and effectiveness on outcomes other than pain and function.

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Executive Summary

Background

Nature and Burden of Low Back Pain

Low back pain is one of the most frequently encountered conditions in clinical practice. Up to 84 percent of adults have low back pain at some time in their lives, and over one-quarter of U.S. adults report recent (in the last 3 months) low back pain.[1,2] Low back pain can have major adverse impacts on quality of life and function. Low back pain is also costly: total U.S. health care expenditures for low back pain in 1998 were estimated at $90 billion.[3] Since that time, costs of low back pain care have risen at a rate higher than observed for overall health expenditures.[4] In addition to high direct costs, low back pain is one of the most common reasons for missed work or reduced productivity while at work, resulting in high indirect costs.[5]

The prognosis for acute low back pain (generally defined as an episode lasting less than 4 weeks) is generally favorable. Most patients experience a rapid improvement in (and often a complete resolution of) pain and disability, and are able to return to work.[6] In those with persistent symptoms, continued improvement is often seen in the subacute phase between 4 and 12 weeks, although at a slower rate than observed at first. In a minority of patients, low back pain lasts longer than 12 weeks, at which point it is considered chronic; levels of pain and disability often remain relatively constant thereafter.[7] Recently, a National Institutes of Health Research Task Force defined chronic low back pain as a back pain problem that has persisted at least 3 months and has resulted in pain on at least half the days in the past 6 months.[8] Patients with chronic back pain account for the bulk of the burdens and costs of low back pain.[9,10] Predictors of chronicity are primarily related to psychosocial factors, such as presence of psychological comorbidities, maladaptive coping strategies (e.g., fear avoidance [avoiding activities because of fears that they will further damage the back] or catastrophizing [anticipating the worst possible outcomes from low back pain]), presence of nonorganic signs (symptoms without a distinct anatomical or physiological basis),[11] high baseline functional impairment, and low general health status.[7] Back pain is frequently associated with presence of depression and anxiety.

Attributing symptoms of low back pain to a specific disease or spinal pathology is a challenge.[12] Spinal imaging abnormalities, such as degenerative disc disease, facet joint arthropathy, and bulging or herniated intervertebral discs, are extremely common in patients with or without low back pain, particularly in older adults, and such findings are poor predictors for the presence or severity of low back pain.[13] Radiculopathy from nerve root impingement (often due to a herniated intervertebral disc) and radiculopathy from spinal stenosis (narrowing of the spinal canal) are each present in about 4 to 5 percent of patients with low back pain and can cause neurological symptoms, such as lower extremity pain, paresthesias, and weakness; the natural history and response to treatment for these conditions may differ from back pain without neurologic involvement.[14]

Interventions for Low Back Pain

Multiple treatment options for acute and chronic low back pain are available. Broadly, these can be classified as pharmacological treatments,[15] noninvasive nonpharmacological treatments,[16] injection therapies,[17] and surgical treatments.[18] This report focuses on the comparative benefits and harms of pharmacological and noninvasive nonpharmacological treatments; each of these categories encompasses a number of different therapies. Pharmacological treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, and corticosteroids; nonpharmacological treatments include exercise and related interventions (e.g., yoga), complementary and alternative therapies (e.g., spinal manipulation, acupuncture, and massage), psychological therapies (e.g., cognitive-behavioral therapy, relaxation techniques, and multidisciplinary rehabilitation), and physical modalities (e.g., traction, ultrasound, transcutaneous electrical nerve stimulation [TENS], low-level laser therapy, interferential therapy, superficial heat or cold, back supports, and magnets).

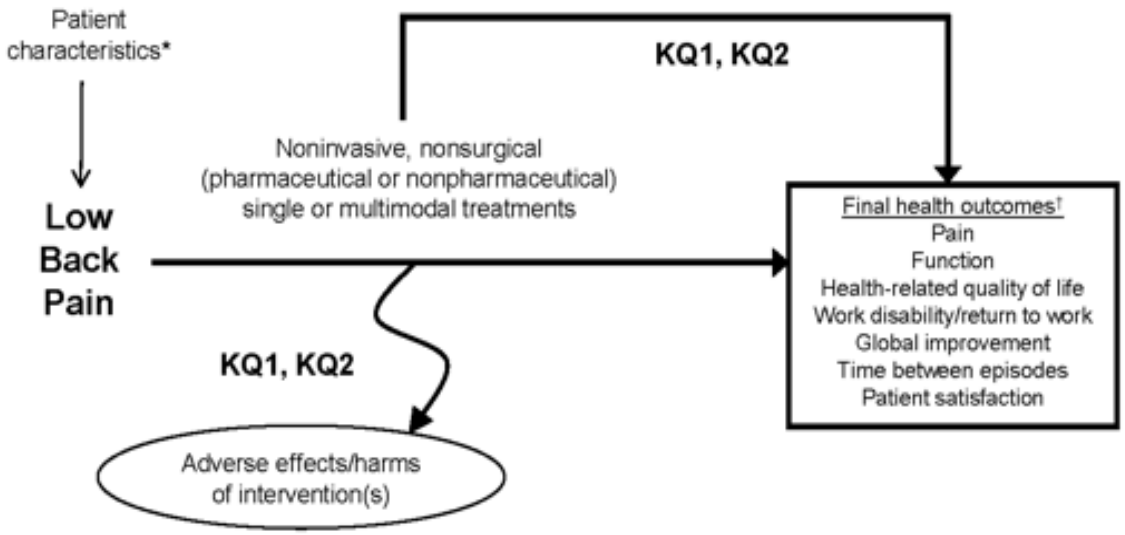
Scope of Review and Key Questions

The provisional Key Questions; populations, interventions, comparators, outcomes, timing, settings, and study designs (PICOTS); and analytic framework for this topic (Figure A) were posted on the Agency for Healthcare Research and Quality (AHRQ) Web site for public comment from December 17, 2013, through January 17, 2014.

Key Question 1. What are the comparative benefits and harms of different pharmacological therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis? Includes NSAIDs, acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, corticosteroids, and topical/patch-delivered medications.

Key Question 2. What are the comparative benefits and harms of different nonpharmacological noninvasive therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis? Includes but is not limited to multidisciplinary rehabilitation, exercise (various types), physical modalities (ultrasound, transcutaneous electrical nerve stimulation, electrical muscle stimulation, interferential therapy, heat [various forms], and ice), traction tables/devices, back supports/bracing, spinal manipulation, various psychological therapies, acupuncture, massage therapy (various types), yoga, magnets, and low-level lasers.

Figure A. Analytic framework



*Patient characteristics include clinical, demographic, and psychosocial risk factors associated with low back pain outcomes.
†Intermediate outcomes (e.g., inflammation) are typically not measured.
KQ = Key Question.

Methods

This Comparative Effectiveness Review follows the methods suggested in the AHRQ "Methods Guide for Effectiveness and Comparative Effectiveness Reviews" (hereafter, "AHRQ Methods Guide").[19] Our methods are summarized in this section; for additional details, see the review protocol posted on the AHRQ Effective Health Care Program Web site (www.effectivehealthcare.ahrq.gov).

Literature Search and Selection

A research librarian conducted searches in Ovid MEDLINE®, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews through August 2014. We restricted search start dates to January 2008 because searches in a prior American Pain Society/American College of Physicians (APS/ACP) review were conducted through October 2008; the APS/ACP review was used to identify studies published prior to 2008.[20] For interventions not addressed in the APS/ACP review, we searched the same databases without a search date start restriction. We also hand searched the reference lists of relevant studies and searched for unpublished studies in ClinicalTrials.gov. Scientific information packets were solicited from drug and device manufacturers, and a notice published in the Federal Register invited interested parties to submit relevant published and unpublished studies. We conducted an update search in April 2015 using the same search strategy as in the original search.

We developed criteria for inclusion and exclusion of studies based on the Key Questions and PICOTS. Abstracts were reviewed by two investigators, and all citations deemed potentially

appropriate for inclusion by at least one of the reviewers were retrieved. Two investigators then independently reviewed all full-text articles for final inclusion. Discrepancies were resolved by discussion and consensus.

Population and condition of interest. This report focuses on adults with low back pain of any duration (categorized as acute [<4 weeks], subacute [4–12 weeks], and chronic [≥12 weeks]), including nonradicular low back pain, radicular low back pain (e.g., due to herniated disc), and symptomatic spinal stenosis.

Interventions, comparisons, and study designs of interest. We included pharmacological and noninvasive nonpharmacological therapies for low back pain. For opioids, we excluded the drug propoxyphene, a weak analgesic associated with risk of cardiac arrhythmia that is no longer available in the United States or Europe. For skeletal muscle relaxants and benzodiazepines, we included drugs not available in the United States but available in Europe and noted such instances. Comparisons were of an included therapy versus placebo (drug trials), sham treatments (nonpharmacological intervention), no treatment, wait list, or usual care, as well as comparisons of one included therapy versus another. We also evaluated comparisons of the combination of one included therapy plus another included therapy versus one of the therapies alone.

Outcomes of interest. We evaluated effects of interventions on reduction or elimination of low back pain, including related leg symptoms, improvement in back-specific and overall function, improvement in health-related quality of life, reduction in work disability/return to work, global improvement, number of back pain episodes or time between episodes, and patient satisfaction. We also evaluated adverse effects, including serious adverse events (e.g., anaphylaxis with medications, neurological complications, death) and less serious adverse events.

Timing and settings of interest. When possible, timing of outcomes was stratified as long term (at least 1 year) and short term (up to 6 months); we also noted outcomes assessed immediately after the completion of a course of treatment. We included studies conducted in inpatient or outpatient settings.

Study designs. Given the large number of interventions and comparisons addressed in this review, we included systematic reviews of randomized trials.[21,22] For each intervention, we selected the systematic review that was the most relevant to our Key Questions and scope (as defined in the PICOTS), had the most recent search dates, and was of highest quality based on assessments using the AMSTAR (A Measurement Tool to Assess Systematic Reviews) tool.[23] We supplemented systematic reviews with randomized trials that were not included in the reviews. For harms, we included cohort studies for interventions and comparisons when randomized trials were sparse or unavailable. We did not include systematic reviews identified in the update searches but checked reference lists for additional randomized trials. We excluded case-control studies, case reports, and case series.

Data Extraction

For systematic reviews we abstracted the following data: inclusion criteria, search strategy, databases searched, search dates, the number of included studies, study characteristics of included studies (e.g., sample sizes, interventions, duration of treatment, duration of followup,

comparison, and results), methods of quality assessment, quality ratings for included studies, methods for synthesis, and results. For primary studies not included in systematic reviews, we abstracted the following data: study design, year, setting, country, sample size, eligibility criteria, population and clinical characteristics, intervention characteristics, and results. Information relevant for assessing applicability was also abstracted, including the characteristics of the population, interventions, and care settings; the use of run-in or washout periods; and the number of patients enrolled relative to the number assessed for eligibility. All study data were verified for accuracy and completeness by a second team member.

Risk-of-Bias Assessment of Individual Studies

Two investigators independently assessed quality (risk of bias) of systematic reviews and primary studies not included in systematic reviews using predefined criteria, with disagreements resolved by consensus. Randomized trials were evaluated using criteria and methods developed by the Cochrane Back Review Group,[24] and cohort studies were evaluated using criteria developed by the U.S. Preventive Services Task Force.[25] Systematic reviews were assessed using the AMSTAR quality rating instrument.[22] These criteria and methods were used in conjunction with the approach recommended in the AHRQ Methods Guide.[21] Studies were rated as good, fair, or poor. We re-reviewed the quality ratings of studies included in the prior APS/ACP review to ensure consistency in quality assessment.[23]

For primary studies included in systematic reviews, we relied on the quality ratings or risk-of-bias assessments performed in the systematic reviews as long as they used a standardized method for assessing quality (e.g., Cochrane Back Review Group, Cochrane Risk of Bias tool, PEDro [Physiotherapy Evidence Database] tool). If we were uncertain about the methods used to assess risk of bias or quality, we assessed the quality of individual studies ourselves, using the methods described previously.

We did not exclude studies rated poor quality a priori, but they were considered the least reliable when synthesizing the evidence, particularly when discrepancies among studies were present.

Data Synthesis

We synthesized data qualitatively, based on the totality of evidence (i.e., evidence included in the prior APS/ACP review plus new evidence). We synthesized results for continuous as well as dichotomous outcomes. We reported binary outcomes based on the proportion of patients achieving successful pain reduction, improvement in function, or some composite overall measure of success as defined in the trials, which varied in how they categorized successful outcomes.

In addition, we reported meta-analysis from systematic reviews that reported pooled estimates from studies that were judged to be homogeneous enough to provide a meaningful combined estimate and used appropriate pooling methods (e.g., random-effects model in the presence of statistical heterogeneity). When statistical heterogeneity was present, we examined the type of inconsistency present and evaluated subgroup and sensitivity analyses based on

study characteristics, intervention factors, and patient factors. We did not conduct updated meta-analysis with new studies. Rather, we qualitatively examined whether results of new studies were consistent with pooled or qualitative findings from prior systematic reviews. When we included more than one systematic review for a particular intervention and comparison, we evaluated the consistency of results among reviews.

We assessed the strength of evidence (i.e., evidence in prior reviews as well as new evidence) for each Key Question and outcome using the approach described in the AHRQ Methods Guide19 based on the overall quality of each body of evidence.

Results

Database searches resulted in 2,545 potentially relevant articles. After dual review of abstracts and titles, 1,310 articles were selected for full-text dual review; 156 publications were determined to meet inclusion criteria and were included in this review.

Most trials were conducted in patients with nonradicular low back pain or mixed populations with primarily nonradicular low back pain. Some trials enrolled mixed populations of patients with acute and subacute symptoms, with few trials restricted to patients with subacute low back pain. Therefore, acute and subacute low back pain were grouped together when summarizing findings. Pain was the most commonly reported outcome in the trials, followed by function, with evidence on other efficacy outcomes generally too limited to reach reliable conclusions. In addition, most trials focused on short-term outcomes, frequently with followup limited to the active treatment period. Assessment and reporting of harms were suboptimal, particularly for the nonpharmacological therapies. Summarizing evidence on nonpharmacological therapies was also complicated by variability in the techniques used; in the number, length, and intensity of sessions; and in the duration of treatment. Common methodological shortcomings included failure to report randomization or allocation concealment methods, unblinded or unclearly blinded design, and high or unclear attrition.

Key Question 1. Pharmacological Therapies

For acute or subacute low back pain, NSAIDs, opioids (buprenorphine patch), and skeletal muscle relaxants were associated with small effects on pain versus placebo, and NSAIDs were associated with small effects on function (Table A). Acetaminophen and systemic corticosteroids were associated with no beneficial effects versus placebo. Head-to-head comparisons were limited but indicated no clear differences between acetaminophen versus NSAIDs or between different NSAIDs (Table B).

For chronic low back pain, NSAIDs and tramadol were associated with moderate effects on pain versus placebo, and opioids, duloxetine, and benzodiazepines were associated with small effects (Table C). Effects on function were small for NSAIDs, opioids, tramadol, and duloxetine. Tricyclic antidepressants were not associated with beneficial effects, and there was insufficient evidence to determine effects of gabapentin or pregabalin. Head-to-head comparisons were limited but showed no clear differences between different NSAIDs, different long-acting opioids, or long-acting versus short-acting opioids. Evidence was too inconsistent to determine effects of opioids versus NSAIDs (Table D).

Evidence on effects of pharmacological therapies for radiculopathy was extremely limited (Table E). There were no differences in pain or function between systemic corticosteroids versus placebo, and evidence was insufficient to determine effects of gabapentin or pregabalin.

Pharmacological therapies were associated with an increased risk of adverse events versus placebo. However, serious harms were rare in clinical trials, with no clear increase in risk based on clinical trials. In particular, trials of opioids were not designed to assess for serious harms, such as overdose, abuse, and addiction. Such harms have been reported in observational studies of opioids for chronic pain, although such studies did not meet inclusion criteria because they were not restricted to patients with low back pain.[26]

Key Question 2. Nonpharmacological Noninvasive Therapies

Evidence on the effectiveness of nonpharmacological therapies for acute low back pain was limited. There was limited evidence that spinal manipulation, heat, massage, and low-level laser therapy are associated with some beneficial effects versus a sham therapy, no intervention, or usual care (Table F). Effects on pain or function were moderate for exercise, massage, and heat, and otherwise small.

For chronic low back pain, a number of nonpharmacological therapies appear to be effective for improving pain or function (Table G). These include exercise, yoga, and tai chi; various psychological therapies; multidisciplinary rehabilitation; acupuncture; spinal manipulation (vs. an inert treatment); and low-level laser therapy. Effects were small to moderate in magnitude. Other physical modalities were not associated with beneficial effects, or evidence was insufficient to estimate effects. Based on head-to-head comparisons, multidisciplinary rehabilitation was associated with small to moderate beneficial effects on pain and function versus standard physical therapy, and spinal manipulation and massage were associated with small beneficial effects versus other active interventions (Table H). There was no strong evidence of differences in effectiveness among different exercise, massage, spinal manipulation, or acupuncture techniques, or among different types of psychological therapies.

Assessment and reporting of harms for nonpharmacological therapies were suboptimal but indicated no serious harms. Reported harms were generally related to superficial symptoms at the application site or a temporary increase in pain.

Table A. Pharmacological therapies versus placebo for acute low back pain

Drug	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Acetaminophen	No effect	1 RCT	Low	No effect	1 RCT	Low
NSAIDs	Small (pain intensity); no effect (pain relief)	1 SR (4 RCTs)	Moderate	Small	2 RCTs	Low
Opioids (buprenorphine patch)	Small	2 RCTs	Low	No evidence	--	--
Skeletal muscle relaxants	Pain relief: RR, 1.72 (95% CI, 1.32 to 2.22) at 5–7 days	1 SR (3 RCTs) + 1 RCT	Moderate	No evidence	--	--
Benzodiazepines	Unable to estimate	2 RCTs	Insufficient	Unable to estimate	2 RCTs	Insufficient
Antiseizure medications	No evidence	--	--	No evidence	--	--
Systemic corticosteroids	No effect	2 RCTs	Low	No effect	2 RCTs	Low

CI = confidence interval; NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized controlled trial; RR = relative risk; SOE = strength of evidence; SR = systematic review.

Table B. Pharmacological therapies versus active comparators for acute low back pain

Drug	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Acetaminophen vs. NSAID	Unable to estimate	1 RCT	Insufficient	Unable to estimate	1 RCT	Insufficient
NSAID vs. NSAID	No difference	6 RCTs	Moderate	--	--	--
Opioid vs. NSAID	Unable to estimate (inconsistent)	3 RCTs	Insufficient	No difference	1 RCT	Insufficient
Long-acting opioid vs. long-acting opioid	No clear difference	4 RCTs	Moderate	No clear difference	4 RCTs	Moderate
Long-acting opioid vs. short-acting opioid	No clear difference*	6 RCTs	Low	--	--	--
Benzodiazepine (diazepam) vs. skeletal muscle relaxant	No difference	1 RCT	Low	--	--	--
Skeletal muscle relaxant vs. skeletal muscle relaxant	No clear difference	1 SR (2 RCTs)	Low	--	--	--

CI = confidence interval; NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized controlled trial; RR = relative risk; SOE = strength of evidence; SR = systematic review; SSRI = selective serotonin reuptake inhibitor.

Table C. Pharmacological therapies versus placebo for chronic low back pain

Drug	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Acetaminophen	No evidence	--	--	No evidence	--	--
NSAIDs	Moderate	1 SR (4 RCTs)	Moderate	Small	1 SR (2 RCTs)	Low
Opioids	Small	1 SR (6 RCTs)	Moderate	Small	1 SR (4 RCTs)	Moderate
Skeletal muscle relaxants	Unable to estimate	3 RCTs	Insufficient	--	--	--
Tramadol	Moderate	1 SR (5 RCTs) + 2 RCTs	Moderate	Small	1 SR (5 RCTs) + 2 RCTs	Moderate
Benzodiazepines: tetrazepam	Failure to improve at 10–14 days: RR, 0.71 (95% CI, 0.54 to 0.93)	1 SR (2 RCTs)	Low	--	--	--
Tricyclic antidepressants	No effect	1 SR (4 RCTs)	Moderate	No effect	1 SR (2 RCTs)	Low
Antidepressants: SSRI	No effect	1 SR (3 RCTs)	Moderate	--	--	--
Antidepressants: duloxetine	Small	3 RCTs	Moderate	Small	3 RCTs	Moderate
Gabapentin/pregabalin	Unable to estimate	2 RCTs	Insufficient	Unable to estimate	2 RCTs	Insufficient

CI = confidence interval; NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized controlled trial; RR = relative risk; SOE = strength of evidence; SR = systematic review; SSRI = selective serotonin reuptake inhibitor.

Table D. Pharmacological therapies versus active comparators for chronic low back pain

Drug	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Acetaminophen vs. NSAID	Unable to estimate	1 RCT	Insufficient	Unable to estimate	1 RCT	Insufficient
NSAID vs. NSAID	No difference	6 RCTs	Moderate	--	--	--
Opioid vs. NSAID	Unable to estimate (inconsistent)	3 RCTs	Insufficient	No difference	1 RCT	Insufficient
Long-acting opioid vs. long-acting opioid	No clear difference	4 RCTs	Moderate	No clear difference	4 RCTs	Moderate
Long-acting opioid vs. short-acting opioid	No clear difference*	6 RCTs	Low	--	--	--
Benzodiazepine (diazepam) vs. skeletal muscle relaxant	No difference	1 RCT	Low	--	--	--
Skeletal muscle relaxant vs. skeletal muscle relaxant	No clear difference	1 SR (2 RCTs)	Low	--	--	--

*Although some RCTs found long-acting opioids to be associated with greater pain relief than short-acting opioids, patients randomized to long-acting opioids also received higher doses of opioids.
NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized controlled trial; SOE = strength of evidence; SR = systematic review.

Table E. Pharmacological therapies versus placebo for radicular low back pain

Drug	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
NSAIDs	Small	1 SR (2 RCTs)	Low	--	--	--
Benzodiazepines: diazepam	RR, 0.5 (95% CI, 0.3 to 0.8)	1 RCT	Low	No effect	1 RCT	Low
Systemic corticosteroids	No effect	5 RCTs	Moderate	No effect	5 RCTs	Moderate
Gabapentin/pregabalin	Unable to estimate	5 RCTs	Insufficient	Unable to estimate	5 RCTs	Insufficient

CI = confidence interval; NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized controlled trial; RR = relative risk; SOE = strength of evidence; SR = systematic review.

Table F. Nonpharmacological treatments versus sham, no treatment, or usual care for acute or subacute low back pain

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Exercise vs. usual care	Moderate	1 SR (3 RCTs) + 3 RCTs	Low	Moderate	1 SR (3 RCTs) + 3 RCTs	Low
Acupuncture vs. sham	Small	2 RCTs	Low	No effect	5 RCTs	Low
Massage vs. sham	Moderate	1 SR (2 RCTs)	Low	Moderate	1 SR (2 RCTs)	Low
Massage vs. usual care	Small to no effect	2 RCTs	Low	Small to no effect	2 RCTs	Low
Spinal manipulation vs. sham	Small	2 RCTs	Low	No effect	1 SR (3 RCTs)	Low
Heat wrap vs. placebo	Moderate	1 SR (2 RCTs) + 2 RCTs	Moderate	Moderate	1 SR (2 RCTs)	Moderate
Low-level laser therapy plus NSAID vs. sham plus NSAID	Moderate	1 RCT	Low	Small	1 RCT	Low
Lumbar supports vs. no lumbar supports or inactive treatment	Unable to determine	5 RCTs	Insufficient	Unable to determine	5 RCTs	Insufficient

NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized controlled trial; SOE = strength of evidence; SR = systematic review.

Table G. Nonpharmacological treatments versus sham, no treatment, or usual care for chronic low back pain

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Exercise vs. usual care	Small	1 SR (19 RCTs) + 1 SR	Moderate	Small	1 SR (17 RCTs) + 1 SR	Moderate
Motor control exercises vs. minimal intervention	Moderate (short to long term)	1 SR (2 RCTs)	Low	Small (short to long term)	1 SR (3 RCTs)	Low
Tai chi vs. wait list or no tai chi	Moderate	2 RCTs	Low	Small	1 RCT	Low
Yoga vs. usual care	Moderate	1 RCT	Low	Moderate	1 RCT	Low
Yoga vs. education	Small (short term) and no effect (long term)	5 RCTs (short term) + 4 RCTs (long term)	Low	Small (short term) and no effect (long term)	5 RCTs (short term) + 4 RCTs (long term)	Low
Progressive relaxation vs. wait-list control	Moderate	1 SR (3 RCTs)	Low	Moderate	1 SR (3 RCTs)	Low
EMG biofeedback vs. wait list or placebo	Moderate	1 SR (3 RCTs)	Low	No effect	1 SR (3 RCTs)	Low
Operant therapy vs. wait-list control	Small	1 SR (3 RCTs)	Low	No effect	1 SR (2 RCTs)	Low
Cognitive-behavioral therapy vs. wait-list control	Moderate	1 SR (5 RCTs)	Low	No effect	1 SR (4 RCTs)	Low
Multidisciplinary rehabilitation vs. no multidisciplinary rehabilitation	Moderate	1 SR (3 RCTs)	Low	Small	1 SR (3 RCTs)	Low
Multidisciplinary rehabilitation vs. usual care	Moderate (short term), small (long term), favors rehabilitation	1 SR (9 RCTs) (short term) + 1 SR (7 RCTs) (long term)	Moderate	Small (short and long term)	1 SR (9 RCTs) (short term) + 1 SR (7 RCTs) (long term)	Moderate
Acupuncture vs. sham acupuncture	Moderate	1 SR (4 RCTs) + 4 RCTs	Low	No effect	1 SR (4 RCTs) + 4 RCTs	Low
Acupuncture vs. no acupuncture	Moderate	1 SR (4 RCTs)	Moderate	Moderate	1 SR (3 RCTs)	Moderate
Spinal manipulation vs. sham manipulation	No effect	1 SR (3 RCTs) + 1 RCT	Low	Unable to estimate	1 RCT	--
Spinal manipulation vs. inert treatment	Small	7 RCTs	Low	--	--	--
Massage vs. usual care	No effect	1 RCT	Low	Unable to estimate	2 RCTs	Insufficient
Ultrasound vs. sham ultrasound	No effect	1 SR (3 RCTs)	Low	Unable to estimate	5 RCTs	Insufficient
Ultrasound vs. no ultrasound	No effect	1 SR (2 RCTs)	Low	No effect	1 SR (2 RCTs)	Low
TENS vs. sham TENS	No effect	1 SR (4 RCTs)	Low	No effect	1 SR (2 RCTs)	Low
PENS vs. sham PENS	Unable to estimate	2 RCTs	Insufficient	Unable to estimate	2 RCTs	Insufficient

Electrical muscle stimulation vs. sham, no stimulation, or usual care	No evidence	--	--	No evidence	--	--
Low-level laser therapy vs. sham laser	Small	3 RCTs	Low	Small	3 RCTs	Low
Lumbar supports vs. no lumbar supports	Unable to estimate	2 RCTs	Insufficient	Unable to estimate	2 RCTs	Insufficient
Traction vs. placebo, sham, or no traction	Unable to estimate	1 SR (13 RCTs)	Insufficient	Unable to estimate	1 SR (13 RCTs)	Insufficient
Kinesio taping® vs. sham taping	No effect	2 RCTs	Low	No effects	2 RCTs	Low

EMG = electromyography; PENS = percutaneous electrical nerve stimulation; RCT = randomized controlled trial; SOE = strength of evidence; SR = systematic review; TENS = transcutaneous electrical nerve stimulation.

Table H. Nonpharmacological treatments versus active comparators for chronic low back pain

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
MCE vs. general exercise (short term)	Small, favors MCE for short term	1 SR (6 RCTs)	Low	Small, favors MCE	1 SR (6 RCTs)	Low
MCE vs. general exercise (intermediate term)	Small, favors MCE for intermediate term	1 SR (3 RCTs)	Low	--	--	--
MCE vs. general exercise (long term)	Small, favors MCE for long term	1 SR (4 RCTs)	Low	Small, favors MCE	1 SR (3 RCTs)	Low
MCE vs. multimodal physical therapy (intermediate term)	Moderate, favors MCE	1 SR (4 RCTs)	Low	Moderate, favors MCE	1 SR (3 RCTs)	Low
MCE + exercise vs. exercise alone	No clear difference	2 RCTs	Low	--	--	--
Pilates vs. usual care + physical activity	No effect to small effect, favors Pilates	7 RCTs	Low	No clear difference	7 RCTs	Low
Pilates vs. other exercise	No clear difference	3 RCTs	Low	No clear difference	3 RCTs	Low
Tai chi vs. other exercise	Moderate, favors tai chi	1 RCT	Low	--	--	--
Yoga vs. exercise	Small, favors yoga	1 SR (5 RCTs)	Low	--	--	--
Psychological therapies vs. exercise or physical therapy	No clear difference	1 SR (6 RCTs)	Low	--	--	--
Psychological therapies vs. psychological therapies	No clear difference	10 RCTs	Moderate	No clear difference	10 RCTs	Moderate
Multidisciplinary rehabilitation vs. physical therapy (short term)	Small, favors multidisciplinary rehabilitation	1 SR (12 RCTs)	Moderate	Small, favors multidisciplinary rehabilitation	1 SR (13 RCTs)	Moderate

Multidisciplinary rehabilitation vs. physical therapy (long term)	Moderate, favors multidisciplinary rehabilitation	1 SR (9 RCTs)	Moderate	Moderate, favors multidisciplinary rehabilitation	1 SR (10 RCTs)	Moderate
Spinal manipulation vs. other active interventions (exercise, usual care, medications, massage)	No clear difference	1 SR (6 RCTs)	Moderate	No clear difference	1 SR (6 RCTs)	Moderate
Acupuncture vs. medications	Small, favors acupuncture	1 SR (3 RCTs)	Low	Small, favors acupuncture	1 SR (3 RCTs)	Low

MCE = motor control exercise; RCT = randomized controlled trial; SOE = strength of evidence; SR = systematic review.

Discussion

Key Findings and Strength of Evidence

The key findings of this review are described in the summary-of-evidence table (Table I).

Table I. Summary of evidence

Key Question	Intervention	Outcome	Strength of Evidence	Conclusion
Key Question 1. Pharmacological therapies	Acetaminophen	Acetaminophen vs. placebo, acute LBP: Pain and function	Low	One good-quality trial found no difference between acetaminophen vs. placebo in pain intensity or function through 3 weeks.
		Acetaminophen vs. NSAID, acute LBP: Pain and global improvement	Insufficient	A systematic review found no difference between acetaminophen vs. NSAIDs in pain intensity (3 trials; pooled SMD, 0.21; 95% CI, −0.02 to 0.43) or likelihood of experiencing global improvement (3 trials; RR, 0.81; 95% CI, 0.58 to 1.14) at ≤3 weeks, although estimates favored NSAIDs.
		Acetaminophen vs. placebo, chronic LBP	Insufficient	No study evaluated acetaminophen vs. placebo.
		Acetaminophen vs. NSAID, chronic LBP	Insufficient	There was insufficient evidence from 1 trial to determine effects of acetaminophen vs. NSAIDs.
		Acetaminophen vs. other interventions, acute LBP	Insufficient	There was insufficient evidence from 4 trials to determine effects of acetaminophen vs. other interventions.
		Acetaminophen vs. placebo: Adverse events (serious adverse events)	Moderate	One trial found no difference between scheduled acetaminophen, as-needed acetaminophen, or placebo in risk of serious adverse events (~1% in each group).
		Acetaminophen vs. NSAIDs: Adverse events	Moderate	A systematic review found that acetaminophen was associated with lower risk of side effects vs. NSAIDs.
		Acetaminophen vs placebo, NSAID, or other intervention, radicular LBP	Insufficient	No study evaluated acetaminophen for radicular low back pain.

Key Question 1. Pharmacological therapies	NSAIDs	NSAIDs vs. placebo, acute LBP: Pain and function	Moderate for pain, low for function	A systematic review found NSAIDs to be associated with greater improvement in pain intensity vs. placebo (4 studies; WMD, −8.39; 95% CI, −12.68 to −4.10; chi-square, 3.47; p >0.1), but 4 trials found no clear effects on the likelihood of achieving significant pain relief. One subsequent trial also found lower pain intensity after the first dose vs. placebo. One trial found NSAIDs to be associated with better function vs. placebo.
		NSAIDs vs. placebo, chronic LBP: Pain and function	Moderate for pain, low for function	A systematic review found NSAIDs to be associated with greater improvement in pain vs. placebo (4 trials; WMD, −12.40; 95% CI, −15.53 to −9.26; chi-square, 1.82; p >0.5); 2 trials found NSAIDs to be associated with greater improvement in function.
		NSAIDs vs. placebo, radicular LBP: Pain	Low	A systematic review found no difference in pain intensity between NSAIDs vs. placebo (2 trials; WMD, −0.16; 95% CI, −11.92 to 11.59; chi-square, 7.25; p <0.01).
		NSAID plus another intervention vs. other intervention alone	Insufficient	There was insufficient evidence from 2 trials of an NSAID plus another intervention vs. the other intervention alone to determine effectiveness.
		NSAIDs vs. interventions other than acetaminophen and opioids	Insufficient	There was insufficient evidence from 2 trials to determine the effects of NSAIDs vs. interventions other than acetaminophen and opioids.
		NSAID vs. NSAID, acute or chronic LBP: Pain	Moderate	A systematic review found that most trials of 1 NSAID vs. another found no differences in pain relief in patients with acute LBP (15 of 21 trials) or chronic LBP (6 of 6 trials).
		NSAIDs vs. placebo: Adverse events	Moderate	A systematic review found NSAIDs to be associated with more side effects vs. placebo (10 trials; RR, 1.35; 95% CI, 1.09 to 1.68).
		COX-2-selective NSAIDs vs. nonselective NSAIDs: Adverse events	Moderate	COX-2-selective NSAIDs were associated with lower risk of side effects vs. nonselective NSAIDs (4 trials; RR, 0.83; 95% CI, 0.70 to 0.99).
		Opioids vs. placebo, chronic LBP: Pain and function	Moderate	A systematic review found opioids to be associated with greater short-term improvement vs. placebo in pain scores (6 trials; SMD, −0.43; 95% CI, −0.52 to −0.33; I2 = 0.0%, for a mean difference of ~1 point on a 0–10 pain scale) and function (4 trials; SMD, −0.26; 95% CI, −0.37 to −0.15; I2 = 0.0%, for a mean difference of ~1 point on the RDQ); 3 additional trials reported results consistent with the systematic review.

Key Question 1. Pharmacological therapies	Opioids, tramadol, and tapentadol	Tramadol vs. placebo, chronic LBP: Pain and function	Moderate	A systematic review found tramadol to be associated with greater short-term pain relief vs. placebo (5 trials; SMD, −0.55; 95% CI, −0.66 to −0.44; I2 = 86%, for a mean difference of 1 point or less on a 0–10 pain scale) and function (5 trials; SMD, −0.18; 95% CI, −0.29 to −0.07; I2 = 0%, for a mean difference of ~1 point on the RDQ); 2 trials not included in the systematic review reported results consistent with the systematic review findings.
		Buprenorphine patch vs. placebo, subacute or chronic LBP: Pain and function	Low for pain, insufficient for function	A systematic review included 2 trials that found buprenorphine patches to be associated with greater short-term improvement in pain vs. placebo patches; effects on function showed no clear effect or were unclearly reported.
		Opioids vs. NSAIDs, chronic LBP: Pain relief, function	Insufficient	Three trials reported inconsistent effects of opioids vs. NSAIDs for pain relief; 1 trial found no difference in function.
		Opioids vs. acetaminophen, acute LBP: Days to return to work, pain	Insufficient	One trial found no significant differences between opioids vs. acetaminophen in days to return to work; pain was not reported.
		Long acting opioids vs. long-acting opioids: Pain and function	Moderate	Four trials found no clear differences among different long-acting opioids in pain or function.
		LongL-acting opioids vs. short-acting opioids: Pain	Low	Six trials found no clear differences between long-acting vs. short-acting opioids in pain relief. Although some trials found long-acting opioids to be associated with greater pain relief, patients randomized to long-acting opioids also received higher doses of opioids.
		Opioids vs. placebo: Adverse events	Moderate	Short-term use of opioids was associated with higher risk vs. placebo of nausea, dizziness, constipation, vomiting, somnolence, and dry mouth; risks of opioids were higher in trials that did not use an enriched enrollment and withdrawal design.
	Skeletal muscle relaxants	SMRs vs. placebo, acute LBP: Pain	Moderate	A systematic review found SMRs to be superior to placebo for short-term pain relief (≥2-point or 30% improvement on a 0–10 VAS pain scale) after 2 to 4 days (4 trials; RR, 1.25; 95% CI, 1.12 to 1.41; I2 = 0%) and 5 to 7 days (3 trials; RR, 1.72; 95% CI, 1.32 to 2.22; I2 = 0%); a more recent large (n = 562) trial was consistent with the systematic review.
		SMR plus NSAID vs. NSAID alone, acute LBP: Pain	Low	A systematic review found no difference between an SMR plus an NSAID vs. the NSAID alone in the likelihood of experiencing pain relief, although the estimate favored combination therapy (2 trials; RR, 1.56; 95% CI, 0.92 to 2.70; I2 = 84%); 1 other trial (n = 197) also reported results that favored combination therapy.
		SMR vs. placebo, chronic LBP: Pain	Insufficient	Evidence from 3 placebo-controlled trials was insufficient to determine effects due to imprecision and inconsistent results.

Key Question 1. Pharmacological therapies	Skeletal muscle relaxants	SMR vs. SMR, acute or chronic LBP: Pain	Low	Three trials in a systematic review found no differences in any outcome among different SMRs for acute or chronic low back pain.
		SMR vs. placebo, acute LBP: Adverse events	Moderate	A systematic review found skeletal muscle relaxants for acute LBP to be associated with increased risk of any adverse event vs. placebo (8 trials; RR, 1.50; 95% CI, 1.14 to 1.98) and increased risk of central nervous system events, primarily sedation (8 trials; RR, 2.04; 95% CI, 1.23 to 3.37; I2 = 50%); 1 additional placebo-controlled trial was consistent with these findings.
	Benzodiazepines	Benzodiazepines vs. placebo, acute LBP: Pain and function	Insufficient	There was insufficient evidence from 2 trials with inconsistent results to determine effectiveness of benzodiazepines vs. placebo.
		Tetrazepam vs. placebo, chronic LBP: Pain, overall improvement	Low	A systematic review included 2 trials that found tetrazepam to be associated with lower likelihood of no improvement in pain at 5–7 days (RR, 0.82; 95% CI, 0.72 to 0.94) and at 10–14 days (RR, 0.71; 95% CI, 0.54 to 0.93) vs. placebo, and lower likelihood of no overall improvement at 10–14 days (RR, 0.63; 95% CI, 0.42 to 0.97).
		Diazepam vs. placebo, acute or subacute radicular pain: Pain and function	Low	One trial found no difference between diazepam 5 mg twice daily for 5 days vs. placebo in function at 1 week through 1 year or in other outcomes, including analgesic use, return to work, or likelihood of surgery through 1 year of followup. Diazepam was associated with lower likelihood of experiencing ≥50% improvement in pain at 1 week (41% vs. 79%; RR, 0.5; 95% CI, 0.3 to 0.8).
		Benzodiazepines vs. SMRs, chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 2 trials with inconsistent results to determine effects of benzodiazepines vs. SMRs.
		Diazepam vs. cyclobenzaprine, chronic LBP: Muscle spasms	Low	One trial found no difference between diazepam vs. cyclobenzaprine in outcomes related to muscle spasm.
		Benzodiazepines vs. placebo: Adverse events	Low	A systematic review found that central nervous system adverse events such as somnolence, fatigue, and lightheadedness were reported more frequently with benzodiazepines vs. placebo, although harms were not reported well; no trial was designed to evaluate risks with long-term use of benzodiazepines such as addiction, abuse, or overdose.

Key Question 1. Pharmacological therapies	Antidepressants	Tricyclic antidepressants or SSRIs vs. placebo, chronic LBP: Pain and function	Moderate for pain, low for function	A systematic review found no differences in pain between tricyclic antidepressants vs. placebo (4 trials; SMD, −0.10; 95% CI, −0.51 to 0.31; I2 = 32%) or SSRIs vs. placebo (3 trials; SMD, 0.11; 95% CI, −0.17 to 0.39; I2 = 0%); there was also no difference between antidepressants vs. placebo in function (2 trials; SMD, −0.06; 95% CI, −0.40 to 0.29; I2 = 0%).
		Duloxetine vs. placebo, chronic LBP: Pain and function	Moderate	Three trials found duloxetine to be associated with lower pain intensity (differences, 0.58 to 0.74 on a 0 to 10 scale) and better function (differences, 0.58 to 0.74 on the Brief Pain Inventory-Interference scale) vs. placebo.
		Duloxetine vs. tricyclic antidepressants	Insufficient	No study compared duloxetine vs. a tricyclic antidepressant.
		Antidepressants vs. placebo: Adverse events, serious adverse events	Moderate	Antidepressants were associated with higher risk of any adverse events compared with placebo, with no difference in risk of serious adverse events.
Key Question 1. Pharmacological therapies	Antiseizure medications	Antiseizure medications, acute nonradicular LBP	Insufficient	No trial evaluated antiseizure medications for acute nonradicular LBP.
		Gabapentin vs. placebo, chronic nonradicular LBP	Insufficient	One trial found no difference between gabapentin (up to 3600 mg/day) vs. placebo but did not meet inclusion criteria because it was published only as an abstract.
		Gabapentin vs. placebo, chronic radicular LBP: Pain and function	Insufficient	There was insufficient evidence from 3 poor-quality trials with inconsistent findings to determine effects of gabapentin vs. placebo.
		Topiramate vs. placebo, chronic radicular or mixed radicular and nonradicular LBP: Pain	Insufficient	Two trials reported inconsistent results for effects of topiramate vs. placebo.
		Pregabalin vs. placebo, chronic radicular LBP: Pain and function	Insufficient	Two trials reported inconsistent effects of pregabalin vs. placebo for pain or function.
		Pregabalin vs. amitriptyline: Pain	Insufficient	There was insufficient evidence from 1 poor-quality trial to determine effects of pregabalin vs. amitriptyline.
		Pregabalin plus transdermal buprenorphine vs. transdermal buprenorphine, chronic nonradicular LBP: Pain	Insufficient	One small trial found that the addition of pregabalin 300 mg/day to transdermal buprenorphine was associated with substantially lower pain scores than transdermal buprenorphine alone at 3 weeks (difference, ~26 points on a 0 to 100 scale; $p < 0.05$), but the estimate was very imprecise

Key Question 1. Pharmacological therapies	Antiseizure medications	Pregabalin plus another analgesic vs. the other analgesic alone: Pain	Insufficient	One trial found pregabalin (mean, 2.1 mg/kg/day) plus celecoxib to be associated with lower pain scores than celecoxib alone (difference, 11 points on a 0–100 scale; p = 0.001) after 4 weeks, and 1 trial found no effects of adding pregabalin (titrated to 300 mg/day) to tapentadol prolonged release vs. tapentadol prolonged release alone on pain or the SF-12 after 8 weeks.
		Gabapentin vs. placebo: Adverse events	Low	Two trials of gabapentin vs. placebo reported no clear differences in risk of adverse events.
		Topiramate vs. placebo: Withdrawal due to adverse events, sedation, diarrhea	Insufficient	Two trials of topiramate vs. placebo reported inconsistent effects on risk of withdrawal due to adverse events; 1 of the trials found topiramate to be associated with higher risk of sedation and diarrhea.
		Pregabalin vs. placebo: Withdrawal due to adverse events, somnolence, dizziness	Insufficient	Two trials of pregabalin vs. placebo reported inconsistent effects on risk of withdrawal due to adverse events, somnolence, and dizziness; 1 of the trials used an enrichment/withdrawal design
	Corticosteroids	Systemic corticosteroids vs. placebo, acute nonradicular LBP: Pain and function	Low	Two trials found no differences between a single intramuscular injection or a 5-day course of systemic corticosteroids vs. placebo for pain or function.
		Systemic corticosteroids vs. placebo, radicular LBP: Pain and function	Moderate	Five trials consistently found no differences between systemic corticosteroids (administered as a single bolus or as a short taper) vs. placebo in pain or function for acute or unspecified-duration LBP; 1 trial found no effect on need for spine surgery.
		Systemic corticosteroids vs. placebo, spinal stenosis: Pain and function	Low	One trial found no differences through 12 weeks of followup between a 3-week course of prednisone vs. placebo in pain intensity, the RDQ, or any SF-36 subscale.
		Systemic corticosteroids: Adverse events	Low	Trials of systemic corticosteroids did not report serious adverse events, including hyperglycemia requiring medical treatment, but adverse events were not reported well in some trials.
Key Question 2. Nonpharmacological noninvasive therapies	Exercise	Exercise vs. no exercise, acute to subacute LBP: Pain and function	Low	A systematic review found no differences between exercise therapy vs. no exercise in pain (3 trials; WMD, 0.59 at intermediate term on a 0 to 100 scale; 95% CI, −11.51 to 12.69) or function (3 trials; WMD at short term, −2.82; 95% CI, −15.35 to 9.71; WMD at intermediate term, 2.47; 95% CI, −0.26 to 5.21). For subacute LBP, there were also no differences in pain (5 trials; WMD, 1.89 on a 100-point scale; 95% CI, −1.13 to 4.91) or function (4 trials; WMD, 1.07; 95% CI, −3.18 to 5.32). Three subsequent trials for acute to subacute LBP reported inconsistent effects of exercise vs. usual care on pain and function

Key Question 2. Nonpharmacological noninvasive therapies	Exercise	Exercise vs. no exercise, chronic LBP: Pain and function	Moderate	A systematic review found exercise to be associated with greater pain relief vs. no exercise (19 trials; WMD, 10 on a 0 to 100 scale; 95% CI, 1.31 to 19.09), although the effect on function was small and not statistically significant (17 trials; WMD, 3.00 on a 0 to 100 scale; 95% CI, −0.53 to 6.48). Results from a more recent systematic review using more restrictive criteria and from additional trials not included in the systematic reviews were generally consistent with these findings.
		MCE vs. minimal intervention, chronic LBP: Pain and function	Low	A systematic review included 2 trials that found MCE to be associated with lower pain scores in the short term (WMD, −12.48 on a 0 to 100 scale; 95% CI, −19.04 to −5.93), intermediate term (WMD, −10.18; 95% CI, −16.64 to −3.72), and long term (WMD, −13.32; 95% CI, −19.75 to −6.90) vs. a minimal intervention. MCE was also associated with better function at short term (3 trials; WMD, −9.00 on 0 to 100 scale; 95% CI, −15.28 to −2.73), intermediate term (2 trials; WMD, −5.62; 95% CI, −10.46 to −0.77), and long term (2 trials; WMD, −6.64; 95% CI, −11.72 to −1.57).
		Exercise vs. usual care, nonacute LBP: Work disability	Moderate	A systematic review found no clear effects of exercise therapy versus usual care on likelihood of short- or intermediate-term (~6 months) disability, but exercise was associated with lower likelihood of work disability at long term (~12 months) followup (10 comparisons in 8 trials; OR, 0.66; 95% CI, 0.48 to 0.92).
		Exercise vs. usual care, radicular LBP: Pain and function	Low	Three trials not included in the systematic reviews found effects that favored exercise vs. usual care or no exercise in pain and function, although effects were small.
		MCE vs. general exercise, chronic LBP: Pain and function	Low	A systematic review found MCE to be associated with lower pain intensity at short term (6 trials; WMD, −7.80 on 0 to 100 scale; 95% CI, −10.95 to −4.65) and intermediate term (3 trials; WMD, −6.06; 95% CI, −10.94 to −1.18) vs. general exercise, but effects were smaller and no longer statistically significant at long term (4 trials; WMD, −3.10; 95% CI, −7.03 to 0.83). MCE was also associated with better function in the short term (6 trials; WMD, −4.65 on 0 to 100 scale; 95% CI, −6.20 to −3.11) and long term (3 trials; WMD, −4.72; 95% CI, −8.81 to −0.63). One of 2 subsequent trials found no effect on pain, although effects on function were consistent with the systematic review.
		Exercise vs. exercise, acute or chronic LBP	Moderate	For comparisons involving other types of exercise techniques, there were no clear differences in >20 head-to-head trials of patients with acute or chronic LBP.

Key Question 2. Nonpharmacological noninvasive therapies	Exercise	Exercise: Adverse events	Low	Harms were poorly reported in trials of exercise. When reported, harms were typically related to muscle soreness and increased pain, or no harms were reported; no serious harms were reported.
	Pilates	Pilates vs. usual care plus physical activity, chronic LBP: Pain and function	Low	A systematic review included 7 trials that found Pilates to be associated with small (mean difference, −1.6 to −4.1 points) or no clear effects on pain at the end of treatment vs. usual care plus physical activity and no clear effects on function.
		Pilates vs. other exercise, chronic LBP: Pain and function	Low	Three trials found no clear differences between Pilates vs. other types of exercise in pain or function.
	Tai chi	Tai chi vs. wait list or no tai chi, chronic LBP: Pain and function	Low	Two trials found tai chi to be associated with improved pain-related outcomes vs. wait list or no tai chi (mean differences, 0.9 and 1.3 on a 0 to 10 scale); 1 trial also found tai chi to be associated with better function (mean difference, 2.6 on the RDQ; 95% CI, 1.1 to 3.7).
		Tai chi vs. other exercise, chronic LBP: Pain	Low	One trial found tai chi to be associated with lower pain intensity vs. backward walking or jogging through 6 months (mean differences, −0.7 and −0.8), but there were no differences vs. swimming.
		Tai chi: Adverse events	Low	One trial of tai chi reported a small temporary increase in back pain symptoms, and 1 trial reported no harms.
	Yoga	Yoga vs. usual care, chronic LBP: Pain and function	Low	One trial found Iyengar yoga to be associated with lower pain scores (24 vs. 37 on a 0–100 VAS; $p < 0.001$) and better function (18 vs. 21 on the 0 to 100 ODI; $p < 0.01$, on a 0 to 100 scale) vs. usual care at 24 weeks.
		Yoga vs. exercise, chronic LBP: Pain and function	Low	A systematic review found yoga to be associated with lower pain intensity and better function vs. exercise in most trials, although effects were small and differences were not always statistically significant (5 trials).
		Yoga vs. education, chronic LBP: Pain and function	Moderate	Yoga was associated with lower short-term pain intensity vs. education (5 trials; SMD, −0.45; 95% CI, −0.63 to −0.26; $I2 = 0\%$), but effects were smaller and not statistically significant at long term followup (4 trials; SMD, −0.28; 95% CI, −0.58 to −0.02; $I2 = 47\%$); yoga was also associated with better function at short-term (5 trials; SMD, 0.45; 95% CI, −0.65 to −0.25; $I2 = 8\%$) and long-term followup (4 trials; SMD, 0.39; 95% CI, −0.66 to −0.11; $I2 = 40\%$).
		Yoga: Adverse events	Low	Reporting of harms was suboptimal, but adverse events, when reported, were almost all classified as mild to moderate.

Key Question 2. Nonpharmacological noninvasive therapies	Psychological therapies	Progressive relaxation vs. wait-list control, chronic LBP: Pain and function	Low	A systematic review found progressive relaxation superior to wait-list control for post-treatment pain intensity (3 trials; mean difference, −19.77 on 0 to 100 VAS; 95% CI, −34 to −5.20; I2 = 57%) and functional status (3 trials; SMD, −0.88; 95% CI, −1.36 to −0.39; I2 = 0%)
		EMG biofeedback, chronic LBP: Pain and function	Low	A systematic review found EMG biofeedback to be associated with lower pain intensity at the end of treatment (3 trials; SMD, −0.80; 95% CI, −1.32 to −0.28; I2 = 0%), with no clear effect on function (3 trials).
		Operant therapy, chronic LBP: Pain and function	Low	A systematic review found operant therapy to be associated with lower pain intensity at the end of treatment (3 trials; SMD, −0.43; 95% CI, −0.75 to −0.1; I2 = 0%), with no clear effect on function (2 trials).
		Cognitive therapy vs. wait-list control, chronic LBP	Insufficient	There was insufficient evidence from 2 trials to determine effects of cognitive therapy vs. wait-list control due to inconsistency and imprecision.
		Cognitive-behavioral and other combined therapy vs. wait-list control, chronic LBP: Pain and function	Low	A systematic review found cognitive-behavioral and other combined psychological therapy to be associated with greater improvements in post-treatment pain intensity compared with wait-list control (5 trials; SMD, −0.60; 95% CI, −0.97 to −0.22; I2 = 40%), but effects on function were smaller and not statistically significant (4 trials; SMD, −0.37; 95% CI, −0.87 to 0.13; I2 = 50%).
		Psychological therapies vs. exercise or physical therapy, chronic LBP: Pain and function	Low	A systematic review found no clear differences between psychological therapies vs. exercise therapy in pain intensity (2 trials) or between psychological therapies plus physiotherapy vs. physiotherapy alone (6 trials) in pain or function, although 1 small subsequent trial found combination therapy to be associated with greater improvements in pain and function immediately after treatment.
		Psychological therapies vs. psychological therapies: Pain and function	Moderate	Ten trials found no clear differences among different psychological therapies in pain or function.
		Psychological therapies: Adverse events	Low	Harms were not well reported, but no included trial reported any adverse events associated with psychological therapies.

Key Question 2. Nonpharmacological noninvasive therapies	Multidisciplinary rehabilitation	Multidisciplinary rehabilitation vs. usual care, chronic LBP: Pain, function, return to work	Moderate	A systematic review found multidisciplinary rehabilitation, compared with usual care, to be associated with lower short-term pain intensity (9 trials; SMD, −0.55; 95% CI, −0.83 to −0.28; I2 = 72%, or ~1.4-point mean difference on a 0 to 10 point numeric rating scale) and disability (9 trials; SMD, −0.41; 95% CI, −0.62 to −0.19; I2 = 58%, or ~2.5-point mean difference on the RDQ); effects on long-term pain intensity and disability also favored multidisciplinary rehabilitation but were smaller (7 trials; SMD, −0.21; 95% CI, −0.37 to −0.04; I2 = 25% and 6 trials; SMD,−0.23; 95% CI, −0.40 to −0.06; I2 = 19%, respectively), with no difference in likelihood of return to work (7 trials; OR, 1.04; 95% CI, 0.73 to 1.47; I2 = 31%).
		Multidisciplinary rehabilitation vs. no multidisciplinary rehabilitation, chronic LBP: Pain and function	Low	A systematic review found multidisciplinary rehabilitation, compared with no multidisciplinary rehabilitation, to be associated with lower short-term pain intensity (3 trials; SMD, −0.73; 95% CI, −1.22 to −0.24; I2 = 64%, or ~1.7-point mean difference on a 0 to 10 numeric rating scale) and disability (3 trials; pooled SMD, −0.49; 95% CI, −0.76 to −0.22; I2 = 0%, or ~2.9-point mean difference on the RDQ); there was insufficient evidence to assess effects on long-term outcomes.
		Multidisciplinary rehabilitation vs. physical therapy, chronic LBP: Pain and function	Moderate	A systematic review found multidisciplinary rehabilitation, compared with nonmultidisciplinary physical therapy, to be associated with lower short-term pain intensity (12 trials; SMD, −0.30; 95% CI, −0.54 to −0.06; I2 = 80%, or an approximate 0.6-point mean difference on a 0 to 10 point numeric rating scale) and disability (13 trials; SMD, −0.39; 95% CI, −0.68 to −0.10; I2 = 88%, or an approximate 1.2-point mean difference on the RDQ); multidisciplinary rehabilitation was also associated with lower long-term pain intensity (9 trials; SMD, −0.51; 95% CI, −1.04 to 0.01; I2 = 92%) and function (10 trials; SMD, −0.68; 95% CI, −1.19 to −0.16; I2 = 94%) and greater likelihood for return to work (8 trials; OR, 1.87; 95% CI, 1.39 to 2.53; I2 = 0%).
		Multidisciplinary rehabilitation, acute LBP, radicular LBP	Insufficient	No study evaluated the effectiveness of multidisciplinary rehabilitation for acute LBP or for radicular LBP.
		Multidisciplinary rehabilitation: Adverse events	Low	Harms were poorly reported in trials of multidisciplinary rehabilitation, although no serious harms were reported.

Key Question 2. Nonpharmacological noninvasive therapies	Acupuncture	Acupuncture vs. sham acupuncture, subacute LBP: Pain	Low	A systematic review found acupuncture to be associated with lower pain intensity vs. sham acupuncture using nonpenetrating needles (2 trials; mean difference, 9.38 on a 0 to 100 VAS; 95% CI, 1.76 to 17.0; I2 = 27%); 3 other trials reported effects consistent with these findings. One trial of sham acupuncture using penetrating needles to nonacupuncture points found no effect on pain. There were no clear effects on function in 5 trials.
		Acupuncture vs. sham acupuncture, chronic LBP: Pain and function	Moderate	A systematic review found acupuncture to be associated with lower pain intensity vs. sham acupuncture (superficial needling at acupuncture or nonacupuncture points or nonpenetrating pressure at acupuncture points) immediately at the end of treatment (4 trials; WMD, −16.76; 95% CI, −33.3 to −0.19; I2 = 90%) and at up to 12 weeks (3 trials; WMD, −9.55; 95% CI, −16.5 to −2.58; I2 = 40%), but there were no differences in function. Four additional trials reported results consistent with these findings.
		Acupuncture vs. no acupuncture, chronic LBP	Moderate	A systematic review found acupuncture to be associated with lower pain intensity (4 trials; SMD, −0.72; 95% CI, −0.94 to −0.49; I2 = 51%) and better function (3 trials; SMD, −0.94; 95% CI, −1.41 to −0.47; I2 = 78%) immediately after treatment vs. no acupuncture. Mean effects on pain ranged from 7 to 24 points on a 0 to 100 point scale; for function, 1 trial reported a difference of 8 points on a 0 to 100 scale and the other 2 trials showed small or no clear differences at long-term followup.
		Acupuncture vs. NSAIDs, acute LBP: Overall improvement	Low	A systematic review found acupuncture to be associated with slightly greater likelihood of overall improvement vs. NSAIDs at the end of treatment (5 trials; RR, 1.11; 95% CI, 1.06 to 1.16; I2 = 0%).
		Acupuncture vs. medications (NSAIDs, muscle relaxants and analgesics), chronic LBP: Pain and function	Low	A systematic review found acupuncture to be associated with better pain relief (3 trials; WMD, −10.56 on a 0 to 100 scale; 95% CI, −20.34 to −0.78; I 2 = 0%) and improvement in function (3 trials; SMD, −0.36; 95% CI, −0.67 to −0.04; I2 = 7%) immediately postintervention.
		Acupuncture: Adverse events	Low	Harms of acupuncture were poorly reported in the trials, although no serious adverse events were reported.
	Massage	Massage vs. sham massage, acute LBP: Pain and function	Low	A systematic review included 2 trials that found massage to be associated with greater short-term (1 week) improvement in pain (SMD, −0.92; 95% CI, −1.35 to −0.48) and function (SMD, −1.76; 95% CI, −3.19 to −0.32) vs. sham therapy, but there was no difference in pain or function at 5 weeks in 1 trial.

Key Question 2. Nonpharmacological noninvasive therapies	Massage	Massage vs. usual care, chronic LBP: Pain and function	Low	One trial found no difference between foot reflexology vs. usual care in pain or function, and 1 trial found structural or relaxation massage to be associated with better function (mean, 2.5 to 2.9 points on the RDQ) vs. usual care at 10 weeks; effects were less pronounced at 52 weeks.
		Massage vs. other interventions, subacute to chronic LBP: Pain and function	Moderate	A systematic review found massage to be associated with better effects on short-term pain in 7 of 9 trials (mean differences, −0.6 to −0.94 points on a 0 to 10 scale) and better effects on short-term function in 3 of 4 trials.
		Massage plus another active intervention vs. the other intervention alone, subacute to chronic LBP: Pain and function	Low	A systematic review included 5 trials that generally found massage plus another intervention to be superior to the other intervention without massage for short-term pain, with effects somewhat stronger in trials in which massage was combined with exercise; few differences were observed for function or long-term pain. Two subsequent trials of massage plus exercise reported findings generally consistent with these findings.
		Massage vs. massage: Pain and function	Insufficient	Comparisons of different massage techniques were too heterogeneous and effects were too small from 6 trials to determine effects on pain and function.
		Massage: Adverse events	Low	Harms were not well reported in trials of massage, although no serious adverse events were reported; 2 trials reported soreness during or shortly after the treatment.
	Spinal manipulation	Spinal manipulation, acute LBP: Pain and function	Low for function, insufficient for pain	Two trials (1 included in a systematic review) found spinal manipulation to be associated with better effects on function vs. sham manipulation (statistically significant in 1 trial); in 1 trial, effects on pain favored manipulation but were small and not statistically significant (mean difference, −0.50; 95% CI, −1.39 to 0.39).
		Spinal manipulation vs. sham manipulation, chronic LBP: Pain and function	Low for pain, insufficient for function	A systematic review found spinal manipulation to be associated with small, statistically nonsignificant effects vs. sham manipulation on pain at 1 month (3 trials; WMD, −3.24; 95% CI, −13.62 to 7.15 on a 0 to 100 scale; I2 = 53%); 1 trial reported similar results for function (SMD, −0.45; 95% CI, −0.97 to 0.06); 1 trial not included in the systematic review reported generally consistent results.
		Spinal manipulation vs. inert treatment, acute LBP: Pain and function	Low	A systematic review found no differences between spinal manipulation vs. inert treatment in pain relief at 1 week (3 trials; WMD, 0.14 on a 0 to 10 scale; 95% CI, −0.69 to 0.96; I2 = 27%), although 1 trial found spinal manipulation to be associated with better long term pain relief (mean difference, −1.20 at 3 months; 95% CI, 2.11 to −0.29); there were no differences in function at 1 week (2 trials; SMD, −0.08; 95% CI, −0.37 to 0.21; I2 = 0%) or at 3 months (1 trial; SMD, −0.28; 95% CI, −0.59 to 0.02).

Key Question 2. Nonpharmacological noninvasive therapies	Spinal manipulation	Spinal manipulation vs. inert treatment, chronic LBP	Low	One trial with low risk of bias found spinal manipulation to be associated with greater improvement in the “main complaint” vs. an inert treatment (mean difference, 0.9 on a 0 to 10 scale; 95% CI, 0.1 to 1.7); results from 3 trials with high risk of bias and 3 additional trials not included in the systematic review were somewhat inconsistent, although some trials reported effects that favored manipulation.
		Spinal manipulation vs. other active interventions, acute LBP: Pain and function	Moderate	A systematic review found no difference between spinal manipulation vs. other active interventions in pain relief at 1 week (3 trials; WMD, 0.06 on a 0 to 10 scale; 95% CI, −0.53 to 0.65; I2 = 0%), 1 month (3 trials; WMD, −0.15; 95% CI, −0.49 to 0.18; I2 = 0%), 3 to 6 months (2 trials; WMD, −0.20; 95% CI, −1.13 to 0.73; I2 = 81%), or 1 year (1 trial; mean difference, 0.40; 95% CI, −0.08 to 0.88). Findings were similar for function, with no differences observed at any timepoint. A subsequent trial of patients with acute or subacute LBP found that spinal manipulation was associated with moderate effects vs. usual care on pain and small effects on function at short-term followup, but effects were smaller and no longer statistically significant at 3 and 6 months.
		Spinal manipulation vs. other interventions, chronic LBP: Pain and function	Moderate	A systematic review found spinal manipulation to be associated with better short-term pain relief vs. other active interventions at 1 month (10 comparisons from 6 trials; WMD, −2.76 on a 0 to 100 scale; 95% CI, −5.19 to −0.32; I2 = 27%) and 6 months (7 comparisons from 4 trials; WMD, −3.07; 95% CI, −5.42 to −0.71; I2 = 0%), although the magnitude of effects was below the small/slight threshold. There was no difference at 12 months (3 trials; WMD, −0.76; 95% CI, −3.19 to 1.66; I2 = 0%). Manipulation was also associated with greater improvement in function vs. other active interventions at 1 month (10 comparisons from 6 trials; SMD, −0.17; 95% CI, −0.29 to −0.06; I2 = 3%); effects were smaller and no longer statistically significant at 6 and 12 months. Three trials not included in the systematic reviews reported results consistent with these findings.
		Spinal manipulation plus exercise or advice vs. exercise or advice alone, acute LBP: Function	Low	Four trials in a systematic review found spinal manipulation plus either exercise or advice to be associated with greater improvement in function at 1 week (SMD, −0.41; 95% CI, −0.73 to −0.10; I2 = 18%) vs. exercise or advice alone, but there were no differences at 1 month (3 trials; SMD, −0.09; 95% CI, −0.39 to 0.21; I2 = 37%) or 3 months (2 trials; SMD, −0.22; 95% CI, −0.61 to 0.16; I2 = 41%).

Key Question 2. Nonpharmacological noninvasive therapies	Spinal manipulation	Spinal manipulation plus another active treatment, chronic LBP: Pain and function	Low	A systematic review found spinal manipulation plus another active treatment to be associated with greater pain relief at 1 month (3 trials; WMD, −5.88 on a 0 to 100 scale; 95% CI, −10.85 to −0.90; I2 = 0%), 3 months (2 trials; mean difference, −7.23; 95% CI, −11.72 to −2.74; I2 = 43%), and 12 months (2 trials; mean difference, −3.31; 95% CI, −6.60 to −0.02; I2 = 12%) vs. the other treatment alone. Combination therapy was also associated with better function at 1 month, (2 trials; SMD, −0.40; 95% CI, −0.73 to −0.07; I2 = 0%), 3 months (2 trials; SMD, −0.22; 95% CI, −0.38 to −0.06; I2 = 33%), and 12 months (2 trials; SMD, −0.21; 95% CI, −0.34 to −0.09; I2 = 0%). One trial not included in the systematic review reported results consistent with these findings.
		Spinal manipulation plus home exercise and advice, radicular LBP	Low	One good-quality trial found spinal manipulation plus home exercise and advice to be associated with greater improvement in leg and back pain at 12 weeks vs. home exercise and advice alone (mean differences about 1 point on a 0 to 10 scale), but effects were smaller (0.3 to 0.7 points) and no longer statistically significant at 52 weeks.
		Spinal manipulation: Adverse events	Low	Harms were not reported well in most trials of spinal manipulation. No serious adverse events were reported, and most adverse events were related to muscle soreness or transient increases in pain.
	Ultrasound	Ultrasound vs. sham ultrasound, chronic LBP: Pain and function	Low for pain, insufficient for function	A systematic review found no difference between ultrasound vs. sham ultrasound in pain at the end of treatment (3 trials; mean difference, −7.12 on 0 to 100 scale; 95% CI, −18.0 to 3.75; I2 = 77%), and 2 trials found no effects on pain 4 weeks after the end of treatment. Evidence from 5 trials was too inconsistent to determine effects on function, although a larger good-quality trial found no effect on the RDQ.
		Ultrasound vs. no ultrasound, chronic LBP: Pain and function	Low	A systematic review found no differences between ultrasound vs. no ultrasound in pain (2 trials; mean difference, −2.16; 95% CI, −4.66 to 0.34; I2 = 0%) or back-specific function (2 trials; mean difference, −0.41; 95% CI, −3.14 to 2.32), but estimates were imprecise.
		Ultrasound plus exercise vs. exercise, chronic LBP: Pain and function	Insufficient	Evidence from 3 trials was insufficient to determine effects of ultrasound plus exercise vs. exercise alone on pain or function due to imprecision and methodological shortcomings.
		Ultrasound plus exercise vs. exercise, radicular LBP: Back pain, leg pain	Insufficient	A small trial found no differences between ultrasound plus exercise vs. sham ultrasound plus exercise in back pain, leg pain, or the ODI after 3 weeks of therapy.
		Ultrasound vs. other interventions	Insufficient	There was insufficient evidence from 3 small trials with methodological shortcomings to determine effects of ultrasound vs. other interventions.

Key Question 2. Nonpharmacological noninvasive therapies	Ultrasound	Ultrasound vs. other interventions, radiculopathy	Insufficient	There was insufficient evidence from 2 small trials with methodological shortcomings to determine effects of ultrasound vs. other interventions.
		Ultrasound, acute nonradicular LBP	Insufficient	No study evaluated the effectiveness of ultrasound for acute nonradicular LBP.
		Ultrasound vs. sham ultrasound: Adverse events	Low	One trial found no differences between ultrasound vs. sham ultrasound in risk of any adverse event (6.0% vs. 5.9%; RR, 1.03; 95% CI, 0.49 to 2.13) or serious adverse events (1.3% vs. 2.7%; RR, 0.48; 95% CI, 0.12 to 1.88).
	Transcutaneous electrical nerve stimulation	TENS vs. sham TENS, acute or subacute LBP: Pain and function	Insufficient	Evidence from single trials with methodological shortcomings was too limited to permit reliable conclusions regarding effectiveness.
		TENS vs. sham TENS, chronic LBP: Pain and function	Low	A systematic review found no differences between TENS vs. sham TENS in pain intensity (4 trials; WMD, −4.47 on a 0 to 100 scale; 95% CI, −12.84 to 3.89) or function (2 trials; WMD, −1.36 on a 0 to 100 scale; 95% CI, −4.38 to 1.66) at short-term followup; most trials found no effect on pain or function at the end of a course of treatment.
		TENS vs. acupuncture, chronic LBP: Pain	Low	A systematic review found no differences between TENS vs. acupuncture for short- (4 trials; SMD, 0.15; 95% CI, −0.33 to 0.63) or long-term pain (2 trials; SMD, 0.32; 95% CI, −0.33 to 0.96). Evidence for TENS vs. other interventions was too limited to permit reliable conclusions.
		TENS: Adverse events	Low	Evidence on harms associated with TENS was limited but suggests an increased risk of skin-site reactions without an increased risk of serious adverse events.
	Electrical muscle stimulation	EMS plus exercise vs. exercise, EMS vs. other interventions, acute or chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 5 RCTs to determine effects of EMS plus exercise vs. exercise alone or vs. other interventions due to methodological limitations and imprecision.
		EMS: Adverse events	Insufficient	There was insufficient evidence to determine harms of EMS.
	Percutaneous electrical nerve stimulation	PENS vs. sham PENS, PENS plus exercise vs. exercise, PENS vs. other interventions, chronic LBP (with or without radiculopathy)	Insufficient	There was insufficient evidence from 7 trials to determine effects of PENS vs. sham, PENS plus exercise vs. exercise alone, or PENS vs. other interventions due to methodological limitations, inconsistency, and imprecision.
		PENS: Adverse events	Insufficient	Harms were poorly reported in trials of PENS.

Key Question 2. Nonpharmacological noninvasive therapies	Interferential therapy	IFT vs. other interventions, IFT plus another intervention vs. the other intervention, subacute to chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 4 trials to determine effects of IFT vs. other interventions or IFT plus another intervention vs. the other intervention alone, due to methodological limitations and imprecision.
		IFT: Adverse events	Insufficient	No study evaluated harms of IFT.
	Superficial heat or cold	Heat wrap vs. placebo, acute or subacute LBP: Pain and function	Moderate	A systematic review found a heat wrap to be more effective than placebo for pain relief at 5 days (2 trials; mean difference, 1.06 on a 0 to 5 scale; 95% CI, 0.68 to 1.45) and disability at 4 days (mean difference, −2.10 on the RDQ; 95% CI, −3.19 to −1.01). Two subsequent trials also found a heat wrap to be associated with decreased pain intensity at 3 to 4 days (differences, 16 to 20 points on a 0 to 100 point VAS) or increased pain relief at 8 hours (difference, ~1.5 points on a 0 to 5 scale). Another trial found a heat wrap during emergency transport to be associated with substantially lower pain intensity vs, an unheated blanket on arrival to the hospital.
		Heat plus exercise vs. exercise alone, acute LBP: Pain and function	Low	One higher quality trial found heat plus exercise to be associated with greater pain relief (mean difference, 1.40 on 0 to 10 scale; 95% CI, 0.69 to 2.11) and higher function (mean RDQ difference, −3.20; 95% CI, −5.42 to −0) vs. exercise without heat at day 7.
		Heat plus NSAID vs. NSAID alone, acute LBP: Pain	Insufficient	One fair-quality trial found heat plus an NSAID to be associated with better pain scores versus an NSAID without heat at day 15 based on the McGill Pain Questionnaire (scoring methods unclear).
		Heat vs. simple analgesics, acute or subacute LBP: Pain and function	Low	A systematic review included 1 trial that found heat to be more effective for pain relief than acetaminophen (mean difference, 0.90 on a 0 to 10 scale; 95% CI, 0.50 to 1.30) or ibuprofen (0.65; 95% CI, 0.25 to 1.05) after 1 to 2 days of treatment; the heat wrap was also associated with greater improvement on the RDQ (mean differences, 2.00 on a 0 to 24 scale; 95% CI, 0.86 to 3.14, and 2.20; 95% CI, 1.11 to 3.29, respectively).
		Heat vs. exercise, acute LBP: Pain and function	Low	A systematic review included 1 trial that found no clear differences between heat vs. exercise in pain relief or function.
		Superficial cold vs. placebo	Insufficient	No study compared superficial cold vs. placebo or no cold treatment.
		Cold plus naproxen vs. naproxen alone, acute LBP: Pain	Insufficient	One small trial with methodological shortcomings found cold plus naproxen to be associated with better pain scores vs. naproxen alone based on the McGill Pain Questionnaire (scoring methods unclear)

Key Question 2. Nonpharmacological noninvasive therapies	Superficial heat or cold	Heat vs. cold	Insufficient	There was insufficient evidence from 3 trials to determine effects of heat vs. cold due to methodological limitations and imprecision.
		Heat vs. no heat or placebo: Adverse events, flushing	Low	Heat was not associated with increased risk of skin flushing vs. no heat or placebo in 2 trials; no serious adverse events were reported with use of heat.
		LLLT vs. sham laser, acute LBP	Insufficient	There was insufficient evidence from 1 trial to determine effectiveness of LLLT vs. sham laser due to serious methodological shortcomings and imprecision.
		LLLT vs. sham laser, chronic LBP: Pain and function	Low	Three of 4 trials found LLLT to be more effective than sham laser for pain, although methods for assessing pain and duration of followup varied; 2 trials found LLLT to be more effective than sham laser for function, with small magnitude of effect.
		LLLT plus NSAID vs. sham plus NSAID, acute or subacute LBP: Pain and function	Low	One trial found LLLT plus an NSAID to be associated with lower pain intensity vs. sham laser plus an NSAID or the NSAID alone (mean differences, 9 to 14 points on a 0 to 100 VAS); effects on the ODI also favored combination treatment but were smaller (differences <6 points).
		LLLT plus another intervention vs. the other intervention alone, chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 3 trials to determine effects of LLLT plus exercise vs. sham laser plus exercise alone due to methodological shortcomings and inconsistency.
		LLLT vs. another intervention: Pain and function	Insufficient	There was insufficient evidence to determine effects of LLLT vs. another intervention due to methodological shortcomings and imprecision.
		LLLT, differing wavelengths or doses	Insufficient	There was insufficient evidence to determine effects of different wavelengths or doses of LLLT due to methodological limitations and imprecision.
		LLLT: Adverse events	Low	Harms were not well reported in trials of LLLT, but no serious adverse events and no harms were reported.

Key Question 2. Nonpharmacological noninvasive therapies	Low- level laser therapy	LLLT vs. sham laser, acute LBP	Insufficient	There was insufficient evidence from 1 trial to determine effectiveness of LLLT vs. sham laser due to serious methodological shortcomings and imprecision.
		LLLT vs. sham laser, chronic LBP: Pain and function	Low	Three of 4 trials found LLLT to be more effective than sham laser for pain, although methods for assessing pain and duration of followup varied; 2 trials found LLLT to be more effective than sham laser for function, with small magnitude of effect.
		LLLT plus NSAID vs. sham plus NSAID, acute or subacute LBP: Pain and function	Low	One trial found LLLT plus an NSAID to be associated with lower pain intensity vs. sham laser plus an NSAID or the NSAID alone (mean differences, 9 to 14 points on a 0 to 100 VAS); effects on the ODI also favored combination treatment but were smaller (differences <6 points).
		LLLT plus another intervention vs. the other intervention alone, chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 3 trials to determine effects of LLLT plus exercise vs. sham laser plus exercise alone due to methodological shortcomings and inconsistency.
		LLLT vs. another intervention: Pain and function	Insufficient	There was insufficient evidence to determine effects of LLLT vs. another intervention due to methodological shortcomings and imprecision.
		LLLT, differing wavelengths or doses	Insufficient	There was insufficient evidence to determine effects of different wavelengths or doses of LLLT due to methodological limitations and imprecision.
		LLLT: Adverse events	Low	Harms were not well reported in trials of LLLT, but no serious adverse events and no harms were reported.
	Short-wave diathermy	Short-wave diathermy vs. sham diathermy, mixed-duration LBP: Effectiveness and adverse events	Insufficient	There was insufficient evidence from 5 RCTs to determine effects of short-wave diathermy vs. sham diathermy due to methodological limitations and imprecision.
		Short-wave diathermy: Adverse events	Insufficient	No study evaluated harms of short-wave diathermy.
	Lumbar supports	Lumbar supports vs. no lumbar supports or an inactive treatment, acute or subacute LBP: Pain and function	Insufficient	There was insufficient evidence from 5 trials to determine effects of lumbar supports vs. no lumbar supports or an inactive treatment due to methodological shortcomings and inconsistent results
		Lumbar supports vs. no lumbar supports, chronic LBP	Insufficient	There was insufficient evidence from 2 trials to determine effects of lumbar supports vs. no lumbar supports due to methodological shortcomings and inconsistent results.

Key Question 2. Nonpharmacological noninvasive therapies	Lumbar supports	Lumbar supports vs. no lumbar supports, mixed-duration LBP: Pain and function	Low	One trial found an inextensible, but not an extensible, lumbar supports to be associated with greater improvement in function vs. no lumbar support, but effects were small. There was no clear effect on function.
		Lumbar support plus education vs. education, acute or subacute LBP: Pain and function	Low	One trial found no differences between a lumbar support plus an education program vs. an education program alone in pain or function after 1 year
		Lumbar support plus exercise vs. exercise alone, chronic LBP: Pain and function	Low	One trial found no difference between a lumbar support plus exercise (muscle strengthening) vs. exercise alone in short-term (8 week) or long-term (6 month) pain or function.
		Lumbar support vs. other active treatments: Pain and function	Low	Three trials found no clear differences between lumbar supports vs. other active treatments in pain or function.
		Lumbar supports vs. lumbar supports: Pain and function	Insufficient	There was insufficient evidence from 2 trials to determine comparative effects of different types of lumbar supports for chronic LBP or back pain of mixed duration due to heterogeneous comparisons, methodological shortcomings, and imprecision.
		Lumbar supports: Adverse events	Low	Trials reported no harms associated with use of lumbar supports.
	Traction	Traction vs. placebo, sham, or no treatment, LBP with or without radicular symptoms: Pain, function, other outcomes	Insufficient	A systematic review included 13 trials that found no clear differences and inconsistent effects of traction vs. placebo, sham, or no treatment in pain, function, or other outcomes, although 2 trials reported favorable effects on pain in patients with radicular back pain.
		Traction vs. physiotherapy, LBP with or without radicular symptoms	Low	A systematic review included 5 trials that found no clear differences between traction plus physiotherapy vs. physiotherapy alone.

Key Question 2. Nonpharmacological noninvasive therapies	Traction	Traction vs. other interventions, LBP with or without radicular symptoms: Pain and function	Low	A systematic review included 15 trials of traction vs. other interventions that found no clear between traction vs. other active interventions in pain or function.
		Traction vs. traction	Low	A systematic review included 5 trials that found no clear differences among different types of traction.
		Traction: Adverse events	Low	Eleven trials of traction in a systematic review reported no adverse events or no difference in risk of adverse events vs. placebo or other interventions. Three subsequent trials reported findings consistent with the systematic review.
	Taping	Kinesio Taping® vs. sham taping, chronic LBP: Pain and function	Insufficient for pain, low for function	Two trials found no differences between Kinesio Taping vs. sham taping in back-specific function after 5 to 12 weeks; effects on pain were inconsistent.
		Functional Fascial Taping® plus exercise vs. sham taping plus exercise, chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 1 trial to determine effects of Functional Fascial Taping plus exercise vs. sham taping plus exercise due to methodological limitations and imprecision.
		Kinesio Taping vs. exercise therapy, chronic LBP: Pain and function	Low	Two trials found no differences between Kinesio Taping vs. exercise therapy in pain or function.
		Taping: Adverse events	Insufficient	No trial of taping reported harms.

CI = confidence interval; EMG = electromyography; EMS = electrical muscle stimulation; IFT = interferential therapy; LBP = low back pain; LLLT = low-level laser therapy; MCE = motor control exercise; NSAID = nonsteroidal anti-inflammatory drug; ODI = Oswestry Disability Index; OR = odds ratio; PENS = percutaneous electrical nerve stimulation; RDQ = Roland-Morris Disability Questionnaire; RR = relative risk; SF-12 = 12-item short form health survey; SF-36 = 36-item short form health survey; SMD = standardized mean difference; SMR = skeletal muscle relaxant; SSRI = selective serotonin reuptake inhibitor; TENS = transcutaneous electrical nerve stimulation; VAS = visual analog scale; WMD = weighted mean difference.

This report updates and expands on a previous review[15,16] that we conducted for the APS and ACP. Because of the large number of interventions addressed in this review, we used relevant well-conducted systematic reviews when available. All conclusions are based on the totality of evidence (i.e., studies included in systematic reviews plus additional primary studies). Across interventions, pain intensity was the most commonly reported outcome, followed by back-specific function, typically measured using the Roland-Morris Disability Questionnaire (RDQ) or the Oswestry Disability Index (ODI). When present, observed benefits were generally small (5 to 10 points on a 100-point visual analog scale or equivalent, or standardized mean difference [SMD] of 0.2 to 0.5) to moderate (10 to 20 points, or SMD of 0.5 to 0.8) for pain. Effects on function were typically smaller than effects on pain or were unclear; other outcomes (such as quality of life, mood, work, analgesic use, or use of resources) were generally reported inconsistently, and data were too sparse to reach reliable conclusions.

New evidence affected conclusions for several classes of medications. The prior review concluded that acetaminophen was effective for acute low back pain, primarily based on indirect evidence from trials of acetaminophen for other conditions and trials of acetaminophen versus other analgesics. However, a recent well-conducted trial—the first placebo-controlled trial in patients with acute low back pain—found acetaminophen to be no more effective than placebo (strength of evidence [SOE]: low).[27] For antidepressant drugs, no studies in the prior review evaluated drugs in the serotonin norepinephrine reuptake inhibitor class. Evidence from several trials indicates that duloxetine is more effective than placebo for pain and function in patients with chronic low back pain (SOE: moderate).[28-30] However, effects were small (less than 1 point on a 0 to 10 scale), and all trials were funded by the manufacturer of duloxetine and led by the same researcher. For antiseizure medications, new evidence is available on pregabalin for radicular low back pain, but the studies had methodological shortcomings and were too inconsistent to reliably estimate effects (SOE: insufficient).[31,32] The prior review found no studies on the effects of benzodiazepines for radiculopathy. One recent trial found that benzodiazepines were no more effective than placebo for this condition (SOE: low).[33] The trial also found that for some outcomes, such as return to work, benzodiazepines were associated with worse outcomes than placebo.

Main conclusions regarding the benefits and harms of pharmacological therapies for low back pain were otherwise relatively unchanged from the prior review and are summarized in Tables A–E. One area in which conclusions changed was the effectiveness of tricyclic antidepressants. In our prior review, tricyclic antidepressants were found to be associated with small beneficial effects for chronic low back pain. However, evidence reviewed for this report suggests that tricyclic antidepressants are not effective versus placebo (4 trials; SMD, −0.10; 95% confidence interval [CI], −0.51 to 0.31; I2 = 32%; SOE: moderate).[34] As noted previously, duloxetine, a serotonin norepinephrine reuptake inhibitor that is not associated with the anticholinergic and cardiac side effects of tricyclics, is now available as a potential alternative antidepressant.

Evidence on the effectiveness of opioids for low back pain remains limited to short-term trials showing modest effects versus placebo on short-term pain and function[35] (SOE: moderate). Findings regarding the increased risk of opioids versus placebo for harms such as constipation, nausea, sedation, and dry mouth are also unchanged. Trials of opioids for low back pain were not designed to assess risk of serious adverse events, such as overdose, abuse or addiction, or

accidental injuries, because of their relatively small samples and short duration of followup. In addition, trials of opioids typically excluded patients with risk factors for overdose, abuse, or addiction. However, observational studies of opioids for chronic pain in general (not restricted to low back pain) have shown an association with serious harms that appears to be dose dependent.[36]

Serious harms were generally not observed in trials of nonopioid medications, although harms were generally not reported well. Like trials of opioids, trials of nonopioid medications were not designed to assess risk of serious uncommon harms (e.g., liver toxicity with acetaminophen, bleeding with NSAIDs, fracture or infection with corticosteroids, or abuse or addiction with benzodiazepines).

The current report reviews several nonpharmacological therapies not addressed in the prior APS/ACP review. Evidence on taping (using techniques to increase skin tension) did not clearly show beneficial effects versus sham taping comparisons, although findings were limited by methodological shortcomings and inconsistency (SOE: insufficient to low). There was insufficient evidence to determine the effects of electrical muscle stimulation because of methodological shortcomings in the trials and imprecision (SOE: insufficient). Two trials found that tai chi was more effective than wait-list control for pain intensity and function[37] (SOE: low); effects appeared to be similar to those observed for other types of exercise and related interventions.

As in the APS/ACP review, we found little evidence to support the use of most passive physical modalities for low back pain. An exception was superficial heat, which was found to be more effective than a nonheated control for acute or subacute low back pain (SOE: moderate). Although evidence on effectiveness of ultrasound and TENS was previously classified as insufficient, additional evidence now supports the findings that ultrasound is not effective versus sham ultrasound[38] and that TENS is not effective versus sham TENS,[39] although the strength of evidence remains low because of methodological limitations in the trials and imprecision. Based on three trials,[40-42] low-level laser therapy was more effective than sham laser for pain, although methods for assessing pain and duration of followup varied; there was insufficient evidence from one trial to determine effects on function. Evidence to compare effects of one physical modality versus another, or a physical modality versus another active intervention, was generally too limited to reach reliable conclusions.

Harms were not well reported in trials of nonpharmacological therapies, although serious adverse events appear to be rare. For physical modalities, harms, when reported, were mostly related to superficial effects at the application site. Severe neurological complications were not reported in trials of lumbar spinal manipulation, and serious infections, bleeding, or other complications were not reported in trials of acupuncture.

Findings in Relationship to What Is Already Known

Our findings are generally consistent with those of prior systematic reviews on noninvasive treatments for low back pain, in part because our report builds on a prior review and utilizes previously published high-quality systematic reviews to inform its findings.

Our prior report and other previous systematic reviews[43,44] found that tricyclic antidepressants were associated with small beneficial effects for low back pain. However, the evidence reviewed for this report suggests that they are not effective versus placebo for pain relief (4 trials; SMD, −0.10; 95% CI, −0.51 to 0.31; I2 = 32%) or function.[34] One potential reason for the discrepancy between this finding and prior reviews is that some of the prior reviews did not conduct a meta-analysis.[44,45] A review[43] that conducted meta-analysis included a study that did not report being randomized and reported the largest effect in favor of antidepressants,[46] did not include relevant studies that were in the more current review,[47-49] and included two relevant studies in the meta-analysis for which data had to be imputed,[50,51] but did not report methods for imputation.

For nonpharmacological treatments, our findings are also generally consistent with other systematic reviews. Like other reviews, we found some evidence to support use of complementary and alternative medicine therapies, such as acupuncture, spinal manipulation, and massage.[52-56] Although acupuncture was no more effective than sham acupuncture in some trials, other reviews found that the overall evidence (including pooled estimates) suggests beneficial effects on pain.[57,58]

Findings regarding the effectiveness of exercise are similar to our prior review and other reviews.[59-61] Our findings are also consistent with reviews that focused on more specific types of exercise, such as aquatic exercise,[62] sling exercise,[63] walking, stability exercises,[64,65] or modifying patterns of movement.[66] Our findings that psychological therapies and multidisciplinary rehabilitation are both effective are consistent with our prior review and other reviews.[67] Other reviews that focused on related interventions, such as functional restoration or cognitive-behaviorally based physical therapy (in which the literature overlaps with that on multidisciplinary rehabilitation), have also reached positive conclusions.[68-70] As in our prior review, we found that for most physical modalities, evidence was too weak to determine effectiveness.

As in other reviews, we found that evidence on the effectiveness of therapies for radicular low back pain was quite limited.[71,72] As in other reviews, including our prior report, we found that systemic corticosteroids are not effective for radicular low back pain.[72, 73]

Applicability

A number of issues could impact the applicability of our findings. Some studies did not specifically enroll patients with acute, subacute, or chronic low back pain, but rather enrolled mixed populations or did not clearly describe the duration of symptoms. Relatively few studies enrolled patients specifically with radicular symptoms, and many studies did not specifically describe whether patients with radicular symptoms were excluded. Of studies of patients with nonradicular symptoms, most did not attempt to evaluate whether effectiveness varied in subgroups of patients defined by clinical, demographic, imaging, or other characteristics.

For nonpharmacological treatments, the applicability of our findings is affected by the variability among trials in the interventions and comparators evaluated. In trials that evaluated "usual care" comparators, the components of usual care were often not well described or standardized, making it difficult to apply findings to clinical practice. Other factors that could impact the applicability of our findings regarding nonpharmacological interventions include

differences related to the setting in which the intervention was performed (e.g., United States vs. another country, specialist vs. primary care setting) or to the training or skill of the person performing the intervention.

To help interpret the results of the trials, we categorized the magnitude of effects for pain and function using the system in the APS/ACP review. Based on these categories, beneficial effects, when present, were in the small or moderate range. However, effects that we classified as small (e.g., 5–10 points on a 0 to 100 scale for pain or function) are below some proposed thresholds for minimum clinically important differences (e.g., 15 points on a 0 to 100 visual analog scale for pain, 2 points on a 0 to 10 numeric rating scale for pain or function, 5 points on the RDQ, and 10 points on the ODI, or a 30% change from baseline).[74] Nonetheless, our classification system provides some objective benchmarks for assessing magnitude of effects, including the smaller effects typically observed in low back pain trials. We also evaluated the proportion of patients who experienced a clinically important improvement in pain or function (e.g., 50% improvement in pain or on the RDQ). However, many studies did not report such dichotomous outcomes, and among those that did, definitions for clinically important improvements varied. When present, most beneficial effects were observed at shorter term followup; effects were typically attenuated or no longer present at long term followup.

Implications for Clinical and Policy Decisionmaking

Our findings have implications for clinical and policy decisionmaking. Clinical practice guidelines recommend acetaminophen as a first-line pharmacological therapy for acute and chronic low back pain.[14,75] New evidence[27] that acetaminophen is ineffective for acute low back pain calls into question its appropriateness as a recommended therapy, although other factors, such as low cost, favorable side-effect profile, and effectiveness for other acute pain conditions, could also impact decisions regarding its use.[76] Although tricyclic antidepressants have long been recommended as a secondary treatment option for chronic low back pain, duloxetine has specifically been approved by the U.S. Food and Drug Administration for this condition and appears to be more effective than tricyclic antidepressants, as well as being associated with a more favorable safety profile, which could impact the selection of drugs within the antidepressant class.

The use of opioids for chronic pain has become an area of increasing concern because of uncertain long-term effectiveness and marked increases in the number of accidental overdoses, as well as other harms related to their abuse potential.[36] Patients with low back pain are frequently prescribed opioids and account for a high proportion of the patients prescribed opioids. Decisions regarding the appropriate use of opioids for low back pain must weigh short-term, relatively modest benefits against potential harms. Guidelines recommend risk assessment, careful patient selection, and close monitoring and followup in patients prescribed opioids.[77]

The continued paucity of evidence to determine effective treatments for radicular low back pain necessitates that most decisions are based on extrapolation of evidence on the effectiveness of treatments for nonradicular low back pain or other non–back-related neuropathic pain conditions. This could explain why antiseizure medications, such as gabapentin and pregabalin, are being prescribed more for radicular low back pain than other back pain, despite the lack of evidence showing that they are effective. Systemic corticosteroids continue to be used for

treatment of radicular back pain, presumably based on their known anti-inflammatory properties and use in epidural injections, despite trials showing that they are ineffective.

Our review supports clinical practice guidelines that found insufficient evidence to recommend most physical modalities other than superficial heat. However, these therapies are still commonly used in clinical practice. Among nonpharmacological therapies that were found to be effective, there was insufficient evidence to determine which patients are most likely to benefit from specific therapies. However, a recent trial found that a stratified approach (in which patients are assessed for risk factors for chronicity and higher risk patients receive more intensive cognitive-behavioral–based physical therapy) is more effective than usual care without a stratified approach, suggesting that psychologically based therapies and multidisciplinary rehabilitation may be the most effective approach in higher risk patients.[78] Other factors that may impact decisions regarding which nonpharmacological therapies to use include cost, availability, and patient preferences. There is some evidence that greater patient expectations of benefit from a particular treatment are associated with greater benefits,[79,80] suggesting that patient preferences should be considered in the selection of therapies. Barriers to use of some nonpharmacological therapies include high out-of-pocket expenses (e.g., for complementary and alternative medicine therapies) and nonavailability depending on locale or other factors (e.g., multidisciplinary rehabilitation).

Limitations of the Review Process

We included previously published systematic reviews. The reliability of systematic reviews depends on the rigor with which they are conducted.[81] Therefore, we focused on higher quality reviews. We did not conduct meta-analyses or update meta-analyses included in prior systematic reviews. However, for comparisons without a meta-analysis, we synthesized results qualitatively, using the methods in the AHRQ Methods Guide. For comparisons for which pooled results were available from prior systematic reviews, we evaluated the consistency of results from new trials against the pooled estimates.

Other limitations of the review process are that we excluded non–English language articles and did not search for studies published only as abstracts. We were unable to assess for publication bias using graphical or statistical methods to detect small sample effects; methodological limitations in the trials; heterogeneity in the interventions, populations, and outcomes addressed; and small numbers of trials for many comparisons. However, based on searches of reference lists, clinical trials registries, and peer review suggestions, we did not find evidence to suggest that unpublished trials would impact conclusions.

There are other noninvasive interventions for low back pain that we did not address—herbal medicines,[82] educational interventions,[83,84] advice to remain active,[83,85] mattresses, shoe insoles,[86] and others.[87,88] We also did not include comparisons of noninvasive therapies versus surgery or interventional procedures; trials of such comparisons appear to be relatively uncommon.

Limitations of the Evidence Base

The evidence base had a number of important limitations. As noted previously, evidence on the effectiveness of interventions for radicular low back pain was sparse. Most trials of nonpharmacological treatments focused on patients with chronic low back pain. A number of interventions were evaluated in small numbers of trials or in trials that had important methodological limitations, precluding strong conclusions. There were relatively few head-to-head trials of different interventions.

Another limitation of the evidence base is that studies were frequently short term and often evaluated patients only at the end of a course of therapy, making it difficult to determine long-term effects. In addition, many trials reported mean changes in outcome measures (typically pain and function) but did not report dichotomized outcomes (e.g., ≥30% or ≥50% pain relief or functional improvement). Because responses to pain treatments tend to be bimodal,[89] with patients tending to experience no benefit or marked benefit, assessment of outcomes based on continuous outcomes could obscure treatment effects.

Some limitations of the evidence were particularly relevant for trials of nonpharmacological interventions. Studies of nonpharmacological interventions were typically characterized by marked heterogeneity in the specific intervention techniques evaluated, as well as in the duration and intensity of treatments, which could attenuate treatment benefits if suboptimal treatment techniques or intensity of therapy were evaluated. In addition, a number of nonpharmacological therapies (e.g., psychological therapies, exercise therapy, massage, spinal manipulation) are difficult to blind effectively. Therefore, observed benefits could be due in part to placebo, attentional, or other nonspecific effects, and results are susceptible to performance and other biases, although it is not possible to reliably quantify the extent of such effects. Finally, trials of nonpharmacological therapies did not report harms well; this could be in part because serious harms are not expected with most of these treatments.

Research Gaps

A number of research gaps limit the full understanding of the effectiveness, comparative effectiveness, and harms of therapies for low back pain. More research is needed to determine effective treatments for low back pain with radicular symptoms. Trials should be designed to evaluate patients not just immediately after they have completed therapy but for longer periods of time, in order to help understand how long effects of treatment persist. For nonpharmacological treatments, research to identify optimal treatment techniques and regimens (including intensity and duration of treatments) would be helpful for defining more standardized interventions to be evaluated in trials.

Studies are needed to determine the long-term effectiveness and harms of opioids for chronic low back pain, including higher risk patients similar to those commonly encountered in clinical practice. Observational studies that are designed to assess serious long-term harms provide some evidence regarding risks of opioids for chronic pain in general, but data specifically on patients with low back pain are lacking.[36] For systemic corticosteroids, the largest trial to date was recently completed and should help further characterize the effectiveness (or lack thereof) of this treatment.[90]

More research is needed to help understand which patients are most likely to benefit from specific therapies.[91-95] Trials are also needed to confirm whether effects of risk-stratified approaches are reproducible in the United States[96,97] and to optimize their implementation.[98] More research is also needed to better understand whether combination therapy with different pharmacological or nonpharmacological treatments is associated with incremental benefits versus individual components of the combination therapy, and which combinations and sequences of therapy are the most effective.

Pain relief was the most commonly assessed outcome in trials of treatment for low back pain, followed by back-specific function. Trials should consistently assess other outcomes related to return to work, quality of life, and health care use in order to provide a more complete picture of treatment effects. Studies that evaluate the effectiveness of interventions for preventing future episodes of low back pain would also be very helpful, as low back pain can be a recurrent episodic condition and these patients are likely to account for a high proportion of resources. In order to provide balanced assessments of low back pain interventions, trials should more consistently and rigorously evaluate and report harms.

Conclusions

A number of pharmacological and nonpharmacological noninvasive treatments for low back pain are associated with small to moderate, primarily short-term, effects on pain versus placebo, sham, wait list, or no treatment. Effects on function are generally smaller than effects on pain. More research is needed to understand optimal selection of treatments, effective combinations and sequencing of treatments, and effectiveness of treatments for radicular low back pain.

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Introduction

Background

Nature and Burden of Low Back Pain

Low back pain is one of the most frequently encountered conditions in clinical practice. Up to 84 percent of adults have low back pain at some time in their lives, and over one quarter of U.S. adults report recent (in the last 3 months) low back pain.[1, 2] Low back pain can have major adverse impacts on quality of life and function. Low back pain is also costly—in 1998, total US health care expenditures for low back pain were estimated at $90 billion.[3] Since that time, costs of low back pain care have risen at a rate higher than observed for overall health expenditures.[4] In addition to high direct costs, low back pain is one of the most common reasons for missed work or reduced productivity while at work, resulting in high indirect costs.[5]

The prognosis for acute low back pain (generally defined as an episode lasting less than 4 weeks) is generally favorable. Most patients experience a rapid improvement in (and often a complete resolution of) pain and disability and are able to return to work.[6] In those with persistent symptoms, continued improvement is often seen in the subacute phase between 4 to 12 weeks, though at a slower rate than observed at first. In a minority of patients, low back pain lasts longer than 12 weeks, at which point it is considered chronic; levels of pain and disability often remain relatively constant thereafter.[7] Recently, a National Institutes of Health Research Task Force defined chronic low back pain as a back pain problem that has persisted at least 3 months and has resulted in pain on at least half the days in the past 6 months.[8] Patients with chronic back pain account for the bulk of the burdens and costs of low back pain.[9, 10] Predictors of chronicity are primarily related to psychosocial factors, such as presence of psychological comorbidities, maladaptive coping strategies (such as fear avoidance [avoiding activities because of fears that they will further damage the back] or catastrophizing [anticipating the worst possible outcomes from low back pain]), presence of nonorganic signs (symptoms without a distinct anatomical or physiological basis),[11] high baseline functional impairment, low general health status, and others.[7] Back pain is frequently associated with presence of depression and anxiety.

Attributing symptoms of low back pain to a specific disease or spinal pathology is a challenge.[12] Spinal imaging abnormalities such as degenerative disc disease, facet joint arthropathy, and bulging or herniated intervertebral discs are extremely common in patients with or without low back pain, particularly in older adults, and such findings are poor predictors for the presence or severity of low back pain.[13] Radiculopathy from nerve root impingement (often due to a herniated intervertebral disc) or spinal stenosis (narrowing of the spinal canal) are each present in about 4 to 5 percent of patients with low back pain and can cause neurological symptoms such as lower extremity pain, paresthesias, and weakness; the natural history and response to treatment for these conditions may differ from back pain without neurologic involvement.[14]

Interventions for Low Back Pain

Multiple treatment options for acute and chronic low back pain are available. Broadly, these can be classified as pharmacological treatments,[15] noninvasive nonpharmacological treatments,[16]

injection therapies,[17] and surgical treatments.[18] This report focuses on the comparative benefits and harms of pharmacological and noninvasive nonpharmacological treatments; each of these categories encompasses a number of different therapies. Pharmacological treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, and corticosteroids; nonpharmacological treatments include exercise and related interventions (e.g., yoga), complementary and alternative therapies (e.g., spinal manipulation, acupuncture, and massage), psychological therapies (e.g., cognitive-behavioral therapy, relaxation techniques, and operant therapy), physical modalities (e.g., traction, ultrasound, transcutaneous electrical nerve stimulation [TENS], low level laser therapy, interferential therapy, superficial heat or cold, back supports, and magnets), and multidisciplinary rehabilitation.

Rationale for Evidence Review

The burden of low back pain, the numerous noninvasive treatment options to be considered by clinicians and patients, and the availability of new evidence and interventions (e.g., duloxetine) warrant a comprehensive comparative effectiveness review of this topic. An existing guideline[14] and associated systematic reviews[15, 16] from the American College of Physicians and the American Pain Society were published in 2007, emphasizing the role of pharmacological therapies and noninvasive nonpharmacological therapies for low back pain in most situations. A systematic evidence review that includes recently published research, explores potential variability in response to treatment depending on patient characteristics, considers multiple outcomes related to pain and function, and separately considers benefits and harms of interventions for acute or chronic nonradicular low back pain, as well as conditions such as radiculopathy and spinal stenosis, may provide a better understanding of the comparative effectiveness of treatment options for acute and chronic low back pain and could be used to update existing clinical recommendations. To aid in the efficiency of the review process, this review will be conducted as an update of prior systematic reviews on pharmacological and nonpharmacological noninvasive treatments used to develop the 2007 APS/ACP clinical practice guideline and conducted by the same review team.[15, 16]

Scope of Review and Key Questions

The Key Questions; populations, interventions, comparators, outcomes, timing, settings, and study designs (PICOTS); and analytic framework used to guide this review are shown below.

Key Question 1. What are the comparative benefits and harms of different pharmacological therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis? Includes NSAIDs, acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, corticosteroids, and topical/patch-delivered medications.

Key Question 2. What are the comparative benefits and harms of different nonpharmacological noninvasive therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis?

Includes but is not limited to multidisciplinary rehabilitation, exercise (various types), physical modalities (ultrasound, transcutaneous electrical nerve stimulation, electrical muscle stimulation, interferential therapy, heat [various forms], and ice), traction tables/devices, back supports/bracing, spinal manipulation, various psychological therapies, acupuncture, massage therapy (various types), yoga, magnets, and low-level lasers.

PICOTS

Population(s)

- Adults with acute (<4 weeks), subacute (4 to 12 weeks), or chronic (>12 weeks) nonradicular low back pain, radicular low back pain, or symptomatic spinal stenosis.
- Exclude: Children, pregnant women
- Exclude: Patients with low back pain related to cancer, infection, inflammatory arthropathy, high velocity trauma, fracture; or low back pain associated with severe or progressive neurological deficits

Interventions

KQ1: Oral or Topical Pharmacologic Therapies (Or Combinations Thereof)

- Nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, naproxen, celecoxib, acetylsalicylic acid (aspirin)
- Nonopioid analgesics, such as acetaminophen
- Opioid analgesics, such as oxycodone, hydrocodone, hydromorphone, morphine, fentanyl
- Tramadol and tapentadol (medications with dual mechanisms of action on the opioid receptor and as a norepinephrine reuptake inhibitor)
- Antidepressants, such as tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors (SNRIs), and selective serotonin-reuptake inhibitors (SSRIs), or serotonin antagonist and reuptake inhibitors (SARIs)
- Skeletal muscle relaxants
- Benzodiazepines
- Corticosteroids, such as prednisone or prednisolone
- Antiepileptic drugs, such as gabapentin or pregabalin
- Capsaicin or topical lidocaine
- Exclude: Intravenously administered medications

KQ2: Noninvasive, Nonpharmacological Therapies (Or Combinations Thereof)

- Interdisciplinary or multicomponent rehabilitation
- Psychological therapies, such as cognitive behavioral therapy
- Exercise and related interventions, such as yoga or tai chi
- Complementary and alternative medicine therapies: spinal manipulation, acupuncture, massage
- Passive physical modalities: heat, cold, ultrasound, transcutaneous electrical nerve stimulation (TENS), electrical muscle stimulation (EMS), interferential therapy (IFT), short-wave diathermy, traction, low level laser therapy, lumbar supports/braces
- Other noninvasive treatments, such as taping
- Exclude: Invasive, nonsurgical therapies (e.g., injections) and surgical therapies

Comparisons

- Any included pharmacological or nonpharmacological intervention or combination of interventions (combinations may include both pharmacological and nonpharmacological components) versus any other included intervention or combination of interventions, placebo (drug trials), sham (functionally-inert) treatments, or no treatment.

Outcomes

- Final health outcomes
  - Reduction or elimination of low back pain, including related leg symptoms
  - Improvement in back-specific and overall function
  - Improvement in health-related quality of life (HRQOL)
  - Reduction in work disability/return to work
  - Global improvement
  - Number of back pain episodes or time between episodes
  - Patient satisfaction
- Adverse effects of intervention(s)
  - Pharmaceutical: serious (anaphylaxis, death) and nonserious (mild allergic or untoward) drug reactions or effects; opioid addiction or overdose
  - Nonpharmaceutical: serious (death, neurological including cauda equine syndrome, fracture, local skin burns, etc.) and nonserious (mild transient local or general soreness, stiffness, aching; local skin irritation, etc.)

Timing

- Duration of followup: Short term (up to 6 months) and long term (at least 1 year)

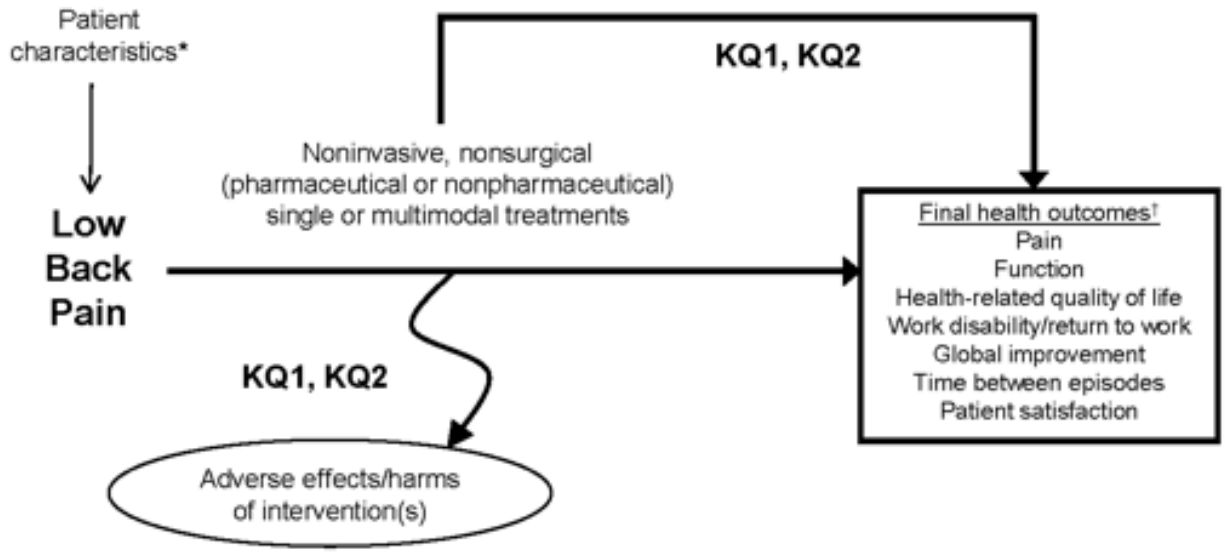
Setting

- Any nonhospital setting or in self-directed care

Analytic Framework

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

Figure 1. Analytic framework



* Patient characteristics include clinical, demographic, and psychosocial risk factors associated with low back pain outcomes.
† Intermediate outcomes are typically not measured (e.g., inflammation).
KQ = Key Question.

Methods

The methods for this Comparative Effectiveness Review (CER) follow the guidance in the Agency for Healthcare Research and Quality (AHRQ) "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[19]

Topic Refinement and Review Protocol

This topic was nominated to AHRQ for a CER through a public process. The Scientific Resource Center developed preliminary Key Questions based on input from the topic nominator. An Evidence-based Practice Center further revised the Key Questions and defined the populations, interventions, comparators, outcomes, timing, and study designs (PICOTS) of interest with input from a group of Key Informants assembled for this purpose. Key Informants disclosed financial and other conflicts of interest prior to participation. The AHRQ Task Order Officer and the investigators reviewed the disclosures and determined that the Key Informants had no conflicts of interest that precluded participation. The provisional Key Questions, PICOTS, and analytic framework were posted on the AHRQ Web site for public comment from December 17, 2013, through January 17, 2014.

After reviewing public comments, the research team at our Evidence-based Practice Center developed the final protocol with input from AHRQ and a Technical Expert Panel (TEP) convened for this report. The TEP consisted of 14 members with expertise in primary care, pain medicine, behavioral sciences, physical medicine and rehabilitation, complementary and alternative therapies, physical therapy, occupational medicine, and pharmacology. TEP members disclosed financial and other conflicts of interest prior to participation. The AHRQ Task Order Officer and the investigators reviewed the disclosures and determined that the Key Informants had no conflicts of interest that precluded participation. Some changes were made in response to public comments. The PICOTS were revised to include tai chi as an intervention and the time between back pain episodes was added as an outcome. The Key Questions and PICOTS were also revised to include combinations of therapies as interventions and comparators. We made additional wording edits to the Key Questions to clarify inclusion of oral and topical pharmacological therapies and to group the nonpharmacological noninvasive therapies into related categories (e.g., exercise and related interventions, complementary and alternative therapies, psychological therapies, and physical modalities). We also revised the PICOTS to be clearer that the population included patients with acute, subacute, or chronic low back pain, and added self-directed care to the setting description.

The final version of the protocol for this CER was posted on the AHRQ Effective Health Care Program web site (www.effectivehealthcare.ahrq.gov) on October 9, 2014. The protocol was registered in the PROSPERO international database of prospectively registered systematic reviews.

Literature Search Strategy

A research librarian conducted searches in Ovid MEDLINE, the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews, through August 2014 (see Appendix A for full search strategies). We restricted search start dates to January 2008

because searches in the prior APS/ACP review, were conducted through October 2008; the APS/ACP review was used to identify studies published prior to 2008.[20] For interventions (electrical muscle stimulation, taping, tai chi) not addressed in the APS/ACP review, we searched the same databases without a search date start restriction.

We also hand-searched the reference lists of relevant studies and searched for unpublished studies in ClinicalTrials.gov.

We conducted an update search in April 2015 using the same search strategy as in the original search.

Study Selection

We developed criteria for inclusion and exclusion of studies based on the Key Questions and PICOTS, in accordance with the AHRQ Methods Guide.[21] Inclusion and exclusion criteria are summarized below and described in more detail in Appendix B. Abstracts were reviewed by two investigators, and all citations deemed potentially appropriate for inclusion by at least one of the reviewers was retrieved. 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 can be found in Appendix C; excluded studies and primary reason for exclusion can be found in Appendix D.

Population and Condition of Interest

This report focuses on adults with low back pain of any duration (categorized as acute [<4 weeks], subacute [4 to 12 weeks], and chronic [≥12 weeks]), including nonradicular and radicular low back pain. Radicular pain was defined as back pain with leg pain, with or without sensory or motor deficits in a nerve root distribution; radicular pain could be based on clinical presentation or require imaging correlation (e.g., due to herniated disc or spinal stenosis). Patients with nonradicular low back pain could have nonspecific imaging findings such as degenerative disc disease, bulging intervertebral disc, or facet joint arthropathy. Patients with low back pain due to cancer, infection, inflammatory arthropathy, high velocity trauma, fracture, low back pain during pregnancy, and low back pain associated with severe or progressive neurological deficits were excluded.

Interventions and Comparisons

We included pharmacologic and noninvasive, nonpharmacological therapies for low back pain. Pharmacological therapies were restricted to those administered orally or topically; we evaluated nonsteroidal anti-inflammatory drugs, acetaminophen, opioids, tramadol and tapentadol, antidepressants, skeletal muscle relaxants, benzodiazepines, corticosteroids, anti-epileptic medications, capsaicin, and lidocaine. We excluded studies of medications administered intravenously but included studies of medications administered intramuscularly. Nonpharmacological therapies were multidisciplinary rehabilitation (also known as interdisciplinary rehabilitation, which we defined as a coordinated program with both physical and biopsychosocial treatment components (e.g., exercise therapy and cognitive behavioral

therapy) provided by professionals from at least two different specialties; psychological therapies; exercise and related interventions (e.g., yoga and tai chi); complementary and alternative therapies (spinal manipulation, acupuncture, and massage); passive physical modalities (heat, cold, ultrasound, transcutaneous electrical nerve stimulation [TENS], electrical muscle stimulation [EMS], interferential therapy [IFT], short-wave diathermy, low level laser therapy [LLLT], and lumbar supports or braces); and taping. Although we placed nonpharmacological interventions into broad groupings for the purpose of organizing the report, this was not meant to imply that they are associated with similar effectiveness or necessarily based on similar mechanisms of action, and the benefits and harms of each intervention was evaluated separately. Interventional therapies involving injections to the spine, ablative therapies, and surgical therapies were excluded. For opioids, we excluded the drug propoxyphene, a weak analgesic associated with risk of cardiac arrhythmia which is no longer available in the United States or Europe. For skeletal muscle relaxants and benzodiazepines, we included drugs not available in the United States but available in Europe, but noted such instances.

Comparisons were of an included therapy versus placebo (drug trials), sham (functionally inert) treatments (nonpharmacological intervention), no treatment, wait list, or usual care (usually defined as care as typically provided at the discretion of the clinician, though components of usual care varied across studies and settings), as well as comparisons of one included therapy versus another. We also evaluated comparisons of the combination of one included therapy plus another included therapy, versus one of the therapies alone. We excluded comparisons involving multicomponent therapy that did not meet the definition for multidisciplinary rehabilitation and did not compare the effects of the multicomponent therapy versus individual components, because it is not possible to determine the incremental benefits of multicomponent therapy over its individual components from such comparisons.

Outcomes, Timing, and Setting

We evaluated effects of interventions on reduction or elimination of low back pain, including related leg symptoms, improvement in back-specific and overall function, improvement in health-related quality of life (HRQOL), reduction in work disability/return to work, global improvement, number of back pain episodes or time between episodes, and patient satisfaction. Of these outcomes, pain and function were the most consistently reported, and we designated them as priority outcomes for the purpose of reporting results. We also evaluated adverse effects, including serious adverse events (e.g., anaphylaxis with medications, neurological complications, and death) and less serious adverse events. When possible, timing of outcomes was stratified as long term (at least 1 year) and short term (up to 6 months); we also noted outcomes assessed immediately after the completion of a course of treatment. We included studies conducted in inpatient or outpatient settings.

Study Designs

Given the large number of interventions and comparisons addressed in this review, we included systematic reviews of randomized trials.[22, 23] For each intervention, we selected the systematic review that was the most relevant to our Key Questions and scope (as defined in the PICOTS), had the most recent search dates, and was of highest quality based on assessments

using the AMSTAR tool.[24] We included nonoverlapping reviews of the same intervention that addressed specific outcomes, populations, or interventions, and in some cases included more than one overlapping review that was similar in terms of search dates and quality, if we could not identify a single best "match." If good-quality systematic reviews were not available, we included fair-quality systematic reviews only if we could address the methodological shortcomings of the review (e.g., if a review reported overall risk of bias of studies but did not report details regarding specific methodological shortcomings, we assessed the risk of bias in the primary studies ourselves). We preferentially selected good-quality systematic reviews that were more comprehensive (e.g., a systematic review on exercise therapy in general, versus a specific type of exercise therapy) or were updates of reviews included in the APS/ACP review. We compared the results of our report with the findings from systematic reviews that were not included in the discussion.

We supplemented systematic reviews with randomized trials that were not included in the reviews. We did not include systematic reviews identified in update searches, but checked reference lists for additional randomized trials. For harms, we included cohort studies for interventions and comparisons when randomized trials were sparse or unavailable. We excluded case-control studies, case reports, and case series.

We only included non-English language articles included in English-language systematic reviews. We noted English language abstracts of non-English language articles to identify studies that would otherwise meet inclusion criteria, in order to help assess for the likelihood of language bias. Studies only published as conference abstracts were excluded, but we noted studies published only as abstracts that otherwise met inclusion criteria, to help assess for potential publication bias.

Data Extraction and Data Management

For systematic reviews we abstracted the following data: inclusion criteria, search strategy, databases searched, search dates, the number of included studies, study characteristics of included studies (e.g., sample sizes, interventions, duration of treatment, duration of followup, comparison, and results), methods of quality assessment, quality ratings for included studies, methods for synthesis, and results.

We did not abstract data for primary studies included in systematic reviews. Rather, we relied on the information provided in the review. For primary studies not included in systematic reviews, we abstracted the following data: study design, year, setting, country, sample size, eligibility criteria, population and clinical characteristics, intervention characteristics, and results. Information relevant for assessing applicability was also abstracted, including the characteristics of the population, interventions, and care settings; the use of run-in or washout periods, and the number of patients enrolled relative to the number assessed for eligibility.

All study data were verified for accuracy and completeness by a second team member. See Appendix E for evidence tables with extracted data.

Assessing Methodological Quality of Individual Studies

Two investigators independently assessed quality (risk of bias) of systematic reviews and primary studies not included in systematic reviews using predefined criteria, with disagreements resolved by consensus. Randomized trials were evaluated using criteria and methods developed by the Cochrane Back Review Group[25] and cohort studies were evaluated using criteria developed by the US Preventive Services Task Force.[26] Systematic reviews were assessed using the AMSTAR quality rating instrument.[23] These criteria and methods were used in conjunction with the approach recommended in AHRQ Methods Guide.[22] Studies were rated as "good," "fair," or "poor." We re-reviewed the quality ratings of studies included in the prior American Pain Society review to ensure consistency in quality assessment.[24]

For primary studies included in systematic reviews, we relied on the quality ratings or risk of bias assessments as performed in the systematic reviews, as long as they used a standardized method for assessing quality (e.g., Cochrane Back Review Group, Cochrane Risk of Bias tool, PEDro tool). We used the overall grade (e.g., good, fair, or poor; or high or low) as presented in the systematic review, and provided details about the methods used to categorize studies (e.g., "higher quality" defined as meeting more than 6 of 11 Cochrane Back Review Group criteria). If we were uncertain about the methods used to assess risk of bias, or quality, we assessed the quality of individual studies ourselves, using the methods described above. In some cases, we supplemented the quality ratings from the reviews with additional methodological considerations.

Primary studies rated "good" are considered to have the least risk of bias, and their results are generally considered valid. Good-quality studies use valid methods to select patients for inclusion and allocate patients to treatment; report similar baseline characteristics in different treatment groups; clearly report attrition and have low attrition; use appropriate methods to reduce performance bias (e.g., blinding of patients, care providers, and outcome assessors), and use appropriate analytic methods (e.g., intention-to-treat analysis; for cohort studies, adjustment for potential confounders).

Studies rated "fair" are susceptible to some bias, though not enough to necessarily invalidate the results. These studies may not meet all the criteria for a rating of good quality, but no flaw is likely to cause major bias. The study may also be missing information, making it difficult to assess limitations and potential problems. The fair-quality category is broad, and studies with this rating will vary in their strengths and weaknesses. The results of some fair-quality studies are likely to be valid, while others may be only possibly valid.

Studies rated "poor" have significant flaws that imply biases of various types that may invalidate the results. They have a serious or "fatal" flaw in design, analysis, or reporting, such as inadequate methods for allocating patients to treatment; large amounts of missing information; discrepancies in reporting; or serious problems in the delivery of the intervention. The results of these studies are at least as likely to reflect flaws in the study design as the true difference between the compared interventions. We did not exclude studies rated poor quality a priori, but such studies were considered to be less reliable than higher-quality studies when synthesizing the evidence, particularly when discrepancies among studies were present.

For systematic reviews that classified studies as "higher" versus "lower" quality, we considered "higher" to incorporate good-quality and better fair-quality studies, and "lower" to include poor-quality studies and fair-quality studies with more methodological shortcomings.

Systematic reviews rated "good" had to use of multiple sources in the literature search, apply predefined inclusion and exclusion criteria, assess quality using an appropriate tool, use methods to reduce errors in data abstraction and quality rating (e.g., multiple independent reviewers), use appropriate methods for evidence synthesis (qualitative or quantitative), and use an explicit system for considering the body of evidence that includes the major domains of strength of evidence (risk of bias, consistency, precision, and directness). As noted above, we included systematic reviews that had shortcomings in one or more of these areas only if we could address the shortcomings (e.g., by assessing quality of the primary studies ourselves or independently determining strength of evidence from the information provided in the review).

For further details about the quality of included studies see Appendix F.

Assessing Applicability

We recorded factors important for understanding the applicability of studies, such as whether the publication adequately described the study sample, the country in which the study was conducted, the characteristics of the patient sample (e.g., age, sex, race, duration and severity of pain, presence of radicular symptoms, medical comorbidities, and psychosocial factors), the characteristics of the interventions used (e.g., specific intervention, dose or intensity, duration of treatment), the clinical setting (e.g., primary care or specialty setting), and the magnitude of effects on clinical outcomes, as well as timing of assessments.[27] We classified the magnitude of effects for pain and function using the same system as in the APS/ACP review.[14, 28] 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 analogue scale (VAS), 0.5 to 1.0 points on a 0- to 10-point numerical 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. Proposed thresholds for minimum clinically important changes in studies of low back pain are 15 on a 0- to 100-point visual analogue pain scale, 5 points on the RDQ, or 10 for the ODI, roughly correlating with the "moderate" classification.[28] However, 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. We also recorded the funding source and role of the sponsor.

Applicability depends on the particular question and the needs of the user of the review. There is no generally accepted universal rating system for applicability. In addition, applicability depends in part on context. Therefore, a rating of applicability (such as "high" or "low") was not assigned because applicability may differ based on the user of this report.

Evidence Synthesis and Rating the Body of Evidence

We synthesized data qualitatively (see Grading the Strength of Evidence, below). Results are organized by Key Question and intervention, organized according to the duration of symptoms (acute, subacute, or chronic), type of low back pain (nonradicular or radicular low back pain), and type of comparison (e.g., versus placebo or sham, versus usual care, or versus another active intervention) with prioritized outcomes (pain, function) presented first. Synthesis was based on the totality of evidence (i.e., evidence included in the prior APS/ACP review plus new evidence). We synthesized results for continuous as well as dichotomous outcomes. We reported binary outcomes based on the proportion of patients achieving successful pain, function, or some composite overall measure of success as defined in the trials, which varied in how they categorized successful outcomes (e.g., >30% improvement in pain score vs. >50% improvement vs. "good" or "excellent" outcomes on a categorical scale). See Appendix G for descriptions of the outcome measures used in the included studies.

In addition, we reported meta-analysis from systematic reviews that reported pooled estimates from studies that were judged to be homogeneous enough to provide a meaningful combined estimate and used appropriate pooling methods (e.g., random effects model in the presence of statistical heterogeneity). When statistical heterogeneity was present, we examined the type of inconsistency present (e.g., did some trials find that an intervention was more effective than placebo and other no effect, or did most trials find that the intervention was more effective, but varied in the strength of the estimate) and evaluated subgroup and sensitivity analyses based on study characteristics, intervention factors, and patient factors.

We did not conduct updated meta-analysis with new studies. Rather, we qualitatively examined whether results of new studies were consistent with pooled or qualitative findings from prior systematic reviews.

When we included more than one systematic review for a particular intervention and comparison, we evaluated the consistency of results among reviews. When findings among reviews were discordant, we evaluated potential sources of discordance, such as differential inclusion of studies, differences in ratings for risk of bias, or differences in methods used to synthesize evidence.

Grading the Strength of Evidence for Each Key Question

We assessed the strength of evidence for each Key Question and outcome using the approach described in the AHRQ Methods Guide,[21] based on the overall quality of each body of evidence, the quality (graded good, fair, or poor); the consistency of results across studies (graded consistent, inconsistent, or unable to determine when only one study was available); the directness of the evidence linking the intervention and health outcomes (graded direct or indirect); the precision of the estimate of effect, based on the number and size of studies and confidence intervals (CI) for the estimates (graded precise or imprecise); and reporting bias (suspected of undetected). The strength of evidence was based on the totality of evidence (i.e., evidence in prior reviews as well as new evidence).

Assessments of reporting bias were based on whether studies defined and reported primary outcomes, identification of relevant unpublished studies, and when available, by comparing

published results to results reported in trial registries.

We graded the strength of evidence for each Key Question using the four key categories recommended in the AHRQ Methods Guide.[21] A "high" grade indicates high confidence that the evidence reflects the true effect and that further research is very unlikely to change our confidence in the estimate of effect. A "moderate" grade indicates moderate confidence that the evidence reflects the true effect and further research may change our confidence in the estimate of effect and may change the estimate. A "low" grade indicates low confidence that the evidence reflects the true effect and further research is likely to change the confidence in the estimate of effect and is likely to change the estimate. An "insufficient" grade indicates evidence either is unavailable or is too limited to permit any conclusion, due to the availability of only poor-quality studies, extreme inconsistency, or extreme imprecision.

See Appendix H for the strength of evidence table.

Peer Review and Public Commentary

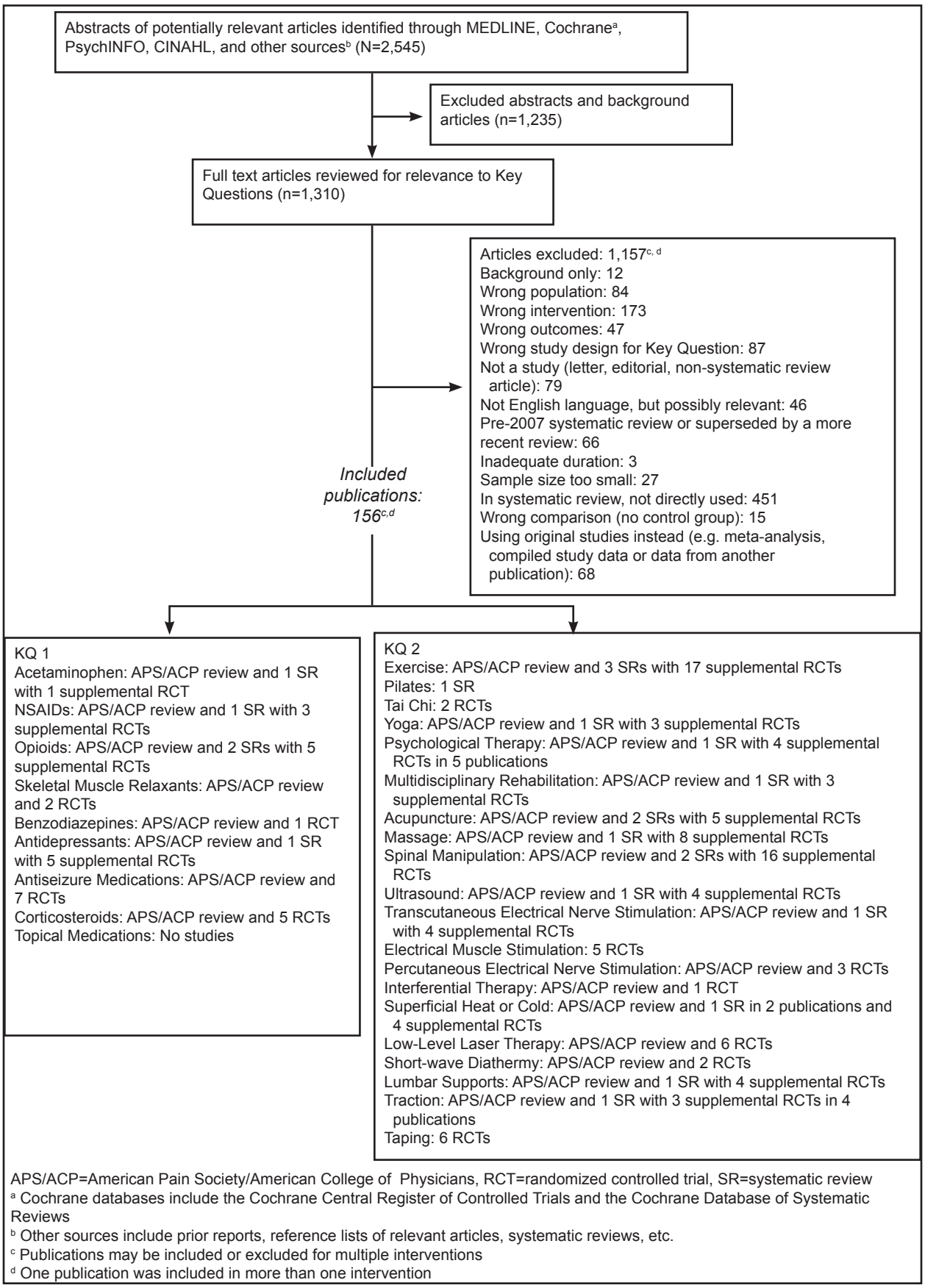
Peer reviewers with expertise in primary care and back pain have been invited to provide written comments on the draft report. The AHRQ Task Order Officer and an Evidence-based Practice Center Associate Editor will also provide comments and editorial review. The draft report will be posted on the AHRQ 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 CER on the public Web site.

Results

Results of Literature Searches

The search and selection of articles are summarized in the literature flow diagram (Figure 2). Database searches resulted in 2,545 potentially relevant articles. After dual review of abstracts and titles, 1,310 articles were selected for full-text dual review and 156 publications were determined to meet inclusion criteria and were included in this review. Data extraction and quality assessment tables for all included studies are available in Appendixes E and F.

Figure 2. Literature flow diagram



APS/ACP=American Pain Society/American College of Physicians, RCT=randomized controlled trial, SR=systematic review

[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] One publication was included in more than one intervention

Key Question 1. What are the comparative benefits and harms of different pharmacological therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis? Includes NSAIDs, acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, corticosteroids, and topical/patch-delivered medications.

Acetaminophen

Key Points

- For acute low back pain, one good-quality trial found no difference between acetaminophen versus placebo in pain intensity or function through 3 weeks (strength of evidence [SOE]: low for pain and function).
- For acute low back pain, a systematic review found no difference between acetaminophen versus nonsteroidal anti-inflammatory drugs (NSAIDs) in pain intensity (3 trials, pooled standard mean difference (SMD) 0.21, 95% confidence interval [CI] −0.02 to 0.43) or likelihood of experiencing global improvement (3 trials, relative risk [RR] 0.81, 95% CI 0.58 to 1.14) at ≤3 weeks, though estimates favored NSAIDs and the estimate was imprecise (SOE: insufficient)
- For chronic low back pain, no study evaluated acetaminophen versus placebo, and there was insufficient evidence from one trial to determine effects of acetaminophen versus NSAIDs (SOE: insufficient).
- There was insufficient evidence from four trials to determine effects of acetaminophen versus other interventions (SOE: insufficient).
- No study evaluated acetaminophen for radicular low back pain.
- One trial found no difference between scheduled acetaminophen, as-needed acetaminophen, or placebo in risk of serious adverse events (~1% in each group) and a systematic review found acetaminophen associated with lower risk of side effects versus NSAIDs (3 trials, RR 0.57, 95% CI 0.36 to 0.89) (SOE: moderate).

Detailed Synthesis

The APS/ACP review[29] included eight trials of acetaminophen (Appendix Tables E1, F1). One trial evaluated acetaminophen versus no treatment,[30] five trials included in a systematic review[31, 32] evaluated acetaminophen versus various NSAIDs,[30, 33-36] and three trials evaluated acetaminophen versus other interventions (amitriptyline,[37] electroacupuncture,[38] and manipulation, corset, or physical therapy[39]). The sample size was 456 in one trial[39] and ranged from 40 to 70 in the others. One trial evaluated acetaminophen for chronic low back pain,[34] one mixed acute to chronic low back pain,[39] and the remainder acute low back pain. No trial specifically focused on patients with radiculopathy. Acetaminophen doses were 4 g/day in 3 trials,[33-35] 3 g/day in 1 trial,[30] 2 g/day in one trial,[37] and unclear in 3 trials.[37-39] Duration of treatment ranged from 1 to 5 weeks. Four trials evaluated patients at 3 to 9 weeks after the

completion of therapy[30, 35, 38, 39] and the remainder evaluated patients at the end of therapy. Two trials[34, 37] were classified as higher quality (based on meeting fewer than 6 of 11 validity criteria) and the remainder classified as lower quality. Methodological shortcomings included inadequate or unclear randomization and allocation concealment methods, unblinded design, and failure to avoid cointerventions. The APS/ACP review concluded that there was good evidence that acetaminophen was associated with moderate effects for acute and chronic low back pain, based primarily on evidence that acetaminophen and NSAIDs were associated with similar effectiveness in most trials, and trials that evaluated effects of acetaminophen for other pain conditions.

An update[40, 41] to the systematic review[32] of acetaminophen versus NSAIDs included one additional high-quality trial (n=371) of patients with acute pain (Table 1).[42] Acetaminophen was compared against ibuprofen, a heat wrap, an unheated wrap, and placebo after a 4-day course of therapy. However, results were only reported for the comparisons of acetaminophen versus ibuprofen or heat wrap.

We identified one additional good-quality trial (n=1643) of scheduled (~4 g/day) or as-needed (up to 4 g/day) acetaminophen for up to 4 weeks versus placebo for acute low back pain (Table 2, Appendix Tables E2, F2).[43] Followup was conducted through 12 weeks.

Acetaminophen Versus Placebo or No Treatment

Acute Low Back Pain

One good-quality trial (n=1093) published subsequent to the systematic reviews found no differences between scheduled acetaminophen ~4 g/day, as-needed acetaminophen up to 4 g/day, and placebo in pain, function, sleep quality, and SF-12 measures in patients with acute low back pain (~20% with radicular symptoms) through 12 weeks.[43] Differences between acetaminophen and placebo were ≤0.2 points on a 0-10 pain scale and ≤0.6 on the 0-24 Roland-Morris Disability Questionnaire (RDQ). There were also no differences in days to recovery, use of concomitant medications or health services, or hours absent from work.

A low-quality trial (n=70) included in the APS/ACP review found no differences between acetaminophen (3 g/day) versus no treatment in likelihood of recovery (54% vs. 82%, p>0.05) after a 1-week course of treatment.[30] However, more patients had thoracic than lumbar back pain in this trial.

Chronic Low Back Pain

No trial evaluated acetaminophen versus placebo or no treatment for chronic low back pain.

Acetaminophen Versus NSAIDs

Acute Low Back Pain

For acute low back pain, a systematic review of low-quality trials found no difference between acetaminophen versus NSAIDs in pain intensity (3 trials, pooled SMD 0.21, 95% CI −0.02 to 0.43) or likelihood of experiencing global improvement (3 trials, RR 0.81, 95% CI 0.[58]

to 1.14) at ≤3 weeks, though estimates favored NSAIDs.[41] Another low-quality trial (n=50) that was not included in the meta-analysis also found no differences.[35]

Chronic Low Back Pain

For chronic low back pain, a small (n=29), high-quality trial found diflunisal associated with higher likelihood of a patient rating of therapeutic efficacy as "good" or "excellent" versus acetaminophen after 4 weeks, but the difference was not statistically significant (62% vs. 33%, RR 1.88, 95% CI 0.77 to 4.55).[34]

Acetaminophen Versus Other Interventions

Acute Low Back Pain

Four trials found no clear differences between acetaminophen versus nonpharmacologic therapies (heat wrap therapy, electroacupuncture, physical therapy, corset, or spinal manipulation)[38, 39, 42] or amitriptyline,[37] but there was insufficient evidence to reach reliable conclusions because each comparison was only evaluated in one trial and the studies had methodological shortcomings.

Chronic Low Back Pain

No trial evaluated acetaminophen versus other interventions for chronic low back pain.

Harms

One good-quality trial found no difference between scheduled acetaminophen, as-needed acetaminophen, or placebo in risk of serious adverse events (~1% in each group).[43] A systematic review found acetaminophen associated with lower risk of side effects versus NSAIDs (3 trials, RR 0.57, 95% CI 0.36 to 0.89).[41] One trial found no difference between acetaminophen versus a heat wrap in risk of systemic adverse events (4.4% vs. 6.2%, RR 0.71, 95% CI 0.23 to 2.18), with no serious adverse events in either group.[42] Adverse events were not reported in other trials of acetaminophen versus other interventions.[37-39]

NSAIDs

Key Points

- For acute low back pain, a systematic review found NSAIDs associated with greater improvement in pain intensity versus placebo (4 studies, weighted mean difference [WMD] −8.39, 95% CI −12.68 to −4.10; chi-square 3.47, p>0.1), but four trials found no clear effects on the likelihood of achieving significant pain relief. One subsequent trial was consistent with these findings. One trial found NSAIDs associated with better function versus placebo (SOE: moderate for pain, low for function).
- For chronic low back pain, a systematic review found NSAIDs associated with greater improvement in pain versus placebo (4 trials, WMD −12.40, 95% CI −15.53 to −9.26; chi-square 1.82, p>0.5); two trials found NSAIDs associated with greater improvement in function (SOE: moderate for pain, low for function).

- For radicular low back pain, a systematic review found no difference in pain intensity between NSAIDs versus placebo (2 trials, WMD −0.16, 95% CI −11.92 to 11.59, chi-square 7.25, p<0.01) (SOE: low).
- There was insufficient evidence from two trials of an NSAID plus another intervention (skeletal muscle relaxants or massage) versus the other intervention alone to determine effectiveness (SOE: insufficient).
- There was insufficient evidence from two trials to determine the effects of NSAIDs versus doloteffin or exercise (SOE: insufficient)
- A systematic review found that most trials of one NSAID versus another found no differences in pain relief in patients with acute low back pain (15 of 21 trials) or chronic low back pain (6 of 6 trials) (SOE: moderate).
- A systematic review found NSAIDs associated with more side effects versus placebo (10 trials, RR 1.35, 95% CI 1.09 to 1.68); COX-2-selective NSAIDs were associated with lower risk of side effects versus nonselective NSAIDs (4 trials; RR 0.83, 95% CI 0.70 to 0.99). Serious harms were rare. (SOE: moderate)

Detailed Synthesis

The APS/ACP review[29] included a good-quality systematic review with 51 trials of NSAIDs.[31, 44] The review found nonselective NSAIDs for acute (6 trials) and chronic (1 trial) low back pain moderately more effective than placebo for outcomes related to pain and function. The APS/ACP review also found no evidence that any nonselective NSAID is superior to another for pain relief based on 24 trials, or when compared with other active interventions (e.g., other medications or passive physical modalities.) None of the trials in the systematic review evaluated a COX-2 selective NSAID.

We identified an updated version of the systematic review described above (Table 1, Appendix Tables E3, F3).[41] It included 65 trials (total n=11,237) of NSAIDs versus placebo (16 trials), other active interventions (13 trials), or one type of NSAID versus another (33 trials), including five trials of COX-2 inhibitors (meloxicam, nimesulide, valdecoxib or etoricoxib) versus nonselective NSAIDs.[45-49] Of the COX-2-selective NSAIDs evaluated in the trials, the only one available in the United States is meloxicam. Eleven trials investigated diclofenac sodium, eight trials ibuprofen, seven trials piroxicam, seven trials diflunisal, four trials naproxen, and 23 trials evaluated other NSAIDs. Nine trials of NSAIDs versus acetaminophen are discussed in the acetaminophen section of this report. Four trials in the systematic review of NSAIDs plus vitamin B versus NSAIDs alone are outside the scope of this review and not discussed further. Of the studies in the systematic review, 37 were conducted in patients with acute low back pain, nine in patients with chronic low back pain, and the remainder in patients with mixed or unclear duration of pain. Six studies included only patients with sciatica, 25 included low back pain without sciatica and 34 evaluated a mixed population or did not specify whether or not patients had sciatica. Treatment schedules and doses varied across studies. Medications were taken 1 to 6 times per day, and doses varied widely (i.e., ibuprofen doses ranged from 800 to 2400 mg per day, diclofenac doses ranged from 48 to 150 mg per day). Duration of treatment ranged from 1 day to 12 weeks, and followup ranged from 2 days to 6 months. 28 studies were rated high-

quality by the systematic review, based on meeting at least 6 of 11 Cochrane Back Review Group criteria; the other 37 were rated low quality. Common methodological shortcomings of the low-quality studies included inadequate details regarding randomization and allocation concealment methods and cointerventions.[41]

We identified three additional trials (n=54 to 193) not included in the systematic review of NSAIDs for acute (including recurrent)[50] or subacute[51, 52] low back pain (Table 3; Appendix Tables E4, F4). One trial compared lornoxicam, diclofenac, and placebo,[50] one trial an NSAID plus deep tissue massage versus deep tissue massage alone,[51] and one trial an NSAID (loxoprofen sodium, diclofenac sodium, or zaltoprofen) versus exercise.[52] One trial was rated good quality,[52] and two were rated fair quality.[50, 51] Methodological shortcomings of the fair-quality trials included inadequate description of randomization, blinding and avoidance of cointerventions.

NSAID Versus Placebo

Acute Low Back Pain

The systematic review included 11 studies of NSAIDs versus placebo for acute low back pain;[45, 53-62] studies that focused on patients with acute sciatica are discussed separately. In studies of patients without sciatica or in mixed populations with or without sciatica,[45, 53, 54, 60] NSAIDs were associated with greater improvements in pain intensity versus placebo (4 studies, WMD −8.39, 95% CI −12.68 to −4.10; chi-square 3.47, p>0.1).[41] Four studies reported did not report changes in mean pain intensity but reported the proportion of patients with pain relief.[55, 57, 59, 61] One trial each of indomethacin, phenylbutazone, and diflunisal found no differences between the NSAID versus placebo in the likelihood of achieving pain relief.[55, 57, 61] One trial found piroxicam associated with greater likelihood of pain improvement versus placebo in the subgroup of patients with moderate to severe pain at baseline (82% vs. 53%), but no clear effect in patients with mild pain (49% vs. 38%).[59]

Most trials did not report effects of NSAIDS on function. One trial found diclofenac and ibuprofen each associated with greater improvement in the RDQ versus placebo (p<0.001 and p=0.001, respectively).[56] Pooled results from seven studies of NSAIDs versus placebo found a higher proportion of patients taking NSAIDs experienced global improvements after followup of 3 weeks or less (RR 1.19, 95% CI 1.07 to 1.33; chi-square 8.39, p>0.1).[45, 55-58, 60, 61]

We identified one additional trial (n=171) of lornoxicam or diclofenac versus placebo for acute low back pain or acute exacerbation of low back pain.50 Lornoxicam was associated with lower pain intensity at 3, 4, 6 and 8 hours after the first dose (p≤0.05 at each time point versus placebo), as measured on a 100 mm point visual analogue scale (VAS). There were no significant differences between lornoxicam and diclofenac for pain intensity or pain relief; function was not assessed.

Chronic Low Back Pain

The systematic review included four trials of NSAIDs versus placebo for chronic low back pain.[63-66] NSAIDS were associated with greater improvement in pain from baseline to 12 weeks versus placebo (WMD −12.40, 95% CI −15.53 to −9.26; chi-square 1.82, p>0.5).[41] Two of the trials found etoricoxib 60 mg 90 mg per day associated with greater improvement on the RDQ

versus placebo (mean differences −2.42, 95% CI −3.87 to −0.98 and −2.06, 95% CI −3.46 to −0.65)[64] and rofecoxib 25 mg or 50 mg per day associated with greater improvement versus placebo (mean differences −2.2, 95% CI −3.2 to −1.3 and −2.3, 95% CI −3.3 to −1.3).[66]

Radicular Low Back Pain

The systematic review found no difference in pain intensity between NSAIDs versus placebo in two trials of patients with sciatica (WMD −0.16, 95% CI −11.92 to 11.59).[45, 62] Statistical heterogeneity was present (chi-square 7.25, p<0.01). One trial found no difference after 4 weeks of followup between piroxicam for 14 days versus placebo (mean difference 6.00, 95% CI −0.75 to 12.75),[62] but the other trial found meloxicam associated with greater reduction in pain versus placebo after 7 days (mean difference −6.00, 95% CI −11.54 to −0.46).45 One trial included in the systematic review found indomethacin significantly more effective than placebo in the subgroup of patients with nerve root pain, but not in patients without nerve root pain.[58] None of the studies assessed effects on function.

NSAIDs Plus Another Intervention Versus the Other Intervention Without NSAIDs

One trial (n=175) in the systematic review found no differences between diflunisal plus the skeletal muscle relaxant cyclobenzaprine versus cyclobenzaprine alone in global improvement at 2 or 7 days.[55]

One trial (n=54) of deep tissue massage plus NSAID versus deep tissue massage alone for subacute low back pain found no significant differences on the RDQ, Oswestry Disability Index (ODI), or pain intensity during rest, motion or mobility of the aching area.[51]

NSAIDs Versus Other Interventions

The systematic review included one trial (n=88) of rofecoxib versus doloteffin for chronic low back pain that found no difference in the likelihood of being pain free after 3 or 6 weeks.[67] Studies of NSAIDs versus acetaminophen or opioids are discussed in the acetaminophen and opioids sections of this report.

One trial (n=193) of an NSAID (loxoprofen, diclofenac, or zaltoprofen) versus trunk strengthening and stretching exercises in patients with chronic low back pain was not included in the systematic review.[52] It found NSAIDs associated with less improvement in quality of life measured by change ratio (improvement from baseline/baseline) on the RDQ (−0.47 versus −0.72, p=0.023) and the Japan Low Back Pain Questionnaire (−0.44 versus −0.58, p=0.021).

One NSAID Versus Another NSAID

The systematic review included thirty-three trials that compared at least two different types of NSAIDs; four evaluated injected NSAIDs which were outside the scope of the current review.[41] Only two trials compared the same two NSAIDs (meloxicam versus diclofenac); both found no significant differences.[45, 68] Most (15 of 21) head-to-head trials of different NSAIDs for acute low back pain found no differences in pain or function, and six head-to-head trials of different NSAIDs for chronic low back pain also found no differences.

COX-2-Selective NSAID Versus Traditional NSAID

The systematic review included 4 trials of COX-2-selective NSAIDs versus traditional NSAIDs for acute low back pain: meloxicam versus diclofenac,[45] nimesulide versus diclofenac,[46] nimesulide versus ibuprofen,[47] and valdecoxib versus diclofenac.[48] Of the COX-2-selective NSAIDs evaluated in these trials, meloxicam is the only one available in the United States. A pooled analysis of three trials, including the meloxicam trial, found no differences between the COX-2 selective and nonselective NSAIDs in pain (WMD −1.17, 95% CI −4.67 to 2.33);[45, 47, 48] the fourth trial[46] also found no difference.[41]

The systematic review included one trial of etoricoxib (not available in the United States) versus diclofenac for chronic low back pain that found no difference in pain relief.[49]

Harms

The systematic review included 10 trials that found NSAIDs associated with more side effects versus placebo (RR 1.35, 95% CI 1.09 to 1.68).[41] It also found COX-2-selective NSAIDs were associated with lower risk of side effects versus traditional NSAIDs (4 trials; RR 0.83, 95% CI 0.70 to 0.99). Serious harms were rare in the trials.

Opioids, Tramadol, and Tapentadol

Key Points

- For chronic low back pain, a systematic review found opioids associated with greater short-term improvement in pain scores (6 trials, SMD −0.43, 95% CI −0.52 to −0.33, I2=0.0%, for a mean difference of ~1 point on a 0−10 pain scale) and function (four trials, SMD −0.26, 95% CI −0.37 to −0.15; I2=0.0%, for a mean difference of ~1 point on the RDQ) versus placebo; three additional trials reported results consistent with the systematic review (SOE: moderate for pain and function).
- For chronic low back pain, a systematic review found tramadol associated with greater short-term pain relief versus placebo (5 trials, SMD −0.55, 95% CI −0.66 to −0.44, I2=86%, for a mean difference of 1 point or less on a 0-10 pain scale) and function (5 trials, SMD −0.18, 95% CI −0.29 to −0.07, I2=0%, for a mean difference of ~1 point on the RDQ); two trials not included in the systematic review reported results consistent with the systematic review findings (SOE: moderate for pain and function).
- For subacute or chronic low back pain, a systematic review included two trials that found buprenorphine patches associated with greater short-term improvement in pain versus placebo patches; effects on function showed no clear effect or were unclearly reported (SOE: low for pain, insufficient for function).
- For chronic low back pain, three trials reported inconsistent effects of opioids versus NSAIDS for pain relief, one trial found no difference in function. (SOE: insufficient for pain and function).
- For acute low back pain, one trial found no significant differences between opioids versus acetaminophen in days to return to work; pain was not reported (SOE: insufficient).

- Four trials found no clear differences among different long-acting opioids in pain or function (SOE: moderate for pain and function).
- Six trials found no clear differences between long-acting versus short-acting opioids in pain relief. Although some trials found long-acting opioids associated with greater pain relief, patients randomized to long-acting opioids also received higher doses of opioids (SOE: low).
- Short-term use of opioids was associated with higher risk versus placebo of nausea, dizziness, constipation, vomiting, somnolence, and dry mouth; risks of opioids were higher in trials that did not use an enriched enrollment and withdrawal design (SOE: moderate). Trials were not designed to assess risks of overdose, abuse, and addiction, or long-term harms.

Detailed Synthesis

The APS/ACP review included nine trials of opioid analgesics for low back pain.[29] Sample sizes ranged from 36 to 683 patients. Three trials compared opioids versus placebo or acetaminophen, five trials compared sustained-release versus immediate-release opioid formulations, and two trials compared two different long-acting opioids. Only one trial assessed opioids for acute low back pain; the remainder evaluated opioids for subacute or chronic low back pain. Two trials were rated higher quality. Based on this evidence, the APS/ACP review found fair evidence that opioids are moderately more effective than placebo or no opioid for subacute or chronic low back pain, but insufficient evidence to determine effects for acute low back pain.

A recent, good-quality systematic review[69] of opioids for low back pain included 16 randomized controlled trials (RCTs) (reported in 15 publications) (Table 1; Appendix Tables E5, F5).[70-84] Sample sizes ranged from 55 to 981 patients. The opioids evaluated were tapentadol (1 trial), oxycodone (2 trials), long-acting oxycodone (1 trial), long-acting morphine (2 trials), extended-release hydromorphone (1 trial), extended-release oxymorphone (3 trials), combinations of oxycodone with naloxone or naltrexone (2 trials), tramadol or the combination of tramadol and acetaminophen (7 trials), and buprenorphine patches (2 trials). In many trials the dose of opioids was titrated to achieve pain relief; maximal doses ranged from 20 to 256 mg of morphine-equivalent doses per day. Tapentadol, morphine, oxymorphone, and hydromorphone were classified as "strong" opioids and analyzed together; tramadol and buprenorphine (a partial opioid agonist) were analyzed separately. Fourteen trials compared an opioid versus placebo and two trials compared an opioid versus an NSAID. The duration of treatment ranged from 2 weeks to 13 weeks following titration, and outcomes were assessed through the end of therapy in all trials. The systematic review assessed 13 trials as being at low risk of bias based on meeting ≥6 of 12 Cochrane Back Review Group criteria. Methodological shortcomings included high attrition, uncertain adherence to treatment, and uncertainty about blinding of outcome assessments. Five trials used the enriched enrollment and randomized withdrawal design described below.

We also included three trials (one higher quality[85] and two lower quality[36, 86]) from the APS/ACP review that were not included in the systematic review and 4 additional newer trials (Table

4; Appendix Tables E8, F6).[87-90] Sample sizes ranged from 36 to 302 subjects. One trial evaluated patients with acute low back pain[36] and the others evaluated patients with subacute or chronic low back pain. The opioids evaluated were long-acting oxymorphone, combined oxycodone and naloxone, long-acting morphine plus oxycodone, short-acting oxycodone alone, oxycodone plus aspirin, and codeine. Two trials compared opioids versus placebo, one compared an opioid plus naproxen versus naproxen alone, and one compared opioids versus acetaminophen. Two newer trials compared tramadol plus acetaminophen versus placebo, and one compared long-acting hydrocodone versus placebo. The duration of treatment ranged from 15 days to 16 weeks, with outcomes assessed at the end of treatment. Two of the newer trials were rated good quality,[87, 88] one fair quality,[90] and one poor quality.[89] Methodological shortcomings in the poor- and fair-quality trials included failure to describe adequate randomization methods, failure to report baseline differences, unblinded design, and high attrition. We also identified a post-hoc analysis of one of the trials included in the systematic review that stratified results according to presence of neuropathic pain.[91]

Of the 23 total trials, 8 employed an enriched enrollment and withdrawal design. In this design, all potential subjects receive the study drug for a period of time in a prerandomization, open label phase. Only those who benefit from the drug and tolerate side effects are then randomized to continue the active drug, or have it withdrawn and replaced with a placebo. Thus, every patient entering the trial has already demonstrated benefit from the opioid and been shown to be free of intolerable side effects at the time of randomization. This strategy can help reduce dropout rates following randomization and reduce the number of unresponsive subjects. However, it may also overestimate efficacy, and has been shown to underestimate adverse events.[92]

Despite frequent use of the enriched enrollment and withdrawal design, dropout rates from the trials were high. Only 2 trials had a dropout rate of less than 20 percent,[86, 90] and most had rates of 30 to 60 percent.[70, 72-80, 82, 84, 87, 89] The most common reasons for dropout were discontinuation due to adverse events (more common in the opioid arms than placebo) or lack of effect (more common in the placebo arms).

Another limitation of all the trials was short duration. The longest trial was 16 weeks (18).86 Many trials excluded patients with a history of substance abuse or depression, though these were groups that were more likely than others to receive opioids in clinical practice.[93] Seventeen trials were industry sponsored and all involved tramadol, new long-acting preparations of older drugs, or new drug combinations.

We also included findings from a good-quality comparative effectiveness review94 of opioids for chronic noncancer pain that included three head-to-head trials of different long-acting opioids for low back pain[85, 95, 96] and five trials of long-acting versus short-acting opioids,86, 97-100 and two other trials that evaluated comparisons among opioids.101, 102

Strong Opioids Versus Placebo

Subacute or Chronic Low Back Pain

Seven trials included in the systematic review[69] (five rated low risk of bias[70, 72, 74-76, 87]) compared strong opioids versus placebo[70-76, 85, 87] for subacute or chronic back pain. The opioids

evaluated were extended-release tapentadol (1 trial), oxycodone (2 trials), long-acting oxycodone (1 trial), long-acting morphine (2 trials), extended release-hydromorphone (1 trial), extended-release oxymorphone (2 trials), and oxycodone with or without naltrexone (1 trial).

Strong opioids were associated with greater improvement in pain scores versus placebo (6 trials, SMD −0.43, 95% CI −0.52 to −0.33).[70-72, 74-76] The findings were consistent among trials (I2=0.0%). The clinical magnitude of effects was small, typically equivalent to about 1 point on a 0-10 pain scale. Strong opioids were also associated with greater improvement in function versus placebo (4 trials, SMD −0.26, 95% CI −0.37 to −0.15; I2=0.0%). The effect was typically equivalent to about 1 point on the 24-point RDQ. Three trials not included in the meta-analysis that evaluated oxycodone, oxycodone plus naloxone, or extended-release hydrocodone reported results consistent with the findings of the systematic review.[85, 87, 89]

Radicular Low Back Pain

One trial[72] included in the systematic review[69] found that effects on pain were similar in patients with neuropathic and non-neuropathic pain in a post-hoc stratified analysis.[91]

Tramadol Versus Placebo

Subacute or Chronic Low Back Pain

Five higher-quality trials of tramadol versus placebo were included in the systematic review.[69] Sample sizes ranged from 254 to 386. Two trials evaluated a tramadol/acetaminophen combination[77, 78] and two trials evaluated extended-release tramadol.[80, 81] Doses were titrated in four trials and the fifth evaluated fixed dosing.

Tramadol was associated with greater pain relief versus placebo (5 trials, SMD −0.55, 95% CI −0.66 to −0.44, I2=86%). Effects generally averaged the equivalent of 1 point or less on a 0-10 pain scale. Although statistical heterogeneity was present, effects in all trials favored tramadol (standard mean differences ranged from −0.10 to −1.01). Tramadol was also associated with greater improvement in function versus placebo, though the average effect was smaller than for pain (5 trials, SMD −0.18, 95% CI −0.29 to −0.07, I2=0%). Four of the trials measured function using the RDQ, with a typical difference between tramadol and placebo of about 1 point. Two newer trials not included in the systematic review of tramadol plus acetaminophen versus placebo reported results consistent with the findings of the systematic review.[88, 90]

Buprenorphine Versus Placebo

Subacute or Chronic Low Back Pain

Two trials in the systematic review compared buprenorphine patches (titrated dose) versus placebo patches for subacute or chronic back pain (n=78 and n=541).[82, 84] Both reported a statistically significant advantage of buprenorphine for pain, though the effect was smaller than the equivalent of 1 point on a 0-10 pain scale. One reported no significant difference in functional outcome;[82] the other reported that buprenorphine was associated with better functional outcomes, but did not report a p value or other statistical testing.

Opioids Versus NSAIDs

Chronic Low Back Pain

Three trials in the systematic review compared opioids versus NSAIDs. Two larger trials (n=796 and n=802) of identical design (both rated higher quality) were reported in a single publication.[83] They compared a fixed dose of the weak opioid tramadol (50 mg three times daily) versus a fixed dose of celecoxib (200 mg twice daily). The third was a small (n=36), older trial comparing three regimens: (1) Long acting morphine + titrated doses of oxycodone + naproxen, (2) fixed-dose short-acting oxycodone + naproxen, and (3) naproxen alone (titrated dose).[86]

The two trials of tramadol versus celecoxib reported the percent of patients with a reduction in pain scores of at least 30 percent on a 0-10 rating scale.[83] One trial reported a statistically significant but small advantage for celecoxib (66% responders vs. 57% for tramadol). The other trial reported no statistically significant difference (65% responders for celecoxib, 60% for tramadol), though results also favored celecoxib. Functional outcomes were not reported.

The small, older trial reported greater average pain relief with both strong opioid regimens than with naproxen, by about 6-10 mm on a 100 mm visual analog scale.[86] There were no significant differences in self-reported activity levels.

Opioid Versus Acetaminophen

Acute Low Back Pain

One small trial of military trainees (n=75) with acute low back pain found no differences between codeine, oxycodone plus aspirin, or acetaminophen in days to return to work (11 vs. 12 vs. 13 days, respectively).[36] Pain scores were not reported.

Opioid Versus Opioid

Chronic Low Back Pain

A systematic review included three head-to-head trials of long-acting opioids for chronic low back pain.[94] In the trials, patients were titrated for effective pain relief in both arms. One trial[95] found no differences between oral morphine versus transdermal fentanyl and one trial[85] found no differences between long-acting oxymorphone versus long-acting oxycodone in measures of pain relief or function. A third trial found long-acting morphine associated with higher likelihood of experiencing >2-point improvement on the Brief Pain Inventory versus long-acting oxycodone (55% vs. 44%, p=0.03) and greater improvement in sleep quality (mean improvement from baseline 33% vs. 17% on the Pittsburgh Sleep Quality Index, p=0.006), but had important methodological shortcomings, including open-label design, high attrition, and failure to report intention-to-treat analysis.[96] One other trial found no differences between extended-release morphine versus controlled-release oxycodone in pain or function.101

Long-Acting Versus Short-Acting Opioid

Chronic Low Back Pain

A systematic review included five head-to-head trials of a long-acting versus short-acting opioid for chronic low back pain.[94] Three trials found no differences between long-acting versus immediate-release preparations in pain control.[97, 98, 100] In two trials, long-acting opioids were more effective than short-acting opioids for pain control, but patients who received long-acting opioids also received higher doses of opioids. One other trial also found long-acting tramadol associated with better pain relief and function than short-acting tramadol, but the dose of tramadol in the long-acting treatment arm was nearly double that of the short-acting arm.[102]

Harms

The systematic review found short-term use of opioids associated with higher risk versus placebo of nausea, dizziness, constipation, vomiting, somnolence, and dry mouth.[69] As noted previously, a number of trials used an enriched enrollment and withdrawal design, which has been shown to underestimate risk of harms. A systematic review of opioids for chronic pain in general (not restricted to low back pain) reported nausea in 28 percent of patients randomized to opioids versus 9 percent randomized to placebo among trials that did not use an enrichment design (difference 17%, 95% CI 13 to 21), 26 versus 7 percent for constipation (difference 20%, 95% CI 15 to 25), 24 versus 7 percent for somnolence/drowsiness (difference 14%, 95% CI 10 to 18), and 15 versus 2 percent for pruritus (difference 10%, 95% CI 5 to 15).[92] In trials that used an enrichment design, rates were 16 versus 8 percent for nausea (difference 7%, 95% CI 0% to 14%), 15 versus 3 percent for constipation (difference 11%, 95% CI 6 to 16), 10 versus 5 percent for somnolence/drowsiness (difference 3%, 95% CI 1 to 7), 10 versus 5 percent for dizziness/vertigo (difference 5%, 95% CI 2 to 8), and 5% versus 2 percent for pruritus (difference 3%, 95% CI 0 to 5).

The trials were not designed to assess risks of harms such as abuse and addiction, overdose, fractures, cardiovascular events, sexual dysfunction, and motor vehicle accidents. Although observational studies on risk for such harms in patients prescribed opioids specifically for low back pain is lacking, we recently reviewed evidence on the long-term risks of opioid therapy for chronic pain in general, including risks of abuse and addiction, overdose, fractures, cardiovascular events, sexual dysfunction, and motor vehicle accidents.[15] Evidence from observational studies suggested an increased risk of overdose, as well as abuse and addiction, fractures, motor vehicle accidents, and sexual dysfunction, which appeared to be dose-dependent after adjusting for potential confounders.

Skeletal Muscle Relaxants

Key Points

- For acute low back pain, a systematic review found skeletal muscle relaxants superior to placebo for short-term pain relief (≥two-point or 30% improvement on a 0-10 VAS pain scale) after 2 to 4 days (4 trials; RR 1.25, 95% CI 1.12 to 1.41; I2=0%) and 5 to 7 days (3 trials; RR 1.72, 95% CI 1.32 to 2.22; I2=0%); a more recent, large (n=562) trial was consistent with the systematic review (SOE: moderate).
- For acute low back pain, a systematic review found no difference between a skeletal muscle relaxant plus an NSAID versus the NSAID alone in the likelihood of experiencing pain relief, though the estimate favored combination therapy (2 trials; RR 1.56, 95% CI 0.92 to 2.70; I2=84%); one other trial (n=197) also reported results that favored combination therapy (SOE: low).
- For chronic low back pain, evidence from three placebo-controlled trials was insufficient to determine effects, due to imprecision and inconsistent results (SOE: insufficient).
- Three trials in a systematic review found no differences in any outcome among different skeletal muscle relaxants for acute or chronic low back pain (SOE: low).
- A systematic review found skeletal muscle relaxants for acute low back pain associated with increased risk of any adverse event versus placebo (8 trials; RR 1.50, 95% CI 1.14 to 1.98) and increased risk of central nervous system events (primarily sedation) (8 trials; RR 2.04, 95% CI 1.23 to 3.37; I2=50%); one additional placebo-controlled trial was consistent with these findings (SOE: moderate).

Detailed Synthesis

The APS/ACP review[29] included a good-quality systematic review of skeletal muscle relaxants103 with 22 studies.[104-125] Twelve trials compared a skeletal muscle relaxant versus placebo,[104-107, 109, 112, 114-116, 118, 119, 121] four compared a skeletal muscle relaxant plus an NSAID versus an NSAID alone,[110, 113, 123, 125] two compared a skeletal muscle relaxant versus another active treatment,[117, 124] and three compared one skeletal muscle relaxant versus another.[111, 120, 122] The skeletal muscle relaxants evaluated were tizanidine (4 to 12 mg/day; 7 trials), cyclobenzaprine (30 to 40 mg/day; 4 trials), oral (dose range 100 to 200 mg/day; 3 trials) or intravenous (single 60 mg dose;1 trial) orphenadrine, carisoprodol (1400 mg/day; 2 trials), chlorzoxazone (1500 mg/day; 1 trial), dantrolene (dose not reported; 1 trial), baclofen (30 to 40 mg/day;1 trial), pridinol (8 mg IM, then oral 4 mg/day; 1 trial), tolperisone (300 mg/day; 1 trial) and meprobamate 450 mg/day; 1 trial). Duration of treatment ranged from 4 to 21 days in 21 trials, except for one trial of single dose intravenous orphenadrine.[118] Only three trials followed patients after treatment had been completed.[106, 123, 125] Sample sizes ranged from 20 to 405 (median n=80). Eighteen of the trials enrolled patients with acute back pain and four[106, 112, 120, 121] enrolled patients with chronic back pain. The review classified 17 trials[104, 105, 107-109, 111-114, 116-123, 125] as high quality based on meeting at least 6 of 11 Cochrane Back Review criteria; the other five trials were classified as low quality.[106, 110, 115, 120, 124] Methodological shortcomings in most trials included inadequate reporting of randomization and allocation concealment methods; low-quality

trials also did not report attrition, had unbalanced groups at baseline, and/or did not conduct intention-to-treat analyses. The APS/ACP review concluded that there was good evidence for moderate effects of skeletal muscle relaxants versus placebo for acute low back pain, but insufficient (poor) evidence to determine effects for chronic low back pain.

We identified two fair-quality trials of skeletal muscle relaxants for acute or subacute back pain published since the APS/ACP review (Table 5; Appendix Tables E7, F7).[126, 127] One trial evaluated carisoprodol 1000 mg/day (250 mg three times daily) versus placebo (n=562)[127] and the other (n=197) tizanidine 4 mg/day (2 mg twice daily) plus aceclofenac (an NSAID not available in the United States) 200 mg/day (100 mg twice daily) versus aceclofenac alone.[126] In both studies, duration of treatment was 7 days, with no post-treatment followup. Neither trial provided information regarding methods of randomization or allocation concealment, or methods of blinding of study personnel.

Skeletal Muscle Relaxants Versus Placebo

Acute Low Back Pain

The systematic review found skeletal muscle relaxants superior to placebo for short-term pain relief (defined as at least a two-point or 30% improvement on a 0-10 VAS pain scale) after 2 to 4 days (4 trials; RR 1.25, 95% CI 1.12 to 1.41; I2=0%) and 5 to 7 days of treatment (3 trials; RR 1.72, 95% CI 1.32 to 2.22; I2=0%.)103 The review also found skeletal muscle relaxants superior to placebo for short-term improvement in global efficacy after 2 to 4 days (4 trials; RR 2.04, 95% CI 1.05 to 4.00), though heterogeneity was very high (I2=89%); the difference was no longer statistically significant after 5 to 7 days (RR 1.47, 95% CI 0.88 to 2.44; I2=34%)

A more recent fair-quality trial of carisoprodol versus placebo (n=562) was consistent with the systematic review. This trial found carisoprodol associated with greater improvements in patient-rated pain relief at day 3 (mean 1.8 vs. 1.1 on a 0 to 4 scale, $p<0.0001$) and day 7 ($p<0.0001$; data not shown.)[127] Patient-rated global improvement was also greater with carisoprodol at day 3 (2.3 vs. 1.7, $p<0.0001$) and day 7 ($p<0.0001$, data not provided).

Chronic Low Back Pain

Evidence on effects of skeletal muscle relaxants versus placebo for chronic back pain is extremely limited. Of three placebo-controlled trials included in the systematic review, one small (n=20), high-quality trial[112] found dantrolene associated with better pain-related outcomes versus placebo and one low-quality trial (n=69)106 found no differences between cyclobenzaprine and placebo for pain. A third, high-quality trial (n=112) found no difference between tolperisone versus placebo in global impression of efficacy after 21 days (mean 2.85 versus 2.45 on 1 to 4 scale).[121]

Skeletal Muscle Relaxants Plus Another Intervention Versus the Other Intervention Without Skeletal Muscle Relaxants

Acute Low Back Pain

The systematic review found no difference between a skeletal muscle relaxant plus an NSAID versus the NSAID alone in the likelihood of experiencing a 2-point or greater difference or 30 percent improvement on a 0-10 VAS after 2 to 4 days (2 trials; RR 1.56, 95% CI 0.92 to 2.70; I2=84%), though the estimate favored the combination. The combination was associated with greater likelihood of experiencing global improvement at 2 to 4 days (4 trials; RR 2.04, 95% CI 1.05 to 4.00; I2=89%); the estimate was not as strong and no longer statistically significant at 5 to 7 days (4 trials; RR 1.47, 95% CI 0.88 to 2.44; I2=34%).103

One fair-quality (n=197) trial not included in the systematic review compared tizanidine plus aceclofenac with aceclofenac alone.126 The combination was associated with greater improvement in resting pain after 3 days (mean change −3.01 vs. −1.90 on 0 to 10 VAS, p=0.0001) and 7 days (−5.88 vs. −4.35, p=0.0001).126Results for pain with movement were similar (mean change −2.94 vs. −1.81 at day 3, p=0.0001 and −6.09 vs. −3.98 at day 7, p=0.0001.) The combination was also associated with higher likelihood of experiencing a good or excellent treatment response (75% vs. 34%; RR 1.28, 95% CI 1.07 to 1.52.)

Skeletal Muscle Relaxants Versus Other Interventions

Three trials[106, 128, 129] of skeletal muscle relaxants versus benzodiazepines are discussed in the benzodiazepine section of this report.

Effectiveness of One Skeletal Muscle Relaxant Versus Another Skeletal Muscle Relaxant

Three trials in the systematic review103 found no differences in any outcome between carisoprodol versus cyclobenzaprine (1 trial [n=78]),[122] or tizanidine versus chlorzoxazone (1 trial [n=27]),[111] for acute back pain or pridinol versus thiocolchicoside (1 trial [n=120]) for chronic back pain.[120]

Harms

For acute low back pain, the systematic review found skeletal muscle relaxants associated with increased risk of any adverse event versus placebo (8 trials; RR 1.50, 95% CI 1.14 to 1.98; I2=50%).[103] There were no differences in risk of any adverse event between skeletal muscle relaxants plus an NSAID versus the NSAID alone (2 trials RR 1.30, 95% CI 0.62 to 2.75; I2=84%). Skeletal muscle relaxants were associated with increased risk of central nervous system events (primarily sedation) versus placebo (8 trials; RR 2.04, 95% CI 1.23 to 3.37; I2=50%), or when added to an NSAID (3 trials; RR 2.77, 95% CI 1.18 to 6.46; I2=51%). Skeletal muscle relaxants were not associated with increased risk of gastrointestinal events versus placebo (7 trials; RR 0.95, 95% CI 0.29 to 3.19; I2=50%) or when added to an NSAID (3 trials; RR 0.48, 95% CI 0.23 to 1.00; I2=50%).103

One trial published subsequent to the systematic review found no significant difference between tizanidine plus aceclofenac versus aceclofenac alone in risk of central nervous system events (drowsiness) (RR 1.19, 95% CI 0.33 to 4.29).[126] One other trial found carisoprodol associated with increased risk of sedation (RR 2.92, 95% CI 1.59 to 5.37) and dizziness (RR 3.08, 95% CI 1.47 to 6.42) versus placebo, though there was no difference in withdrawals due to adverse events.[127] No serious adverse events were reported in either study.[126, 127]

Two trials of skeletal muscle relaxants for chronic low back pain found no increase in risk of experiencing any adverse event versus placebo (RR 1.02, 95% CI 0.67 to 1.57; I2=0%).[103] Other harms were not reported.

Benzodiazepines

Key Points

- For acute low back pain, there was insufficient evidence from two trials with inconsistent results to determine effectiveness of benzodiazepines versus placebo (SOE: insufficient).
- For chronic low back pain, a systematic review included two trials that found tetrazepam associated with lower likelihood of no improvement in pain at 5-7 days (RR 0.82, 95% CI 0.72 to 0.94) and at 10 to 14 days (RR 0.71, 95% CI 0.54 to 0.93) versus placebo, and lower likelihood of no overall improvement at 10 to 14 days (RR 0.63, 95% CI 0.42 to 0.97) (SOE: low).
- For acute or subacute radicular pain, one trial found no difference between diazepam 5 mg twice daily for 5 days versus placebo in function at 1 week through 1 year, or other outcomes including analgesic use, return to work, or likelihood of surgery through 1 year of followup. Diazepam was associated with lower likelihood of experiencing ≥50% improvement in pain at 1 week (41% vs. 79%, RR 0.5, 95% CI 0.3 to 0.8) (SOE: low).
- For acute low back pain, there was insufficient evidence from two trials with inconsistent results to determine effects of benzodiazepines versus skeletal muscle relaxants (SOE: insufficient).
- For chronic low back pain, one trial found no difference between diazepam versus cyclobenzaprine in outcomes related to muscle spasm (SOE: low).
- A systematic review found central nervous system adverse events such as somnolence, fatigue, and lightheadedness were reported more frequently with benzodiazepines versus placebo, though harms were not reported well; no trial was designed to evaluated risks with long-term use of benzodiazepines such as addiction, abuse, or overdose (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included a systematic review of skeletal muscle relaxants for low back pain[103] that included eight trials of benzodiazepines.[106, 128-134] The sample size was 152 in one trial;[133] and ranged from 30 to 80 in the other trials. Four trials compared a benzodiazepine versus placebo,[106, 130-132] one trial compared a benzodiazepine plus physical therapy versus placebo plus physical therapy,[133] and three trials compared a benzodiazepine versus a skeletal muscle relaxant

(carisoprodol,[128] cyclobenzaprine,[106] or tizanidine[129]). One other trial evaluated a benzodiazepine versus drugs that are not available in the United States.[134] Four trials in the systematic review evaluated benzodiazepines for acute low back pain[128, 129, 131, 132] and three for chronic low back pain.[106, 130, 133] Two trials specifically enrolled patients with muscle spasms.[106, 129] No trial focused on patients with radiculopathy; in one trial the proportion of patients with radiculopathy was 40 percent.[131] Five trials evaluated diazepam[106, 128, 129, 131, 132] and two trials evaluated tetrazepam (not available in the United States).[130, 133] Diazepam was administered orally at doses of 5 to 10 mg three or four times daily in three trials;[106, 128, 129] two trials evaluated regimens that included initial intramuscular diazepam and oral doses.[131, 132] In both trials of tetrazepam, the dose was 50 mg by mouth three times daily.[130, 133] The duration of therapy ranged from 6 to 14 days; two trials[106, 130] evaluated patients 4 days after the completion of therapy and the others evaluated patients at the end of therapy. The review classified five trials as high quality[128-131, 133] based on meeting at least 6 of 11 Cochrane Back Review group criteria; the other two trials were classified as low quality.[106, 132] All trials used a blinded design. Methodological shortcomings included inadequate reporting of randomization and allocation concealment methods; some trials also did not report attrition or intention-to-treat analyses. The APS/ACP review concluded that there was fair evidence of a moderate effect of benzodiazepines for acute and chronic low back pain, based in part on evidence from populations with mixed back and neck pain, but noted that there were no reliable data on the risk of abuse of addiction.

We identified one good-quality trial (n=60) published since the APS/ACP review of diazepam 5 mg three times daily for 5 days versus placebo for acute radiculopathy due to prolapse lumbar disc (with computed tomography scan or magnetic resonance imaging confirmation) (Table 6; Appendix Tables E8, F8).[135] Outcomes were evaluated through 1 year.

Benzodiazepines Versus Placebo

Acute Low Back Pain

For acute nonradicular low back pain, one high-quality trial (n=50)[131] included in the APS/ACP review found no differences between diazepam and placebo in likelihood of improved pain and tenderness at the end of 5 days of treatment (76% vs. 72%, RR 1.06, 95% CI 0.76 to 1.47), but a low-quality trial (n=68)[132] found diazepam superior to placebo for likelihood of experiencing good or very good benefit at the end of 10 days of treatment (57% vs. 17%, RR 3.31, 95% CI 1.52 to 7.23).

Chronic Low Back Pain

For chronic nonradicular low back pain, pooled results from two high-quality trials (n=50 and 152)[130, 133] included in the APS/ACP review found tetrazepam associated with lower likelihood of no improvement in pain at 5-7 days (RR 0.82, 95% CI 0.72 to 0.94) and at 10 to 14 days (RR 0.71, 95% CI 0.54 to 0.93) versus placebo, and lower likelihood of no overall improvement at 10 to 14 days (RR 0.63, 95% CI 0.42 to 0.97). In one trial, all patients also underwent physical therapy.133 One low-quality trial (n=76) found no difference between diazepam versus placebo in outcomes related to muscle spasm.106

Radicular Low Back Pain

For acute or subacute radicular pain due to herniated disc, one good-quality trial (n=60) published subsequent to the APS/ACP review found no difference between oral diazepam 5 mg twice daily for 5 days versus placebo in improvement in the RDQ (median improvement 3.0 vs. 5.0 at 1 week, p=0.67; median RDQ 2 vs. 1 at 1 year), request for additional analgesics, likelihood of improvement in neurological deficits, return to work, or likelihood of undergoing surgery through 1 year of followup.[135] Diazepam was associated with lower likelihood of experiencing ≥50% improvement in pain at 1 week (41% vs. 79%, RR 0.5, 95% CI 0.3 to 0.8)

Benzodiazepines Versus Skeletal Muscle Relaxants

Acute Low Back Pain

Two high-quality trials included in the APS/ACP review evaluated diazepam versus skeletal muscle relaxants for acute low back pain.[128, 129] One trial (n=30) found no differences between diazepam versus tizanidine in measures of pain relief or daily activities.129 The other trial found diazepam inferior to carisoprodol for likelihood of overall improvement (45% vs. 70%, RR 0.64, 95% CI 0.43 to 0.96) and measures of activity, sleep impairment, and overall relief at the end of a 7-day course of treatment (differences on continuous measures ranged from 12 to 19 points on a 100-point scale).[128]

Chronic Low Back Pain

For chronic low back pain, one trial included in the APS/ACP review found no difference between diazepam versus cyclobenzaprine in outcomes related to muscle spasm.[106]

Harms

In the trials of benzodiazepines included in the APS/ACP review, central nervous system adverse events such as somnolence, fatigue, and lightheadedness were reported more frequently with benzodiazepines versus placebo, though harms were not reported well.[103] No trial was designed to evaluate risks with long-term use of benzodiazepines such as addiction, abuse, or overdose. Harms were not reported in one short-term trial of diazepam versus placebo published subsequent to the APS/ACP review.[135]

Antidepressants

Key Points

- For chronic low back pain, a systematic review found no differences in pain between tricyclic antidepressants versus placebo (4 trials; SMD −0.10, 95% CI −0.51 to 0.31; I2=32%) or SSRIs versus placebo (3 trials; SMD 0.11, 95% CI −0.17 to 0.39; I2=0%); there was also no difference between antidepressants versus placebo in function (2 trials, SMD −0.06, 95% CI −0.40 to 0.29; I2=0%) (SOE: moderate for pain, low for function).
- For chronic pain, three trials, found duloxetine associated with lower pain intensity (differences 0.58 to 0.74 on a 0 to 10 scale) and better function (differences 0.58 to 0.74 on

the Brief Pain Inventory-Interference scale) versus placebo (SOE: moderate for pain and function).

- No study evaluated the effectiveness of antidepressants specifically for radicular low back pain.
- No study compared duloxetine versus a tricyclic antidepressant.
- Antidepressants were associated with higher risk of any adverse events compared with placebo, with no difference in risk of serious adverse events (SOE: moderate).

Detailed Synthesis

The APS/ACP review[29] included three higher-quality systematic reviews[136-138] of antidepressants for low back pain. The reviews included a total of 10 unique trials (8 placebo controlled). Based on the systematic reviews, the APS/ACP review[29] concluded that that tricyclic antidepressants were slightly more effective than placebo for pain relief for chronic back pain, with no significant effects on function. There was insufficient evidence to determine the effectiveness of antidepressants for acute low back pain.

We identified a good-quality systematic review[139] on antidepressants for low back pain published subsequent to the APS/ACP review (Table 1; Appendix Tables E9, F9). The review included 10 trials (n=16 to 121);[140-149] seven of the trials were included in one or more of the older systematic reviews.[140, 142-145, 147, 148] Only two trials required patients to have depression in addition to low back pain;[144, 148] the other trials excluded patients with depression,[141-143, 146] patients with depression accounted for a minority of enrollees,[140, 145, 149] or depression status was not reported.[147] The antidepressants assessed were tricyclic antidepressants (desipramine [3 trials], imipramine [2 trials], amitriptyline and nortriptyline [1 trial each]), selective serotonin reuptake inhibitors (paroxetine [3 trials], fluoxetine [2 trials]), tetracyclic antidepressants (maprotiline, trazodone [1 trial each]), and bupropion (1 trial.) One trial[149] evaluated injectable clomipramine, an intervention which is not widely used and outside the scope of this review. All studies included a placebo arm, though three used an active placebo (either diphenhydramine,[142] benztropine,[141] or atropine[148]) meant to mimic the side effects of antidepressants without therapeutic effects on pain. One trial also compared a tetracyclic antidepressant (maprotiline) versus an SSRI (paroxetine).[142] Duration of followup in the trials ranged from 10 days to 12 weeks. Nine of the trials enrolled participants with chronic pain; duration of pain was not reported in the other trial.[140] Seven trials were assessed as high quality based on meeting at least 6 Cochrane Back Review Group criteria. Methodological limitations in the three lower-quality trials included inadequate description of randomization and allocation concealment methods and high rates of attrition.[139]

We identified five additional trials (n=60 to 404) not included in the prior systematic reviews of antidepressants for chronic low back pain (Table 7; Appendix Tables E10, F10).[150-154] Three trials compared duloxetine (a serotonin-norepinephrine reuptake inhibitor) versus placebo,[152-154] one trial duloxetine versus escitalopram,[151] and one trial amitriptyline versus bupropion.[150] One trial was rated good quality,[152] three trials fair quality,[151, 153, 154] and one trial poor quality.[150] Methodological shortcomings in the poor- and fair-quality trials included inadequate description of randomization, allocation concealment, and blinding methods.

Antidepressants Versus Placebo

Chronic Low Back Pain

The systematic review found no difference between antidepressants versus placebo on pain for chronic low back pain (9 trials, SMD −0.04, 95% CI −0.25 to 0.17; I2=0%), with a point estimate close to 0 (no effect).[139] In stratified analyses, there were also no differences between antidepressants versus placebo for tricyclic antidepressants (4 trials; SMD −0.10, 95% CI −0.51 to 0.31; I2=32%) or SSRIs (3 trials; SMD 0.11, 95% CI −0.17 to 0.39; I2=0%). The review also found that antidepressants were not associated with reduced depression (SMD 0.06, 95% CI −0.29 to 0.40; I2=0%) or improved function (SMD −0.06, 95% CI −0.40 to 0.29; I2=0%), but each of these outcomes was only evaluated in two trials.

One good-quality[152] and two fair-quality[153, 154] trials evaluated duloxetine versus placebo for chronic low back pain and were not included in the systematic review. In all three trials, duloxetine 60 mg daily was associated with better scores based on the Brief Pain Inventory-Severity Scale (differences 0.60 to 0.79 points on a 0 to 10 scale) after 12 to 13 weeks followup. Results were similar, but not statistically significant, for duloxetine 20 or 120 mg/day doses versus placebo.[152] One of the trials also found 60 mg duloxetine associated with a greater likelihood of at least 50 percent improvement in pain score after 12 weeks (49% vs. 35%; RR 1.41, 95% CI 1.11 to 1.78).[153]

All three trials found duloxetine 60 mg daily associated with greater improvement in function versus placebo on the Brief Pain Inventory-Interference scale (mean between-group difference 0.58 to 0.74), but there were no differences on the RDQ (reported in one study; mean change from baseline −2.69 vs. −2.22; p=0.26).[153] The good-quality trial found both 60 and 120 mg daily doses of duloxetine associated with greater global improvement versus placebo (mean change −0.94 vs. −1.06 vs. −0.53; p<0.05 for both comparisons), measured using the Clinical Global Impressions of Severity (CGI-S) scale, although absolute differences between the groups were small (about 0.5 point on an 0- to 7-point scale).[152] Two other fair-quality trials found no differences between duloxetine and placebo in mean change in CGI-S scores.[153, 154] There were also few differences between duloxetine and placebo in quality-of-life outcomes, although one study found significant improvements in insomnia scores with duloxetine (mean change from baseline −1.92 versus −1.18 on the 0 to 24 Athens Insomnia Scale; p≤0.01).[154]

Antidepressants Plus Another Intervention Versus the Other Intervention Without Antidepressants

No study evaluated an antidepressant plus another intervention versus the other intervention alone.

Antidepressants Versus Other Interventions

One trial[37] included in the APS/ACP review[29] of acetaminophen versus amitriptyline is discussed in the acetaminophen section of this report.

Effectiveness of One Antidepressant Versus Another Antidepressant

Chronic Low Back Pain

Two trials included in prior reviews compared the effects of different antidepressants for chronic low back pain. One trial (n=108) found a tetracyclic antidepressant (maprotiline) superior to an SSRI (paroxetine) for pain relief after 8 weeks using the Descriptor Differential Scale (−5.41 vs. −2.34 on a 0 to 20 scale; p=0.013).[142] A smaller (n=40), lower-quality trial found no difference between a tricyclic antidepressant (amitriptyline) versus an SSRI (fluoxetine) in the likelihood of experiencing at least moderate pain relief after 6 weeks (82% [14/17] vs. 78% [14/18]; RR 1.06, 95% CI 0.76 to 1.47.)[155]

We identified one fair-quality study (n=85) not included in prior systematic reviews that compared the effects of different antidepressants for low back pain.[151, 152] It found no differences between duloxetine versus an SSRI (escitalopram) in pain, function, or quality of life. A third, poor-quality study (n=60) found no differences between a tricyclic antidepressant (amitriptyline) versus bupropion in pain after 8 weeks of use.[150]

Harms

The APS/ACP review[29] found antidepressant use associated with a higher risk for any adverse event compared with placebo (22% vs. 14%; RR 1.73, 95% CI 1.17 to 2.55) based on an older systematic review.[137] However, there were no differences between antidepressants versus placebo in rates of specific adverse events, including drowsiness (p=0.61), dizziness (p=0.84), dry mouth (p=0.55), constipation (p=0.28), or sexual dysfunction (p=0.23). The trials were not designed to assess for risk of serious adverse events.

Three recent trials found no differences between duloxetine versus placebo in risk of serious adverse events, with no deaths reported.[152-154] Duloxetine was associated with increased risk of withdrawal due to adverse events (3 trials, duloxetine any dose vs. placebo [OR 2.72, 95% CI 1.74 to 4.24; I2=0%]; duloxetine 60 mg versus placebo [OR 2.52, 95% CI 1.58 to 4.03; I2=0%]). Duloxetine was also associated with increased risk of nausea (p<0.05), but there was no clear increase in risk of other specific adverse events. Trials of escitalopram versus duloxetine[151] or amitriptyline versus bupropion[150] found no differences in risk of adverse events.

Antiseizure Medications

Key Points

- No trial evaluated antiseizure medications for acute nonradicular low back pain.
- One trial found no difference between gabapentin (up to 3600 mg/day) versus placebo for chronic nonradicular low back pain, but did not meet inclusion criteria because it was only published as an abstract (SOE: insufficient).
- For chronic radicular low back pain, there was insufficient evidence from three poor-quality trials with inconsistent findings to determine effects of gabapentin versus placebo (SOE: insufficient).

- For chronic radicular low back pain or mixed radicular and nonradicular low back pain, two trials reported inconsistent results for effects of topiramate versus placebo (SOE: insufficient).
- For chronic radicular low back pain, two trials reported inconsistent effects of pregabalin versus placebo for pain or function (SOE: insufficient).
- For chronic radicular or nonradicular low back pain, there was insufficient evidence from one poor-quality trial to determine effects of pregabalin versus amitriptyline (SOE: insufficient).
- For chronic nonradicular low back pain, one small trial found the addition of pregabalin 300 mg/day to transdermal fentanyl associated with substantially lower pain scores than transdermal buprenorphine alone at 3 weeks (difference ~26 points on a 0 to 100 scale, $p<0.05$) but the estimate was very imprecise (SOE: insufficient).
- For chronic radicular pain, one trial found pregabalin (mean 2.1 mg/kg/day) plus celecoxib associated with lower pain scores than celecoxib alone (difference 11 points on a 0-100 scale, $p=0.001$) after 4 weeks and one trial found no effects of adding pregabalin (titrated to 300 mg/day) to tapentadol PR versus tapentadol PR alone on pain or the SF-12 after 8 weeks (SOE: insufficient).
- Two trials of gabapentin versus placebo reported no clear differences in risk of adverse events (SOE: low).
- Two trials of topiramate versus placebo reported inconsistent effects on risk of withdrawal due to adverse events; one of the trials found topiramate associated with higher risk of sedation and diarrhea (SOE: insufficient).
- Two trials of pregabalin versus placebo reported inconsistent effects on risk of withdrawal due to adverse events, somnolence, and dizziness; one of the trials used an enrichment/withdrawal design (SOE: insufficient).

Detailed Synthesis

The APS/ACP review[29] included four trials of antiseizure medications for low back pain.[156-159] Two trials (n=50 and 65)[157, 159] evaluated gabapentin and two trials (n=29 and 96)[156, 158] evaluated topiramate. All trials compared antiseizure medications versus placebo, with one trial[156] utilizing an "active" placebo (diphenhydramine). Three trials[156, 157, 159] evaluated patients with radicular symptoms and one trial (of topiramate)[158] evaluated a mixed population of patients with radicular or nonradicular pain.

We identified seven trials of antiseizure medications for low back pain published subsequent to the APS/ACP review (Table 8; Appendix Tables E11, F11).[160-166] Sample sizes were 200 to 309 in the three largest trials[160-162] and ranged from 26 to 55 in the other four trials. Six trials[160-165] evaluated pregabalin and one trial166 evaluated gabapentin. Two trials compared pregabalin versus placebo[160] or active placebo (diphenhydramine)[163] and one trial[166] compared gabapentin versus no gabapentin. Three trials compared pregabalin plus another medication (tapentadol,[161] transdermal buprenorphine,[164] or celecoxib[165]) versus the other medication without pregabalin

and one trial[162] compared pregabalin versus amitriptyline. The celecoxib trial also compared pregabalin alone versus celecoxib alone.[165] Five trials evaluated patients with radicular symptoms,[160, 161, 163, 165, 166] with two trials[163, 166] focusing on patients with spinal stenosis. One trial was restricted to patients with nonradicular back pain[164] and one trial enrolled a mixed population of radicular and nonradicular back pain.[162]

All of the trials, including those in the APS/ACP review, evaluated patients with chronic symptoms. Dosing of antiseizure medications varied. One trial evaluated fixed-dose pregabalin 300 mg/day in combination with transdermal buprenorphine.[164] In the other pregabalin trials, doses were titrated, though titration protocols and maximum doses varied. Two trials[156, 158] of topiramate titrated doses to 300 or 400 mg/day and three trials titrated gabapentin to a maximum dose that ranged from 1200 to 3600 mg/day.[157, 159, 166] The duration of therapy ranged from 2 weeks to 4 months; outcomes were assessed at the end of or during therapy in all trials except for one,[161] which evaluated patients 1-2 weeks after completing 8 weeks of therapy.

Three trials[156, 163, 165] used a crossover design and the rest were parallel-group trials. Six trials[158, 160, 161, 163-165] were rated fair quality and four[156, 157, 159, 166] poor quality. Methodological shortcomings included inadequate description of randomization and allocation concealment methods and unclear blinding of outcome assessors. Additional shortcomings in the poor-quality trials included unblinded design or unclear blinding status, high attrition, and failure to perform intention-to-treat analysis. One trial of pregabalin used an enrichment/withdrawal design.[160] None of the crossover trials reported results of the first intervention period and two of the crossover trials[163, 165] did not assess for carryover effects, though all employed a washout period between interventions.

We excluded one trial (n=113) of gabapentin (up to 3600 mg/day) versus placebo for chronic nonradicular pain only published as an abstract.[167]

Antiseizure Medications Versus Placebo

Acute Low Back Pain

No trial evaluated antiseizure medications for acute nonradicular low back pain.

Chronic Low Back Pain

One trial (n=113) of gabapentin (titrated up to 3600 mg/day) versus placebo for nonradicular low back pain was excluded because it has only been published as an abstract, but otherwise met inclusion criteria.[167] It found no differences between gabapentin versus placebo in outcomes related to pain, function, or quality of life.

Radicular Low Back Pain

Two poor-quality trials included in the APS/ACP review evaluated gabapentin versus placebo for chronic radicular back pain.[157, 159] One trial (n=80) found no clear differences between gabapentin (titrated up to 1200 mg/day) versus placebo in back pain at rest, back pain with movement, or leg pain (mean differences ~0.3 to 0.5 points on a 0 to 10 scale, p for between-group differences not reported).[157] The other trial (n=50), which used higher doses of gabapentin

(titrated up to 3600 mg/day) found gabapentin associated with greater improvement in back pain at rest versus placebo (mean change from baseline −1.04 vs. −0.32 on a 0 to 3 scale, p<0.01).[159]

One subsequent poor-quality trial (n=55) of patients with chronic radicular symptoms due to spinal stenosis found gabapentin (titrated up to 2400 mg/day) associated with lower pain scores at 4 months (2.8 vs. 4.7 on 0 to 10 scale, p=0.006), increased likelihood of being able to walk >1000 m (65% vs. 21% at 4 months, p=0.001), and decreased likelihood of sensory deficit (32% vs. 63%).[166] However, it was unclear if patients were blinded and attrition was not reported.

Two trials included in the APS/ACP review evaluated topiramate (titrated up to 300 or 400 mg/day) versus placebo or active placebo.[156, 158] For chronic radicular or nonradicular pain, a fair-quality trial (n=96) found topiramate moderately more effective than placebo for improving Pain Rating Index scores (about 11 points on a 0 to 100 scale, p<0.001).[158] Topiramate was also more effective than placebo for improving scores on all SF-36 subscales. The largest difference was on the physical function subscale (9.1 points, range 0.6 to 8.3 points for other subscales). For chronic radicular pain, a poor-quality trial (n=41)[156] found topiramate more effective than diphenhydramine for improving back and overall pain, though mean differences were small (less than one point on a 0 to 10 scale). There were no statistically significant differences in leg pain, ODI scores, or SF-36 scores. Topiramate was also associated with a higher likelihood of patients reporting moderate to complete pain relief (54% vs. 24%, p=0.005).

Two fair-quality trials published subsequent to the APS/ACP review evaluated pregabalin versus placebo. One trial (n=211) that used an enrichment/withdrawal design found no differences between pregabalin (mean dose 410 mg/day) versus placebo in pain (mean change from baseline −0.16 vs. 0.05 on a 0-10 scale, p=0.33), the EQ-5D, or the RDQ.[160] Pregabalin was superior for outcomes related to sleep and Hospital Anxiety and Depression Scale (HADS), but effects were small (difference in sleep quality less than 0.5 hours, and differences in HADS anxiety and depression scores ~1 point on a 0 to 21 scale). The other, smaller (n=26) trial, which evaluated patients with neurogenic claudication due to spinal stenosis, found no differences between pregabalin (titrated to 150 mg twice daily) versus an active placebo (diphenhydramine) in the ODI, pain with ambulation, walking distance, or the Swiss Spinal Stenosis Questionnaire after 10 days.[163] Pregabalin was associated with slightly worse mean RDQ at 2 weeks (13 vs. 11, p=0.01).

Antiseizure Medications Versus Another Medication

Radicular Low Back Pain

For chronic radicular pain, one fair-quality trial (n=36) found no differences between pregabalin (mean 2.1 mg/kg/day) versus celecoxib (mean 4.2 mg/kg/day) in pain scores after 4 weeks (mean 43 vs. 40 on a 0-100 scale).[165]

Mixed (Radicular or Nonradicular) Low Back Pain

For chronic radicular or nonradicular low back pain, one poor-quality trial (n=200) found no clear differences between pregabalin (mean dose ~430 mg/day) versus amitriptyline (mean dose 38 mg/day) in mean pain (3.8 vs. 2.8 on 0 to 10 VAS, p>0.05) or function scores (22 vs. 17 on the ODI, p>0.05) through 14 weeks, though pregabalin was associated with greater likelihood of

≥50% improvement in pain score (RR 0.68, 95% CI 0.51 to 0.92) or >20% improvement in the ODI (RR 0.76, 95% CI 0.59 to 0.97).[162]

Antiseizure Medications Plus Another Medication Versus the Other Medication Alone

Chronic Low Back Pain

For chronic nonradicular low back pain, one fair-quality trial (n=44) found the addition of pregabalin 300 mg/day to transdermal buprenorphine associated with substantially lower pain scores versus transdermal buprenorphine alone at 3 weeks (difference ~26 points on a 0 to 100 scale, $p<0.05$).[164]

Radicular Low Back Pain

For chronic radicular pain, one trial (n=36) found pregabalin (mean 2.1 mg/kg/day) plus celecoxib associated with lower pain scores versus celecoxib alone (difference 11 points on a 0-100 scale, $p=0.001$) after 4 weeks[165] and one trial (n=309) found no effects of adding pregabalin (titrated to 300 mg/day) to tapentadol PR versus tapentadol PR alone on pain, the SF-12, the EQ-5D, or HADS anxiety or depression scores 1 to 2 weeks after an 8-week course of therapy.[161] Both trials were rated fair quality.

Harms

Two trials of gabapentin versus placebo evaluated harms. In one trial, withdrawal due to adverse events occurred in 2 of 25 patients randomized to gabapentin versus none of 25 randomized to placebo.[159] In the other trial, no withdrawals due to adverse events occurred, though drowsiness (6%), loss of energy (6%), and dizziness (6%) were reported with gabapentin.[157] One subsequent trial of gabapentin versus placebo also reported no withdrawals, though ataxia (7%) was reported with gabapentin.[166]

Harms were reported in two trials of topiramate versus placebo.[156, 158] One trial found topiramate associated with higher likelihood of withdrawal due to adverse events versus diphenhydramine (33% vs. 15%),[156] but there was no difference between topiramate versus placebo in rates of withdrawal due to adverse events in the other (4% vs. 4%).[158] Topiramate was also associated with higher rates of withdrawal due to adverse events (33% vs. 15%), sedation (34% vs. 3%) and diarrhea (30% vs. 10%) compared with diphenhydramine in one trial.[156]

Two trials published reported harms associated with pregabalin versus placebo.[160, 163] One trial[163] found pregabalin associated with greater risk of any adverse event versus diphenhydramine (active placebo) (64% vs. 35%), though the other trial[160] found no difference versus inert placebo (41% vs. 42%). Serious adverse events were rare (2 events in one trial and none in the other). The trials also reported inconsistent results for somnolence and dizziness, with one trial[163] reporting increased risk and the other[160] no difference. In the trial that reported no differences, patients randomized to placebo were withdrawn from pregabalin after being stabilized on it (enrichment/withdrawal design).[160]

Three trials of pregabalin plus another drug (transdermal buprenorphine, celecoxib, or tapentadol PR) versus the other drug alone found no differences in risk of withdrawal due to adverse events or other side effects, though estimates were imprecise due to small samples.[161, 164, 165]

Corticosteroids

Key Points

- For acute nonradicular low back pain, two trials found no differences between a single intramuscular injection or a 5-day course of systemic corticosteroids versus placebo for pain or function (SOE: low for pain and function).
- For radicular low back pain (acute or unspecified duration) five trials consistently found no differences between systemic corticosteroids (administered a single bolus or as a short taper) versus placebo in pain or function; one trial found no effect on need for spine surgery (SOE: moderate for pain and function).
- For spinal stenosis, one trial found no differences through 12 weeks of followup between a 3-week course of prednisone versus placebo in pain intensity, the RDQ, or any SF-36 subscale (SOE: low for pain and function).
- Trials of systemic corticosteroids did not report serious adverse events, including hyperglycemia requiring medical treatment, but adverse events were not reported well in some trials (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included four trials of systemic corticosteroids.[168-171] Three trials (n=49 to 60)[168, 170, 171] evaluated systemic corticosteroids in patients with radiculopathy and one trial (n=86)[169] evaluated patients with nonradicular back pain. For radiculopathy, the APS/ACP review concluded that there was consistent evidence that systemic corticosteroids were not associated with clinically significant benefits when given as a single large parenteral bolus or as a short oral or intramuscular taper.

We identified four trials[172-175] of systemic corticosteroids published subsequent to the APS/ACP review and one older trial[176] that was not included in the APS/ACP review (Table 9; Appendix Tables E12, F12). Three trials (n=27 to 78)[173, 174, 176] evaluated patients with radicular pain, one trial (n=61) evaluated patients with spinal stenosis[175] and one trial (n=67)[172] evaluated patients with nonradicular pain.

All of the trials were placebo-controlled. Five trials[168, 169, 172-174] evaluated patients with acute low back pain (including the two trials of nonradicular back pain)[169, 172] and the other four[170, 171, 175, 176] did not specify the duration of symptoms. Three trials were conducted in emergency department settings,[169, 172, 173] one trial in an inpatient setting,[168] and in the other trials the clinical setting was not reported or mixed. The doses and mode of administration of corticosteroids varied. Three trials evaluated a single dose of parenteral (intravenous or intramuscular) methylprednisolone (150 to 500 mg, equivalent to 187.5 to 625 mg of prednisone).[168, 169, 173] In

the other trials, the duration of treatment ranged from 5 to 21 days. Three trials evaluated similar tapering courses of oral or intramuscular dexamethasone (64 mg for 1 day, 32 mg for 1 day, 24 mg for 1 day, 12 mg for 1 day, and 8 mg for 3 days [64 mg of dexamethasone equivalent to 400 mg of prednisone]).[170, 171, 176] The other three trials evaluated different courses of oral prednisone (50 mg for 5 days,[172] 60 mg for 3 days, 40 mg for 3 days, and 20 mg for 3 days,[174] or 1 mg/kg/day for 1 week, with a one-third dose reduction each week[175]). The three single-dose trials evaluated patients at 10 days to 1 month after administration; in the other trials followup ranged from within 2 days after a 5 or 7 day course of therapy[171, 172] to 1 to 4 years after a 1-week course of therapy.[170]

Among the trials of systemic corticosteroids for radiculopathy, two trials[173, 174] required a positive straight leg raise for inclusion and four others[168, 170, 171, 176] required a positive straight leg raise or other signs of radiculopathy (e.g., sensory, motor, or reflex deficit). One of the latter trials also required imaging findings of a herniated disc that correlated with radicular symptoms.168 The trial of patients with spinal stenosis required presence of neurogenic claudication symptoms and imaging findings of central stenosis.[175]

Three trials[168, 169, 173] were rated good quality, five trials fair quality,[170-172, 175, 176] and one trial poor quality.[174] Methodological shortcomings in the fair-quality trials included inadequate description of allocation concealment, unclear blinding of outcomes assessors, and unclear compliance to interventions. The poor-quality trial allocated patients sequentially.[174]

One trial (n=100) of dexamethasone versus placebo for nonradicular low back pain was excluded because it was published in German, but otherwise met inclusion criteria.[177]

Systemic Corticosteroids Versus Placebo

Acute Low Back Pain

Two trials evaluated the effects of systemic corticosteroids versus placebo for acute nonradicular low back pain.[169, 172] The APS/ACP review included one good-quality trial (n=86) that found no differences between a single intramuscular injection of 160 mg daily methylprednisolone versus placebo in pain relief or improvement in the RDQ at 1 week or 1 month.[169] A subsequent trial (n=67) also found no difference between a 5-day course of oral prednisone 50 mg daily versus placebo in measures of pain, days of work lost, or likelihood of seeking care at 5-7 days, though estimates favored the placebo group.[172]

One other trial (n=100) was excluded because it was published in German, but also found no effects of dexamethasone versus placebo for nonradicular pain.[177]

Radicular Low Back Pain

For radiculopathy, three trials included in the APS/ACP review found no differences between systemic corticosteroids (administered as a single large parenteral bolus or as a short oral or intramuscular taper) versus placebo.[168, 170, 171] One good-quality trial (n=60), which was also the only trial to require imaging correlation of radicular symptoms, found a single large bolus of methylprednisolone associated with small (average 6 mm on a 0-100 scale) early improvement in leg pain versus placebo, but the benefits was no longer present after the first 3 days.[168] There were

no differences in the degree of pain relief, functional disability, the proportion requiring spine surgery within the first month, or medication use. In two fair-quality trials (n=33 and 49), 7-day tapering courses of either oral or intramuscular dexamethasone (initial dose 64 mg/day) were not associated with differences in overall effect or likelihood of subsequent surgery, either at the end of treatment or after 1 to 4 years of followup.[170, 171]

Two subsequent trials of patients with acute radicular low back pain also found no differences between systemic corticosteroids versus placebo in improvement in pain, the RDQ, return to work, use of medications, or the likelihood of seeking additional health care.[173, 174] A good-quality trial (n=78)[173] evaluated outcomes through 1 month after a single dose of intramuscular methylprednisolone 160 mg and one poor-quality trial (n=27)[174] evaluated outcomes through 6 months after a tapering course of prednisone (initial dose 60 mg/day. One other older, fair-quality trial (n=39) that was not included in the APS/ACP review also found no difference between a tapering course of intramuscular dexamethasone (initial dose 64 mg/day) versus placebo in likelihood of experiencing "clear improvement" through 3 months.[176]

Spinal Stenosis

For spinal stenosis, one trial not included in the APS/ACP review found no differences through 12 weeks of followup between a 3-week course of prednisone versus placebo in pain intensity, the RDQ, or any SF-36 subscale.[175]

Harms

One trial reported two cases of transient hyperglycemia and one case of facial flushing following administration of a large (500 mg) intravenous methylprednisolone bolus.[168] In two trials, a smaller (160 mg) intramuscular methylprednisolone injection was associated with no cases of hyperglycemia requiring medical attention, infection, or gastrointestinal bleeding.[169, 173] One other older trial not included in the APS/ACP review found a tapering course of intramuscular dexamethasone (initial dose 64 mg/day) associated with increased risk of any side effect (32% vs. 5.0%, RR 6.32, 95% CI 0.84 to 47.7), but no patients in either group withdrew due to adverse events.[176] Adverse events were not reported well in the other trials of systemic corticosteroids.

Topical Medications

No study evaluated topical capsaicin or lidocaine for low back pain.

Key Question 2. What are the comparative benefits and harms of different nonpharmacological noninvasive therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis? Includes but is not limited to multidisciplinary rehabilitation, exercise (various types), physical modalities (ultrasound, transcutaneous electrical nerve stimulation, electrical muscle stimulation, interferential therapy, heat [various forms], and ice), traction tables/devices, back supports/bracing, spinal manipulation, various psychological therapies, acupuncture, massage therapy (various types), yoga, magnets, and low-level lasers.

Exercise and Related Interventions: Exercise

Key Points

- For acute low back pain, a systematic review found no differences between exercise therapy versus no exercise in pain (3 trials, WMD 0.59 at intermediate term on a 0 to 100 scale, 95% CI −11.51 to 12.69) or function (3 trials, WMD at short term −2.82, 95% CI −15.35 to 9.71 and WMD 2.47 at intermediate term, 95% CI −0.26 to 5.21). For subacute low back pain, there were also no differences in pain (5 trials, WMD 1.89 on a 100-point scale, 95% CI −1.13 to 4.91) or function (4 trials, WMD 1.07, 95% CI −3.18 to 5.32). Three subsequent trials for acute to subacute low back pain reported inconsistent effects of exercise versus usual care on pain and function (SOE: low for pain and function).
- For chronic low back pain, a systematic review found exercise associated with greater pain relief versus no exercise (19 trials, WMD 10 on a 0 to 100 scale, 95% CI 1.31 to 19.09), though the effect on function was small and not statistically significant (17 trials, WMD 3.00 on a 0 to 100 scale, 95% CI −0.53 to 6.48). Results from a more recent systematic review using more restrictive criteria and additional trials not included in the systematic reviews were generally consistent with these findings (SOE: moderate for pain and function).
- For chronic low back pain, a systematic review included two trials that found motor control exercise (MCE) associated with lower pain scores in the short term (WMD −12.48 on a 0 to 100 scale, 95% CI−19.04 to −5.93), intermediate term (WMD −10.18, 95% CI −16.64 to −3.72) and at long term (WMD −13.32 95% CI −19.75 to −6.90) versus a minimal intervention. MCE was also associated with better function at short term (3 trials WMD −9.00 on 0 to 100 scale, 95% CI −15.28 to −2.73), intermediate term (2 trials WMD −5.62, 95% CI−10.46 to −0.77) and long term (2 trials, WMD −6.64, 95% CI −11.72 to −1.57) (SOE: low for pain and function).
- For nonacute low back pain, a systematic review found no clear effects of exercise therapy versus usual care on likelihood of short- or intermediate-term (~6 months) disability, but exercise was associated with lower likelihood of work disability at long-term (~12 months) followup (10 comparisons in 8 trials, OR 0.66, 95% CI 0.48 to 0.92) (SOE: moderate for pain and function).
- For radicular low back pain, three trials not included in the systematic reviews found effects that favored exercise versus usual care or no exercise in pain and function, though effects were small (SOE: low for pain and function).
- For chronic low back pain, a systematic review found MCE associated with lower pain intensity at short term (6 trials, WMD −7.80 on 0 to 100 scale, 95% CI −10.95 to −4.65) and intermediate term (3 trials, WMD −6.06, 95% CI −10.94 to −1.18) versus general exercise, but effects were smaller and no longer statistically significant at long-term (4 trials, WMD −3.10, 95% CI −7.03 to 0.83). MCE was also associated with better function in the short term (6 trials, WMD −4.65 on 0 to 100 scale, 95% CI −6.20 to −3.11) and long term (3 trials, WMD −4.72, 95% CI −8.81 to −0.63). One of two subsequent trials found no

effect on pain, though effects on function were consistent with the systematic review (SOE: low for pain and function).

- For comparisons involving other types of exercise techniques, there were no clear differences in >20 head-to-head trials of patients with acute or chronic low back pain (SOE: moderate).
- Harms were poorly reported in trials of exercise. When reported, harms were typically related to muscle soreness and increased pain, or no harms were reported; no serious harms were reported (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included six systematic reviews[178-184] with a total of 79 unique trials and one additional large, lower-quality trial.[185] The most comprehensive systematic review in the APS/ACP review found no differences between exercise therapy versus no exercise for acute low back pain in pain (3 trials, WMD 0.59 at intermediate term on a 0 to 100 scale, 95% CI −11.51 to 12.69) or function (3 trials, WMD at short term −2.82, 95% CI −15.35 to 9.71 and WMD 2.47 at intermediate term, 95% CI −0.26 to 5.21).[179] For subacute low back pain, there were also no differences in pain (5 trials, WMD 1.89 on a 100-point scale, 95% CI −1.13 to 4.91) or function (4 trials, WMD 1.07, 95% CI −3.18 to 5.32). For chronic low back pain, the APS/ACP review found good evidence that exercise is moderately superior to no exercise for pain relief (19 trials, WMD 10 on a 0 to 100 scale, 95% CI 1.31 to 19.09), though the effect on function was small and not statistically significant (17 trials, WMD 3.00 on a 0 to 100 scale, 95% CI −0.53 to 6.48). Results of the other reviews were generally consistent with these findings. Based on this evidence, the APS/ACP review concluded that there was fair evidence of no benefit for exercise versus no exercise for acute or subacute low back pain, and good evidence for moderate benefits of exercise versus no exercise for chronic low back pain.

We included three fair-quality systematic reviews of exercise for low back pain published subsequent to the APS/ACP review (Table 10; Appendix Tables E13, F13).[186-188] One focused on exercise for nonspecific chronic low back pain[187] one evaluated effects of exercise on work disability in patients with nonacute, nonspecific low back pain (duration >4 weeks),[188] and the third focused on effects of motor control exercise (MCE), which was not addressed in the APS/ACP review and not covered well in the other reviews.[186]

The first review focused on various types of exercise therapy for chronic low back pain and included 37 RCTs (n=3957).[187] Shortcomings of this review included limited description of included trial characteristics (including exercise treatments) failure to report statistical heterogeneity for pooled analyses, and lack of sensitivity or subgroup analyses. The systematic review included eight trials from a previous review[179] plus 29 additional trials; it excluded a number of trials in the previous review because it applied more strict criteria to define chronic low back pain (≥ 12 weeks), and only enrolled trials of patients with nonspecific low back pain. Exercise was compared against wait list/no treatment (8 RCTs), usual care (6 RCTs), back school or education (3 RCTs), and other forms of exercise therapy (11 RCTs). Exercise interventions varied and included general strengthening, stretching, or aerobic exercise; motor control and stabilization exercises; physiotherapy; multidisciplinary programs; and specific

techniques such as the active trunk exercise protocol.[187] Comparisons of exercise versus other active interventions (behavioral treatment, passive modalities [TENS, laser, ultrasound, massage], spinal manipulations and psychotherapy), are discussed in the sections of this report addressing those interventions. Outcomes were assessed at the end of treatment, at short term (3 months), intermediate term (6 months), and long term (>6 months). Of the 27 trials providing data for the above comparisons,[189-215] 11 (41%) were rated low risk of bias, based on meeting ≥6 of 11 Cochrane Back Review Group criteria.[191-193, 197, 198, 201-203, 207, 209, 214, 216] Methodological flaws included failure to describe adequate randomization methods (26% of trials) or allocation concealment (48%), inadequate description of cointerventions(63%), unclear compliance with treatment (56%), failure to report intention-to-treat analysis (48%), and high or unreported attrition (33%). Given the nature of exercise interventions, blinding of patients and care providers was generally not possible; in addition, 67 percent of trials did not report blinding of outcome assessors.

The second review evaluated effects of exercise specifically on work disability in patients with nonacute (>4 weeks), nonspecific low back pain.[188] It included 23 trials (n=4138), 20 of which were included in meta analyses. Sample sizes ranged from 49 to 476 and duration of low back pain varied from 4 weeks to greater than 12 months. Exercise was compared against usual care (13 RCTs, n=3181) and other forms of exercise (11 RCTs). Exercise interventions varied and included stabilization, strengthening, stretching, and mobilization, though exercise regimens were most frequently mixed. About half of the exercise interventions were administered in the context of a cognitive behavioral approach. The majority of interventions (91%) were supervised exercise conducted in an outpatient setting (77%). Nine trials[206, 217-224] (39%) were rated high quality and the remainder were rated low quality, based on risk of bias criteria by Juni et al. Methodological shortcomings included detection bias in 12 trials (52%), selection bias in 9 trials (39%), and attrition bias in 8 trials (35%).

The third review included 16 trials of MCE (sample size range 30 to 346, total n=1993).[186] MCE (also referred to as specific stabilization exercise) focuses on strengthening of deep muscles of the spine through a specific stabilization protocol, while reducing unwanted overactivity of other muscles.[225] Methodological limitations of the review are that it did not report details regarding study quality (it reported an overall assessment only), did not report statistical heterogeneity in pooled analyses, and did not report harms. We addressed these issues through additional review and assessment of the primary studies. The review included seven trials of MCE versus various types of general exercise (including sling exercise, trunk strengthening, walking, cardiovascular and McKenzie exercises),[192, 226-231] three trials of MCE versus a minimal intervention (no intervention, advice/education or placebo short-wave therapy and ultrasound),[196, 232, 233] and four trials of MCE versus multimodal physical therapy (including ultrasound, electrotherapy, lumbar strengthening, passive physical therapy and general exercise).[230, 234-236] Two trials evaluated MCE as part of a multimodal intervention versus other components of that intervention.[237, 238] Eight trials included only chronic low back pain patients;[192, 196, 226, 228-230, 232, 233] three trials also included patients with subacute low back pain, but mean duration of symptoms was 25 to 34 months.[231, 234, 236] Three trials focused on patients with recurrent low back pain, with the duration of the current episode ranging from >6 weeks to >3 months.[231, 235, 237] Most trials selected patients for inclusion on the basis of tests showing deficits in motor control, but the specific methods and criteria for inclusion varied. The duration of treatment ranged from 6 to10

weeks; six trials evaluated patients 10 to 28 months after the end of treatment. In two trials, MCE was administered through 20 treatment sessions (time frame not described), with followup for 180 days. The systematic review classified 10 trials as high quality, based on scoring ≥6 points on the 10 point PEDro scale[192, 226, 227, 229, 230, 232-238] and six low quality.[196, 227, 229, 231, 233, 234] Common methodological shortcomings included unclear or inappropriate randomization methods and unclear allocation concealment; patients and care providers generally could not be blinded. Some trials also reported discrepancies in baseline characteristics or differential attrition. Data were pooled for short term (≥6 weeks to <4 months) intermediate term (≥4 months to <8 months) and long term (≥8 months <15 months).

We identified 17 trials with sample sizes >100 of exercise for low back pain that were not included in the systematic reviews (Table 11; Appendix Tables E14, F14).[239-255] Three trials evaluated exercise versus no exercise or usual care for acute to subacute low back pain,[244, 254, 255] two trials compared different types of exercise for patients primarily with subacute low back pain,[243, 246] four trials compared exercise versus no exercise or usual care for chronic low back pain,[250-252, 256] four trials compared different types of exercise for chronic low back pain,[241, 249, 251, 253] and four trials evaluated exercise versus various other interventions for radicular low back pain.[239, 240, 242, 248] Exercise techniques varied but included general exercise, strengthening, the McKenzie method, exercise based on a treatment-based classification (TBC) system, the Alexander technique, periodized musculoskeletal rehabilitation, walking, MCE and others. Four trials were rated good quality,[241, 242, 250, 252] seven trials fair quality,[239, 240, 244, 245, 249, 253-255] and five poor quality.[243, 246, 248, 251, 256] Methodological shortcomings included inadequate allocation concealment, failure to clearly described cointerventions, and failure to report compliance to treatment. Patients and people administering exercise could not be effectively blinded given the nature of the interventions.

We also identified 28 trials not included in the systematic reviews that evaluated exercise therapy for subacute to chronic low back pain, but enrolled fewer than 100 patients. Eighteen trials compared exercise versus no exercise or usual care[197, 200, 257-272] and 15 compared different forms of exercise.[197, 200, 258, 261, 271, 273-282] Given the number of larger trials on exercise, we did not abstract these studies in detail.

Exercise Therapy Versus Placebo, Usual Care, or No Treatment

Acute to Subacute Low Back Pain

As noted above, a systematic review included in the prior APS/ACP review found no differences between exercise therapy versus usual care for acute low back pain in pain (3 trials, WMD 0.59 at intermediate term on a 0 to 100 scale, 95% CI −11.51 to 12.69) or function (3 trials, WMD at short term −2.82, 95% CI −15.35 to 9.71 and WMD 2.47 at intermediate term, 95% CI −0.26 to 5.21).179 For subacute low back pain, there were also no differences in pain (5 trials, WMD 1.89 on a 100-point scale, 95% CI −1.13 to 4.91) or function (4 trials, WMD 1.07, 95% CI −3.18 to 5.32).

We identified three subsequent trials of exercise therapy for acute to subacute low back pain.[244, 254, 255] For acute or subacute low back pain, a fair-quality trial (n=259) found the combination of exercise plus advice associated with lower pain scores versus no exercise or

advice at the end of the 6-week intervention (mean difference –1.5 on a 0 to 10 scale, 95% CI –2.2 to –0.7); the difference favored exercise plus advice at 3 months (mean difference –1.1, 95% CI–2.0 to –0.3), but was smaller and no longer statistically significant at 12 months (mean difference −0.8, 95% CI –1.7 to 0.1).[255] Exercise plus advice was also associated with better scores on the Patient-Specific Functional Scale (PSFS) (differences 1.1 to 1.3 on a 0 to10 scale) and on a Global Perceived Effect scale at 3 months. Differences on the RDQ tended to favor exercise plus advice (mean differences −0.9 to −1.3) but were small and not statistically different. For acute low back pain, one fair-quality trial (n=148) found six sessions of McKenzie exercise over 3 weeks associated with lower pain intensity at one (mean difference, −0.4 points on a 0 to 10 scale, 95% CI –0.8 to –0.1) and 3 weeks (–0.7, 95% CI –1.2 to –0.1) versus usual care, though effects were small.[254] There were no differences in disability at either time point (mean differences −0.2 and −0.3 on the RDQ), global perceived effects (mean differences 0.3 to 0.5 on a −5 to 5 scale), or risk of developing persistent low back pain (RR 1.1, 95% CI 0.8 to 1.6). The third, fair-quality trial (n=246) found no differences between 8 weeks of trunk muscle stabilization exercise versus no treatment in patients with 8 to 12 weeks of low back pain, with outcomes measured as 6 to 24 months.[244]

Chronic Low Back Pain

As described above, a systematic review included in the APS/ACP review found exercise moderately superior to placebo for pain relief (19 trials, WMD 10 on a 0 to 100 scale, 95% CI 1.31 to 19.09), though the effect on function was small and not statistically significant (17 trials, WMD 3.00 on a 0 to 100 scale, 95% CI −0.53 to 6.48).[179] A more recent systematic review[187] that used more restrictive inclusion criteria also found exercise therapy associated with decreased pain intensity (3 trials, WMD −9.23, 95% CI –16.02 to –2.43)[193, 200, 210] and better function (3 RCTs, WMD −12.35 on a 0 to 100 scale, 95% CI –23.0 to –1.69)[193, 200, 210] versus usual care at the end of treatment. Effects on function were smaller but remained statistically significant at intermediate- and long-term followup (mean differences −5.23 and −3.17). Effects on pain were also smaller, and no longer statistically significant at long-term followup (mean difference −4.94, 95% CI −10.45 to 0.58).[193, 203, 214]

One good-quality trial (n=579) not included in the systematic review used a factorial design that randomized patients to usual care, massage, 6 sessions of Alexander, or 24 sessions of Alexander; half of the patients in each group was also randomized to exercise.[252] Exercise was associated with fewer days with low back pain (in the previous 4 weeks) at 3 months (difference −6 days, 95% CI −9 to −3) versus no exercise but the effect was not significant at 12 months (difference −2 days, 95% CI −5 to 1). Effects on the RDQ also favored exercise at 3 months (mean difference −0.9, 95% CI −1.76 to 0.04) and 12 months (−1.29, 95% CI −2.25 to −0.43). There were no differences between exercise versus no exercise in the SF-36 Pain Catastrophizing Scale (PCS) at 3 or 12 months (mean differences of 3.0 and 1.9 on a 0-100 scale); exercise was associated with small positive effects on the mental component score of the SF-36 (MCS) at 3 months (mean difference 4.4, 95% CI 0.65 to 7.43 on 0 to 100 scale) that were not sustained to 12 months (mean difference, 0.9 95% CI (−2.8 to 4.6).

In the same trial, compared with usual care, 24 Alexander technique sessions were associated with fewer days with back pain at 3 months (difference −16 days, 95% CI −21 to −11) and 12 months (difference −18 days, 95% CI −23 to −13) and with better function at both time frames

(mean differences on the RDQ −2.91, 95% CI 4.16 to 1.66 at 3 months and −3.4, 95% CI −4.6 to −0.03 at 12 months). The 24 session intervention was also associated with better scores on the SF-36 PCS at both time points (mean differences 7.5 and 11.3); effects on the MCS were smaller and not statistically significant (mean differences 3.4 and 4.0). Although six Alexander technique sessions were also associated with fewer low back pain days (mean differences −11 days at 3 months and −10 days at 12 months) and better scores on the RDQ (mean differences at 3 and 12 months −1.71 and −1.4, respectively) compared with usual care, effects were smaller and not as well sustained. For all outcomes, the addition of exercise to Alexander method had little impact compared with Alexander method sessions alone for all outcomes. For example, the reduction in low back pain days was similar (20 days) following 24 sessions with or without exercise, as were mean effects on the RDQ. Six sessions of Alexander plus exercise were almost as beneficial as 24 sessions without exercise with respect to effects on the number of low back pain days and function.

Two trials[196, 232] included in another systematic review186 found MCE associated with lower pain scores in the short term (WMD, −12.48 on a 0 to 100 scale, 95% CI −19.04 to −5.93), intermediate term (WMD, −10.18, 95% CI −16.64 to −3.72), and at long term (WMD, −13.32 95% CI −19.75 to −6.90) versus a minimal intervention. Each trial favored MCE at all time points. MCE was also associated with lower disability at short term (3 trials, WMD −9.00 on 0 to 100 scale, 95% CI −15.28 to −2.73).196, 232, 233 Effects on disability were somewhat smaller at intermediate term (WMD −5.62, 95% CI−10.46 to −0.77) and long term (WMD, −6.64, 95% CI −11.72 to −1.57),based on two trials.[196, 232] Across trials, estimates consistently favored MCE.

A poor-quality trial (n=240) not included in the systematic reviews found different intensities of periodized musculoskeletal rehabilitation (PMR) training (2, 3, and 4 days per week for 12 weeks) for chronic low back pain associated with lower pain intensity at 13 weeks versus no training (mean differences ranged from −0.74 for twice per week to −1.35 for four times per week on 0-10 scale) and better function based on the ODI (mean differences ranged from −7.3 for twice per week to −12 for four times per week, 0 to 100 scale).[251] It also found training associated with better (higher) SF-36 PCS scores (mean differences ranged from 5.2 for twice per week to 10.7 for four times per week, 0 to 100 scale) and MCS scores (mean differences ranged from 7.1 for twice per week to 11.7 for four times per week, 0 to 100 scale) at 13 weeks versus no training.

We also identified two additional trials (n=100 and 105) of exercise for subacute to chronic low back pain (mean duration of symptoms not reported).[250, 256] One good-quality trial found no differences between 10 weeks of supervised general exercise including back and abdomen muscle stabilization) versus avoidance of hard physical activity, at the end of treatment or at 12 months (mean differences 0.07, 95% CI −0.9 to 0.70 and 0.3, 95% CI −1.3 to 0.6 on a 0 to10 scale, respectively).[250] There were also no differences on the RDQ (mean differences 0.6, 95% CI −2.2 to 1.0 and 1.2, 95% CI −3.3 to 1.0, respectively) or on the EQ5D. A poor-quality trial (n=105) found no differences between exercise versus usual care on the ODI at the end of 12 weeks of treatment (mean difference −1.9 on 0 to 100-point scale) and at 1 year (mean difference −1.8) among patients who had undergone functional multidisciplinary rehabilitation.[256]

A systematic review of exercise therapy for nonacute low back pain versus usual care that specifically evaluated the outcome work disability found no effects at short-term (~4 weeks) or

intermediate-term (~6 months) followup, based on pooled analyses of high-quality studies (6 comparisons in 5 trials, OR 0.80, 95% CI 0.51 to 1.25 and 5 comparisons in 4 trials, OR 0.78, 95% CI 0.45 to 1.34, respectively).188 However, exercise, was associated with lower likelihood of work disability at long-term (~12 months) followup (10 comparisons in 8 trials, OR 0.66, 95% CI 0.48 to 0.92).

An additional 16 trials with fewer than 100 participants compared exercise versus no exercise or usual care for chronic low back pain.[197, 200, 257-267, 270-272] For pain, 11 trials reported differences favoring exercise;[257, 258, 260, 261, 263, 264, 266, 267, 270-272] the other five found no differences among groups.[197, 200, 259, 262, 265] Of the 12 trials that reported on function, results favored exercise in nine[258, 260, 261, 263-265, 270-272] and three found no differences.[197, 200, 262] Quality of life was reported by five trials, three of which favored exercise[260-262] and two of which found no difference among groups.[197, 200] Global improvement was reported by two studies, with results favoring exercise in one trial[264] but not the other.[197]

Exercise Therapy Versus Advice

Subacute to Chronic Low Back Pain

Two trials not included in the systematic reviews evaluated exercise therapy versus advice for subacute to chronic low back pain.[245, 268] One fair-quality trial (n=136) found no differences between 8 weeks of supervised Nordic walking or unsupervised Nordic walking versus advice to remain active at the end of treatment for pain (mean improvement 8.8, 3.4, 4.8 respectively on the 0-30 Low back pain rating scale [LBRS]) or on the functional portion of the LBRS (mean improvement 7.4, 3.2, 3.8 respectively on a 0 to 30 scale) or Patient-Specific Functional Scale (PSFS) though effects were largest with supervised Nordic walking.[245] No differences between treatments were seen on the EQ-5D. One very small trial (n=21) found 4 weeks of supervised stabilization exercise associated with greater pain reduction versus advice, but there was no difference on the ODI.[268]

Exercise Therapy Versus Education or Back School

Chronic Low Back Pain

The systematic review[187] included three trials of exercise (yoga, Pilates and MCE) versus education or back school.[190, 196, 213] One small trial (n=53) found no differences between 10- to 60-minute sessions of Pilates versus back school in post intervention pain (mean difference 0.2 on a 0 to10 scale) or function (mean difference 0.8 the ODI).190 The trials of yoga[213] and MCE[196] are discussed in those sections of this report.

One subsequent good-quality trial (n=148) of weekly McKenzie exercises versus back school found no differences in mean pain intensity scores at the end of four weeks of treatment or at three or six months (mean differences -0.48 to -0.71 on a 0 to 10 scale).[242] Exercise was associated with better function at the end of therapy (mean difference -2.37, 95% CI -3.99 to -0.76) but effects were smaller and no longer statistically significant at longer followup. Exercise was also associated with a greater likelihood of experiencing a ≥5 point improvement on the RDQ (53% vs. 30%, RR 1.8, 95% CI 1.2 to 2.7).

One other small trial (n=61) reported no differences between exercise therapy versus a single education session or between exercise versus conventional physical therapy in pain of function for subacute to chronic low back pain at 6 or 12 months.[269]

Radicular Low Back Pain

Three trials (n=181 to 348) predominantly enrolled patients with radiculopathy (70 to 100% of sample); the duration of symptoms varied from acute to chronic.[239, 240, 248] None were included in the systematic reviews.

For subacute low back pain with radiculopathy, one fair-quality trial compared 8 weeks of symptom guided, back-related exercise versus sham (nonback related) exercise; >50 percent of the sample had lower extremity motor deficits.[240] Pain scores at the end of the 8-week intervention favored exercise (mean difference −0.8, 95% CI −1.2 to −0.09, on a 0-10 scale) but effects were small. There were no differences on the RDQ or measures of health-related quality of life. Exercise was associated with greater likelihood of patients reporting being "much better" at the end of treatment (8 weeks) versus sham exercises (80% vs. 60%, RR 1.3, 95% CI 1.1 to 1.6) but effects were smaller and not statistically significant at 12 months (84% versus 76%, RR 1.1, 95% CI 1.0 to 1.3). Patient satisfaction was similar at 12 months (93.5% vs. 90.5%).240

In one fair-quality trial, the difference in median pain scores at 6 months for education plus four physical therapy sessions was 3.0 (on 0-10 scale) compared with usual care and 1.0 compared with education alone, both favoring exercise, but tests for statistical significance were not performed.[239] Education plus physical therapy was also associated with better function versus usual care (mean difference in improvement on the RDQ 2.3, 95% CI 1.7 to 2.9) but not versus education alone (mean difference in improvement 0.4, 95% CI −0.26 to 1.06).

A poor-quality trial found no statistically significant differences between a maximum of 8 weeks of physical therapy, bed rest or continuation of usual activities in pain or disability at up to 6 months in patients with acute sciatica, though effects favored physical therapy.[248] Mean differences between physical therapy and control groups at 6 months ranged from −1.4 to −1.0 on a 0-10 scale for pain and for the Quebec Disability Scale from −0.7 to −2.7 on a 0-100 scale. Most patients (70%) had a prior history of low back pain or sciatica.

Exercise Versus Other Active Interventions

Results for comparisons involving exercise versus other active interventions are summarized in the results sections for nonexercise interventions.

Exercise Versus Exercise

Acute and Subacute Low Back Pain

The APS/ACP review included a higher-quality systematic review[183] with one higher-quality trial that found marginal differences between the McKenzie method versus flexion exercises (mean differences, 2 points on a 0 to 100 scale) for acute pain, though a second, lower-quality trial found the McKenzie method associated with large benefits on short-term (5 days) disability (mean difference, −22 points on a 0 to 100 scale, 95% CI −26 to −18).

Two subsequent poor-quality trials which primarily enrolled patients with subacute low back pain found no differences among different types of exercise.[243, 246] One trial compared physical therapy based on a TBC plus graded exposure, TBC plus graded activity, and TBC only[243] and one trial compared lumbar extensor strength training versus "regular" physical therapy.[246] A small (n=33) trial of patients with acute low back pain found no differences between regular trunk exercises versus trunk exercises plus specific core stability core exercises through 3 months.[274]

Chronic Low Back Pain

The APS/ACP review[29] found few trials that directly compared different types of exercise for chronic low back pain, with no clear differences. The APS/ACP review also included a meta-regression that was conducted in conjunction with a higher-quality systematic review.[283] Exercise therapy factors associated with greater effects on pain in the meta-analysis were use of individually designed programs (5.4-point improvement in pain scores, 95% credible interval 1.3 to 9.5), supervised home exercise (6.1 points, 95% CI −0.2 to 12.4), group exercise (4.8 points, 95% CI 0.2 to 9.4), and individually supervised programs (5.9 points, 95% credible interval 2.1 to 9.8). High-dose exercise programs (20 or more hours of intervention time) were not superior to low-dose programs. Interventions that included additional noninvasive therapy were superior (5.1 points, 95% CI 1.8 to 8.4) to those without additional noninvasive therapy. The exercise regimens that were most effective used stretching and strengthening, though there was some overlap with other types of exercise (aerobic, mobilizing, or other specific exercise methods). The meta-regression estimated that an intervention incorporating all of the features of an effective exercise regimen would improve pain scores by 18.1 points (95% CI 11.1 to 25.0) compared with no treatment, and improve function by 5.5 points (95% CI 0.5 to 10.5) compared with no treatment. However, trials to directly confirm the incremental benefits of exercise therapies utilizing these factors are not available.

A more recent systematic review[186] found MCE associated with lower pain intensity at short term (6 trials, WMD −7.80 on 0 to 100 scale, 95% CI −10.95 to −4.65)[192, 226-229, 231] and at intermediate term (3 trials, WMD −6.06, 95% CI −10.94 to −1.18)[192, 227, 230] versus general exercise, but effects were smaller and no longer statistically significant at long term (4 trials, WMD −3.10, 95% CI −7.03 to 0.83).[192, 227, 228, 230] Individual trial estimates at all time points generally favored MCE, though most differences did not reach statistical significance. MCE was also associated with better function in the short term (6 trials, WMD−4.65 on 0 to 100 scale, 95% CI−6.20 to −3.11)[192, 226-229, 231] intermediate term (3 trials, WMD −4.86 95% CI−8.59 to −1.13)192, 227, 230 and long term (3 trials, WMD −4.72, 95% CI −8.81 to −0.63).[192, 227, 230] Individual trial estimates generally favored MCE at all time points, with one trial reporting a statistically significant effect.[227]

A subsequent trial (n=172) found no differences between MCE versus graded activity in pain at 2 (mean difference 0.0 on 0 to 10 scale, 95% CI –0.7 to 0.8), 6 (mean difference 0.0 (95% CI –0.8 to 0.8), or 12 months (mean difference 0.1 (95% CI–0.7 to 0.9).253 MCE was associated with better function at 2 (mean difference –0.8 on 0 to 24 RDQ, 95% CI −2.2 to 0.7), 6 (mean difference –0.8, 95% CI –2.3 to 0.6), and 12 months (mean difference –0.6, 95% CI –2.0 to 0.9), though differences were not statistically significant; there were no differences in Global Perceived Effect Scale scores or SF-36 mental or physical component summary scores.[253]

Another systematic review[187] included 11 trials of other exercise therapy comparisons[191, 192, 197, 199, 201, 202, 205-207, 211, 215] Results could not be pooled because of differences in the exercise regimens and comparisons evaluated. Only two trials reported statistically significant differences among groups. One low risk of bias trial (n=240) found 12 weeks of motor control exercise associated with better function and global perceived effect at 8 weeks (mean adjusted between-group difference 2.9 and 1.7, respectively) versus general exercise, but there were no differences by 6 months.[192] One high risk of bias trial (n=72) found 3 months of aerobic exercise associated with greater pain relief versus lumbar flexion exercise at the end of treatment.[211]

Two subsequent trials that compared various forms of exercise in patients with chronic low back pain found no differences in pain relief.[241, 249] One good-quality trial (n=201) compared supervised exercise focused on core strengthening versus home exercise[241] and the other compared exercise therapy, a walking program or usual physical therapy.[249]

One poor-quality trial (n=180 for exercise groups) that evaluated different intensities of exercise found the greatest intensity of PMR training (4 days per week, 1563 repetitions) associated with greater pain relief (mean difference −0.61 95% CI −0.97 to −0.25, 0-10 scale), reduced disabilities (mean difference −4.7 on the ODI, 95% CI −7.5 to −1.9), and improved quality of life based on SF-36 PCS (mean difference 5.5, 95% CI 2.5 to 8.5, 0 to 100 scale), and MCS (mean difference 4.6, 95% CI 1.6 to 7.6 on 0-100 scale) compared with the least intense regimen (2 days per week, 564 repetitions).[251]

Fourteen smaller trials (n<100) also compared different forms of exercise for chronic low back pain. In four trials, results for pain favored global postural reeducation versus stabilization exercises; exercise and stabilization training versus routine exercises; periodized resistance training versus periodized aerobic exercise, or the addition of static or dynamic back endurance exercise to the McKenzie method versus the McKenzie method alone.[261, 275, 280, 281] Seven other trials found no clear differences among different types of exercises in outcomes related to pain.[200, 258, 271, 273, 277-279, 282] Similar results were reported for other outcomes, with most trials reporting no clear differences.

Radicular Low Back Pain

One small (n=68) trial[284] of patients with spinal stenosis found no clear difference between the addition of unweighted treadmill walking versus stationary cycling to an exercise program in short-term outcomes.

Harms

Harms were poorly reported in trials of exercise.[29, 186, 187] When reported, harms were typically related to muscle soreness and increased pain,[232, 241, 246, 249, 255, 285] or no harms were reported.[192, 230, 236, 239, 243, 250, 252] Serious harms were not reported in patients who underwent exercise therapy.[248, 253]

Exercise and Related Interventions: Pilates

Key Points

- For chronic low back pain, a systematic review included seven trials that found Pilates associated with small (mean difference −1.6 to −4.1 points) or no clear effects on pain at the end of treatment versus usual care plus physical activity and no clear effects on function (SOE: low for pain and function).
- For chronic low back pain, three trials found no clear differences between Pilates versus other types of exercises in pain or function (SOE: low for pain and function).

Detailed Synthesis

The previous APS/ACP review did not specifically evaluate Pilates. A systematic review on exercise therapies included in the APS/ACP review did not include any studies of Pilates.

A fair-quality systematic review published subsequent to the APS/ACP review[28]6 included seven trials of Pilates versus usual care (sample size range17 to 86, total n=301)[195, 287-292] and four trials of Pilates versus other exercise techniques (sample size range 12 to 83, total n=199) (Table 10; Appendix Tables E15; F15).[293-296] The trials exclusively or primarily (~75%)[292, 293] enrolled patients with chronic low back pain. Pilates interventions varied but generally included one or three supervised mat small group classes per week plus home sessions; some included specific Pilates equipment. Usual care was generally less well described, but typically involved no specific treatment apart from medications and no restriction from regular physical activity. One study allowed both groups to continue physical therapy and regular exercise[289] and another provided an educational booklet on low back pain.[290] Exercise techniques in trials of Pilates versus other exercise methods included supervised stationary cycling, traditional lumbar stabilization exercises, McKenzie exercises and a generalized exercise regimen that included aerobics, stretching and strengthening. The duration of interventions in the trials ranged from four to 12 weeks. Three trials followed participants 16 to 18 weeks beyond the end of the active intervention. Most trials were conducted in Brazil, Australia and the United Kingdom and three trials were published as dissertations.[289, 293, 297] Based on the 16-item McMaster Critical Review Form for Quantitative Studies, review authors classified four trials excellent (15 or 16 out of 16 points),[289, 290, 294, 296] four very good (13-14 points),[195, 287, 291, 292] one fair (9-10 points)[293] and four poor (0-8 points).[288, 295-298] Methodological shortcomings included inability to blind patients (most trials blinded outcomes assessors) and high attrition in trials with longer followup.[294, 296]

Pilates Versus Usual Care and Physical Activity

Chronic Low Back Pain

Seven trials[195, 287-292] included in the systematic review evaluated the effects of Pilates on pain.[286] Results across trials were somewhat inconsistent. Although four trials (sample sizes 22 to 86) found Pilates associated with lower pain scores versus usual care plus physical activity at the end of treatment (mean differences −1.6 to −4.1 points on a 0- to 10-point scale), three trials found no significant effects (mean differences −0.2 to −1.9 points). One trial (n=86) found smaller effects 18 weeks after the end of therapy (mean difference −0.9, 95% CI −1.9 to 0.1) that

were no longer statistically significant, compared with the effects at the end of therapy (mean difference −2.2, 95% CI −2.2, 95% CI −3.2 to −1.1).290 The largest effect (−4.1, 95% CI −6.3 to −1.8 on 0−10 scale) was observed in the trial with the highest total class hours (2 hours per week for 15 weeks, n=22).[287] Total hours in the other trials ranged from 12 to 24 hours of class and/or home exercise; there was no clear relationship between the intensity of treatment and estimates of effect. Trial data were not pooled.

Seven trials[195, 289-292, 297, 298] included in the systematic review evaluated effects of Pilates on function.[286] Most trials showed no clear beneficial effects. Two trials found no differences between Pilates versus usual care on the ODI at the end of a 6-195 or 12-week course of therapy[297] (mean difference 0.0 on a 0 to 10 scale, 95% CI −8.5 to 8.5 in one trial and −7.1, 95% CI −17.6 to 3.4 in the other trial). Five trials measured disability with the RDQ. The largest, fair-quality trial (n=86) found Pilates associated with lower (better) RDQ scores at the end of a 6-week intervention of twice weekly 60-minute Pilates sessions (mean difference −2.7, 95% CI −4.4 to −1.0), but effects were smaller and no longer statistically significant at 24 weeks (mean difference,−1.4, 95% CI −3.1 to 0.0 at 24 weeks, 0 to 24 scale).[290] Four smaller trials (n=20 to 39) reported inconsistent effects of Pilates at the end of 4 to 12 weeks of treatment, with two trials finding Pilates associated with better RDQ scores (mean differences −1.2, 95% CI −1.4 to −1.0[292] and −2.6, 95% CI −5.2 to −0.1289) and two trials finding nonstatistically significant differences in favor of Pilates (mean differences −2.1 p>0.21, no CI reported.[283] and −1.7 (95% CI −0.4 to 3.8).[298]

Pilates Versus Other Exercise

Chronic Low Back Pain

There were no differences between Pilates versus traditional lumbar stabilization exercises (1 trial, n=12),[293] Pilates versus McKenzie and daily postural correction exercises (1 trial, n=40[295]), or Pilates versus general exercise (including aerobics, stretching, and strengthening) (1 trial, n=83[296]) in pain or function at the end of a 4- to 7-week course of treatment. One trial (n=64) found 8 weeks of Pilates (50- to 60-minute sessions 3 times a week) associated with lower pain (mean difference −1.1, 95% CI −2.1 to −0.1) and better ODI scores (difference in means −6.5%, 95% CI −11.8 to −1.1) at the end of treatment, but effects were smaller and no longer statistically significant at 24-week followup.[294] Attrition was high in this trial and greater in patients randomized to cycling.

Exercise and Related Interventions: Tai Chi

Key Points

- For chronic low back pain, two trials found tai chi associated with improved pain-related outcomes versus wait list or no tai chi (mean differences 0.9 and 1.3 on a 0 to 10 scale); one trial also found tai chi associated with better function (mean difference 2.6 on the RDQ, 95% CI 1.1 to 3.7) (SOE: low for pain and function).

- For chronic low back pain, one trial found tai chi associated with lower pain intensity versus backward walking or jogging through 6 months (mean differences −0.7 and −0.8), but there were no differences versus swimming (SOE: low).
- • One trial of tai chi reported a small temporary increase in back pain symptoms and one trial reported no harms (SOE: low).

Detailed Synthesis

Tai chi was not specifically evaluated in the APS/ACP review. We identified two trials of tai chi versus no treatment for chronic low back pain with no treatment (2 RCT, n=480) (Table 12; Appendix Tables E16, F16;[285, 299] one of the trials also evaluated tai chi versus other exercise interventions including backward walking, jogging and swimming.[299] Tai chi sessions were eighteen 40-minute sessions over 10 weeks in one trial[285] and 45-minute sessions 5 days a week for 6 months in the other.[299] Both trials were rated fair quality. One trial did not adequately report allocation concealment and attrition[299] and adherence was unclear in both trials. The nature of the intervention precluded blinding of participants and people administering the interventions, but both trials reported blinding of outcomes assessors.

Tai Chi Versus Wait List or No Exercise

Chronic Low Back Pain

Both trials found tai chi for chronic low back pain associated with improved pain-related outcomes versus wait list or no tai chi.[285, 299] One trial (n=160) found 10 weeks of tai chi associated with lower pain intensity versus wait list (mean difference 1.3 on a 0 to 10 scale, 95% CI 07 to 1.9) and better function (mean difference 2.6 on the RDQ, 95% CI 1.1 to 3.7); the proportion of patients who experienced ≥30 percent improvement in pain intensity was 46 percent vs. 15 percent and the proportion who experienced ≥30 percent improvement in RDQ was 50 versus 24 percent.[285] Similar results were seen for pain bothersomeness (mean difference 1.7, 95% CI 0.9 to 2.5; proportion with ≥30% improvement 50% vs. 18%).[285] The other trial (n=188 for this comparison) found tai chi associated with lower pain intensity at 26 weeks versus no exercise (mean scores 2.7 vs. 3.6 on a 0 to 10 scale).[299]

Tai Chi Versus Other Exercise Interventions

Chronic Low Back Pain

One trial (n=273 for this comparison) found Tai chi associated with lower pain intensity versus backward walking or jogging at 3 months (mean differences −0.6 and −0.7 on a 0 to 10 scale, respectively) and 6 months (mean differences −0.7 and −0.8), but there were no differences versus swimming (mean differences −0.1 at both time points).[299]

Harms

One trial reported a small increase in back pain symptoms that resolved by 3-4 weeks in three patients who underwent tai chi,[285] the other trial reported no harms.[299]

Exercise and Related Interventions: Yoga

Key Points

- For chronic low back pain, one trial found Iyengar yoga associated with lower pain scores (24 vs. 37 on a 0-100 VAS, p<0.001) and better function (18 vs. 21 on the 0 to 100 ODI, p<0.01, on a 0 to 100 scale) versus usual care at 24 weeks (SOE: low for pain and function).
- For chronic low back pain, a systematic review found yoga associated with lower pain intensity and better function versus exercise in most trials, though effects were small and differences were not always snot statistically significant (5 trials) (SOE: low for pain and function).
- For chronic low back pain, yoga was associated with lower short-term pain intensity versus education (5 trials, SMD −0.45,- 95% CI −0.63 to −0.26; I2=0%), but effects were smaller and not statistically significant at longer-term followup (4 trials, SMD −0.28, 95% CI−0.58 to −0.02, I2=47%); yoga was also associated with better function at short-term (5 trials, SMD 0.45, 95% CI −0.65 to −0.25; I2=8%) and long-term followup (4 trials, SMD 0.39, 95% CI −0.66 to −0.11; I2=40%) (SOE: moderate for pain and function).
- Reporting of harms was suboptimal, but adverse events when reported were almost all classified as mild to moderate (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included three trials (n=22 to 101) of yoga for chronic low back pain.[194, 207, 213] One trial evaluated Viniyoga[194] and two trials Iyengar yoga;[207, 213] comparator interventions were exercise or self-care. The APS/ACP review concluded that there was fair evidence that Viniyoga is moderately effective for chronic low back pain, with insufficient evidence to judge the effectiveness of other yoga styles, or the effectiveness of yoga for acute low back pain.

A good-quality systematic review[300] published subsequent to the APS/ACP review included 10 trials,[194, 207, 210, 213, 301-306] including the 3 trials described above (Table 10; Appendix Tables E17, F17). All trials enrolled patients with chronic (>3-month duration) low back pain, except for one small trial (n=12) which enrolled patients with back pain for >3 weeks. Sample sizes ranged from 12 to 313 (total sample=1,056). All yoga interventions included specific asanas (poses), pranayama (breathing), and relaxation, and many included meditation or mental focus practices. The most common specific yoga styles evaluated were Iyengar (5 trials) and Viniyoga (2 trials). Most trials evaluated yoga classes lasting 75 minutes once weekly with recommended home practice for 30 minutes 5 to 7 days per week, though one trial[210] evaluated all-day sessions over a 1-week period. Trials generally reported starting out with simple or restorative yoga poses and progressing to more challenging poses. The duration of active intervention ranged from 1 to 24 weeks. Outcomes were assessed at the end of therapy in all trials; five trials also assessed outcomes 14 to 52 weeks after the end of therapy. Yoga was compared versus usual care (2 trials), education (7 trials), and supervised exercise therapy (3 trials). Exercise therapy interventions varied, but included stretching, strengthening, and aerobic exercise. Two trials were conducted in

India,[210, 302] one in the United Kingdom,301 and the remainder in the United States. Two trials[213, 302] were rated high risk of bias (based on meeting fewer than 6 of 10 Cochrane Back Review Group criteria) and the remainder were rated low risk of bias; methodological shortcomings included inadequate reporting of randomization and allocation concealment methods and high attrition. Blinding of patients and caregivers was generally not possible, though 8 of the 10 trials reported blinding of outcome assessors.

We identified two additional trials[307, 308] not included in the systematic review of yoga for chronic low back pain (Table 13; Appendix Tables E18; F18).[307, 308] One Indian trial (n=60) compared a 60-minute class of Iyengar Yoga per week for 4 weeks (plus home practice) versus exercises (primarily strengthening exercises)[307] and a US trial (n=95) compared once versus twice weekly 75-minute hatha yoga classes over 12 weeks.[308] Both trials were rated fair quality; methodological shortcomings included unclear allocation concealment methods and unblinded design.

Yoga Versus Usual Care

Chronic Low Back Pain

Two trials evaluated yoga for 6 or 12 weeks versus usual care.[194, 306] One trial (n=90) found Iyengar yoga associated with lower pain scores (mean 24 vs. 37 on a 0-100 VAS, p<0.001), better function (mean 18 vs. 21 on the 0 to 100 ODI, p<0.01, on a 0 to 100 scale), and better Beck Depression Inventory score (mean 5 vs.8 on 0 to 63 scale, p<0.01) at 24 weeks.[306] Another trial (n=22) found yoga associated with trends towards favorable effects on the ODI and Beck Depression Inventory, but was underpowered and reported large baseline differences among groups, precluding reliable conclusions.[194]

Yoga Versus Exercise

Chronic Low Back Pain

Effects of yoga versus exercise on pain were reported in four trials, with somewhat inconsistent results.[207, 304, 307, 309] The two most well-conducted trials evaluated a 12-week course of yoga. One trial (n=101) found yoga associated with lower pain scores at 26 weeks (mean difference between groups −1.4 on an 0 to 10 scale, 95% CI −2.5, −0.2),[207] but a larger trial (n=228) found small and nonstatistically significant differences between 12 weeks of yoga versus exercise in pain scores at 6, 12, or 26 weeks and in the likelihood of experiencing a 30 or 50 percent improvement in pain.[304] Another (n=80) trial found a weeklong intensive in-residence yoga program associated with lower pain scores than exercise at 1 week (3.40 vs. 4.85 on 0 to 10 scale, p<0.001).[309] Another small (n=60) trial found 4 weeks of yoga associated with lower pain score versus exercise at 6 months (mean 1.8 vs. 3.8 on a 0 to 10 VAS, p=0.001).[307]

Effects of yoga versus exercise on back-specific disability were reported in three trials, with somewhat inconsistent effects.[207, 210, 304] A large (n=228), well-conducted trial found no differences between 12 weeks of yoga versus exercise in the mean RDQ score or in the likelihood of 30 or 50 percent improvement at 6, 12, or 26 weeks,304 but another well-conducted trial (n=101) found 12 weeks of yoga associated with a better (lower) RDQ score versus exercise at 12 weeks

(adjusted mean difference −1.8 on a 0 to 24 scale, 95% CI −3.5 to −0.10), though differences were not statistically significant at 6 or 26 weeks.207 One trial (n=80) found an intensive, weeklong yoga program associated with a lower (better) ODI score versus exercise at 1 week (mean 18.70 versus 35.75 on a 0 to 100 scale, p<0.01).[210]

One trial (n=101) found no difference between yoga versus exercise in health-related quality of life as measured by the SF-36 MCS or PCS.[207] Two smaller trials found yoga associated with better health-related quality of life based on other measures of health-related qualify of life (WHO-QOL-BREF or the CDC-HRQOL-4 questionnaire).[307, 310] One trial found no statistically significant differences between yoga versus exercise in the likelihood of global improvement or patient satisfaction at 6, 12, or 26 weeks, though results favored yoga, particularly at 12 weeks (RR 1.3, 95% CI 0.97 to 1.75).[304] One trial (n=80) found that compared with exercise, an intensive, weeklong yoga program associated with greater improvement in the Beck Depression index (BDI) and measures of anxiety at 1 week (p≤0.001).[309]

Yoga Versus Education

Yoga was associated with better short-term (up to 12 weeks) mean pain scores versus education (5 trials, SMD −0.45, 95% CI −0.63 to −0.26; I2=0%) but effects were smaller and not statistically significant at longer-term (~1 year) followup (4 trials, SMD −0.28, 95% CI −0.58 to −0.02; I2=47%).[300] In the trials, differences in mean pain scores ranged from 0.37 to 2.4 on a 0 to 10 scale at 26 to 28 weeks. One of the trials included in the review (n=228) also found yoga associated with a greater likelihood of experiencing >30 percent improvement in pain at 26 weeks (RR 1.80, 95% CI 1.12 to 2.84); results also favored yoga for likelihood of >50 percent improvement, but the difference was just below the threshold for statistical significance (RR 2.13, 95% CI 0.96 to 4.73).[304] Another small (n=30) trial also found yoga associated with a greater likelihood of experiencing clinically meaningful (≥ 2 points) pain relief, but the estimate was imprecise (OR 5.0, 95% CI 1.13 to 19.1).[303]

Yoga was associated with better back-specific disability versus education at short-term (5 trials, SMD 0.45, 95% CI −0.65 to −0.25; I2=8%) and long-term followup (4 trials, SMD 0.39, 95% CI −0.66 to −0.11; I2=40%).[300] In the three largest trials, mean differences on the RDQ at 26 weeks ranged from 0.37 to 3.6 on a 0 to 24 scale, favoring yoga.[207, 304, 305] The largest (n=313), fair-quality trial reported found 12 weeks of yoga associated with lower (better) RDQ scores through 12 months (mean difference −1.57, 95% CI −2.71 to −0.42).[305] One trial (n=228) included in the review also found yoga associated with greater likelihood of experiencing 50 percent improvement in RDQ at 26 weeks (RR, 1.90, 95% CI 1.21 to 2.99).[304] A smaller trial (n=30) also found yoga associated with greater likelihood of experiencing a ≥30 percent improvement in the RDQ, but the difference was not statistically significant (67% vs. 40%, OR 1.7, 95% CI 0.8 to 3.4).[303]

Yoga was also associated with better SF-12 or SF-36 scores versus education at short-term (up to 12 weeks) followup (3 trials, SMD 0.25, 95% CI 0.02 to 0.47; I2=0%), but the difference was slightly smaller and not statistically significant at longer-term followup (2 trials, SMD 0.18, 95% CI−0.05 to 0.41; I2=0%).[300] In the largest trial (n=313), mean differences on the SF-12 Physical Component and Mental Component Summary Scores were small (0.42 to 2.02) and not statistically significant at any time point. [305]

Yoga was associated with greater likelihood of global improvement at 12 weeks in two trials (RR 3.27, 95% CI 1.89 to 5.66; I2=0%).300 In the larger trial (n=228), a similar effect was also present at 26 weeks (RR 2.57. 95% CI 1.39 to 4.78).[304] It also found yoga associated with greater likelihood of satisfaction with care through12 weeks (RR 3.95, 95% CI 1.90 to 8.21).

Once Versus Twice Weekly Yoga Classes

One fair-quality trial (n=95) compared once versus twice weekly 75-minute Hatha yoga classes for 12 weeks.[308] There were no statistically significant differences in measures of pain, the RDQ, or the SF-36.

Harms

The systematic review reported adverse events from three trials.[300] Reporting of adverse events was suboptimal, though adverse events were almost all classified as mild to moderate, with no clear difference in risk of serious adverse events. One trial published subsequent to the systematic review reported no adverse events[307] and one trial of once versus twice weekly yoga classes reported no differences in risk of any adverse event, which were primarily musculoskeletal.[308]

Psychological Therapies

Key Points

- For chronic low back pain, a systematic review found progressive relaxation superior to wait list control for post-treatment pain intensity (3 trials, mean difference −19.77 on 0 to 100 VAS, 95% CI -34 to −5.20, I2=57%) and functional status (3 trials, standardized mean difference −0.88, 95% CI −1.36 to −0.39, I2=0%) (SOE: low for pain and function).
- For chronic low back pain, a systematic review found electromyography (EMG) biofeedback associated with lower pain intensity at the end of treatment (3 trials, SMD −0.80, 95% CI −1.32 to −0.28, I2=0%), with no clear effect on function (3 trials) (SOE: low for pain and function).
- For chronic low back pain, a systematic review found operant therapy associated with lower pain intensity at the end of treatment (3 trials, standardized mean difference −0.43, 95% CI −0.75 to −0.1, I2=0%), with no clear effect on function (2 trials) (SOE: low for pain and function).
- For chronic low back pain, there was insufficient evidence from two trials to determine effects of cognitive therapy versus wait list control, due to inconsistency and imprecision (SOE: insufficient).
- For chronic low back pain, a systematic review found cognitive-behavioral and other combined psychological therapy associated with greater improvements in post-treatment pain intensity compared with wait list control (5 trials, SMD −0.60, 95% CI −0.97 to −0.22, I2=40%), but effects on function were smaller and not statistically significant (4 trials, SMD −0.37, 95% CI −0.87 to 0.13, I2=50%) (SOE: low for pain and function).

- For chronic low back pain, a systematic review found no clear differences between psychological therapies versus exercise therapy in pain intensity (2 trials) or between psychological therapies plus physiotherapy versus physiotherapy alone (6 trials) in pain or function, though one small subsequent trial found combination therapy associated with greater improvements in pain and function immediately after treatment (SOE: low for pain and function).
- Ten trials found no clear differences between different psychological therapies in pain or function (SOE: moderate for pain and function).
- Harms were not well-reported, but no trial included reported any adverse events associated with psychological therapies (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included two high-quality systematic reviews on psychological therapies for chronic low back pain.[311, 312] One review included 22 trials (6 assessed as higher quality)[311] and the other included 21 trials (7 assessed as higher quality).[312] Together, the two reviews included a total of 35 unique studies. Based on the systematic reviews, the APS/ACP review concluded that there was good evidence that versus no psychological therapy or wait-list control, cognitive-behavioral therapy is associated with moderate benefits, good evidence that operant therapy is associated with no effect, fair evidence that progressive relaxation is associated with substantial net benefits, and insufficient evidence to determine effects of biofeedback. Neither systematic review found any differences between one type of behavioral intervention versus another.

An updated version of one of the reviews[312] included in the APS/ACP review has been published (Table 10; Appendix Tables E19, F19).[313] It included 28 trials relevant to this report (total n=3090, sample sizes ranged from 18 to 409). Compared with the previous version, the updated review included seven additional trials and excluded three previously included trials. The review focused on psychological therapies conducted in an office or group setting, broadly classified into respondent (10 trials), operant (7 trials), cognitive (4 trials), and cognitive-behavioral (7 trials) treatments as well as combinations thereof (8 trials).[313] Operant therapies refer to behavioral therapies that encourage healthy behaviors such as exercise and participation in usual activities, and that do not reinforce patient pain behaviors. Cognitive therapies help patients to identify and challenge maladaptive thoughts that contribute to disability and distress. Respondent therapy includes techniques such as relaxation or biofeedback, and is based on the premise that the physiological response to pain is linked to muscle tension in a negative feedback loop, and that this cycle can be interrupted by reducing muscle tension. Twelve trials compared psychological therapies versus wait list control, seven trials compared psychological therapies versus other interventions, and 10 trials compared one psychological therapy versus another. Several trials evaluated more than one type of psychological therapy. The duration and intensity of treatments were inconsistently described; when reported they varied from 35- to 120-minute sessions over 3 to 10 weeks; one trial evaluated daily 8-hour treatments over 5 weeks. Outcomes were assessed during or at the end of treatment in 25 trials and at 3 to 24 months after treatment in 21 trials.

Thirteen trials were classified as being at low risk of bias (based on meeting at least 6 of the 12 Cochrane Back Review Group criteria). Common methodological shortcomings included inadequate description of randomization and allocation concealment methods, high attrition, and dissimilar cointerventions among groups. The majority of trials used an unblinded design.[313]

We identified five additional trials of psychological therapies for chronic low back pain not included in the systematic review (Table 14; Appendix Tables E20; F20).[314-318] One trial evaluated psychological therapy versus wait list control[317] and three trials (across four publications) psychological therapies plus another noninvasive intervention versus the other intervention alone.[314-316, 318] All of the trials were rated fair quality. In general, neither patients nor care providers could be blinded, compliance to treatment was low or unreported, and some trials did not report allocation concealment methodology or use of intention-to-treat analysis.[315-318]

Respondent Therapy Versus Wait List Control

Chronic Low Back Pain

Two types of respondent therapy, progressive relaxation and biofeedback, were separately evaluated in the systematic review.

Three small trials (total n=74 patients) in the systematic review evaluated relaxation training versus placebo or wait list control for chronic low back pain.[313] All were rated high risk of bias. No information was provided regarding treatment duration except that one study offered eight 45-minute sessions.[319] Outcomes for pain and function favored treatment in all individual trials, as well as in pooled results. Progressive relaxation was superior to wait list control for post-treatment pain intensity (3 trials, mean difference −19.77 on 0 to 100 VAS, 95% CI −34 to −5.20, I2=57%) and functional status (3 trials, standardized mean difference −0.88, 95% CI −1.36 to −0.39, I2=0%).[319-321] For function, one trial reported a 0.5-point difference in favor of progressive relaxation on a 7-point function scale[319] and two trials reported a 4.8 to 11.1-point difference on the 100-point Sickness Impact Profile.[320, 321] Two small studies reported post-treatment depression using the 63-point Beck Depression Inventory. One study[320] (n=25) found a significant effect (14.3 points) in favor of relaxation therapy while the other trial (n=35) found no difference (1.0-point difference between groups),[321] with no difference when results were pooled (2 trials, mean difference −6.80 on 0 to 63 scale, 95% CI −20 to 6.12, I2=85%).[320, 321]

The systematic review included four trials (3 low risk of bias) of auditory and/or visual EMG biofeedback training (plus education and breathing exercises in one study) versus wait list or placebo controls for chronic low back pain.[313] The total sample was 108 patients. When described, session durations generally lasted 45 to 60 minutes and patients were offered 8 to 15 sessions over 3 to 4 weeks. EMG biofeedback was associated with lower pain intensity at the end of treatment (3 trials, SMD −0.80, 95% CI −1.32 to −0.28, I2=0%). Although results were not statistically significant in two of the three trials, they favored treatment in all three trials by 5 to 13 points on a 100-point pain scale.[319, 322, 323] A fourth trial could not be pooled, but reported no effect of biofeedback on pain.[324] There was no clear difference between biofeedback versus wait list control for function, with inconsistent results from three trials.[319, 322, 324]

Operant Therapy Versus Wait List Control

Four trials (three low risk of bias) in the systematic review compared operant therapy versus wait list control for chronic low back pain (total n=243).[313] Interventions varied, but typically included behavioral therapy plus exercise, often involving spousal participation. When reported, treatments lasted 5 to 8 weeks, with sessions lasting 2 to 8 hours per day. Operant therapy was associated with lower pain intensity at the end of treatment (3 trials, standardized mean difference −0.43, 95% CI −0.75 to −0.1, I2=0%).[212, 325, 326] Results favored operant therapy in all three trials (13 points on a 0 to 100 VAS scale in one trial[325] or 3.3 to 3.6 points on the 78-point McGill Pain Questionnaire in two trials,[212, 326] though the difference was statistically significant in only one[325] of the trials. There was no difference between operant therapy versus wait list control for function at the end of treatment as measured by the Sickness Impact Profile (2 trials, mean difference −1.18 on a 100-point scale, 95% CI −3.53, 1.18, I2=0%).[212, 326] Operant therapy also had no effect on depression, based on two trials.[212, 325]

Cognitive Therapy Versus Wait List Control

Two small trials (34 patients in each study) in the systematic review evaluated cognitive therapy versus wait list control for chronic low back pain.[313] In one trial, cognitive therapy consisted of graded exposure to fearful activities plus psychological education over 13 sessions in addition to usual care;[327] treatment details were not reported for the other trial.[321] There was no clear difference between cognitive therapy versus wait list control in pain, though there was inconsistency between trials. One trial reported an 11-point difference on a 100-point VAS and the other reported a 0-point difference.[321, 327] There was also no difference between cognitive therapy versus wait list control for function (one trial reported a 1.6-point difference in the 100-point Sickness Impact Profile and the other reported a 1.4-point difference in the Activities of Daily Living Scale). One other larger (n=156) fair-quality trial not included in the systematic review found cognitive therapy consisting of ten to fourteen 60-minute individual sessions over 18 weeks to associated with greater improvement in activity-specific pain versus wait list control (mean improvement from baseline −19.1 vs. −5.2 on the 0 to 100 Patient Specific Complaints outcome measure, p=0.018), and increased likelihood of experiencing an 18- to 24-point improvement at the end of treatment (49% vs. 26%, odds ratio 2.77, 95% CI 1.28 to 6.01).317 However, there was no effect on function as measured by the 100-point Quebec Back Pain Disability Scale (36.7 vs. 38.7).

Cognitive-Behavioral and Other Combined Psychological Therapies Versus Wait List Control

Five trials (total sample 239 patients) in the systematic review evaluated combined psychological therapies versus wait list control for chronic low back pain.[313] Three trials were assessed as being at low risk of bias. Combined psychological therapy interventions varied and included education, problem solving training, coping techniques, imagery, relaxation, goal setting, cognitive pain control, and exercises. Three of the trials described these interventions as being cognitive-behavioral in nature.[209, 320, 322] When reported, sessions lasted 1 to 2 hours, with 8 to 30 sessions given over 4 to 10 weeks.

Combined psychological therapy was associated with greater improvements in post-treatment pain intensity compared with wait list control (5 trials, SMD −0.60, 95% CI −0.97 to −0.22, I2=40%).[209, 320-322, 326] Effects were statistically significant in two[209, 320] trials and favored treatment in the other three. Specifically, two high risk of bias trials (n=22 and 39) reported a 3.8 to a 40.5-point difference between groups on a 100-point VAS pain scale;[320, 321] one low risk of bias trial (n=45) found a 6.2-point difference between treatment groups in the 78-point McGill Pain Questionnaire;[326] and two low risk of bias trials (n=28 and 105) reported a 7.2 to 14.8-point difference in pain outcomes (scale not reported).[209, 322] There was no difference between combined psychological therapy versus wait list control in function at the end of treatment (4 trials, SMD −0.37, 95% CI −0.87 to 0.13, I2=50%).[320-322, 326] Although one small (n=22) trial at high risk of bias found combined psychological therapy associated with better Sickness Impact Profile Score versus wait list control by about 10 points,[320] the remaining three trials (n=28 to 45) found no differences.[321, 322, 326] There was also no difference between combined psychological therapies versus wait list control on the Beck Depression Inventory (4 trials, SMD −1.92, 95% CI −6.2 to 2.3, I2=70%),[209, 320-322] with only one small (n=22) trial showing an effect that favored treatment.[320]

Psychological Therapy Versus Usual Care

Two high risk of bias trials in the systematic review compared behavioral therapy versus usual care.[313] One trial (n=100) compared 6 weeks of progressive muscle relaxation versus usual care (not otherwise described)[328] and the other (n=230) compared four sessions of cognitive therapy which addressed fears and encouraged exercise and activities versus usual care (pain medications, primary care visits, and other services such as physical therapy).[329] While behavioral therapy was associated with greater improvements in VAS pain scores versus usual care at the end of therapy (2 trials, mean difference −5.2 on a 0 to 100 scale, 95% CI −9.8 to −0.6, I2=20%), there was no difference at 6-month followup (2 trials, mean difference −4.3, 95% CI −9.3 to 0.7, I2=0%).[328, 329] There were no differences in functional status (based on the ODI or the RDQ) at the end of therapy or at 6-month followup in either trial or when results were pooled (2 trials, SMD −0.20 at end of treatment, 95% CI −0.4 to 0.02, I2=0% and SMD −0.12 at 6 months, 95% CI −0.3 to 0.1, I2=0%), though results slightly favored behavioral therapy.[328, 329]

Psychological Therapy Versus Other Noninvasive Treatments

Five trials included in the systematic review[209, 212, 330-332] evaluated psychological therapy versus other noninvasive treatments. The types of psychological therapies and comparator interventions varied across trials. Two trials (one low risk of bias) compared behavioral therapy versus group exercise.[313] One low risk of bias trial (n=107) compared cognitive behavioral therapy with strength and aerobic physical training; both interventions were given for 3 sessions per week for 10 weeks[209] and one smaller (n=39), high risk of bias trial compared operant conditioning (2 hours per week) versus group aerobic exercise (10 to 20 minutes per day, 5 days per week) for 8 weeks.[212] There were no differences in pain intensity as measured by the Pain Rating Index (0-45) at the end of treatment (2 trials, mean difference −2.31, 95% CI −6.3 to 1.7, I2=0%) or at 12 months (2 trials, N=136, mean difference 0.14, 95% CI −4.4 to 4.7, I2=0%). Similarly, there were no differences in depression at the end of therapy at any time point measured through 12 months in either study or when results were pooled.[209, 212]

One high risk of bias trial (n=114) in the systematic review found behavioral therapy (intensive group training via 30 sessions consisting of exercise therapy, back school, and behavioral principles) associated with significantly lower pain at 6 months versus guideline-based care (approximately 13 sessions, though the number varied), although these differences were no longer statistically significant at 12 months (data not reported).[332] There were no differences among groups in functional status at 6 or 12 months.

One small (n=36), high risk of bias trial included in the systematic review found no differences between ten 35-minute sessions of progressive relaxation or biofeedback training versus back education in pain (VAS and McGill Pain Questionnaire) at the end of treatment or at 3-month followup.[330]

One small (n=15), high risk of bias trial included in the systematic review found no differences between eight weekly 50-minute sessions of progressive relaxation versus self-hypnosis in VAS pain and depression at the end of therapy or at 3-month followup.[331]

Psychological Therapy Plus Another Intervention Versus the Other Intervention Alone

Nine trials evaluated the effects of adding psychological therapy to another noninvasive intervention, versus the other intervention alone. Five trials (n=20 to 116)[209, 212, 333-335] in the systematic review[313] compared psychological therapy plus physiotherapy or exercise therapy versus physiotherapy or exercise therapy alone. There were no differences in pain, function, or depression when measured at the end of treatment or through 4 to 6 months. Results were consistent across trials, including one low risk of bias trial.[209] The systematic review also found no differences between psychological therapy plus inpatient rehabilitation versus inpatient rehabilitation alone, based on one low risk of bias (n=30)[336] and two high risk of bias (n=45 and 409)[337, 338] trials.[313] One low risk of bias trial (n=234) in the systematic review found the additional of cognitive-behavioral therapy program to an educational intervention associated with a small, nonstatistically significant effect on pain and functional outcomes versus the educational intervention alone measured immediately after the treatment.[339]

Three fair-quality trials not included in the systematic review also evaluated the effects of combining psychological therapies with another noninvasive intervention.[314-316, 318] One trial (n=88) found the addition of motivational enhancement to physical therapy (ten 30-minute sessions over 8 weeks) associated with no significant differences in pain, function, or quality of life versus physical therapy alone at 1 month.[318] In contrast, another trial (n=54) reported the addition of cognitive behavioral therapy to physical-therapist guided exercise (three sessions per week over 12 weeks plus exercise at home twice a day five times per week) resulted in significantly better pain and RDQ scores post-treatment than physical-therapist guided exercise alone.[314] Another trial (n=701) found the addition of cognitive behavioral therapy to active management advisory consult (one 15-minute session in which advice was given to remain active and use pain medication) associated with greater improvement in pain scores, the RDQ, and EQ-5D through 12-month followup, though effects on pain at 34 months were smaller and no longer statistically significant at 34 months.[315, 316] Through 12 months, differences in pain scores were

about 5 to 8 points and differences on the RDQ 1.0 to 1.5 points (effect sustained through 34 months).

Comparisons of Different Psychological Therapies

Ten trials in the systematic review compared one psychological therapy versus another for chronic low back pain.[313] Sample sizes ranged from 16 to 90 patients. In general, trials found no differences among psychological therapies in pain or function; some trials also found no effect on measures of depression. However, methodological shortcomings in most trials (5 were rated low risk of bias), small numbers of trials for each comparison, and variability in the psychological therapy interventions evaluated within comparisons precluded strong conclusions. Four trials compared various combinations of psychological therapies (e.g., operant and respondent therapy, operant and cognitive with or without group education) versus operant therapy,[326, 334, 340, 341] four trials compared various combinations of psychological therapies versus respondent therapy,[320-322, 342] one trial compared different types of respondent therapy (EMG biofeedback vs. progressive relaxation),[330] two trials compared cognitive therapy versus operant therapy,[334, 343] one trial compared cognitive therapy versus respondent therapy (progressive muscle relaxation), and two trials compared combined psychological therapy versus cognitive therapy.[321, 334] Based on pooled estimates, there were no differences between combined psychological therapies and operant therapy in pain or function. There were also no differences between combined psychological therapies and respondent therapy for pain or function. Although respondent therapy was associated with better outcomes on the Beck Depression Inventory versus combined therapy at the end of treatment (3 trials, mean difference 2.89 on 0 to 63 scale, 95% CI 0.6 to 5.2, I2=0%),[320-322] the effect was smaller and no longer statistically significant at 6 months (2 trials, mean difference on 0-63 scale 1.84, 95% CI −0.4 to 4.1, I2=28%),[321, 322] with no differences at either time point in one low risk of bias trial.[322]

Harms

None of the trials included in the systematic review or subsequent trials reported any adverse events associated with psychological therapies.

Multidisciplinary Rehabilitation

Key Points

- For chronic low back pain, a systematic review found multidisciplinary rehabilitation, versus usual care, associated with lower short-term pain intensity (9 trials, standardized mean difference −0.55, 95% CI −0.83 to −0.28, I2=72%; or ~1.4-point mean difference on a 0- to 10-point numerical rating scale) and disability (9 trials, standardized mean difference −0.41, 95% CI −0.62 to −0.19, I2=58%; or ~2.5-point mean difference on the RDQ); effects on long-term pain intensity and disability also favored multidisciplinary rehabilitation, but were smaller (7 trials, standard mean difference −0.21, 95% CI −0.37 to −0.04, I2=25% and 6 trials, standardized mean difference −0.23, 95% CI −0.40 to −0.06, I2=19%, respectively), with no difference in likelihood of return to work (7 trials, OR 1.04, 95% CI 0.73 to 1.47, I2=31%) (SOE: moderate for pain and function).

- For chronic low back pain a systematic review found multidisciplinary rehabilitation, versus no multidisciplinary rehabilitation, associated with lower short-term pain intensity (3 trials, standardized mean difference −0.73, 95% CI −1.22 to −0.24, I2=64%, or ~1.7-point mean difference on a 0 to 10 numerical rating scale) and disability (3 trials, pooled standardized mean difference −0.49, 95% CI −0.76 to −0.22, I2=0%, or ~2.9-point mean difference on the RDQ); there was insufficient evidence to assess effects on long-term outcomes (SOE: low for pain and function).
- For chronic low back pain, a systematic review found multidisciplinary rehabilitation, versus nonmultidisciplinary physical therapy, associated with lower short-term pain intensity (12 trials, standardized mean difference −0.30, 95% CI −0.54 to −0.06, I2=80%, or an approximate 0.6-point mean difference on a 0- to 10-point numerical rating scale) and disability (13 trials, standardized mean difference −0.39, 95% CI −0.68 to −0.10, I2=88%, or an approximate 1.2-point mean difference on the RDQ); multidisciplinary rehabilitation was also associated with lower long-term pain intensity (9 trials, standardized mean difference −0.51, 95% CI −1.04 to 0.01, I2=92%) and function (10 trials, standardized mean difference −0.68, 95% CI −1.19 to −0.16, I2=94%) and greater likelihood for return to work (8 trials, OR 1.87, 95% CI 1.39 to 2.53, I2=0%) (SOE: moderate).
- No study evaluated the effectiveness of multidisciplinary rehabilitation for acute low back pain or for radicular low back pain.
- Harms were poorly reported in trials of multidisciplinary rehabilitation, though no serious harms were reported (SOE: low).

Detailed Synthesis

Multidisciplinary rehabilitation, also known as interdisciplinary rehabilitation, refers to a coordinated program with both physical and biopsychosocial treatment components (at minimum) and is provided by professionals from at least two different specialties (e.g., physical therapists, occupational therapists, psychologists, physicians, and/or complementary and alternative medicine providers). The previous APS/ACP review[29] identified three systematic reviews of multidisciplinary rehabilitation for chronic low back pain (>3 months duration) and one trial of multidisciplinary rehabilitation for subacute (>4 weeks and <3 months duration) low back pain.[344-347] The systematic reviews were all rated high quality and included 20 unique trials. Based on the systematic reviews, the APS/ACP review concluded that there was good evidence that multidisciplinary rehabilitation interventions for chronic low back pain are moderately more effective than usual care or no multidisciplinary intervention at reducing pain and improving function, including return to work.[344-347]

We identified a subsequent good-quality systematic review of multidisciplinary rehabilitation that included 41 trials of multidisciplinary biopsychosocial rehabilitation (MBR) for chronic (>12 weeks) mechanical or nonspecific low back pain (Table 10; Appendix Tables E21; F21).[348] Thirty-one of the trials were published after the APS/ACP review. The trials in the systematic review enrolled a total of 6,858 subjects (sample size range 20 to 542) from Europe, Iran, North America, and Australia. Sixteen trials compared MBR versus usual care; 4 trials MBR versus wait list controls; 19 trials MBR versus physical treatments (exercise plus

other modalities like back school, massage, traction, and stretching); and 12 trials compared different multidisciplinary rehabilitation interventions versus one other. Trials of MBR versus surgery were included in the systematic review but outside the scope of this report. Fifteen of the MBR interventions were categorized as high-level interventions (>100 hours total and delivered on a daily basis), 15 involved low-level interventions (<30 hours and nondaily), and 11 interventions did not meet criteria for either high- or low-level interventions. Primary outcomes of pain, disability, and work were organized into short-term outcomes (<3 months), medium term-outcomes (3-12 months), and long-term outcomes (>12 months). All of the studies had methodological shortcomings, but 13 trials were assessed by the review as low risk of bias, based on meeting ≥6 of 12 Cochrane Back Review criteria. No trial blinded providers or participants; other methodological shortcomings included failure to describe adequate randomization methods (12 trials) and failure to report intention to treat analysis (25 trials).

We identified three additional trials of multidisciplinary rehabilitation that were not included in the systematic review (Table 15; Appendix Tables E22, F22).[349-351] Two trials evaluated multidisciplinary rehabilitation for subacute (<12 weeks duration) low back pain.[349, 350] One good-quality trial (n=20) compared a low-intensity multidisciplinary program consisting of physician evaluation, acupuncture, chiropractic care, massage, occupational therapy, physical therapy, nutrition counseling, and as-needed psychiatric and rheumatology consults versus usual care.[349] A fair-quality trial (n=70) compared a high-intensity (>100 total hours) multidisciplinary rehabilitation program including physician evaluation, physical therapy, biofeedback/pain management, group didactic sessions, case management/occupational therapy sessions, and interdisciplinary team conference for patients at high risk for chronic disabling low back pain versus usual care.350 A third, good-quality trial (n=20) evaluated multidisciplinary rehabilitation (including exercise and cognitive-behavioral therapy) versus usual care (including passive spinal mobilization and exercise) for chronic low back pain.[351]

Multidisciplinary Rehabilitation Versus Usual Care

Chronic Low Back Pain

For chronic low back pain, the systematic review found multidisciplinary rehabilitation associated with lower pain intensity versus usual care in the short term (less than 3 months) (9 trials, standardized mean difference −0.55, 95% CI −0.83 to −0.28, I2=72%; ~1.4-point mean difference on a 0- to 10-point numerical rating scale).[348] Multidisciplinary rehabilitation was also associated with better short-term disability (9 trials, standardized mean difference −0.41, 95% CI −0.62 to −0.19, I2=58%; ~2.5-point mean difference on the RDQ). Statistical heterogeneity was present in pooled analyses. Restricting analyses to high-quality trials resulted in similar pooled estimates, though results were less precise and differences no longer statistically significant. There was substantial overlap in CIs for pooled estimates when results were stratified according to use of high versus low intensity MBR interventions. Only one trial enrolled patients with high baseline pain and disability intensity, precluding reliable conclusions regarding effects of baseline symptom intensity on estimates of effectiveness. No difference was seen in the proportion of patients working in the short term, based on two trials (OR 1.07, 95% CI 0.60 to 1.90, I2=0%). The odds ratios for return to work in the two included studies were 0.91 and 1.14.329, [352]

The systematic review also found multidisciplinary rehabilitation associated with small beneficial effects on long-term back pain versus usual care (7 trials, standard mean difference −0.21, 95% CI −0.37 to −0.04, I2=25%; ~0.5-point mean difference on a 0 to 10 numerical rating scale). Multidisciplinary rehabilitation was also associated with beneficial effects on long-term functional outcomes (6 trials, standardized mean difference −0.23, 95% CI −0.40 to −0.06, I2=19%; ~1.4-point mean difference on the RDQ). There was no difference between multidisciplinary rehabilitation versus usual care in the likelihood of return to work long-term (7 trials, OR 1.04, 95% CI 0.73 to 1.47, I2=31%). In the included trials, odds ratios for return to work ranged from 0.48 to 2.77.

The systematic review found multidisciplinary rehabilitation associated with better short-term scores on the SF-36 mental component subscale (mean difference 15.25, 95% CI 2.05 to 28.44, I2=73%), with no effect on the SF-36 physical component subscale (mean difference 13.45, 95% CI −9.07 to 35.96, I2=94%).[353, 354] However, estimates were based on only two trials with heterogeneous results (mean differences 9.4 [95% CI 2.7 to 16] and 23 [95% CI 11 to 35] on the mental component subscale and 2.5 [95% CI −1.4 to 6.4] and 26 [95% CI 15 to 36] on the physical component subscale).

Two trials evaluated multidisciplinary rehabilitation versus usual care for subacute low back pain. One trial (n=20) found MBR associated with better pain (mean 1.0 vs. 4.7) and SF-12 Physical Component Subscale scores (mean 51 vs. 44, p=0.03) through 26 weeks.[349] Effects on the RDQ favored MBR at 12 weeks (3.9 vs. 11, p=0.08), but did not reach statistical significance. The second trial (n=70) found multidisciplinary rehabilitation associated with long-term (12 months) improvement in pain based on the Characteristic Pain Inventory (27 vs. 43 on a 0- to 100-point scale, p=0.001), disability days (38 vs. 102, p=0.001), return to work (91% vs. 69%, OR 4.55, p=0.027), use of opioids (27% vs. 44%, OR 0.44, p=0.020), and costs ($12,721 vs. $21,843, p<0.05) in patients at high risk for chronic disabling low back pain.350 Both trials found no differences in days in bed, days of work or school missed, and days that activity levels were reduced.

Multidisciplinary Rehabilitation Versus No Multidisciplinary Rehabilitation

Chronic Low Back Pain

The systematic review found multidisciplinary rehabilitation associated with lower short-term pain intensity versus no multidisciplinary rehabilitation (3 trials, standardized mean difference −0.73, 95% CI −1.22 to −0.24, I2=64%; ~1.7-point mean differences on a 0 to 10 NRS).[348] Although statistical heterogeneity was present, results from all trials favored multidisciplinary rehabilitation (standardized mean differences of −0.45, −0.55, and −1.20). Multidisciplinary rehabilitation was also associated with improved short-term disability (3 trials, pooled standardized mean difference −0.49, 95% CI −0.76 to −0.22, I2=0%; ~2.9-point difference on the RDQ). There was insufficient evidence to assess effects on long-term outcomes. Work-related outcomes were also not reported.

Multidisciplinary Rehabilitation Versus Physical Therapy

Chronic Low Back Pain

The systematic review found multidisciplinary rehabilitation associated with lower short-term pain intensity versus physical therapy (12 trials, standardized mean difference −0.30, 95% CI −0.54 to −0.06, I2=80%; ~0.6-point mean difference on a 0- to 10-point NRS).[348] Multidisciplinary rehabilitation was also associated with better short-term disability (13 trials, standardized mean difference −0.39, 95% CI −0.68 to −0.10, I2=88%; ~1.2-point mean difference on the RDQ). Statistical heterogeneity was present for both short-term pain and function, with 5 trials finding no effect on short-term pain or disability. Exclusion of high risk of bias trials and stratification by intensity of the multidisciplinary rehabilitation intervention resulted in pooled estimates that also favored multidisciplinary rehabilitation, though results were less precise and in some cases no longer statistically significant. Excluding an outlier trial with large effect sizes (e.g., 1.99 for pain vs. 0.04 to 0.65 in the other trials) eliminated statistical heterogeneity for pain and reduced statistical heterogeneity for function, and resulted in similar pooled estimates. Multidisciplinary rehabilitation was also associated with increased likelihood of working versus physical therapy at short term (3 trials, OR 1.60, 95% CI 0.92 to 2.78, I2=23%), though only one of the included trials reported a positive effect (OR 2.4, 95% CI 1.3 to 4.5, versus OR 1.1 in the other two trials).[355]

The systematic review also found multidisciplinary rehabilitation associated with lower long-term pain intensity versus physical therapy (9 trials, standardized mean difference −0.51, 95% CI −1.04 to 0.01, I2=92%; ~1.2-point mean difference on a 0 to 10 NRS). Multidisciplinary rehabilitation was also associated with better long-term function (10 trials, standardized mean difference −0.68, 95% CI −1.19 to −0.16, I2=94%; ~4.0-point difference on the RDQ). Excluding an outlier trial with very large effects in favor of multidisciplinary rehabilitation resulted in a similar pooled estimate that was no longer statistically significant. Multidisciplinary rehabilitation was associated with greater likelihood versus physical therapy for return to work (8 trials, OR 1.87, 95% CI 1.39 to 2.53, I2=0%).

Three trials found no differences between multidisciplinary rehabilitation versus physical therapy in the short or long term for quality of life measures[209, 338, 356-358] and seven trials found no differences in short- or long-term depression or anxiety, or self-efficacy.[209, 212, 334, 335, 338, 356-359]

One subsequent small (n=20), good-quality trial reported results consistent with the systematic review.[351]

Harms

Harms were poorly reported in trials of multidisciplinary rehabilitation, though no serious harms were reported. One trial reported no adverse events in subjects who underwent multidisciplinary rehabilitation[360] and one trial reported one case of pain due to acupuncture.[349] One trial reported three cases of transitory worsening of pain and one case of mood alteration in patients undergoing multidisciplinary rehabilitation.

Acupuncture

Key Points

- For acute low back pain, a systematic review found acupuncture associated with lower pain intensity versus sham acupuncture using nonpenetrating needles (2 trials, mean difference 9.38 on a 0 to 100 VAS, 95% CI 1.76 to 17.0, I2=27%); three other trials reported effects consistent with these findings. One trial of sham acupuncture using penetrating needles to nonacupuncture points found no effect on pain. These were no clear effects on function in 5 trials (SOE: low for pain and function).
- For chronic low back pain, a systematic review found acupuncture associated with lower pain intensity versus sham acupuncture (superficial needling at acupuncture or nonacupuncture points, or nonpenetrating pressure at acupuncture points) immediately at the end of treatment (4 trials, WMD −16.76, 95% CI −33.3 to − 0.19, I2=90%) and at up to 12 weeks (3 trials, WMD −9.55, 95% CI −16.5 to −2.58, I2=40%), but there were no differences in function. Four additional trials reported results consistent with these findings (SOE: moderate for pain and function).
- For chronic low back pain, a systematic review found acupuncture associated with lower pain intensity (4 trials, SMD −0.72, 95% CI −0.94 to −0.49, I2=51%) and better function (3 trials, SMD −0.94, 95% CI −1.41 to −0.47, I2=78%) immediately after treatment versus no acupuncture. Mean effects on pain ranged from 7 to 24 points on a 0- to 100-point scale; for function one trial reported a difference of 8 points on a 0- to 100-point scale and the other two trials; two trials showed small or no clear differences at longer-term followup (SOE: moderate for pain and function).
- For acute low back pain, a systematic review found acupuncture associated with slightly greater likelihood of overall improvement versus NSAIDs at the end of treatment (5 trials, RR 1.11, 95% CI 1.06 to 1.16, I2=0%) (SOE: low).
- For chronic low back pain, a systematic review found acupuncture associated with better pain relief (3 trials, WMD −10.56 on a 0 to 100 scale, 95% CI −20.34 to −0.78, I2=0%) and improvement in function (3 trials, SMD −0.36, 95% CI −0.67 to −0.04, I2=7%) immediately postintervention (SOE: low).
- Harms of acupuncture were poorly reported in the trials, though no serious adverse events were reported (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included three systematic reviews[361-363] with a total of 51 unique trials of acupuncture. Four trials in the systematic reviews evaluated acupuncture for acute low back pain and the remainder evaluated acupuncture for chronic low back pain. Based on the evidence in the systematic reviews, the APS/ACP review found insufficient (poor) evidence to determine effects of acupuncture for acute low back pain and fair evidence of moderate effects of acupuncture versus sham or no acupuncture for short-term pain relief in patients with chronic

low back pain, though some inconsistency was noted in trials of acupuncture versus sham acupuncture, with some trials findings no effects.

We identified two fair-quality recent systematic reviews of acupuncture for low back pain; one evaluated acupuncture for acute or subacute low back pain[364] and the other evaluated acupuncture for chronic low back pain (Table 10, Appendix Tables E23, F23).[365]

The systematic review[364] on acupuncture for acute or subacute low back pain 9<12 weeks in duration) included 11 trials (9 not included in the APS/ACP review).[366-374] Three trials evaluated acupuncture versus sham acupuncture (total n=148), 7 trials evaluated acupuncture versus medications including NSAIDS, muscle relaxants and analgesics (total n=966). and 1 trial compared acupuncture plus medication versus the medication alone (n=49). The acupuncture interventions ranged from a single session[371, 375] to up to 12 sessions over a 4- to 6-week period. Outcomes were assessed immediately at the end of treatment in all trials; longer-term outcomes were assessed at 1 to 6 months in three trials.[374, 376, 377] Five trials were rated low risk of bias,[366, 371, 374-376] based on meeting at least 6 of 12 2009 Cochrane Back Group criteria. Methodological shortcomings in the 6 high-risk of bias trials included inadequate description of randomization and allocation concealment methods, unblinded design, and unclear similarity of the groups at baseline. Three sham-controlled trials had blinding of patients, providers and outcomes assessors.[371, 374, 375]

The systematic review[365] on acupuncture for chronic low back pain included 32 trials (9 not included in the APS/ACP review).[378-385] All of the trials evaluated patients with chronic low back pain for >12 weeks, with the exception of one trial that included people with subacute (>6 weeks) to chronic low back pain (up to 52 weeks).[386] In addition to standard acupuncture needles applied to the body, other acupuncture techniques evaluated in the trials included electroacupuncture and auricular acupuncture. Seven trials evaluated acupuncture versus sham procedures (total sample=638 participants), 3 trials evaluated acupuncture versus medications (total sample=75 participants), and the other 22 trials compared acupuncture versus no acupuncture, usual care, TENS, exercise, inactive treatment, or another active treatment. The number of sessions ranged from 1 to 20, the duration of treatment ranged from 1 day (single treatment) to 12 weeks, and duration of followup ranged from immediately following treatment through up to 48 months. Seven of the trials[378-381, 383, 387, 388] were rated low risk of bias (based on meeting all 2009 Cochrane Back Review Group criteria). Methodological shortcomings in the other trials included inadequate description of randomization and allocation concealment techniques, unblinded design, and unclear similarity of groups at baseline.

We identified three additional good-quality trials of acupuncture for acute[389, 390] or chronic[391] low back pain (Table 16, Appendix Tables E24, F24). One trial (n=80) compared five 30-minute sessions scalp acupuncture plus diclofenac versus sham scalp acupuncture plus diclofenac for acute low back pain; outcomes were assessed at 28 days.[389] Another trial (n=270), randomized patients with acute low back pain to one of four treatment groups: true acupuncture, sham acupuncture (needles inserted at nonacupuncture points), placebo acupuncture (momentary pressure with semiblunted needle applied to back) or no acupuncture.[390] Treatments were administered in five 20-minute sessions over 2 weeks, with outcomes assessed through 48 weeks. The third trial (n=130) evaluated acupuncture versus sham acupuncture for chronic low back

pain.391 Patients received 12 acupuncture or sham acupuncture sessions over a 6 week time period and were followed for up to 6 months.

We also identified one fair-quality trial (n=236) of acupuncture performed at back pain specific acupoints or standard acupuncture performed at nonspecific acupoints (n=82) versus usual care.[392] Methodological limitations included unclear allocation concealment and lack of blinding of patients and providers. Patients in the acupuncture groups received 14 daily treatments and outcomes were assessed through 24 weeks. A poor-quality trial (n=143) (due to unclear randomization and allocation concealment methods, no primary outcome identified and unclear blinding) compared the addition of daily acupuncture to an intensive inpatient 21-day rehabilitation for chronic low back pain and measured outcomes at 3 months after the end of treatment.[393]

Acupuncture Versus Sham Acupuncture

Acute Low Back Pain

Three low risk of bias trials in the systematic review of acupuncture for acute low back pain[364] evaluated acupuncture versus a sham procedure involving nonpenetrating needles to acupuncture points.[371, 374, 375] Two trials (n=40 and 60) found acupuncture associated with immediate pain relief following a single treatment, though effects were small (mean difference 9.38 on a 0 to 100 VAS, 95% CI 1.76 to 17.0, I2=27%).[371, 375] The third trial (n=48) could not be pooled, but found no difference between 3 to 12 sessions of acupuncture versus sham in mean pain intensity at 3 months, though acupuncture was associated with lower scores for worst pain at 3 months (estimated marginal mean difference from baseline 18.7 on 0-100 VAS scale, 95% CI 1.5 to 36.0, p=0.034) as well as analgesic tablet use. There were no differences in function in any of the studies.

One good-quality trial (n=275) not included in the systematic review found no differences between five 20-minute sessions of acupuncture, sham (nonacupuncture points), or placebo (semiblunted needles to the back) acupuncture in the likelihood of experiencing 35 percent improvement in the RDQ at 3 weeks, though the first two were associated with greater likelihood of improvement in the RDQ versus no acupuncture (74% vs. 75% vs. 65% vs. 44%, respectively, RR 1.66, 95% CI 1.23 to 2.24 for acupuncture versus no acupuncture and RR 1.69, 95% CI 1.26 to 2.28 for sham acupuncture versus no acupuncture).390 Changes in pain intensity were not reported, and there were no clear differences between groups in the proportion of patients reporting ongoing or recurring pain at 1 year.

Another good-quality trial (n=80) not included in the systematic review found five 30-minute sessions of scalp acupuncture associated with lower pain intensity (mean improvement from baseline 4.57 vs. 3.30 on a 0-10 VAS, p=0.005) and function (mean improvement from baseline 10.8 vs. 6.6 on the RDQ, p=0.002) at 28 days versus sham acupuncture (nonpenetrating needles), though the magnitude of the difference was below the prespecified threshold for meaningful differences (<2 cm on the 10 cm VAS scale and <5 on the RDQ).[389]

Chronic Low Back Pain

Seven trials in the systematic review of acupuncture for chronic low back pain evaluated acupuncture versus sham acupuncture. One trial evaluated auricular electroacupuncture versus sham electroacupuncture (needles inserted but no current)[394] and the other trials evaluated acupuncture to the body versus superficial needling at acupuncture points,[388, 395] nonpenetrating pressure with a needling tube,[396] or superficial needling at nonacupuncture points.[379, 397, 398] Four trials could be included in pooled analyses.[388, 395-397] Acupuncture was associated with improved pain versus sham immediately at the end of treatment (4 trials, WMD −16.76, 95% CI −33.3 to −0.19, I2=90%) and at up to 12 weeks (3 trials, WMD −9.55, 95% CI −16.5 to −2.58, I2=40%), but there were no differences on function at the end of treatment (p=0.2, data not provided) or at up to 12 weeks (p=0.76). Statistical heterogeneity was substantial and was not explained by the type of sham procedure evaluated. The three trials not included in the meta analysis due to lack of poolable data,[379, 394, 398] including the trial of auricular acupuncture, reported results consistent with the meta-analysis for immediate effects. One trial that evaluated longer-term outcomes found that differences between acupuncture versus sham acupuncture were smaller and no longer statistically significant at 26 and 52 weeks.[397]

One good-quality trial (n=130) published subsequent to the systematic review found acupuncture (up to 12 sessions over 6 weeks) associated with lower low back pain symptom bothersomeness scores (mean change from baseline −3.4 vs. −2.3 on 0 to 10 VAS, p<0.05) and pain intensity (−3.52 vs. −2.27 on 0 to 10 VAS, p=0.008) versus sham acupuncture (semiblunt needles to nonacupuncture points) at 8 weeks, though differences were no longer present at 6-month followup.[391] There was no difference in function (ODI) at any time point through 6 months.

Acupuncture Versus No Acupuncture

Chronic Low Back Pain

The systematic review of acupuncture for chronic low back pain[365] included five trials of acupuncture versus no acupuncture. One trial was rated low risk of bias[378] and the others unclear risk of bias.[384, 397, 399, 400] The systematic review found acupuncture associated with lower pain intensity (4 trials, SMD −0.72, 95% CI −0.94 to −0.49, I2=51%)[384, 397, 399, 40]0 and better function (3 trials, SMD −0.94, 95% CI −1.41 to −0.47, I2=78%)[378, 397, 400] immediately after treatment, versus no acupuncture. Across the trials included in the meta-analyses, mean effects on pain ranged from 7 to 24 points on a 0- to 100-point scale; for function one trial reported a difference of 8 points on the Pain Disability Index[397] and the other two trials[378, 400] reported mean differences of 0.8 and 3.4 points on the RDQ. The low risk of bias trial found no clear differences between acupuncture versus self care alone in the RDQ at the end of treatment (mean 7.9 vs. 8.8, p=0.55) or at 1 year (mean 8.0 vs. 6.4, p=0.10) or in symptom bothersomeness scores (40 vs. 4.6 on a 0 to 10 scale at 10 weeks and 4.5 vs. 3.8 at 1 year, respectively).[378] Another trial also found that effects on pain and function were much larger immediately after a 12-week course of treatment (for pain, mean difference 27 [95% CI 24 to 21] on a 0- to 100-point scale at 3 months and 2.7 [95% CI −0.3 to 5.7] at 6 months; for function, mean difference 22 points [95% CI 95% CI 19 to 25] on the 0 to 100 Hannover Functional Ability Questionnaire at 3 months and 3.7 points [95% CI 0.7 to 6.7] at 6 months).[384]

Acupuncture Versus Medications

Acute Low Back Pain

Five trials[366-369, 373] in the systematic review of acupuncture for acute low back pain[364] found acupuncture associated with slightly greater likelihood of overall improvement versus NSAIDs at the end of treatment (5 trials, RR 1.11, 95% CI 1.06 to 1.16, I2=0%). However, there was no significant difference when the analysis was restricted to two trials rated low risk of bias (pooled RR, 1.14; 95% CI 0.99, 1.30; I2=49%), although the point estimate was similar to the overall analysis and each trial reported results that favored acupuncture versus meloxicam (RR 1.07, 95% CI 1.02 to 1.11)[369] or versus ibuprofen (94% vs. 75% "cured", $p<0.05$).[366] The three high risk of bias trials reported inconsistent effects of acupuncture versus medications on pain intensity. One trial favored acupuncture over ibuprofen[368] immediately following each treatment, but two other trials found no significant differences between acupuncture versus naproxen[377] or diclofenac.[372]

Chronic Low Back Pain

Three trials in a systematic review of acupuncture for chronic low back pain[365] compared acupuncture versus medications (NSAIDs, muscle relaxants and analgesics).[400-402] Two of the trials were rated high risk of bias[401, 402] and the other unclear risk of bias.[400] Compared with medications, acupuncture was associated with better pain relief (WMD −10.56 on a 0 to 100 scale, 95% CI −20.34 to −0.78, I2=0%) and function (SMD −0.36, 95% CI −0.67 to −0.04, I2=7%) immediately postintervention.

Acupuncture Plus Medications Versus the Medication Alone

Acute Low Back Pain

Two high risk of bias trials in the systematic review compared acupuncture plus medications versus the medication alone.[372, 373] One trial (n=200) found 7 days of acupuncture plus nimesulide (an NSAID) associated with better short-term overall improvement the NSAID alone.[373] The other trial (n=69) found five sessions of acupuncture plus diclofenac associated with greater short-term improvements in pain and function versus diclofenac alone at the end of treatment.[372]

Harms

Harms of acupuncture were poorly reported in the trials. Serious adverse events were not reported in any trial. In three trials, the most commonly reported adverse effects in people receiving acupuncture were gastrointestinal problems, changes in energy,[377] mild bleeding at the needling site,[371] and temporarily increased low back pain.[391]

Massage

Key Points

- For subacute low back pain, a systematic review included two trials that found massage associated with greater short-term (1 week) improvement in pain (SMD −0.92, 95% CI −1.35 to −0.48) and function (SMD −1.76, 95% CI −3.19 to −0.32) versus sham therapy, but there was no difference in pain or function at 5 weeks in one trial (SOE: low for pain and function).
- • For chronic low back pain, one trial found no difference between foot reflexology versus usual care in pain or function, and one trial found structural or relaxation massage associated with better function (mean 2.5 to 2.9 points on the RDQ) versus usual care at 10 weeks; effects were less pronounced at 52 weeks (SOE: low for pain and function).
- • For subacute to chronic low back pain, a systematic review found massage associated with better effects on short-term pain in 7 of 9 trials (mean differences −0.6 to −0.94 points on a 0 to 10 scale) and better effects on short-term function in 3 of 4 trials (SOE: moderate for pain and function).
- • For subacute to chronic low back pain, a systematic review included 5 trials that generally found massage plus another intervention superior to the other intervention without massage for short-term pain, with effects somewhat stronger in trials in which massage was combined with exercise; few differences were observed for function or long-term pain. Two subsequent trials of massage plus exercise reported findings generally consistent with these findings (SOE: low).
- • Comparisons of difference massage techniques were too heterogeneous and effects were too small from six trials to determine effects on pain and function (SOE: insufficient).
- • Harms were not well-reported in trials of massage, though no serious adverse events were reported; two trials reported soreness during or shortly after the treatment (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included two good-quality systematic reviews with a total of eight unique trials of massage.[403, 404] Five of the trials were rated higher quality. Based on the systematic reviews, the APS/ACP review concluded that there was fair evidence of moderate net benefits of massage for chronic or subacute low back pain.

One of the systematic reviews[404] has been updated to include 13 trials (total n=1596, range 39 to 262) (Table 10; Appendix Tables E25, F25).[405] The trials evaluated massage for acute (1 RCT), subacute (4 RCTs) and chronic low back pain (8 RCTs). Massage techniques were variable, and included traditional Thai massage, Swedish massage, relaxation massage methods, acupuncture massage, muscle energy technique, roptrotherapy, acupressure, foot reflexology, or combined techniques. Two trials compared massage versus sham/placebo massage, nine trials of massage versus other treatments (manipulation, exercise, relaxation, acupuncture, physiotherapy and self-

care education), five trials of massage versus other interventions versus the other interventions alone, and two trials compared different massage techniques. The number of sessions, duration of sessions, and duration of treatment varied. Two of the studies included were single intervention trials; in the remainder the duration of treatment ranged from three to 10 weeks. The duration of followup ranged from immediately following treatment to 52 weeks post randomization. Six trials were rated low risk of bias (based on meeting ≥6 of 11 Cochrane Back Review group criteria). Methodological shortcomings included lack of blinding of patients and assessors and inadequate or unclearly described allocation concealment methods.

We identified eight additional trials of massage not included in the systematic review.[406-413] One good-quality trial (n=401) evaluated two different types of massage (structural or relaxation) versus usual care for chronic low back pain (Table 17; Appendix Tables E26, F26).[406] Patients randomized to massage received 10 weekly treatments including up to 3 home exercises from a predefined list of seven exercises, six of which were common to both treatments, as well as stretching. The relaxation massage group was also given 2.5-minute home relaxation exercises. A fair-quality trial (n=45) compared acupressure massage versus sham laser or no treatment.[412] Three smaller trials (n=26 to 140) not compared different massage techniques with one another. One trial was rated as good quality,[407] one fair,[409] and one poor quality.[408] Two fair-quality trials compared massage plus an exercise intervention to the exercise intervention alone.[411, 413] One of these trials trial (n=80)[411] evaluated myofascial release for subacute to chronic low back pain and the other[413] evaluated Chinese massage for back pain of mixed duration. The eighth, fair-quality trial (n=32) compared massage plus traction versus traction alone in patients with chronic low back pain.[410] Methodological shortcomings in the fair- and poor-quality trials included unclear randomization and allocation concealment methods, baseline group differences, and inadequate or unclear blinding.

Massage Versus Sham Intervention or No Massage

Subacute Low Back Pain

The updated systematic review included two trials of massage versus sham therapy for subacute low back pain.[414, 415] One low risk of bias trial (n=98) included in the prior APS/ACP review found massage moderately superior to sham laser for short- and long-term pain intensity and functional status.[414] Effects of pain ranged from about 0.8 to 1.3 points on a 10-point pain scale ($p<0.001$) and from 1.2 to 4 points on the RDQ ($p<0.001$). Another, high risk of bias trial (n=60)[415] compared one 30-minute session of deep cross-friction massage with the aid of a copper myofascial T-bar (roptrotherapy) applied to the lumbar pelvic region versus no massage to patients with subacute low back pain (>3 weeks and <12 weeks). In this trial, roptrotherapy was associated with less pain and improved function at 1 week compared with either no treatment or a placebo intervention (endemiology as a massage-like treatment). Mean differences in change from baseline were about 20 points for pain on a 0 to 100 scale and about 20 points on the ODI. In a pooled analysis, massage was associated with greater short-term (1 week) improvement in pain (SMD −0.92, 95% CI −1.35 to −0.48) as well as back-specific function (SMD −1.76, 95% CI −3.19 to −0.32).414, 415 However, one trial that evaluated longer-term outcomes found no statistically significant effects on pain and back-related function at 5 weeks.[415]

One additional fair-quality trial (n=45) found massage associated with decreased low back pain versus sham laser or no treatment at 6 weeks (0.9 vs. 4.7 vs. 5.9 on a 0 to 10 scale, respectively), but there were differences in baseline pain scores (6.4 vs. 5.7 vs. 5.0).[412]

Massage Versus Usual Care

Chronic Low Back Pain

One low risk of bias trial (n=243) included in the systematic review found no differences between foot reflexology versus usual care in short- or long-term pain or function.[328] A recent, good quality, larger (n=401) trial[406] not included in the systematic review found a 10-week course of structural or relaxation massage for chronic low back pain each associated with better RDQ scores versus usual care (differences 2.5 to 2.9 points on a 0- to 24-point scale) and better symptom bothersomeness scores (differences 1.4 and 1.7 points) at 10 weeks. Beneficial effects on function, but not symptom bothersomeness, remained present at 52 weeks for relaxation massage (but not structural massage) versus usual care, but were less pronounced (mean difference in RDQ −1.4, 95% CI −2.6 to −0.2).

Massage Versus Other Treatments

The systematic review included eight trials (5 published since the APS/ACP review) of massage other noninvasive active treatments. Massage was compared versus manipulation (1 trial),[416] exercise therapy (1 trial),[414] relaxation therapy (3 trials),[328, 417, 418] acupuncture (1 trial),[403] or physiotherapy (2 trials).[419, 420] All of the trials evaluated patients with subacute to chronic low back pain. Most trials found massage superior to other treatments for short-term pain, but findings were limited by small samples, small numbers of trials for each comparison, heterogeneous massage and comparator intervention techniques, and methodological limitations in the trials. For short-term pain, results favored massage in 7 of the nine trials, though effects were small (mean differences less than 1 point on a 0 to 10 scale, range −0.6 to −0.94). The largest effect was observed in a low risk of bias trial (n=67) that found Thai massage associated with less pain versus joint mobilization 5 minutes after treatment (mean difference −0.94,95% CI −1.76 to −0.12) for chronic low back pain.[416] The largest trial (n=243) found no differences between reflexology versus progressive muscle relaxation in pain (mean difference 2.90, 95% CI −12.32 to 6.52) or function (−3.60, 95% CI −11.10 to 3.90) immediately post-treatment or at 6 months.[328] Other trials found massage associated with better scores on the RDQ versus acupuncture at the end of a 10-week course of treatment (n=172, mean difference in change from baseline 0.6 points, p=−0.01), with similar effects at 1 year[403] versus exercise 1 month after a 1-month course of treatment (n=47, mean difference in change from baseline 4.2 points, $p<0.05$);[414] or versus a physical therapy intervention (including exercise, manipulation, and physical modalities) at the end of a 1-month course of treatment (n=129, mean difference −4.6, 95% CI −6.4 to −2.9) through 6-month followup.[419]

Massage Plus Another Intervention Versus the Other Intervention Without Massage

Five trials included in the systematic review compared massage plus another intervention (exercise [2 trials],[414, 421] exercise and education [1 trial],[422] or usual care [2 trials][328, 423]) versus the other intervention without massage; three of these trials[328, 422, 423] were not in the prior APS/ACP review. Three trials were assessed as being at low risk of bias.[328, 414, 421] The two studies that included usual care interventions either did not define usual care[423] or included a broad range of possible treatments including no treatment, medications, physical therapy, herbal remedies and aromatherapy.[328] Only one trial included patients with subacute low back pain;[423] the rest included patients with subacute to chronic low back pain. The trials generally found massage plus another intervention to be superior to the treatments without massage for short-term pain, but findings were limited by small samples, few trials for each comparison, evaluation of heterogeneous massage techniques and comparator interventions, and methodological limitations in the trials. Few differences were observed for function or long-term pain. The improvement in short-term pain appeared somewhat stronger in the 3 trials in which massage was combined with either group or individual exercise.[414, 421, 422]

One subsequent, fair-quality trial (n=32) found massage (twice weekly 20 minute sessions) plus traction for three weeks and 32 associated with no clear effects versus traction alone in pain immediately following treatment (mean 1.9 vs. 1.4 on a 0 to 10 scale); function was not reported.[410] Two other fair-quality trials (n=80 and 90) not included in the systematic review found massage plus an exercise intervention associated with small to moderate effects on short-term pain (mean difference of about 5 point on the McGill Pain Questionnaire or 1.4 on a 0 to 10 point VAS) and function (about 3 points on the 0 to 100 point Quebec Back Pain Disability Questionnaire or about 5 point on the ODI) versus the exercise intervention alone.[411, 413]

Comparisons of Different Types of Massage

Six trials compared different types of massage;[406-409, 421, 424] two of these[421, 424] were included in the systematic review.[405] The massage techniques that were compared varied. Although most trials found statistically significant differences among methods, effects were small. One low risk of bias trial (n=190) found acupuncture massage superior to Swedish massage for short-term pain (mean difference about 0.8 on a 0 to 10 VAS) and function (mean difference about 7 points on the 0 to 100 Hanover Function Score Questionnaire).[421] Another trial (n=268 for comparison of massage techniques) found no differences between structural versus relaxation massage on the RDQ (mean difference about 0.4 points) or symptom bothersomeness scores (mean difference about 0.3 points on a 0 to 10 scale).[406] Other, smaller (n=26 to 140) trials also found small differences that favored Chinese massage with oils vs. standard massage,[407] Swedish massage with oils versus Thai massage,[409] traditional Thai versus Swedish massage[424] and deep tissue versus standard massage.[408]

Harms

Harms were not well-reported in trials of massage, though no serious adverse events were reported. In two trials that reported adverse events,[420, 424] soreness was noted during or shortly after the treatment. Some patients also reported a skin reaction (e.g., rash or pimples) in trials that used massage oil.

Spinal Manipulation

Key Points

- For acute low back pain, two trials (one included in a systematic review) found spinal manipulation associated with better effects on function versus sham manipulation (statistically significant in one trial); in one trial effects on pain favored manipulation but were small and not statistically significant (mean difference −0.50, 95% CI −1.39 to 0.39) (SOE: low for function, insufficient for pain).
- For chronic low back pain, a systematic review found spinal manipulation associated with small, statistically nonsignificant effects versus sham manipulation on pain at 1 month (3 trials, WMD −3.24, 95% CI −13.62 to 7.15 on a 0 to 100 scale, I2=53%); one trial reported similar results for function (SMD −0.45, 95% CI −0.97 to 0.06); one trial not included in the systematic review reported generally consistent results (SOE: low for pain, insufficient for function).
- For acute low back pain, a systematic review found no differences between spinal manipulation versus and inert treatment in pain relief at 1 week (3 trials, WMD 0.14 on a 0 to 10 scale, 95% CI −0.69 to 0.96, I2=27%), though one trial found SMT associated with better longer-term pain relief (MD −1.20 at 3 months, 95% CI 2.11 to −0.29); there were no differences in function at 1 week (2 trials, SMD −0.08, 95% CI −0.37 to 0.21, I2=0%) or at 3 months (1 trial, SMD −0.28, 95% CI −0.59 to 0.02) (SOE: low for pain and function).
- For chronic low back pain, one high-quality trial found spinal manipulation associated with greater improvement in the “main complaint” versus an inert treatment (mean difference 0.9 on a 0 to 10 scale, 95% CI 0.1 to 1.7); results from three low risk of bias trials and three additional trials not included in the systematic review were somewhat inconsistent, though some trials reported effects that favored manipulation (SOE: low).
- For acute low back pain, a systematic review found no difference between spinal manipulation versus other active interventions in pain relief at 1 week (3 trials, WMD 0.06 on a 0 to 10 scale, 95% CI −0.53 to 0.65, I2=0%), 1 month (3 trials, WMD −0.15, 95% CI −0.49 to 0.18, I2=0%), 3 to 6 months (2 trials, WMD−0.20, 95%CI −1.13 to 0.73, I2=81%), or 1 year (1 trial, MD 0.40, 95% CI −0.08 to 0.88). Findings were similar for function, with no differences observed at any time point. A subsequent trial of patients with acute or subacute low back pain found spinal manipulation associated with moderate effects versus usual care on pain and small effects on function at short-term followup, but effects were smaller and no longer statistically significant at 3 and 6 months (SOE: moderate for pain and function).

- For chronic low back pain, a systematic review found spinal manipulation associated with better short-term pain relief versus other active interventions at 1 month (10 comparisons from 6 trials, WMD −2.76 on a 0 to 100 scale, 95% CI −5.19 to −0.32, I2=27%) and 6 months (7 comparisons from 4 trials, WMD −3.07, 95% CI −5.42 to −0.71, I2=0%), though the magnitude of effects was below the small/slight threshold. There was no difference at 12 months (3 trials, WMD −0.76, 95% CI −3.19 to 1.66, I2=0%). Manipulation was also associated with greater function improvement in function versus other active interventions at 1 month (10 comparisons from 6 trials, SMD −0.17, 95% CI −0.29 to −0.06, I2=3%); effects were smaller and no longer statistically significant at 6 and 12 months. Three trials not included in the systematic reviews reported results consistent with these findings (SOE: moderate for pain and function).
- For acute low back pain, four trials in a systematic review found spinal manipulation plus either exercise or advice associated with greater improvement in function at 1 week (SMD −0.41, 95% CI −0.73 to −0.10, I2=18%) versus exercise or advice alone, but there were no differences at 1 month (3 trials, SMD −0.09, 95% CI −0.39 to 0.21, I2=37%) or 3 months (2 trials, SMD −0.22, 95% CI −0.61 to 0.16, I2=41%) (SOE: low).
- For chronic low back pain, a systematic review found spinal manipulation plus another active treatment associated with greater pain relief at 1 month (3 trials, WMD −5.88 on a 0 to 100 scale, 95% CI −10.85 to −0.90, I2=0%), 3 months (2 trials, MD −7.23, 95% CI −11.72 to −2.74, I2=43%), and 12 months (2 trials, MD −3.31, 95% CI −6.60 to −0.02, I2=12%) versus the other treatment alone, combination therapy was also associated with better function at 1 month, (2 trials, SMD −0.40, 95% CI −0.73 to −0.07, I2=0%), 3 months (2 trials, SMD −0.22, −0.38 to −0.06, I2=33%), and 12 months (2 trials, SMD −0.21, 95% CI −0.34 to −0.09, I2=0%). One trial not included in the systematic review reported results consistent with these findings (SOE: low).
- For radicular low back pain, one good-quality trial found spinal manipulation plus home exercise and advice associated with greater improvement in leg and back pain at 12 weeks versus home exercise and advice alone (mean differences about 1 point on a 0 to 10 scale), but effects were smaller (0.3 to 0.7 points) and no longer statistically significant at 52 weeks (SOE: low).
- Harms were not reported well in most trials of spinal manipulation. No serious adverse events were reported and most adverse events were related to muscle soreness or transient increases in pain (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included 12 systematic reviews[361, 425-436] with a total of 69 individual trials of spinal manipulation versus sham, an inactive treatment, or another active treatment for acute and chronic low back pain.[16] The APS/ACP review concluded that there was fair evidence that spinal manipulation was associated with moderate benefits for acute and chronic low back pain.

One of the reviews of spinal manipulation in the APS/ACP review was subsequently updated as separate good-quality reviews for acute low back pain[437] and chronic low back pain (Table 10;

Appendix Tables E27, F27)[438] The acute low back pain review included 19 randomized trials; eight of these trials were not included in the APS/ACP review.[439-446] Sample sizes ranged from 36 to 323 participants (total sample=2674). About half of the trials restricted inclusion to patients with acute low back pain,[442-445, 447-451] four included patients with a mix of acute and subacute back pain[439, 441, 446, 452] and six included patients with acute to chronic low back pain.[440, 453-457]

A separate review[438] included 26 trials (sample sizes 29 to 1,334, total sample=6070 participants) of spinal manipulation for chronic low back pain; 18 of these trials were not included in the prior Cochrane review.[185, 192, 196, 402, 458-471] Only eight trials restricted inclusion to patients with symptoms longer than 3 months.[192, 196, 402, 458, 460, 464, 465, 467, 470] The remainder permitted inclusion of patients with nonchronic symptoms, but the mean duration of back pain was generally months to years in duration.

Six studies of acute low back pain were rated as low risk of bias[441-443, 445, 446, 453] and nine studies of chronic low back pain were rated as low risk of bias.[185, 192, 461, 462, 469, 472-474] Methodological shortcomings in the high risk of bias studies included unblinded design, unclear allocation concealment methods, incomplete followup, selective reporting of outcomes and in one study[475] significant baseline differences among groups.

In the trials included in the systematic reviews, spinal manipulation was compared against a wide variety of interventions, including various sham or inert therapies (placebo antiedema gel, detuned short-wave diathermy, bed rest, detuned ultrasound, corset and transcutaneous muscle stimulation, sham SMT), or another active intervention (acupuncture, back school, educational back booklet with or without additional counseling, exercise therapy, myofascial therapy, massage, pain clinic, pharmacological/analgesic therapy, short-wave diathermy, standard medical care [including analgesic therapy and advice/reassurance], standard physiotherapy, and ultrasound). The primary type of thrust technique used in the spinal manipulation interventions also varied. High-velocity low-amplitude (HVLA) thrust was used in most studies, though a combination of manipulation and mobilization or other mobilization techniques such as flexion-distraction or the Maitland method were used in 8 trials and unspecified types of SMT were used in 14 trials.

The number and frequency of manipulation treatments also varied among trials that reported this information. Approximately half of the acute low back pain trials did not report number of treatments, but those that did reported 1 and 10 treatment sessions. For chronic low back pain trials, the average maximum number of treatments allowed was 8 and the average duration of treatment 7 weeks in trials that provided this information. In both acute and chronic low back pain trials, followup ranged from 2 weeks to 2 years, with approximately half of the studies only reporting short-term outcomes (<3 months). One study of SMT for acute low back pain only measured the immediate effect of treatment, 2 days after the end of treatment.[446]

We identified 16 additional trials published subsequent to the updated reviews, 8 of which were trials for chronic low back pain,[241, 476-482] two for acute or subacute low back pain[483-485], one for mixed duration low back pain[466] one for radicular low back pain.[486] (Table 18; Appendix Tables E28, F28). We also included 3 trials that were excluded from the systematic reviews because they enrolled patients with sciatica/radiculopathy.[487-489] Two studies were poor quality[487, 488] and one was good quality.[489] These additional trials varied in terms of the comparators

including epidural steroid injections,[487] chemonucleolysis,[488] McKenzie,[466, 481] physical therapy,[478] active exercise[241, 486] usual care,[483] and inactive or sham treatments including detuned ultrasound,[476] simulated manipulation,[489] side lying,[477] and light massage.[480] The duration of treatment ranged from a single treatment[479] on 1 day to 18 sessions over a period of 9 months.

Spinal Manipulation Versus Sham Therapy

Acute Low Back Pain

The systematic review of spinal manipulation for acute low back pain[437] included one high risk of bias trial (n=192) of SMT versus sham SMT.[444] It found no differences between seven sessions of high velocity low amplitude thrust SMT over 2 weeks versus sham adjustments at 1-month followup (MD −0.50, 95% CI −1.39 to 0.39 for pain; SMD −0.35, 95% CI −0.76 to 0.06, function).

One additional poor-quality study not included in the systematic review[485] (n=100) compared three treatments: SMT (up to 2 treatments over a 3-day period) with placebo diclofenac, sham SMT with diclofenac, and sham SMT with placebo diclofenac. Results at 7 to 9 days post treatment favored SMT with placebo diclofenac versus the sham SMT with diclofenac (mean improvement from baseline on RDQ 7.71 vs. 4.75, p=0.01) and versus sham SMT with placebo diclofenac (data not provided), but effects were small.

Chronic Low Back Pain

The systematic review of manipulation for chronic low back pain included three high risk of bias trials of SMT versus sham SMT.[459, 464, 490] The SMT interventions in these trials ranged from four to seven treatment sessions over 2 weeks to 5 months. There was no difference between SMT versus sham SMT in pain at 1 month (3 trials, WMD −3.24, 95% CI −13.62 to 7.15 on a 0 to 100 scale, I2=53%). Two of the trials (n=64 and 19)[459, 490] reported a nonsignificant effects in favor of SMT, while the third trial (n=65)[464] reported a nonsignificant effect that favored sham SMT. One trial that reported 3- and 6-month outcomes[464] reported nonsignificant effects that favored sham SMT. This was also the only trial to report function; it found a small benefit favoring SMT at 1 month (SMD −0.45, 95% CI −0.97 to 0.06) but there were no differences at 3 or 6 months.

Two additional trials compared SMT versus a sham SMT procedure for chronic low back pain.[479, 482] A good-quality trial (n=148) found no difference between a single treatment of region-specific SMT versus sham SMT (nonregion-specific HVLA) immediately following the procedure.[479] One additional fair-quality trial (n=94) compared two different SMT protocols (12 sessions of SMT over 1 month and 12 sessions of SMT over 1 month plus maintenance SMT for 9 months) versus sham manipulation for chronic low back pain.[482] Both SMT groups were superior to sham at 1 month (mean difference 5.0 on a 0-100 scale, p<0.05), with no difference between active SMT interventions. At 10 months, maintenance SMT was associated with small improvements in both pain (16.3 difference on a 0-100 scale, p<0.05) and function (18.1 difference on ODI, p<0.05) compared with either 1 month of SMT or sham manipulation.

Spinal Manipulation Versus an Inactive Treatment

Acute Low Back Pain

Seven trials included in the systematic review of manipulation for acute low back pain[437] compared SMT versus inert interventions (an educational booklet,[453] detuned ultrasound and cold packs,[447] detuned ultrasound,[443] detuned short-wave diathermy,[491] antiedema gel spread,[456] bed rest,[456] and short-wave diathermy[450, 452]). Two trials were rated low risk of bias.[443, 453] There were no differences between SMT versus inactive treatments for pain relief at 1 week (3 trials, MD on 0-10 scale 0.14, 95% CI −0.69 to 0.96, I2=27%),[447, 452, 453] one trial found SMT associated with better longer-term pain relief (MD −1.20 at 3 months, 95% CI 2.11 to −0.29).[453] There were no differences between SMT versus inert interventions in function at 1 week (2 trials, SMD −0.08, 95% CI −0.37 to 0.21, I2=0%)[447, 453] or at 3 months (1 trial, SMD −0.28, 95% CI −0.59 to 0.02).[453]

Chronic Low Back Pain

The systematic review of manipulation for chronic low back pain[438] included four trials of SMT versus inert interventions (antiedema gel [1 trial], detuned short-wave diathermy [1 trial], detuned ultrasound [1 trial], or corset and transcutaneous muscle stimulation [1 trial]).[456, 474, 475, 492] One trial (n=76) was rated low risk of bias.[474] It found SMT associated with greater improvement in the "main complaint" (mean difference 0.9 on a 0 to 10 scale, 95% CI 0.1 to 1.7) versus detuned therapy at 12 months. Effect also favored SMT for function at 12 months, though the difference was not statistically significant (mean difference 0.6, 95% CI −0.1 to 1.3). Effects at earlier time points were smaller not statistically significant. Three high risk of bias trials found no clear differences between SMT versus various inert interventions in pain or other outcomes.[456, 475, 492]

Three additional trials (n=42, 40, 111 and 400)[476, 477, 480] not included in the systematic review also compared SMT versus other inactive treatments for chronic low back pain. One of the trials was rated good quality[480] and two were rated fair quality.[476, 477] The inactive comparators were detuned ultrasound,[476] side lying without SMT,[477] and light massage for 5 minutes.[480] One trial evaluated effects of a single treatment session immediately after treatment.[477]

The good-quality trial[480] compared 6, 12, or 18 sessions of SMT versus light massage. All patients underwent 18 sessions of therapy; at each session they also received hot packs and low-intensity ultrasound and for sessions in which they did not undergo SMT, they received 5 minutes of light massage instead. At the primary outcome of 12 weeks, both those receiving either 12 or 18 sessions of SMT demonstrated statistically significant, but modest improvements in pain over those receiving light massage only; 12 sessions was associated with slightly greater improvement versus light massage only (MD 8.6 on a 0 to100 scale, 95% CI 3.2, 14.0) than 18 sessions (MD 6.1, 95% CI 1.0 to 11.2). Although 12 sessions of SMT were superior to light massage only for function at 6 weeks (mean difference 7.5 on a 0 to 100 scale, 95% CI 1.7 to 13.3), effects were small. Differences were smaller and not statistically significant at 12 and 24 weeks. Eight sessions of SMT were superior to light massage only at 52 weeks for pain (mean difference 7.6, 95% CI 0.8 to 9.2) and function (mean difference 8.8, 95% CI 3.3 to 14.4). Effects on the SF-

36 physical and mental component scales and EuroQoL were small and did not show any clear differences between the SMT treatments versus light massage only.

One fair-quality trial found SMT associated with greater pain relief versus side lying with SMT (−11 versus −2.2 on a 0 to 100 scale, p=0.04).[477] The third trial found 8 sessions of SMT over 4 to 8 weeks associated with greater pain relief at 6 months versus detuned ultrasound, though the difference was not statistically significant based on a prespecified p-value of <0.025 due to multiple comparisons (mean difference −1.24 on 0-10 scale, 95% CI −2.37 to −0.30, p=0.032).476 SMT was associated with greater improvement in the ODI (mean difference −7.14, 95% CI −12.8 to −1.52, p=0.013).

Spinal Manipulation Versus Another Active Treatment

Acute or Subacute Low Back Pain

Eight trials in the systematic review compared SMT versus another active intervention (exercise;[439, 451] physical therapy [according to McKenzie principles];[448, 452, 453, 456, 457] massage;[454] standard general practitioner [GP] care consisting primarily of prescription [diclofenac or codeine] or nonprescription medication (paracetamol), or both;[451, 456] or back school[452, 456]). One trial was rated as a low risk of bias.[453] There were no differences between SMT versus other active interventions in pain relief (0-10 scale) at 1 week (3 trials, MD 0.06, 95% CI −0.53 to 0.65; I2=0%), 1 month (3 trials, MD −0.15, 95% CI −0.49 to 0.18; I2=0%), 3 to 6 months (2 trials MD −0.20, 95% CI −1.13 to 0.73, I2=81%), or 1 year (1 trial, MD 0.40, 95% CI −0.08 to 0.88). Findings were similar for function, with no differences observed at any time point. Among the trials included in the pooled analyses, the active comparators were exercise or physical therapy in all trials except for one, which evaluated back school.[452] The only low risk of bias trial[453] compared SMT (n=122) versus physical therapy/McKenzie (n=133) versus a minimal intervention (an educational booklet). This trial found no differences between SMT versus physical therapy/McKenzie in pain at 1 week (mean difference 0.20 on a 0 to 10 scale, 95% CI −0.56 to 0.96) or 1 month (mean difference −0.40, 95% CI −0.96 to 0.16), or in function (SMD 0.07 at 1 week, 95% CI −0.18 to 0.33 and SMD −0.09 at 1 month, 95% CI −0.34 to 0.16).

One subsequent good-quality trial (n=112) found manual thrust SMT for acute or subacute low back pain associated with greater effects on pain and the ODI versus mechanical assisted manipulation or usual care at the end of four weeks of treatments (mean differences in pain scores -1.4 to -1.7 point and on the ODI -6.5 to -8.1 points), but differences were smaller and no longer statistically significant at 3 or 6 months.[484]

Chronic Low Back Pain

Fifteen studies in the systematic review of SMT for chronic low back pain compared SMT with another active intervention.[185, 192, 460-463, 465, 466, 468-473, 475] Eight trials were rated low risk of bias. The comparators were acupuncture (1 trial), back school, (2 trials), educational back booklet with or without additional counseling (2 trials), exercise therapy (9 trials), myofascial therapy (1 trial), massage (1 trial), pain clinic (1 trial), pharmaceutical/analgesic therapy only (2 trials), short-wave diathermy (1 trial), and standard medical care, including analgesic therapy and advice/reassurance (4 trials), standard physiotherapy (5 trials), and ultrasound (1 trial).

Based on trials rated low risk of bias, SMT was associated with better short-term pain relief versus other interventions at 1 month (10 comparisons from 6 trials, WMD −2.76 on a 0 to 100 scale, 95% CI −5.19 to −0.32, I2=27%) and 6 months (7 comparisons from 4 trials, WMD −3.07, 95% CI −5.42 to −0.71, I2=0%), though effects were small. Effects on pain relief were even smaller and no longer statistically significant at 12 months in three trials (3 trials, WMD −0.76, 95% CI −3.19 to 1.66, I2=0%).[185, 192, 463] For functional status, SMT was associated with greater functional improvement versus other active interventions at 1 month, though effects were small (10 comparisons from 6 trials, SMD −0.17, 95% CI −0.29 to −0.06, I2=3%); as for pain, effects on function were even smaller and no longer statistically significant at 6 and 12 months (8 comparisons from 6 trials, SMD −0.12, 95% CI −0.23 to 0.00, I2=0% and 9 comparisons from 5 trials, SMD −0.06, 95% CI −0.16 to 0.05, I2=0%, respectively). Exercise and physical therapy were the most commonly evaluated active comparators in the trials included in the meta-analyses; results from this subgroup of trials appeared consistent with the overall estimates.

Three additional trials compared SMT versus other active treatments for chronic low back pain.[241, 478, 481] One good-quality trial (n=301) found no clear differences between 12 weeks of SMT versus supervised or home exercise in pain or function.[241] Effects were small (differences 0.1 to 0.6 points on a 0 to 10 pain scale and 0.2 to 1.3 points on the RDQ) and not statistically significant. A good-quality trial (n=350) found SMT (maximum of 15 sessions over 12 weeks) associated with worse function at 12 months versus exercise (mean difference 1.5 on the RDQ, 95% CI 0.2 to 2.9), though the effect was small.[481] Results for pain also favored exercise, but the difference was not statistically significant (mean difference 2.8 on 0 to 100 scale, 95% CI −0.2 to 5.8). A fair-quality trial (n=210) found SMT (20-minute sessions once a week for 4 to 6 weeks) associated with greater pain relief and improvement in function versus back school or physical therapy (fifteen 1-hour sessions over 3 weeks); differences were less than 1 point on 0-10 pain scale and less than 5 points on the RDQ.[478]

Low Back Pain Of Mixed Duration

One fair-quality trial (n=134)[466] of patients with acute to chronic low back pain that was not included in the systematic reviews found no differences between SMT (3 to 7 session) versus McKenzie exercise (3 to 7 sessions) in pain or function, though SMT was associated with better effects versus advice (one 45- to 60-minute session) on the RDQ (MD –3, 95% CI –6 to 0).

Spinal Manipulation Plus Other Active Treatment Versus the Active Treatment Without Manipulation

Acute Low Back Pain

Four trials in the systematic review of SMT for acute low back pain compared SMT plus another intervention (one trial each of advice on posture, exercise, and avoidance of occupational distress,[455] analgesic medication (parecetamol, diclofenac, or dihydrocodeine),[445] exercise,[440] or physiotherapy[442]). One trial was rated low risk of bias.[445] It found no differences between SMT plus analgesics versus analgesics alone at 1 week or at 3 to 6 months in pain relief (MD 0.84 on a 0 to 100 scale, 95% CI −0.04 to 1.72 and MD 0.65, 95% CI −0.32 to 1.62, respectively). Two high risk of bias trials[440, 455] found SMT plus either exercise or advice associated with greater improvement in function at 1 week (SMD −0.41, 95% CI −0.73 to −0.10, I2=18%) versus

exercise or advice alone, but there were no differences in function at 1 month (3 trials, SMD −0.09, 95% CI −0.39 to 0.21, I2=37%) or 3 months (2 trials, SMD −0.22, 95% CI −0.61 to 0.16, I2=41%).

Chronic Low Back Pain

The systematic review of spinal manipulation for chronic low back pain.[438] included five studies[185, 462, 464, 467, 493] of SMT plus another active treatment versus the other active treatment alone. Two trials were rated low risk of bias.[185, 462] The comparators were extension exercises,[467] best care + exercise,[185] myofascial therapy,[462] or usual care.[464] Combination therapy with SMT was more effective versus active treatment without SMT for pain relief at 1 month (3 trials, MD −5.88 on a 0 to 100 scale, 95% CI −10.85 to −0.90, I2=0%),[462, 464, 467] 3 months (2 trials, MD −7.23, 95% CI −11.72 to −2.74, I2=43%),[185, 464] and 12 months (2 trials, MD −3.31, 95% CI −6.60 to −0.02, I2=12%).[185, 467] Combination therapy with SMT was also more effective versus active treatment without SMT on function at 1 month, (2 trials, SMD −0.40, 95% CI −0.73 to −0.07, I2=0%), 3 months (2 trials, SMD −0.22, −0.38 to −0.06, I2=33%), and 12 months (2 trials, SMD −0.21, 95% CI −0.34 to −0.09, I2=0%). Results from the two trials rated low risk of bias were consistent with the pooled estimates.

One fair-quality trial (n=91) not included in the systematic review found SMT (2 sessions once a week for 4 weeks) plus standard medical therapy associated with lower pain intensity (mean difference 1.2 on a 0 to 10 scale, 95% CI 0.2 to 2.3) and better function (mean difference 4.0 on the RDQ, 95% CI 1.3 to 6.7) at the end of therapy versus standard medical care alone for chronic low back pain.[483]

Radicular Low Back Pain

One fair-quality trial (n=192) of patients with subacute to chronic back-related leg pain (n=192) found SMT plus home exercise and advice associated with greater improvement in leg and back pain at 12 weeks versus home exercise and advice alone (mean differences about 1 point on a 0 to 10 scale), but effects were smaller (0.3 to 0.7 points) and no longer statistically significant at 52 weeks.[486]

Harms

As in the prior APS/ACP review, we found that harms were poorly reported in trials of SMT. For chronic low back pain, ~two-thirds of trials did not report adverse events.[438] When reported, adverse events in patients undergoing SMT were limited to muscle soreness, stiffness, and/or transient increase in pain. None of the studies reported any serious complications in either the experimental or control group.

Physical Modalities: Ultrasound

Key Points

- For chronic low back pain, a systematic review found no difference between ultrasound versus sham ultrasound in pain at the end of treatment (3 trials, mean difference −7.12 on 0 to 100 scale, 95% CI −18.0 to 3.75, I2=77%) and two trials found no effects on pain 4

weeks after the end of treatment. Evidence from 5 trials was too inconsistent to determine effects on function, though a larger, good-quality trial found no effect on the RDQ (SOE: low for pain, insufficient for function).

- For chronic low back pain, a systematic review found no differences between ultrasound versus no ultrasound in pain (2 trials, mean difference −2.16, 95% CI −4.66 to 0.34, I2=0%) or back-specific function (2 trials, mean difference −0.41, 95% CI −3.14 to 2.32), but estimates were imprecise (SOE: low for pain and function).
- For chronic low back pain, evidence from 3 trials was insufficient to determine effects of ultrasound plus exercise versus exercise alone on pain or function, due to imprecision and methodological shortcomings (SOE: insufficient).
- For radicular low back pain due to spinal stenosis, a small trial found no differences between ultrasound plus exercise versus sham ultrasound plus exercise in back pain, leg pain, or the ODI after 3 weeks of therapy (SOE: insufficient)
- There was insufficient evidence from three small trials with methodological shortcomings to determine effects of ultrasound versus other interventions (SOE: insufficient).
- For radiculopathy, there was insufficient evidence from two small trials with methodological shortcomings to determine effects of ultrasound versus other interventions (SOE: insufficient).
- No study evaluated the effectiveness of ultrasound for acute nonradicular low back pain.
- One trial found no differences between ultrasound versus sham ultrasound in risk of any adverse event (6.0% vs. 5.9%, RR 1.03, 95% CI 0.49 to 2.13) or serious adverse events (1.3% vs. 2.7%, RR 0.48, 95% CI 0.12 to 1.88) (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included three small (n=15 to 73) trials of therapeutic ultrasound for low back pain.[494-496] All trials had methodological shortcomings. One trial (n=73) found ultrasound associated with a higher likelihood of being pain-free versus sham ultrasound or analgesics (41% vs. 12% vs. 6.8%, p<0.001 for ultrasound versus placebo), but used a quasi-randomized design (alternate allocation).[495] In addition, all patients were placed on bed rest, a treatment no longer recommended. One small (n=10) trial of patients with chronic low back pain found ultrasound moderately superior to sham ultrasound after 10 treatment sessions, but had high loss to followup and did not perform intention-to-treat analysis.[494] The third trial (n=36), which was published in 1960, found no difference between ultrasound and sham ultrasound for low back pain of unspecified duration in pain improvement after 1 month of therapy.496 The APS/ACP review concluded that there was insufficient evidence to determine effects of ultrasound.

We identified one good-quality systematic review published since the APS/ACP review (Table 10; Appendix Tables E29, F29).[497] It included seven trials, including one of the trials described above[494] and six subsequent trials.[465, 494, 498-502] All trials enrolled patients with chronic nonradicular low back pain. Sample sizes ranged from 15 to 120 subjects. One trial was

published in Croatian.[502] All studies evaluated 1 MHz continuous ultrasound at intensities from 1 to 2.5 W/cm^2, applied for 5 to 10 minutes or based on Gray's formula. The number of sessions ranged from 6 to 18. The review focused on outcomes immediately following the prescribed ultrasound treatment course; two trials also evaluated patients 4 weeks[501] and 6 months[465] after the end of treatment. Four trials evaluated ultrasound versus sham ultrasound,[494, 498, 501, 502] two trials ultrasound versus no ultrasound,[499, 500] and three trials ultrasound versus other treatments (spinal manipulation,[465] electrical stimulation,[499] and phonophoresis[500]). In all of the trials except for one,[494] patients in all treatment groups also underwent exercise therapy. Although all trials had methodological shortcomings, two trials[498, 501] were classified by the systematic review as being at low risk of bias, based on meeting six or more of 12 risk of bias criteria. Patients were blinded to receipt of ultrasound in four trials,[494, 498, 501, 502] care providers were blinded in none of the trials, and intention-to-treat analysis was reported in two trials.[498, 501]

The largest randomized trial (n=455) of ultrasound was published after the systematic review (Table 19; Appendix Tables E30, F30).[503] It compared ultrasound versus sham ultrasound for chronic nonradicular low back pain and evaluated patients 4 weeks after the end of treatment. About 20 percent of patients also underwent exercise therapy. The trial used a 2 x 2 factorial design in which patients were also randomized osteopathic manual treatment versus no manual treatment; there was no interaction between the ultrasound and manual treatment interventions. We also identified three small trials of ultrasound that were not included in the systematic review. One fair-quality trial (n=30) compared ultrasound versus low-level laser therapy for back pain ≥3 weeks,[504] one fair-quality trial (n=45) compared ultrasound plus exercise, sham ultrasound plus exercise, and no treatment for spinal stenosis,[505] and one poor-quality trial (n=60) of ultrasound versus traction or low-level laser therapy for acute radiculopathy due to herniated disc.[506]

Ultrasound Versus Sham Ultrasound

Chronic Low Back Pain

The systematic review found no difference between ultrasound versus sham ultrasound in pain at the end of treatment (3 trials, mean difference −7.12 on 0 to 100 scale, 95% CI −18.0 to 3.75, I2=77%).[497] Statistical heterogeneity was high, with one trial498 reporting an effect favoring ultrasound (mean difference −20.0, 95% CI −31.1 to −8.81) and two trials[501, 502] reporting no effect (mean difference −4.10 and 0.90). Ultrasound was associated with better functional status at the end of treatment than sham ultrasound (3 trials, standardized mean difference −0.45, 95% CI −0.84 to −0.05, I2=0%).[497] Although statistical heterogeneity was not present, only one501 of the trials reported a statistically significant effect (standardized mean difference −0.71, 95% CI −1.30 to −0.13 [~8 points on a 0 to 100 scale], versus −0.26 and −0.20, or [~5 points on a 0 to 100 scale] in the other two trials).[494, 498] One additional good-quality trial not included in the systematic review found no differences between ultrasound versus sham ultrasound on the RDQ (median 3 vs. 4, p=0.76) or the SF-36 General Health score (72 vs. 72, p=0.53) at the end of treatment.[503]

Two trials of ultrasound versus sham ultrasound reported no effects on pain 4 weeks after the end of treatment.[501, 503] In a fair-quality trial,[501] there was no difference in pain scores (28 vs. 26, p=0.48) and in a good-quality trial[503] there was no difference in the likelihood of experiencing ≥30 percent (RR 1.02, 95% CI 0.86 to 1.20) or ≥50% (RR 1.09, 95% CI 0.88 to 1.35)

improvement in pain. Results were inconsistent for function. The fair-quality trial[501] found that ultrasound was superior to sham ultrasound on the Functional Rating Index (23 vs. 30, p=0.04), but the good-quality trial[503] found no effect on the RDQ (median 3 vs. 3, p=0.93).

Ultrasound Plus Exercise Versus Exercise Alone

Chronic Low Back Pain

The systematic review[497] found no differences between ultrasound plus exercise versus exercise alone in pain (mean difference −2.16 on a 0 to 10 scale, 95% CI −4.66 to 0.34, I2=0%) or back-specific function (mean difference −0.41 on the ODI, 95% CI −3.14 to 2.32); pooled estimates favored ultrasound but were imprecise and were based on only two trials with methodological shortcomings.[499, 500] Neither individual trial found a statistically significant effect on either outcome.

Mixed Duration Low Back Pain

A small (n=30), fair-quality trial found no differences between ultrasound plus exercise versus sham ultrasound plus exercise in back pain, leg pain, or the ODI after 3 weeks of therapy in patients with low back pain for ≥3 weeks.[504]

Radicular Low Back Pain

A small (n=45), fair-quality trial found no differences between ultrasound plus exercises versus sham ultrasound plus exercise in back pain, leg pain, the ODI, or paracetamol use after 3 weeks of therapy in patients with spinal stenosis.[505]

Ultrasound Versus Other Interventions

Chronic Low Back Pain

Three nonblinded trials compared ultrasound versus other interventions.[465, 499, 500] In one trial, ultrasound, versus spinal manipulation, was associated with worse pain at the end of treatment (mean difference −16.4 on 0 to 100 scale, −26.8 to −6.1), though the difference was not as pronounced 6 months after the end of treatment (−1.4, 95% CI −2.7 to −0.1).465 Spinal manipulation was also associated with better ODI scores at the end of treatment (mean difference −7.8, 95% CI −13.2 to −2.4), with similar findings 6 months after the end of treatment. One trial each found no differences between ultrasound versus electrical stimulation[499] or ultrasound versus phonophoresis[500] in pain or function.

Mixed Duration Low Back Pain

A small (n=30), fair-quality trial of patients with low back pain ≥3 weeks found ultrasound associated with higher pain intensity (median 4 vs. 3 on a 0 to 10 VAS, p<0.001) and worse function (median 16 vs. 12 on the ODI, p<0.001) versus high-intensity laser therapy after three weeks of treatment.[504]

Radicular Low Back Pain

A small (n=60), poor-quality trial found no differences between ultrasound versus traction or low-level laser therapy for acute radiculopathy in back or leg pain or function as measured by the RDQ or modified ODI.[506]

Harms

Harms were only reported in one good-quality trial of therapeutic ultrasound. This trial found no difference between ultrasound versus sham ultrasound in risk of any adverse event (6.0% vs. 5.9%, RR 1.03, 95% CI 0.49 to 2.13) or serious adverse events (1.3% vs. 2.7%, RR 0.48, 95% CI 0.12 to 1.88).[503]

Physical Modalities: Transcutaneous Electrical Nerve Stimulation

Key Points

- For acute or subacute low back pain, evidence from single trials with methodological shortcomings was too limited to permit reliable conclusions regarding effectiveness (SOE: insufficient).
- For chronic low back pain, a systematic review found no differences between transcutaneous electrical nerve stimulation (TENS) versus sham TENS in pain intensity (4 trials, WMD −4.47 on a 0 to 100 scale, 95% CI −12.84 to 3.89) or function (2 trials, WMD −1.36 on a 0 to 100 scale, 95% CI −4.38 to 1.66) at short-term followup; most trials found no effect on pain or function at the end of a course of treatment (SOE: low for pain and function).
- For chronic low back pain, a systematic review found no differences between TENS versus acupuncture for short- (4 trials; SMD 0.15, 95% CI −0.33 to 0.63) or long-term pain (2 trials; SMD 0.32, 95% CI −0.33 to 0.96). Evidence for TENS versus other interventions was too limited to permit reliable conclusions (SOE: low for TENS vs. acupuncture).
- Evidence on harms associated with TENS was limited, but suggests an increased risk of skin site reactions without an increased risk of serious adverse events (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included a good-quality systematic review[507] of TENS versus sham that included one good-quality trial,[508] and one poor-quality trial.[509] The first (good quality) trial (n=145) compared 4 weeks of treatment with followup 2 months after treatment cessation.[508] The second trial (n=30) compared 2 weeks of TENS versus sham, with no post-treatment followup, and was rated poor quality due to lack of blinding, unclear allocation concealment, and incomplete outcome data.[509] The APS/ACP review also included evidence from systematic reviews of acupuncture,[363] massage,[510] spinal manipulation,[426] traction, and superficial heat and cold[511] that each included one to five trials of TENS versus these interventions. The APS/ACP review concluded that there was insufficient to determine the effects of TENS for acute or chronic low back pain.

We identified a more recent good-quality systematic review of TENS versus sham TENS[512] that included the good-quality trial described above508 and four other trials (Table 10; Appendix Tables E31, F31).[508, 513-516] The poor-quality study discussed above[509] was not included, presumably because there was no post-treatment followup. The studies enrolled between 50 and 324 patients with chronic low back pain. Duration of treatment ranged from 2 to 8 weeks in five trials[508, 513, 514, 516] and duration of followup ranged from 2 to 11 weeks in three trials;[508, 513, 516] duration of followup was not reported in one crossover study.[515] One trial also included an exercise comparison group and one trial[513] included a PENS comparison group. Three trials were classified as higher-quality[508, 514, 516] based on meeting at least six of eleven Cochrane Back Review Group criteria; common methodological shortcomings were failure to repeat adequate allocation concealment techniques, unblinded design or unclear blinding status, and failure to report intention-to-treat analysis.

We identified three other trials of TENS for chronic low back pain that compared TENS versus sham TENS[517, 518] or interventional therapy[519] (Table 20; Appendix Tables E32, F32). Two fair-quality trials (n=236[517] and n=21[518]), one of which included patients with or without radicular symptoms[517] evaluated TENS (3 months or 5 weeks of treatment) versus sham TENS. The third, good-quality trial (n=150), evaluated 2 weeks of TENS treatment versus interferential therapy.[519] All three trials only evaluated outcomes at the end of treatment.

TENS Versus Sham TENS

Chronic Low Back Pain

For chronic low back pain, a good-quality trial (n=145) included in the APS/ACP review found no differences between TENS versus sham TENS in pain, functional status, or other outcomes after 4 weeks of treatment or 11 weeks total followup.[508] A smaller (n=30) trial included in the APS/ACP review found TENS associated with decreased pain versus sham TENS (WMD −33.6, 95% CI −52.3 to −14.0), but only evaluated outcomes immediately after a 60-minute treatment session.[509]

A systematic review which included the good-quality trial described above and three other trials published subsequent to the APS/ACP review found no statistically significant differences between TENS versus sham TENS in pain scores at followup ranging from 2 weeks to 3 months (4 trials, WMD −4.47, 95% CI −12.84 to 3.89).[512] There was also no difference between TENS versus sham in disability (2 trials, WMD −1.36, 95% CI −4.38 to 1.66.)

Two trials (n=21 and n=236) that were not included in the systematic review reported results that were generally consistent.[517, 518] Both trials found no differences between TENS versus sham TENS on any outcome after 6 weeks of treatment, including mean pain scores,[518] patient satisfaction, and functional improvement.[517] However, after 3 months of treatment, one of the trials, which enrolled patients with radicular or nonradicular low back pain, found TENS associated with greater likelihood of experiencing improvement ≥50 percent from baseline in VAS score versus sham for both lumbar (RR 3.71, 95% CI 1.69 to 8.18) and radicular pain (RR 2.26, 95% CI 1.13 to 4.51).[517] However, mean changes in pain scores were not reported, there were no statistically significant differences between TENS versus sham TENS on other 3-month outcomes, including function, quality of life, and patient satisfaction, and the trial did not

report outcomes following the end of treatment. Estimates of effect were somewhat stronger in subgroups of patients with radicular symptoms or a neuropathic pain component, but estimates were imprecise, with overlapping CIs.

TENS Versus Other Interventions

Acute Low Back Pain

Evidence on effectiveness of TENS for acute or subacute low back pain was limited. For acute low back pain, one small fair-quality trial (n=20) found acupuncture superior to TENS for pain (mean difference 21 on a 0 to 100 VAS score, 95% CI 4.13 to 38).520

Chronic Low Back Pain

For chronic low back pain, the APS/ACP review found no difference between TENS versus acupuncture in short- (4 trials; SMD 0.15, 95% CI −0.33 to 0.63) or long-term pain (2 trials; SMD 0.32, 95% CI −0.33 to 0.96)[363] or between TENS versus gentle ice massage (1 trial),[521] though the quality of evidence was fair to poor for both comparisons.[29] Evidence for TENS versus other interventions was limited and mixed. Based on one trial traction was superior to TENS,[522] and minimal ice massage was inferior in one trial[523] with no difference in another trial.[521]

A systematic review[512] published subsequent to the APS/ACP review included one trial of TENS versus exercise[508] and one trial of TENS versus PENS[513] for chronic low back pain. Each review reported no statistically significant differences in pain or disability. One trial not included in prior reviews of TENS versus interferential therapy found no differences in pain or disability, though for one measure (the McGill Pain Questionnaire pain rating index) interferential therapy was superior to TENS (mean change from baseline −17.66 vs. −25.34, p>0.05).[519]

Harms

The APS/ACP review found limited evidence on harms from trials of TENS, though there was no clear difference between active versus sham TENS in likelihood of minor skin irritation at the application site. In one trial published since the APS/ACP review, active TENS was associated with greater likelihood of application skin site reactions versus sham TENS (9% vs. 3%; RR 3.73, 95% CI 1.07 to 13).[517] There were no significant differences in risk of other harms, including withdrawals due to adverse events (3% vs. 0.8%; RR 3.05, 95% CI 0.32 to 29) and serious adverse events (4% vs. 5%; RR 0.73, 95% CI 0.24 to 22), though event rates were low and estimates imprecise.

Physical Modalities: Electrical Muscle Stimulation

Key Points

- There was insufficient evidence from five RCTs to determine effects of electrical muscle stimulation plus exercise versus exercise alone or versus other interventions, due to methodological limitations and imprecision (SOE: insufficient).

- There was insufficient evidence to determine harms of electrical muscle stimulation (SOE: insufficient).

Detailed Synthesis

The APS/ACP review did not evaluate effects of electrical muscle stimulation for low back pain. We identified five trials on the effects of electrical muscle stimulation for low back pain (Table 21; Appendix Tables E33, F33).[492, 499, 524-526] The sample size ranged from 28 to 80 in four trials and was 164 in the fifth trial.[492] Four trials enrolled patients with chronic low back pain and the fifth trial[492] enrolled patients with back pain of 3 weeks to 6 months in duration. Two trials compared electrical muscle stimulation plus exercise versus exercise,[499, 524] one trial electrical muscle stimulation plus exercise versus sham stimulation plus exercise,[525] and three trials electrical muscle stimulation versus other interventions (ultrasound,[499] TENS or sham TENS,[526] and massage, manipulation, or lumbar supports[492]), with or without exercise. The duration of stimulation sessions ranged from 15 minutes to at least 8 hours, the number of sessions ranged from 2 to 60, and the duration of treatment ranged from 2 days to 2 months. The technical parameters of the stimulation varied. Outcomes were assessed at the end of 2 days to 8 weeks of therapy in four trials and at 6 months (4 months after the end of therapy) in the fifth trial.[525] One trial was rated fair quality[492] and the other four poor quality. Methodological shortcomings included unclear randomization and allocation concealment methods, unblinded design, and lack of intention-to-treat analysis. In two trials, some subscales of the SF-36 were analyzed as mean differences and others as median differences without a rationale.[499, 524]

Electrical Muscle Stimulation Plus Exercise Versus Sham Stimulation Plus Exercise

Chronic Low Back Pain

One poor-quality (n=55) trial found no differences between 2 months of therapy with electrical muscle stimulation plus exercise versus sham stimulation plus exercise in subscales of the Low Back Pain Outcome Instrument or the SF-36 mental health subscale after 2 or 6 months.[525] Although the trial reported some differences as statistically significant, this does not appear to be possible based on the mean scores and standard deviations (e.g., for the Low Back Pain Outcome Instrument Expectations Met subscale, scores of 2.71[standard deviation 0.77] vs. 2.56 [0.71] were reported as having a $p<0.05$). The trial reported very high (>50%) attrition at 6 months.

Electrical Muscle Stimulation Plus Exercise Versus Exercise Alone

Chronic Low Back Pain

Two poor-quality trials (n=41 and n=68) each found electrical muscle stimulation plus exercise superior to exercise for pain at the end of a 6- or 8-week course of therapy.[499, 524] Differences in pain scores averaged 2.9 and 1.5 points on a 0-10 VAS scale. Effects on the ODI were mixed (differences 12.6 and 1.6 points). Electrical muscle stimulation was superior to exercise on some SF-36 subscales.

Electrical Muscle Stimulation Versus Other Interventions

Acute/Subacute Low Back Pain

One fair-quality trial (n=164) found no difference between electrical muscle stimulation (at least 8 hours/day) versus manipulation, massage, or lumbar support in improvement in pain (range −9.6 to −24 on a 0-100 VAS) after a 3-week course of therapy.[492]

Chronic Low Back Pain

One poor-quality crossover trial (n=24) found no difference between electrical muscle stimulation versus TENS or sham TENS in pain scores after a 2-day course of therapy (39.7 vs. 40.6 vs. 44.8 on a 0-100 VAS scale).[526] However, the combination of electrical muscle stimulation plus TENS was more effective than sham TENS (36.3 vs. 44.8, p=0.02). Another poor-quality trial (n=59) found no differences between electrical muscle stimulation plus exercise versus ultrasound plus exercise in the pain scores (0.4 vs. 0.9 on 0-10 VAS) or the ODI (6.80 vs. 8.60) after a 6-week course of therapy.[499]

Harms

One trial of electrical muscle stimulation reported no adverse treatment effects.[526] The other trials did not report harms.

Physical Modalities: Percutaneous Electrical Nerve Stimulation

Key Points

- There was insufficient evidence from seven trials to determine effects of percutaneous electrical nerve stimulation (PENS) versus sham, PENS plus exercise versus exercise alone, or PENS versus other interventions, due to methodological limitations, inconsistency and imprecision (SOE: insufficient).
- Harms were poorly reported in trials of PENS (SOE: insufficient).

Detailed Synthesis

Percutaneous electrical nerve stimulation (PENS) involves the application of an electrical nerve stimulus via needles placed at the dermatomal levels corresponding to the pain (rather than at acupuncture sites). The APS/ACP review[29] included four trials (n=34 to 64) of percutaneous electrical nerve stimulation (PENS) for low back pain.[513, 527, 528] Two trials compared PENS versus sham PENS,[513, 527] one trial compared PENS plus physical therapy versus sham PENS plus physical therapy,[528] three trials compared PENS versus TENS,[513, 527, 529] and one trial compared PENS versus exercise.[513] Two trials enrolled patients with nonradicular low back pain,[513, 528] one trial enrolled patients with radicular back pain,[527] and one trial did not specify presence or absence of radicular symptoms.[529] All trials enrolled patients with chronic low back pain; although the trial of radicular back pain enrolled patients with symptoms for >6 weeks, the mean duration was 21 months.[513] PENS was administered two or three times weekly for 2 to 8 weeks, with each session 15 to 45 minutes in duration. Outcomes were assessed at the end of treatment

in two trials,[513, 527] and 8 weeks[529] or 3 months[528] after the end of treatment. The APS/ACP review concluded that there was insufficient evidence to determine the effectiveness of PENS for acute or chronic low back pain.

We also identified three trials not included in the APS/ACP review (Table 22; Appendix Tables E34, F34). One trial (n=200) compared PENS (two 30-minute sessions weekly for 6 weeks), PENS plus supervised and home exercise, control (minimal) PENS plus exercise, and control PENS alone. One trial (n=112) compared PENS (three 30-minute sessions weekly for 3 weeks) versus dry needling for chronic low back pain.[530] The other trial (n=75) compared different durations of PENS therapy (15, 30, or 45 minutes 3 times a week for 2 weeks) versus sham PENS (insertion of needles without stimulation).[531] Outcomes were assessed at the end of treatment in both trials.

Among all trials, two trials were rated fair quality[528, 532] and the rest were rated poor quality. Methodological shortcomings included inadequate description of randomization and allocation concealment methods, failure to report attrition, unblended or unclearly blinded design and failure to report intention-to-treat analysis. Three trials with a crossover design had a 1 week washout between treatments, but did not evaluate for potential carryover effects.[513, 527, 531]

PENS Versus Sham PENS

Chronic Low Back Pain

For chronic non-radicular low back pain, one fair-quality trial (n=200) found no difference between PENS versus a control (minimal) PENS intervention in pain, function, quality of life, or other outcomes at the end of a 6-week course of therapy or through 6-month followup.[532] One poor-quality trial (n=60) of patients with nonradicular low back pain[513] found PENS superior to sham PENS for pain at the end of a 3-week course of therapy. The difference in mean pain scores in was about 2 points ($p<0.05$) on a 0-10 VAS scale. PENS was also associated with greater improvement in SF-36 physical and mental component summary scores, but effects were small (less than 7 points on a 0 to 100 scale for the physical component and <3 points for the mental component). PENS was also associated with better quality of sleep and decreased opioid use.

One poor-quality trial (n=75) not included in the APS/ACP review found PENS administered for varying durations (15, 30, or 45 minutes) similarly effective versus sham PENS for pain relief.[531] Differences ranged from 3.4 to 3.9 points on a 0-10 VAS scale at the end of a 2-week course of treatment. Although the three PENS interventions were also more effective than sham PENS on the SF-36 physical and mental component scores, sleep quality, and use of nonopioid analgesics, there was some evidence of a dose threshold effect, with the 15-minute intervention associated with smaller effects than the 30- and 45-minute interventions.

Radicular Low Back Pain

One poor-quality trial (n=64) of patients with radiculopathy[527] found PENS superior to sham PENS for pain at the end of a 3-week course of therapy. The difference in mean pain scores in was about 2 points ($p<0.05$) on a 0-10 VAS scale. PENS was also associated with greater improvement in SF-36 physical and mental component summary scores, but effects were small

(less than 7 points on a 0 to 100 scale for the physical component and <3 points for the mental component). PENS was also associated with better quality of sleep and decreased opioid use.

PENS Plus Exercise Therapy Versus Sham PENS Plus Exercise Therapy

Chronic Low Back Pain

For chronic nonradicular back pain, one fair-quality trial (n=34) included in the APS/ACP review found PENS plus physical therapy superior to sham PENS plus physical therapy for pain.[528] The difference in the Multidimensional Pain Inventory pain severity score was about 1 point (0 to 6 scale) 3 months after an 8-week course of treatment. Physical therapy consisted of exercise, physical modalities, manual therapies, and education to meet patient goals. There were no differences on the RDQ, Geriatric Depression Scale, or Pittsburgh Sleep Quality Index. However, a fair-quality trial published subsequent to the APS/ACP review found no differences between PENS plus exercise therapy versus control (minimal) PENS plus exercise therapy in pain, the RDQ, or other outcomes through 6-month followup after a 6-week course of treatment.[532]

PENS Versus TENS

Chronic Low Back Pain

Three trials included in the APS/ACP review evaluated PENS versus TENS for chronic low back pain.[513, 527, 529] Two poor-quality trials (n=40 and 60) each found PENS superior to TENS for pain, though effects may not be sustained. In one trial, the difference was 2.1 points on a 0-10 VAS scale at the end of a 3-week course of therapy.[513] In the other, the difference was 17 points on a 0-100 VAS scale at the end of an 8-week course of therapy ($p<0.01$), but the difference was smaller (6 points) and no longer statistically significant 8 weeks later.[529] Effects of therapy consisting of 4 weeks of PENS followed by 4 weeks of TENS were similar to effects of 8 weeks of TENS. PENS was also superior to sham TENS on measures of function, but neither trial reported standardized measures of back-specific function. In one trial, PENS was superior to sham PENS on the SF-36 physical and mental component summary scores, though effects were small (differences of 4.66 and 1.7 points, respectively).[513]

Radicular Low Back Pain

One poor-quality trial (n=64) of patients with radicular back pain included in the APS/ACP review found PENS superior to sham PENS for pain at the end of a 3-week course of therapy (difference 1.3 points on a 0-10 scale, $p<0.01$).[527] PENS was also superior to sham PENS on the SF-36 physical and mental component scores, though effects were small (5.7 and 2.1 points, respectively).

PENS Versus Other Interventions

Chronic Low Back Pain

For chronic low back pain, one poor-quality trial (n=60) included in the APS/ACP review found a 3-week course of PENS more effective than a minimal exercise intervention (flexion and extension while seated) for pain (mean difference 2.1 points on a 0-10 VAS), level of activity, and quality of sleep.[513] PENS was also more effective than exercise on the SF-36 physical and mental component scores, but differences were small. A fair-quality trial (n=200) published subsequent to the APS/ACP review found no difference between PENS versus control (minimal) PENS plus exercise in pain, the RDQ, or other outcomes through 6 months followup after a 6-week course of treatment.[532]

One poor-quality trial (n=112) published subsequent to the APS/ACP review of patients with chronic nonradicular back pain found no differences between a 3-week course of PENS versus dry needling in pain, the ODI, and sleep quality at the end of treatment.[530]

Harms

Harms were poorly reported in trials of PENS therapy. One trial reported no treatment-related adverse events, though one patient withdrew due to worsening low back pain.[532]

Physical Modalities: Interferential Therapy

Key Points

- There was insufficient evidence from four trials to determine effects of interferential therapy versus other interventions, or interferential therapy plus another intervention versus the other interventions lone, due to methodological limitations and imprecision (SOE: insufficient).
- No study evaluated harms of interferential therapy (SOE: insufficient).

Detailed Synthesis

The APS/ACP review[29] included three trials (n=151 to 240) of interferential therapy for low back pain.[533-535] No trial compared interferential therapy versus sham therapy. One trial each compared interferential therapy versus spinal manipulation[533] or traction.[535] One of these trials also compared interferential therapy versus the combination of interferential therapy plus spinal manipulation.[533] The third trial compared interferential therapy applied to the painful area versus to the area of the spinal nerve, each in combination with a self-care book, as well as against the self-care book alone.[534] The trials focused on patients with nonradicular low back pain. The duration of symptoms was 4 to 12 weeks in two trials[533, 534] and unspecified (mainly chronic) in the third.[535] The trials varied in the number (range 3 to 10) and duration (10 to 30 minutes) of interferential therapy sessions and in technical parameters. Outcomes were assessed at 3 to 12 months (1 week to 10 months following the end of therapy). All of the trials were rated poor quality; methodological shortcomings included failure to blind patients or care providers, high

attrition, and failure to perform intention-to-treat analysis; one trial[534] also reported potentially important baseline differences. The APS/ACP review concluded that there was insufficient to determine the effectiveness of interferential therapy for acute or chronic low back pain.

One trial (n=62) published subsequent to the APS/ACP review evaluated interferential therapy versus superficial massage for chronic low back pain (Table 23; Appendix Tables E35, F35).[536] Interferential therapy was administered for 30 minutes in 20 sessions over 10 weeks, with outcomes assessed at the end of therapy. The trial was rated fair quality; methodological shortcomings included unblinded design and failure to report use of cointerventions and compliance to assigned therapies.

Interferential Therapy Versus Other Interventions

The two poor-quality trials included in the APS/ACP review found no differences between interferential therapy versus spinal manipulation for subacute low back pain[533] or interferential therapy versus traction[535] for low back pain of unspecified duration (primarily chronic) on pain, function, or other outcomes.

One subsequent, fair-quality trial (n=62) found interferential therapy associated with greater improvement from baseline in pain (0-10 VAS, difference −1.06, 95% CI −1.91 to −0.22) and the RDQ (0-24, difference −3.01, 95% CI −4.53 to −1.47) versus superficial massage at the end of a 10-week course of therapy, though effects on the ODI were not statistically significant (0-100, difference −5.20, 95% CI −10.82 to 0.42) and longer-term effects were not assessed.536 There were no statistically significant differences on seven of eight SF-36 subscales. The superficial massage intervention appeared to be designed as a sham or subtherapeutic control treatment.

Interferential Therapy Plus Another Intervention Versus the Other Intervention Alone

One poor-quality trial found a 3-week course of interferential therapy applied to the paraspinal area (near the target spinal nerve) plus a back self-care book associated with greater improvement in the RDQ (0-24, −6.0 vs. −4.0, $p<0.05$) after 3 months, though there were no differences in the McGill Pain Rating Index or the EQ-5D.[534] However, effects on the RDQ are difficult to interpret as there were baseline differences (median 9.0 vs. 5.0) and scores at 3 months were identical (1.0 vs. 1.0). There were no differences between interferential therapy applied to the painful area plus a self-care book versus the self-care book alone. One of the trials described above no differences between the combination of interferential therapy plus spinal manipulation versus manipulation alone.[533]

Harms

No trial of interferential therapy reported harms.

Physical Modalities: Superficial Heat or Cold

Key Points

- For acute or subacute low back pain, a systematic review found a heat wrap more effective than placebo for pain relief at 5 days (2 trials, mean difference 1.06 on a 0 to 5 scale, 95% CI 0.68 to 1.45) and disability at 4 days (mean difference −2.10 on the RDQ, 95% CI −3.19 to −1.01). Two subsequent trials also found a heat wrap associated with decreased pain intensity at 3 to 4 days (differences 16 to 20 points on a 0- to 100-point VAS) or increased pain relief at 8 hours (difference ~1.5 points on a 0 to 5 scale). Another trial found a heat wrap during emergency transport associated with substantially lower pain intensity versus an unheated blanket upon arrival to the hospital (SOE: moderate for pain and function).
- For acute low back pain, one higher-quality trial found heat plus exercise associated with greater pain relief at day 7 (mean difference 1.40 on 0 to 10 scale, 95% CI 0.69 to 2.11) and on the RDQ (mean difference −3.20 on the RDQ, 95% CI −5.42 to −0) versus exercise without heat (SOE: low).
- One fair-quality trial found heat plus an NSAID associated with better pain scores versus an NSAID without heat at day 15, based on the McGill Pain Questionnaire (scoring methods unclear) (SOE: insufficient).
- For acute or subacute low back pain, a systematic review included one trial that found heat more effective for pain relief than acetaminophen (mean difference 0.90 on a 0 to 10 scale, 95% CI 0.50 to 1.30) or ibuprofen (0.65, 95% CI 0.25 to 1.05) after 1 to 2 days of treatment; the heat wrap was also associated with greater improvement on the RDQ (mean differences 2.00 on a 0 to 24 scale, 95% CI 0.86 to 3.14 and 2.20, 95% CI 1.11 to 3.29, respectively) (SOE: low for pain and function).
- For acute low back pain, a systematic review included one trial that found no clear differences between heat versus exercise in pain relief or function (SOE: low).
- No study compared superficial cold versus placebo or no cold treatment.
- For acute low back pain, one small trial with methodological shortcomings found cold plus naproxen associated with better pain scores versus naproxen alone, based on the McGill Pain Questionnaire (methods for scoring unclear). (SOE: insufficient).
- There was insufficient evidence from three trials to determine effects of heat versus cold, due to methodological limitations and imprecision (SOE: insufficient).
- Heat was not associated with increased risk of skin flushing versus no heat or placebo in two trials; no serious adverse events were reported with use of heat (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included a good-quality systematic (Cochrane) review[511] of nine controlled clinical trials on the effects of heat or cold on low back pain. An updated version of the review was published in 2011, but included no additional trials (Table 2; Appendix Tables

E36, F36).[537] Of the studies included in the systematic review, five were randomized parallel-group trials.[42, 538-541] The other four used alternate allocation or did not describe the allocation method;[521, 542-544] one was a parallel group trial[542] and the other three used a crossover design.[521, 543, 544] Four trials evaluated hot packs or heated wraps versus placebo or nonheated wraps,[42, 539-541, 544] one trial heat plus exercise versus heat or exercise alone,[538] one trial heat versus ibuprofen or acetaminophen,[42] and two trials hot packs versus ice massage.[542, 543] One trial[521] compared ice massage versus TENS and is discussed in the TENS section of this report. The sample sizes ranged from between 36 and 371 participants with acute pain (1 trial); mixed acute and subacute pain (4 trials); chronic (3 trials) or mixed acute pain; and subacute and chronic (1 trial) pain. Duration of treatment was generally 1 week or less, with followup no longer than 1 or 2 days after the end of treatment. In one trial, treatment duration was 25 to 27 minutes, with immediate post-treatment followup.[541]

The systematic review rated the five RCTs[42, 538-541] higher quality, based on meeting at least 6 of 11 Cochrane Back Review Group criteria,[545] and the remaining studies were rated lower quality.[521, 542-544] All studies had methodological limitations, including unblinded design and failure to adequately report methods of randomization and allocation concealment.[511] Four trials reported funding by manufacturers of heat wraps.

We identified two fair-quality trials (n=30 and 51) published subsequent to the systematic review of heat therapy (4 hours daily for 4 days, 8 hours for 1 day) versus no heat therapy (Table 24; Appendix Tables E37, F37).[546, 547] One trial[547] enrolled patients with acute low back pain and the other [546] included patients with acute or subacute low back pain. Methodological shortcomings included inadequate description of randomization and allocation concealment methods and nonblinded design; one trial[546] also had high (21%) attrition. Both trials were funded by a manufacturer of heat wraps. We also identified a fair-quality trial (n=87) that compared superficial heat (hot water bottle 20 minutes twice daily for 1 week) plus naproxen 500 mg bid, superficial cold (ice 20 minutes twice daily for 1 week) plus naproxen, or naproxen alone for acute low back pain[548] and a small (n=43), poor-quality trial of patients with acute low back pain in an occupational health setting evaluated3 days of heat-wrap therapy plus education versus education only through 14 days.[549] Methodological shortcomings included inadequate description of randomization and allocation concealment, failure to report attrition, and unblinded design.

Heat Versus Placebo

Acute or Subacute Low Back Pain

For acute or subacute low back pain, the systematic review[511] found a heat wrap more effective versus placebo for short-term pain relief (mean difference at 5 days 1.06 on a 0 to 5 scale, 95% CI 0.68 to 1.45) and improvement in disability (mean difference at 4 days −2.10 on the RDQ, 95% CI −3.19 to −1.01) based on pooled results from two trials.[539, 540] Effects on pain intensity were about 10-13 points on a 0- to 100-point scale in one trial and about 0.7 to 1 point on a 0- to 10-point scale in the other trial, and effects on the RDQ were about 2-3 points in both trials. One other trial that could not be pooled found a heat wrap applied during emergency transport associated with substantial lower pain intensity upon arrival at the hospital versus an unheated blanket (mean difference from baseline −32.3 vs. 0.8 on a 0 to 100 VAS).[541] A fourth trial did not report effects on pain or disability.[544]

A small, fair-quality trial (n=38) not included in the systematic review found a heat wrap for acute or subacute low back pain associated with decreased pain versus no heat wrap after 3 (mean 31 versus 57 on a 0 to 100 VAS; p=0.02 [data estimated from graph]) or 4 days (27 versus 47; p=0.04); effects at 1 to 2 days also favored the heat wrap, but were smaller and not statistically significant.[546] The heat wrap was also associated with lower likelihood of waking in the night due to pain at day 2 (7% [1/15] versus 53% [8/15]; RR 0.13, 95% CI 0.02 to 0.88); no patients in the heat wrap group reported night waking on days 3 and 4 (compared with 67% and 59% of no heat wrap patients) Another fair-quality trial (n=51) found a heat wrap for acute low back pain associated with increased pain relief versus oral placebo, but only evaluated outcomes after 8 hours of treatment (mean pain relief score 3.0 vs. 1.5 on 0 [very poor] to 5 [excellent] scale).[547]

Heat Versus Another Intervention Versus the Other Intervention Without Heat

One higher-quality trial (n=100) included in the systematic review found heat plus exercise for acute low back pain superior to exercise alone for pain relief at day 7 (mean difference 1.40 on 0 to 10 scale, 95% CI 0.69 to 2.11). Effects were smaller (mean differences 0.50 to 0.80) on days 2 and 4 and not statistically significant.[538] Heat plus exercise was also superior to exercise alone at day 7 (mean difference −3.20 on the RDQ, 95% CI −5.42 to −0.0), but not at day 2 (0.60, 95% CI −0.79 to 1.99) or day 4 (−1.20, 95% CI −3.14 to 0.74).

Two trials not included in the systematic review compared heat versus another intervention versus the other intervention without heat. A fair-quality trial (n=58) found a hot water bottle for 20 minutes plus naproxen 500 mg twice daily associated with better scores on the McGill Pain Questionnaire (scoring methods unclear).[548] A poor-quality trial (n=43) found 3 days of heat wrap therapy plus education associated with decreased pain intensity at day 3 (mean difference −2.05, 95% CI −3.34 to −0.76 on a 0 to 10 pain scale) through day 14 (mean difference −1.63, 95% CI −2.92 to −0.34) as well as on the RDQ (difference −2.37, 95% CI −5.62 to 0.85 at day 4 and −4.02, 95% CI −7.82 to −0.24 at day 14), versus education without heat wrap.[549]

Heat Versus Other Active Treatments

For acute or subacute pain, the systematic review[537] included one higher-quality trial (n=371) that found heat more effective for pain relief than acetaminophen (mean difference 0.90 on a 0 to 10 scale, 95% CI 0.50 to 1.30) or ibuprofen (0.65, 95% CI 0.25 to 1.05) after 1 to 2 days of treatment.42 The heat wrap was also associated with greater improvement on the RDQ versus acetaminophen (mean difference 2.00 on a 0 to 24 scale, 95% CI 0.86 to 3.14) and ibuprofen (2.20, 95% CI 1.11 to 3.29).[42]

One higher-quality trial (n=100) included in the systematic review found small, nonstatistically significant differences favoring heat versus exercise in pain relief (mean difference 0.40 on a 0 to 10 scale at days 1 to 2, 95% CI −0.15 to 0.95; mean difference 0.30 at day 7, 95% CI −0.68 to 1.28) and function (mean difference −0.70 on the RDQ at day 4, 95% CI −2.09 to 0.69; mean difference −0.90 at day 7, 95% CI −2.84 to 1.04).[538]

Cold Versus Placebo

No study compared cold versus placebo or no cold.

Cold Versus Another Intervention Versus the Other Intervention Without Cold

A fair-quality trial (n=58) found ice for 20 minutes plus naproxen 500 mg twice daily associated with better scores based on the McGill Pain Questionnaire (scoring methods unclear).[548]

Cold Versus Other Active Treatments

One lower-quality trial included in the systematic review[537] found no differences between ice massage versus TENS (see the TENS section of this report.)[521]

Heat Versus Cold

Two lower-quality trials (n=117 and 36) included in the systematic review[537] evaluated heat versus cold.[542, 543] One trial found no difference between hot packs versus ice massage for back pain of mixed duration (treatment duration and followup not reported)[542] and one trial found ice massage superior to hot packs for chronic pain following two 20-minute treatments.[543] One fair-quality trial (n=58) not included in the systematic review found a hot water bottle twice daily for 1 week associated with no clear differences versus ice twice daily through 2 weeks, based on the McGill Pain Questionnaire (scoring methods unclear).[548]

Harms

The only adverse events reported in the systematic review[537] were from two trials that found no difference between heat wrap versus no heat or placebo in the risk of skin flushing at the application site in two trials of heat wrap versus no heat/placebo (5% [6/128] versus 0.8% [1/130]; RR 6.09, 95% CI 0.74 to 50; Appendix Table E36).[539, 540] No serious adverse events were reported. One trial not included in the systematic review reported two cases of headache with heat, versus no cases in the oral placebo group.[547]

Low-Level Laser Therapy

Key Points

- For acute low back pain, there was insufficient evidence from one trial to determine effectiveness of low-level laser therapy versus sham laser, due to serious methodological shortcomings and imprecision (SOE: insufficient).
- For chronic low back pain, three of four trials found low-level laser therapy more effective than sham laser for pain, though methods for assessing pain and duration of followup varied; two trials found low-level laser therapy more effective than sham laser for function, with small magnitude of effects (SOE: low for pain and function).

- For acute or subacute low back pain, one trial found low-level laser therapy plus an NSAID associated with lower pain intensity versus sham laser plus an NSAID or the NSAID alone (mean differences 9 to 14 points on a 0 to 100 VAS); effects on the ODI also favored combination treatment but were smaller (differences <6 points) (SOE: low).
- For chronic low back pain, there was insufficient evidence from three trials to determine effects of low-level laser therapy plus exercise versus the other sham laser plus exercise alone, due to methodological shortcomings and inconsistency (SOE: insufficient).
- There was insufficient evidence to determine effects of low-level laser therapy versus another intervention, due to methodological shortcomings and imprecision (SOE: insufficient).
- There was insufficient evidence to determine effects of different wavelengths of low-level laser therapy or different doses, due to methodological limitations and imprecision (SOE: insufficient).
- Harms were not well-reported in trials of low-level laser therapy, but no serious adverse events and no harms were reported (SOE: low)

Detailed Synthesis

Low level laser therapy involves administration of a single wavelength of light (usually from 632 to 904 nm) that does not emit heat but may affect underlying connective tissues and have potential anti-inflammatory effects. The APS/ACP review[29] included seven trials[550-556] of low-level laser therapy for low back pain. Four trials were conducted in patients with chronic low back pain, one trial in patients with acute low back pain, and two trials did not specify the duration of symptoms. The APS/ACP review found insufficient evidence to determine effectiveness of low-level laser therapy versus sham or other interventions, due to variability across trials in terms of laser types and doses, outcomes, duration of followup, and inconsistency in results. A recent systematic review[557] included six[550-555] of the trials included in the APS/ACP review plus one additional trial (Table 2).[558] We also identified five recently published trials not included in prior reviews (Table 25; Appendix Tables E38, F38).[559-563]

In total, after excluding one poor-quality trial with uninterpretable findings,[556] 10 trials assessed low-level laser therapy for low back pain.[550-555, 558-563] Laser wavelengths ranged from 830 to 10600 nm and five of the trials used a 904 nm laser.[551, 552, 555, 560, 562] Duration of treatment ranged from 1 day to 6 weeks, followup was from 1 day to 1 year, and there were 6 to 20 laser treatment sessions (1 trial[555] did not report the treatment protocol and 1 trial[553] assessed outcomes after a single treatment). Five trials compared laser versus sham[550-553, 559] and two trials compared different laser doses, either with[555] or without[562] a sham group. The other five trials compared laser plus another treatment (heat, exercise, or NSAID) versus the other treatment, either alone or in combination with sham laser.[554, 558, 560, 561, 563] Sample sizes in nine of the trials ranged from 20 to 120 and in the tenth (largest) study was [546.560] Patients had chronic low back pain in seven trials[550-552, 554, 558, 559, 563] and acute low back pain in three trials.[555, 560, 562] One trial enrolled both subacute and chronic pain patients[561] and one trial did not report the duration of pain.[553] Two trials[560, 561] were rated good quality, two[554, 555] poor quality, and eight trials fair quality. Methodological limitations in the fair- and poor-quality studies included inadequate reporting of

treatment allocation, unblinded design, use of cointerventions, unclear or low compliance, and high or unclear attrition.

Low-Level Laser Therapy Versus Sham or Placebo

Acute Low Back Pain

One poor-quality trial (n=120) of patients with acute low back pain compared two different laser wavelengths versus sham.[555] A higher proportion of patients in both active laser groups reported effective (undefined) treatment versus sham, with no difference among active groups, but point estimates were very imprecise. The number of treatments given in each group was not reported.

Chronic Low Back Pain

Three fair-quality trials[550, 552, 553] included in the APS/ACP review found laser more effective than sham treatment for pain and disability. All three trials (n=41 to 71)[550, 552, 553] reported significant differences between laser and sham for pain outcomes, though duration of followup (range 1 day to 6 months) and methods for assessing pain varied among the trials. One trial found a higher proportion of laser-treated patients reported >60% pain relief after 2 weeks of treatment (71% [27/38] vs. 36% [12/33]; RR 1.95, 95% CI 1.19 to 3.21)[552] and another found laser associated with higher likelihood of "effective" (undefined) treatment (94% [15/16] vs. 48% [12/25]; RR 1.95, 95% CI 1.27 to 2.99).[553] The third trial reported significantly different mean pain VAS scores (scale 0 to 100) between laser and sham after 4 weeks (19.1 vs. 35.1; mean difference −16.00, 95% CI −27.95 to −4.05).[550] One additional fair-quality trial (n=60) published subsequent to the APS/ACP review found no difference in improvement in VAS pain scores between laser versus sham laser after 2 weeks of treatment (0-10 scale, difference -0.3, 95% CI -1.0 to 0.3).[559]

One trial included in the APS/ACP review and one subsequent trial found low-level laser therapy associated with significantly better ODI scores versus sham (14.7 vs. 22.9; mean difference −8.20, 95% CI −13.44 to −2.96[550] and mean difference in improvement -0.3, 95% CI -0.6 to -0.1 [scale unclear][559]).

Low-Level Laser Therapy Plus Another Intervention Versus the Other Intervention Without Low-Level Laser Therapy

Acute or Subacute Low Back Pain

Two good-quality trials (n=80 and 546)[560, 561] assessed low-level laser therapy for acute or subacute low back pain. The larger trial found low-level laser therapy plus an NSAID, versus sham laser plus an NSAID or the NSAID alone, associated with improved pain (mean change −30.0 vs. −15.7 vs. −20.8 on 0 to 100 VAS), function (mean change −12.0 vs. −6.5 vs. −10.0 on the ODI) and the SF-36 physical component score (−4 vs. −2 vs. −3 on a 0 to 100 scale) after 3 weeks of treatment, although differences in disability and quality of life scores were small (<6 points on the ODI and 1 to 2 points on the SF-36 physical component score).[560] The smaller (n=80) trial found no difference between low-level laser therapy plus heat versus sham plus heat in pain (mean change from baseline −4.0 vs. −4.15 on 0 to 10 VAS; p=0.07) or disability (RDQ

mean change from baseline -6.0 vs. −5.65; p=0.39; ODI mean change from baseline −8.2 vs. −8.7; p=0.15); patient global assessment of pain was significantly worse with laser versus sham (mean change from baseline −3.0 vs. −4.7; p=0.006.)[561]

Chronic Low Back Pain

Four trials compared low-level laser therapy plus another intervention versus the other intervention alone for chronic low back pain.[551, 558, 561, 563] A good-quality trial (n=40) found laser plus heat associated with smaller improvements versus sham laser plus heat in pain scores (mean change −3.35 versus −3.95 on a 0 to 10 scale; p=0.03) and physician global assessment of pain (mean change −3.15 versus −4.05; p=0.01) at 3 weeks,[561] but differences were small (less than 1 point on a 0 to 10 scale).[564] Low-level laser therapy plus heat was associated with greater improvement in the RDQ (mean change −6.7 vs. −4.65 on a 0 to 24 scale; p>0.05) and modified ODI (mean change −9.6 vs. −6.2 on a 0 to 50 scale; p>0.05) versus sham laser plus heat.

Three fair-quality trials compared low level laser therapy plus exercise versus sham laser plus exercise for chronic low back pain.[551, 558, 563] The one small trial (n=20) found no differences in pain (mean change −1.3 vs. −1.2 on 0 to 7.5 scale; p=0.5) or the RDQ (mean change −1.8 vs. −3.0, p=0.9) at 1-month followup.[551] However, two other trials (n=54 and 100) found the combination associated with lower pain intensity (2.4 vs. 4.3 at 12 weeks; p=0.0005558 and 2.68 vs. 4.08 at 3 weeks on a 0 to 10 VAS563) and disability (16.8 vs. 24.1 on the 0 to 50 modified ODI; p=0.0001558).

Low-Level Laser Therapy Versus Other Interventions

The APS/ACP review included two poor-quality trials of low-level laser therapy versus other interventions, though one was uninterpretable due to methodologic and reporting limitations.[556] The other trial (n=75) found no differences between low-level laser therapy versus exercise in pain (mean change −4.2 vs. −3.60 on 0 to 10 VAS) or disability (mean change −16.4 vs. −16.9 on modified ODI).[554] A trial not included in the APS/ACP review found no difference between low-level laser therapy versus sham laser plus exercise for pain (4.4 vs. 4.3 on 0 to 10 VAS; p=0.87) or disability (20.8 vs. 24.1 on modified ODI; p=0.06).

Low-Level Laser Therapy Versus Low-Level Laser Therapy

One fair-quality trial (n=66) found no differences between 904 nm laser therapy at doses of 0.1, 1.0, and 4.0 joules per point (corresponding to 0.4, 4.0, and 16.0 joules daily) in pain scores after 2 weeks of followup, but 16.0 joules daily was associated with better functional outcomes related to walking (p=0.007), sitting (p=0.005), and standing (p=0.013) versus the lower doses.562 A poor-quality trial (n=120) found no difference between 904 nm versus 10600 nm low-level laser therapy in the likelihood of experiencing complete resolution of pain at 1-month followup (95% vs. 83%; RR 1.15; 95% CI 0.98 to 1.35.)[555]

Harms

Harms were not well-reported in trials of low-level laser therapy. The APS/ACP review[29] reported no harms associated with low-level laser therapy. Three subsequent trials described no

adverse events (including local adverse events), without providing further data.[558, 560, 562] One trial reported two withdrawals due to worsening pain across groups.[562]

Short-Wave Diathermy

Key Points

- For back pain of mixed duration, there was insufficient evidence from five RCTs to determine effects of short-wave diathermy versus sham diathermy, due to methodological limitations and imprecision (SOE: insufficient).
- No study evaluated harms of short-wave diathermy.

Detailed Synthesis

The APS/ACP review[29] included three trials (n=24 to 400) of short-wave diathermy for low back pain.[450, 475, 565] Two trials[475, 565] compared short-wave diathermy versus sham diathermy and all three trials compared short-wave diathermy versus other interventions (exercises,[565] traction,[565] or manipulation[450 , 475]). The trials focused on patients with nonradicular low back pain. One trial enrolled patients with acute (<3 weeks) back pain,[450] one trial patients with low back pain for 2 to 12 months,(Gibson) and the third patients with back pain for >1 week.[565] The trials varied in the number of sessions (6, 12, or not specified); only one trial[565] specified the duration of each session (20 minutes). Outcomes were assessed at the end of a 2-week course of therapy in two trials[450, 565] and at 12 weeks (8 weeks after the end of therapy) in the third trial.[475] Two trials[475, 565] were rated fair quality and one trial[450] poor quality; methodological shortcomings included unclear randomization and allocation concealment methods, failure to blind care providers and outcome assessors, and failure to report use of cointerventions and compliance. The poor-quality trial also did not blind patients. The APS/ACP review found insufficient evidence to determine effects of short-wave diathermy for acute or chronic low back pain.

Two trials (n=97 and 102) published subsequent to the APS/ACP review evaluated short-wave diathermy versus sham diathermy for chronic low back pain (Table 26; Appendix Tables E39, F39).[566, 567] Short-wave diathermy was administered for 15 minutes in 18 sessions over 6 weeks, with outcomes assessed at the end of therapy. Both trials were rated poor quality; methodological shortcomings included unclear randomization and allocation concealment methods, failure to report attrition, lack of intention-to-treat analysis, and failure to blind caregivers and outcome assessors.

Short-Wave Diathermy Versus Sham Diathermy

Mixed Duration Low Back Pain

Two fair-quality trials included in the APS/ACP review found no difference between 2 weeks of short-wave diathermy versus sham diathermy. In one trial of patients with low back pain for 2 to 12 months, short-wave diathermy was not superior to sham diathermy in median pain scores, the proportion free of pain, or the proportion with work or activity limitations through 12 weeks, with some trends favoring sham therapy.[475] In a trial of patients with back pain for >1 week, there

was no difference in the likelihood of a positive global response at the end of therapy (39% vs. 37%, RR 1.05, 95% CI 0.74 to 1.50).[565]

Two subsequent, poor-quality trials each found short-wave diathermy for chronic low back pain associated with better pain scores at the end of a 6-week course of therapy.[566, 567] However, in addition to the methodological shortcomings in the trials, they also used a nonstandardized method to assess pain (sum of Lattinen's score plus tenderness score plus 0-10 VAS). Other outcomes were not assessed.

Short-Wave Diathermy Versus Other Interventions

Mixed Duration Low Back Pain

Two fair-quality trials included in the prior APS/ACP review found no differences between a 2-week course of short-wave diathermy versus spinal manipulation[475] in pain, use of analgesics, or work or activity limitations through 12 weeks or versus extension exercises or traction565 in the likelihood of a positive global effect at the end of therapy. A small (n=24), poor-quality trial of patients with acute low back pain found short-wave diathermy associated with a lower likelihood of being "fully restored" than spinal manipulation at the end of a 2-week course of therapy (25% vs. 92%, RR 0.27, 95% CI 0.10 to 0.74).[450]

Harms

No trial of short-wave diathermy reported harms.

Lumbar Supports

Key Points

- For acute or subacute low back pain, there was insufficient evidence from five trials to determine effects of lumbar supports versus no lumbar supports or an inactive treatment, due to methodological shortcomings and inconsistent results (SOE: insufficient).
- For chronic low back pain, there was insufficient evidence from two trials to determine effects of lumbar supports versus no lumbar supports, due to methodological shortcomings and inconsistent results (SOE: insufficient).
- For back pain of mixed duration, one trial found an inextensible but not extensible lumbar support associated with greater improvement in function versus no lumbar support, but effects were small. There was no clear effect on function (SOE: low).
- For acute or subacute low back pain, one trial found no differences between a lumbar support plus an education program versus an education program alone in pain or function after 1 year (SOE: low for pain and function).
- For chronic low back pain, one trial found no difference between a lumbar support plus exercise (muscle strengthening) versus exercise alone in short-term (8 weeks) or long-term (6 months) pain or function (SOE: low for pain and function).

- Three trials found no clear differences between lumbar supports versus other active treatments in pain or function (SOE: low for pain and function).There was insufficient evidence from 3 trials to determine comparative effects of different types of lumbar supports for chronic low back pain or back pain of mixed duration, due to heterogeneous comparisons, methodological shortcomings and imprecision (SOE: insufficient).
- Trials reported no harms associated with use of lumbar supports (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included a good-quality systematic review[44] with six trials[39, 568-572] of lumbar supports for low back pain. Sample sizes ranged from 19 to 456 subjects. One of the trials was classified as high quality.[569] The APS/ACP review concluded that there was insufficient evidence to determine effects of lumbar supports for acute or chronic low back pain.

An updated version of the systematic review[573] with two additional trials[574, 575] (eight total) has since been published (Table 2; Appendix Tables E40, F40). Six trials compared lumbar supports versus no lumbar supports,3[9, 568, 569, 571, 572, 575] three trials lumbar supports versus other active interventions (e.g., spinal manipulation therapy, exercise, massage),[39, 568, 569, 575] and two trials compared different types of lumbar supports[570, 574] The types of lumbar supports included flexible and semi-rigid corset made of various materials and a pneumatic lumbar support. Duration of treatment ranged from 3 weeks to 2 months. Trials evaluated patients at the end of treatment; three trials[39, 568, 574] also evaluated patients 6 to 16 months after the end of treatment. Three trials enrolled patients with chronic pain[570, 574, 575] and four enrolled patients with low back pain of mixed duration;[39, 568, 569, 572] one trial[571] did not report the duration of pain. Sample sizes ranged from 19 to 456 (total n=1,361). All of the studies except for one[569] were rated lower quality by the systematic review, based on meeting at least 5 of 10 Cochrane Back Review Group criteria.[545] Methodological shortcomings in the trials included failure to describe adequate randomization and allocation concealment methods, lack of blinding of outcome assessors, inadequate or unclear compliance, and possible differential use of cointerventions.[573]

We identified three trials (n=50, 98 and 217) published since the updated Cochrane review of lumbar supports versus no support for subacute,[576] chronic,[577] or mixed duration low back pain578 and one trial (n=433) of lumbar supports plus education versus education alone for acute or subacute low back pain[579] (Table 27; Appendix Tables E41, F41). One of the trials also compared two types of lumbar supports (inextensible [stiffer] versus extensible).[578] Treatment duration was 2 weeks, 3 months, or 6 months in three trials, with followup up through the end of treatment. The fourth trial did not report treatment duration, but followed patients for 1 year. All four trials were rated fair quality; methodological limitations included unclear allocation concealment methods, unclear compliance and unblended design.

Lumbar Support Versus No Lumbar Support or an Inactive Therapy

Acute or Subacute Low Back Pain

The systematic review[573] included four trials of lumbar supports versus no lumbar support or an inactive therapy (light massage)[569] for acute or subacute low back pain. Meta-analysis was not performed due to clinical heterogeneity. One higher-quality trial (n=164)[569] and two lower-quality

trials (n=334 and 456)[39, 568] found no difference between lumbar supports versus no lumbar support in pain. The fourth, a lower-quality trial (n=216), found lumbar supports associated with higher likelihood of improvement in pain (95% [106/111] vs. 77% [79/103]; RR 1.25, 95% CI 1.11 to 1.40).[572] Only one trial evaluated function using standardized measures; it found no differences between a corset versus light message on the RDQ or ODI.[569] Evidence on return to work was mixed in two lower-quality trials one trial found no difference between lumbar support versus no support in time to return to work,[568] while the other trial found lumbar supports associated with greater likelihood of return to work at 3 weeks (85% [94/111] vs. 67% [70/105]; RR 1.27, 95% CI 1.09 to 1.49).[572] Two lower-quality trials (n=790) reported no difference in measures of global improvement.[39, 568]

A fair-quality trial (n=217) published subsequent to the systematic review evaluated lumbar supports versus no lumbar support for subacute low back pain.[576] It found lumbar supports associated with greater improvement in pain after 30 days (mean change −26.8 vs. −21.3; p=0.04) and 90 days (mean change −41.5 vs. −32.0; p=0.002) of use. Lumbar supports were also associated with greater improvement in function, based on the EIFEL score (mean change −5.4 vs. −4.0 at 30 days on a 0 to 24 scale; p=0.02 and −7.6 vs. −6.1 at 90 days; p=0.02).

Mixed Duration Low Back Pain

One fair-quality trial (n=98) of patients with acute to chronic low back pain found an inextensible lumbar support associated with better scores on the ODI (mean difference 9.4, 95% CI 2.2 to 16.6) and the Patient Specific Activity Scale (mean difference -1.4 on a 0 to 10 scale, 95% CI -2.3 to -0.4) and greater likelihood of ≥50 percent improvement in the ODI (RR 3.40, 95% CI 1.07 to 10.8) versus no lumbar support after 2 weeks of therapy among patients who also underwent physical therapy.[578] Effects on pain were small (<1 point on a 0-10 NRS) and were not statistically significant. Differences between an extensible lumbar support versus no lumbar support were smaller and did not reach statistical significance.

Chronic Low Back Pain

One lower-quality trial (n=79)[575] of lumbar supports versus no support for chronic pain found no differences in pain or functional outcomes after 2 months of treatment.[573] A small trial (n=50) published since the systematic review found use of lumbar supports associated with better pain and functional outcomes versus no lumbar support at 1 month (p<0.01; no data reported) based on assessment using the Japanese Orthopedic Association criteria, but effects were not sustained after 3 and 6 months of use.[577]

Lumbar Support Plus Another Intervention Versus the Other Intervention Without Lumbar Support

Acute and Subacute Low Back Pain

One fair-quality trial (n=433) published subsequent to the systematic review found no differences between a lumbar support plus an education program versus an education program alone in pain or function after 1 year, in patients with acute or subacute work-related back pain.[579]

Chronic Low Back Pain

One small, lower-quality trial (n=63) included in the systematic review found no difference between a lumbar support plus exercise (muscle strengthening) versus exercise alone in short-term (8 weeks) or long-term (6 months) pain or function.[574]

Lumbar Support Versus Other Treatments

Acute, Subacute, or Chronic Low Back Pain

The systematic review included one higher-quality (n=164)[569] and two lower-quality (n=334 and 456) trials[39, 568] of lumbar supports versus other active treatments.[573] None of the trials found a significant difference among lumbar supports and other treatments, including traction, spinal manipulation, exercise, physiotherapy or TENS, and pain outcomes. For function, results from the higher-quality trial were mixed,[569] with the lumbar support associated with better function versus spinal manipulation or transcutaneous muscle stimulation based on the RDQ, but no difference based on the ODI. There were no differences between lumbar supports and other active treatment for either time to return to work (1 trial) or global improvement (2 trials).[573]

One Type of Lumbar Support Versus Another

Chronic or Mixed Duration Low Back Pain

For chronic low back pain, one trial (n=79; lower quality) included in the systematic review[573] found no differences between a flexible versus semi-rigid corset in pain or functional outcomes after 2 months of use.[575] Another, small (n=19), lower-quality trial included in the systematic review found a lumbar support plus nonsupportive corset associated with greater improvement in short-term pain and back-specific function after 8 weeks followup versus the nonsupportive corset alone.[570]

A fair-quality trial (n=98) of patients with back pain of mixed duration found no clear differences between an inextensible versus extensible lumbar support in pain or the ODI after 2 weeks, though effects on the ODI favored the inextensible support (difference 4.1 points, 95% CI -2.8 to 11.1).[578]

Harms

No harms associated with use of lumbar supports were reported in the systematic review, and none of the four subsequent trials, though harms were not well reported.[576-579]

Traction

Key Findings

- For low back pain with or without radicular symptoms, a systematic review included 13 trials that found no clear differences with inconsistent effects of traction versus placebo, sham, or no treatment in pain, function, or other outcomes, though two trials reported favorable effects on pain in patients with radicular back pain (SOE: insufficient for pain and function).

- For low back pain with or without radicular symptoms, a systematic review included five trials that found no clear differences between traction versus physiotherapy versus physiotherapy alone (SOE: low).
- For low back pain with or without radicular symptoms, a systematic review included 15 trials of traction versus other interventions that found no clear between traction versus other active interventions in pain or function (SOE: low for pain and function).
- A systematic review included five trials that found no clear differences between different types of traction (SOE: low).
- Eleven trials of traction in a systematic review reported no adverse events or no difference in risk of adverse events versus placebo or other interventions. Three subsequent trials reported findings consistent with the systematic review (SOE: low).

Detailed Synthesis

The APS/ACP review[29] included a large, good-quality systematic review[580] with 23 trials of traction versus sham or no treatment, sham versus other interventions, or one type of traction versus another. The review was subsequently updated to include 32 trials with 2,762 patients (Table 2; Appendix Tables E42, F42).[581] Thirteen trials compared traction versus placebo, sham traction, or no treatment; 15 trials compared traction versus other active treatments (including exercise [6 trials], heat therapy [2 trials], or other passive physical modalities [7 trials]); and five trials compared one type of traction versus another. Ten trials assessed participants with chronic pain and participants with subacute pain were included in one trial. In the remaining trials, duration of pain was mixed (17 trials) or not clearly reported (5 trials). Of the 32 included trials, 23 enrolled populations with radicular low back pain. Among the other nine studies, eight enrolled a mixed population with radicular and nonradicular pain and one enrolled only patients with nonradicular low back pain. Duration of followup ranged from 1 week to 1 year. Only three studies[460, 582, 583] reported outcomes beyond 6 months followup. Sixteen of the 32 included trials were judged to have a low risk of bias (i.e., quality score ≥6/12.)

We also identified three trials (in four publications) not included in the updated systematic review (Table 28; Appendix Tables E43, F43).[584-587] Each trial (n=24 to 80) compared combination treatment with traction plus another active intervention versus the active intervention alone. None of the trials clearly stated the duration of low back pain in study participants, but inclusion criteria for two trials[584-586] required 3 months or more of pain at baseline (subacute/chronic) and the third[587] required no more than 6 months of pain at baseline (acute/subacute). Two trials compared 10 weeks of traction in combination with usual care (infrared lamp and stretching[584, 585] or hot packs and interferential therapy[586]) versus usual care alone. The third trial compared inversion traction plus physiotherapy with physiotherapy alone.[587] Study participants received treatment for 10 weeks in two trials[584-586] and for 4 weeks in the third,[587] with respective followup of 6 months and 56 weeks. Two trials were rated fair quality[584-586] and one poor quality.[587] Methodological shortcomings included unblinded design and in the case of the poor-quality study,[587] inadequate description of randomization and allocation concealment techniques, and incomplete followup.

Traction Versus Placebo, Sham, or No Treatment

Low Back Pain With or Without Radiculopathy

Although the updated systematic review included 13 trials of traction versus placebo, sham, or no treatment, few studies reported data suitable for meta-analysis.[581] For low back pain with or without radiation, two trials found traction associated with lower pain scores at 3- to 5-week followup (2 trials; mean difference VAS −18.49, 95% CI −24.12 to −12.87) but not at longer followup (6 weeks to 1 year). There were also no significant differences between traction versus placebo, sham or no treatment in functional status, global improvement, or return to work after 3 weeks to 6 months, though evidence was limited to one to four trials for each outcome. Among the trials not included in meta-analyses, there was no significant difference at 3- to 5-week followup in pain,[582, 588] functional status,[588] or global improvement.[588, 589]

Traction Plus Another Intervention Versus Another Intervention Alone

Low Back Pain With or Without Radiculopathy

The systematic review found few differences between traction plus another intervention versus the other intervention alone in pain, function, or global improvement for nonradicular or radicular low back pain based on five trials. All five trials compared traction plus physiotherapy versus physiotherapy alone, though evidence was limited to one to two trials for outcome and time point.[581]

Two trials published subsequent to the systematic review evaluated traction plus an active "usual care" intervention (infrared lamp and stretching or hot packs and interferential therapy) versus the usual care intervention alone.[584-586] One trial (n=80) found traction associated with better pain scores at 10 weeks (mean difference −1.20 on a 0 to 10 scale, 95% CI −1.87 to −0.53) and 6 months (mean difference −0.90, 95% CI −1.41 to −0.39) and improved function (mean difference in ODI scores −1.60 on 0 to 100 scale at 6 weeks, 95% CI −1.41 to −0.39 and −3.30 at 6 months, 95% CI −4.57 to −2.03).[584, 585] The other trial (n=64) found traction associated with better pain scores (mean difference −2.20 on 0 to 100 scale, 95% CI −2.79 to −1.62) and function (mean difference −8.10 on the ODI, 95% CI −9.60 to −6.60) at 6 months, though the differences were small.[586] A small (n=24), poor-quality trial of traction plus physiotherapy versus physiotherapy alone for radicular low back pain found no differences in pain, disability, or quality-of-life scores after 4 weeks of treatment and 6 weeks of followup, though traction was associated with lower likelihood of back surgery (23% vs. 82%; RR 0.28, 95% CI 0.10 to 0.79.)[587]

Traction Versus Other Active Treatments

Low Back Pain With or Without Radiculopathy

Although the updated systematic review included 15 trials of traction versus other active interventions, few of the included trials provided data suitable for inclusion in meta-analysis.[581] The review found no differences between traction versus other active treatments in two trials of low back pain with radicular symptoms (followup at 1 to 16 weeks) or in four trials of patients

with low back pain with or without radicular symptoms (followup at 1 year) in pain, functional status, and global improvement. We identified no trial published subsequent to the systematic review on traction versus other active treatments.

One Type of Traction Versus Another

Low Back Pain With or Without Radiculopathy

Five trials included in the updated systematic review compared different types of traction.[581] For low back pain of varying duration with or without radicular symptoms, one trial (n=26) found no difference between static versus intermittent traction in the likelihood of experiencing global improvement after 1 to 2 weeks (risk difference −0.08, 95% CI −0.46 to 0.30)[590] and one trial (n=67) found autotraction superior to mechanical traction (risk difference 0.53, 95% CI 0.32 to 0.73.)[591] For radicular low back pain, there were no differences among different types of traction (autotraction versus manual or mechanical traction [2 trials] and water versus land-based traction [1 trial]) in pain scores (3 trials; mean difference 6.58, 95% CI −2.77 to 16) or likelihood of global improvement (1 trial; risk difference −0.16, 95% CI −0.40 to 0.09.)

Harms

Eleven (of 32) studies included in the updated systematic review[581] reported adverse events; of those, four reported no events in either group. In the other seven trials, most found no difference between traction versus placebo or other treatments in risk of adverse events (including aggravation or worsening of symptoms), or with one type of traction versus another. However, one trial found inversion traction associated with increased likelihood of worsened pain versus conventional traction, although the estimate was imprecise (79% [11/14]) versus 15% [2/13]; RR 5.00, 95% CI 1.39 to 19.) Three trials published subsequent to the updated systematic review did not report adverse events[584-586] or reported no adverse events.587

Taping

Key Points

- For chronic low back pain, three trials found no differences between a Kinesio Taping® versus sham taping in back-specific function after 5 to 12 weeks; effects on pain were inconsistent (SOE: low for function, insufficient for pain).
- For chronic low back pain, there was insufficient evidence from 1 trial to determine effects of Functional Fascial Taping plus exercise versus sham taping plus exercise, due to methodological limitations and imprecision (SOE: insufficient).
- For chronic low back pain, two trials found no differences between Kinesio Taping® versus exercise therapy in pain or function (SOE: low for pain and function).
- No trial of taping reported harms.

Detailed Synthesis

The APS/ACP review did not evaluate taping for low back pain. We identified six trials on the effects of taping (Table 29; Appendix Tables E44, F44).[592-597] Sample sizes ranged from 20 to 60 in five trials and was 148 in the fifth trial.[597] Five trials evaluated Kinesio Taping®[592, 593, 595-597] and one trial Functional Fascial Taping.[594] Three trials of Kinesio Taping[592, 593, 597] and the trial of Functional Fascial Taping®[594] evaluated a sham taping (taping applied without tension) comparison. In the Functional Fascial Taping trial, patients in both groups also received instruction in home trunk flexion exercises. Among the Kinesio Taping trials, one trial[595] compared Kinesio Taping versus exercise therapy without Kinesio Taping, one trial[596] compared Kinesio Taping versus exercise therapy or the combination of taping and exercise, and one trial[592] compared Kinesio Taping plus physical therapy (hot pack, ultrasound, and TENS) versus sham taping plus physical therapy. The five trials of Kinesio Taping enrolled patients with chronic low back pain and the trial of Functional Fascial Taping enrolled patients with back pain for >6 weeks, though the median duration was 32 to 39 weeks. The taping techniques all involved some degree of tension, though the taping pattern, reapplication interval, and duration of treatment (7 days to 12 weeks) varied. Outcomes were assessed at the end of a 4-week course of therapy in two trials[595, 596] and at 5 to 12 weeks (4 to 10 weeks after the end of therapy in three trials and at the end of therapy in one trial[592]). Two trials were rated good quality,[593, 597] three fair quality,[592, 594, 596] and one poor quality.[595] Methodological shortcomings in the fair- and poor-quality trials included unclear randomization and allocation concealment methods, unblinded design, failure to report attrition, and unclear use of intention-to-treat analysis.

Taping Versus Sham Taping

Chronic Low Back Pain

Two good-quality trials (n=60 and 148) and one fair-quality trial (n=20) found no differences between a Kinesio Taping® versus sham taping in back-specific function (RDQ or ODI) after 5 weeks (following 1 week of therapy)[593] or 12 weeks (following 4 or 12 weeks of therapy).[592, 597] Effects on pain were somewhat mixed, with one trial finding a 1-week course of taping associated with greater improvement in pain (mean difference, 0-10 VAS −1.0, 95% CI −1.7 to 0.2) after 5 weeks,[593] but two trials finding no effect of a 4-week course of taping (mean difference, 0-10 VAS −0.5, 95% CI −1.4 to 0.4)597 or a 12-week course of taping (mean, 0-10 VAS 5.07 vs. 5.14).[592]

Taping Plus Exercise Versus Exercise Alone

Chronic Low Back Pain

A fair-quality trial (n=43) found no difference between 2 weeks of Functional Fascial Taping plus exercise versus sham taping plus exercise in pain or ODI scores when outcomes were assessed at 6 or 10 weeks.[594]

Taping Versus Exercise

Chronic Low Back Pain

One fair-quality (n=39)[596] and one poor-quality (n=40) trial[595] found no differences between a 4-week course of Kinesio Taping® versus exercise therapy in pain or the RDQ when outcomes were assessed at the end of therapy. Differences in pain scores favored taping by less than 1 point on a 0-10 scale, though effects on the RDQ were in opposite directions (favored taping in one trial and exercise in the other). One of the trials also found no differences between taping and taping plus exercise.

Harms

No trial of taping reported harms.

Table 1. Summary of systematic reviews of pharmacological treatments for low back pain

Treatment	Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Acetaminophen	Roelofs, 2008[41]	65 RCT and controlled clinical trials Acute low back pain (25 trials), chronic low back pain (9 trials) mixed or unclear low back pain population (31 trials) 6 trials NSAIDs versus paracetamol or acetaminophen	A. NSAIDs (nonselective and selective) B. Other medications C. Other active interventions (i.e., passive physical modalities) D. Placebo Total n=11,237	For acute LBP, NSAIDs were no different for improvement in pain intensity vs. paracetamol/acetaminophen (3 studies; SMD -0.21, 95% CI -0.43 to 0.02) One study found limited evidence that parcacetamol was less effective than NSAIDs for chronic low back pain. Other comparisons of NSAIDs are discussed in the NSAIDs or opioids section. NSAIDs were associated with more side effects than paracetamol (4 trials, RR 1.76, 95% CI 1.12 to 2.76)
Antidepressants	Urquhart, 2010[139]	10 RCTs; 9 trials conducted in pts with chronic low back pain; 1 trial duration of low back pain not reported. Duration of followup 10 days to 12 weeks.	A. Antidepressants (n=315): paroxetine (3 studies); desipramine (3 studies); imipramine (2 studies); maprotiline (2 studies); fluoxetine (2 studies); bupropion, trazodone, amitriptyline, nortriptyline and clomipramine IV (1 study each) B. Placebo (n=252)	There were no significant differences between antidepressants and placebo for pain relief (6 trials; SMD -0.04, 95% CI -0.25 to 0.17) or depression (2 trials; SMD 0.06 (95% CI -0.29 to 0.40) in patients with chronic low back pain.

NSAIDs	Roelofs, 2008[41]	65 RCT and controlled clinical trials Acute low back pain (25 trials), chronic low back pain (9 trials) mixed or unclear low back pain population (31 trials)	A. NSAIDs (nonselective and selective) B. Other medications C. Other active interventions (i.e., passive physical modalities) D. Placebo Total n=11,237	For acute LBP, NSAIDs associated with greater improvement in pain intensity vs. placebo (4 studies; WMD -8.39, 95% CI -12.68 to -4.10), but no clear effects on pain relief. For chronic LBP, NSAIDs associated with greater improvement in pain vs. placebo (4 trials, WMD -12.40, 95% CI -15.53 to -9.26). For radicular LBP, there was no difference in pain intensity between NSAIDs versus placebo. There was no difference in likelihood of pain relief for rofecoxib vs. diolefin. Studies of NSAIDs vs. acetaminophen or opioids are discussed in those sections. NSAIDs were associated with more side effects than placebo (10 trials, (10 trials, RR 1.35, 95% CI 1.09 to 1.68) COX-2-selective NSAIDs were associated with lower risk of side effects versus nonselective NSAIDs (4 trials; RR 0.83, 95% CI 0.70 to 0.99). Serious harms were rare.

Opioids	Carson, 2011[94]	41 RCTs: 10 comparing long-acting with another long-acting opioid; 3 were for low back pain. 27 trials comparing long-acting opioid to placebo (for indirect comparisons); 4 for back pain 7 trials comparing long-acting vs. short-acting opioids; 5 for back pain	Comparisons of long-acting opioids: total 1310 patients in trials for LBP 4 trials for low back pain comparing long-acting opioid to placebo are all summarized elsewhere Comparisons of long vs. short acting opioids: 284 total patients in trials for LBP	Insufficient evidence from 10 head-to-head trials to suggest that a long-acting opioid is superior to another in terms of efficacy in adult patients with chronic noncancer pain. No useful indirect evidence for determining the comparative efficacy of long-acting opioids was found in 27 placebo-controlled trials In 7 fair-quality trials directly comparing a long-acting opioid to a short-acting opioid there was no good quality evidence to suggest superior efficacy of long-acting opioids as a class over short-acting opioids Insufficient evidence from 10 head-to-head trials of long acting opioids that any drug safer than others. No trials adequately assessed addiction or abuse. There was insufficient evidence from 27 placebo-controlled trials to suggest that a long-acting opioid was superior in terms of adverse events to any other. No convincing evidence from 7 RCTs to suggest lower adverse event rates with long-acting opioids as a class compared with short-acting opioids for all assessed adverse events. No data compared rates of addiction or abuse of long-acting and short-acting opioids.
	Chaparro, 2013[598]	A. Strong opioids vs. placebo: 7 trials B. Tramadol vs. placebo: 5 trials C. Buprenorphine vs. placebo: 2 trials D. Opioids vs. NSAIDs: 2 trials in 1 article all subacute or chronic low back pain Duration of followup 4 weeks to 13 weeks	A. Strong opioids, n=1154, placebo n=733 adol, n=689, placebo n=689 C. Buprenorphine, n=312, placebo=341 D. Opioids n=785 celecoxib, n=798	A.Pain: moderate-quality evidence that strong opioids are better than placebo; SMD 0.43 lower (95% CI 0.52 to 0.33); Function: Moderate-quality evidence better than placebo in improving function (SMD 0.26 lower disability score [95% CI 0.37 to 0.15])

Opioids	Chaparro, 2013[598]	A. Strong opioids vs. placebo: 7 trials B. Tramadol vs. placebo: 5 trials C. Buprenorphine vs. placebo: 2 trials D. Opioids vs. NSAIDs: 2 trials in 1 article all subacute or chronic low back pain Duration of followup 4 weeks to 13 weeks	A. Strong opioids, n=1154, placebo n=733 adol, n=689, placebo n=689 C. Buprenorphine, n=312, placebo=341 D. Opioids n=785 celecoxib, n=798	B. Pain: low-quality evidence tramadol is better than placebo, SMD 0.55 lower, 95% CI 0.66 to 0.44; Function: Moderate evidence tramadol is better than placebo, SMD 0.18 lower (95% CI 0.29 to 0.07) C. Pain: very low-quality evidence that transdermal buprenorphine is better than placebo (mean difference 0.58 lower, 95% CI 0.61 to 0.55; Function: very low-quality evidence of no difference in function (mean difference 3 lower (95% CI 11.44 lower to 5.44 higher) D. Pain: very low-quality evidence that tramadol is better than celecoxib; this seems to be a misprint; in fact, celecoxib appeared to be better than tramadol (at least 30% pain reduction: 63.7% with celecoxib; 52.5% with tramadol, OR 0.63 [95% CI 0.52, 0.77])

CI = confidence interval; IV = intravenous; LBP = low back pain; NSAIDs = nonsteroidal anti-inflammatory drug;
OR = odds ratio; RCT = randomized controlled trial; RR = relative risk; SMD = standard mean difference; WMD = weighted mean difference

Table 2. Characteristics and conclusions of included acetaminophen trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Williams, 2014[43] 12 weeks Acute *Good*	A: Acetaminophen: 665 mg 2 tablets orally every 6-8 hours (6 tabs/day) + placebo 1-2 tabs orally every 4-6 hours as needed (up to 8 tabs/day) (n=550) B: Acetaminophen: Placebo 2 tablets orally every 6-8 hours (6 tabs/day) + 500 mg 1-2 tablets orally every 4-6 hours as needed (up to 8 tablets/day) (n=546) C: Placebo: Placebo 2 tablets orally every 6-8 hours (6 tablets/day) + placebo 1-2 tablets orally every 4-6 hours as needed (up to 8 tablets/day) (n=547) Medications taken until *recovery* or for 4 weeks	A. vs. B. vs. C. Mean age: 44 vs. 45 vs. 45 years Female: 48% vs. 47% vs. 45% Baseline pain (mean, 0-10 NRS): 6.3 vs. 6.3 vs. 6.2 Baseline RDQ (mean, 0-24): 3.5 vs. 3.6 vs. 3.7 Pain below knee: 20% vs. 21% vs. 18	A. vs. B. vs. C. Pain (mean, 0-10): 3.7 vs. 3.8 vs. 3.6 at week 1, 2.6 vs. 2.6 vs. 2.5 at week 2, 1.7 vs. 1.8 vs. 1.7 at week 4, 1.2 vs. 1.3 vs. 1.3 at w 12 RDQ (mean, 0-24): 7.7 vs. 8.0 vs. 8.3 at week 1, 5.2 vs. 5.4 vs. 5.3 at week 2, 3.2 vs. 3.5 vs. 3.3 at week 4, 2.4 vs. 2.6 vs. 2.4 at week 12 Patient Specific Functional Scale (mean, 0-10): 6.2 vs. 6.1 vs. 6.2 at week 1, 7.3 vs. 7.2 vs. 7.4 at week 2, 8.2 vs. 8.1 vs. 8.2 at week 4, 8.7 vs. 8.7 vs. 8.7 at week 12 Global change (mean, -5 to +5): 2.1 vs. 2.0 vs. 2.1 at week 1, 2.8 vs. 2.7 vs. 2.8 at week 2, 3.4 vs. 3.4 vs. 3.5 at week 4, 3.8 vs. 3.7 vs. 3.8 at week 12 SF12 Physical score (mean, 0-100): 50 vs. 50 vs. 51 at week 4, 55 vs. 55 vs. 55 at week 12 SF12 Mental score (mean, 0-100): 44 vs. 44 vs. 44 at week 4, 46 vs. 46 vs. 45 at week 12	A. vs. B. vs. C. Sleep quality “fairly bad” or “very bad”: 28% (143/514) vs. 26% (129/501) vs. 26% (127/496) at week 1, 17% (85/508) vs. 18% (88/495) vs. 17% (85/497) at week 2, 12% (59/507) vs. 11% (57/500) vs. 10% (52/503) at week 4, 11% (54/506) vs. 11% (55/503) vs. 8.6% (44/514) at week 12 No differences in use of concomitant medications or health services or hours absent from work Days to recovery (median, days): 17 vs. 17 vs. 16 Satisfied with treatment: 76% (365/478) vs. 72% (342/472) vs. 73% (335/458)

LBP=low back pain, Mg = milligrams; NRS=numeric rating scale, RDQ=Roland-Morris Disability Questionnaire;
SF-12 = 12 item short form health survey

Table 3. Characteristics and conclusions of included NSAID trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Herrmann, 2009[50] 5 days Acute *Fair*	A: Lornoxicam 8mg tablets, with 16 mg loading dose on day 1, then 8mg after 8 hours; 8 mg twice per day on days 2-4; 8 mg on day 5 B: Diclofenac: 50 mg twice per day on days 1 and 5; 50mg three times per day on days 2-4. C: Placebo capsules in lornoxicam or diclofenac blister packs Day 5 treatment was optional	A. vs. B. vs. C. Mean age: 51.8 vs. 48.9 vs. 48.4 Female: 44% vs. 47% vs. 42% Pain etiology: Sciatica or lumbo-sciatica	A. vs. B. vs. C. Pain intensity difference, mm: 3 hours: -21.0 vs. -18.7 vs. -15.3, p≤0.05 for A. vs. C. 4 hours: -22.0 vs. -21.5 vs. -14.8, p≤0.05 for A. vs. C. 6 hours: -20.5 vs. -22.4 vs. -14.9, p≤0.05 for A. vs. C. 8 hours: -22.0 vs. -24.1 vs. -13.7, p≤0.05 for A. vs. C. Sum of time-weighted pain intensity difference, mm x minute: 0-4 hours: -4020 vs. -3879 vs. -2901, p≤0.05 for A. vs. C. 0-6 hours: -6486 vs. -6358 vs. -4713, p≤0.05 for A. vs. C. 0-8 hours: -9125 vs. -8833 vs. -6257, p≤0.05 for A. vs. C. Pain Relief (mm) 3 hours: 30.1 vs. 30.8 vs. 26.6 4 hours: 31.7 vs. 33.9 vs. 26.6 6 hours: 31.1 vs. 34.3 vs. 26.1 8 hours: 31.9 vs. 35.6 vs. 23.9, p≤0.05 for A. vs. C. Peak pain intensity difference, A. vs. C: -27.9 mm vs. -19.9 mm, p=0.01 Time to peak pain intensity difference, A. vs. C: 243 vs. 240 minutes, no difference Peak pain relief, A. vs. C. : 38.0 mm vs. 31.1 mm, p=0.05 Time to peak pain relief: no difference Start of peak pain relief: no difference End of peak pain relief: no difference Duration of peak pain relief: no difference	

Majchrzycki, 2014[51] 2 weeks Acute, subacute *Fair*	A. Deep tissue massage + NSAID (n=26) B. Deep tissue massage (n=28)	A. vs. B. Mean age: 50.8 vs. 52.6 Female: 50.0% vs. 46.4% Chronic pain: 100% Baseline pain: NR Baseline function: NR QOL: NR	A. vs. B. VAS1 (0-100): pain intensity during resting: 16.5 vs. 13.9 VAS2 (0-100): pain intensity during motion: 3.2 vs. 3.4 VAS3 (0-100): pain intensity during mobility of the aching area of the spine: 4.8 vs. 8.2	A. vs. B. Difference scores, no significantly different results between groups on: Roland-Morris questionnaire: 21.2 vs. 16.1 Oswestry disability index: 24.7 vs. 19.6
Shirado, 2010[52] 12 months Subacute *Good*	A: NSAIDs: loxoprofen sodium, 60 mg tablet 3 times daily; diclofenac sodium, 25 mg tablet 3 times daily; or zaltoprofen, 80 mg tablet 3 times daily B: Exercise: medical professionals at each clinic gave instruction of the exercise. 2 types of exercise: trunk strengthening and stretching. 2 sets of 10 repetitions of each exercise per day were encouraged.	A. vs. B. Mean age: 42.5 vs. 42.0 Female: 59% vs. 52% Pain type: All chronic pain Baseline pain: VAS (0-10): 3.8 vs. 3.5 QOL scores: RDQ (0-24): 3.7 vs. 3.0 JLEQ score (0-120): 21.8 vs. 20.5	A. vs. B. Baseline to 8 week change ratio: Pain: VAS (0-10): -0.35 vs. -0.44, p=0.332	A. vs. B. Baseline to 8 week change ratio: Function: Finger-floor distance: 0.00 vs. -0.09, p=0.112 RDQ: -0.47 vs. -0.72, p=0.023 JLEQ: -0.44 vs. -0.58, p=0.021

JLEQ = Japan Low Back Pain Evaluation Questionnaire; Mg = milligrams; mm = millimeters; NR = not reported;; QOL = quality of life; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; VAS = visual analog scale

Table 4. Characteristics and conclusions of included opioid trials

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Cloutier, 2013[87] 4 weeks Subacute, chronic *Good*	A. Oxycodone/Naloxone, both controlled release, titrated dose of 10mg/5mg every 12 hours up to 40mg/20mg every 12 hours B. Placebo Crossover design: 4 weeks of each intervention	Due to crossover design, all patients received both A and B. Among the 54 analyzed: Mean age: 50.6 years Female: 50% Baseline score on Pain and Disability Index: 42 on a 0-70 scale (70 worst) Among the full 83 enrolled Mean age: 51.3 years Female: 53%	A. vs. B. ITT Analysis (n=83): Pain VAS (0-100): A. 52.2 mm (SD 23.0; B: 57.8 mm (SD 24.2) (p=0.053) Ordinal pain score: A: 2.3 (SD 0.8); B: 2.5 (SD 0.9), (p=0.086) No other results for ITT analysis Per protocol analysis: Pain VAS (0-100): A. 48.6 mm (SD 23.1); B: 55.9 mm (SD 25.4) (p=0.03) Ordinal pain score: A: 2.1 (SD 0.8); B: 2.4 (SD 0.9), (p=0.042)	A. vs. B. Per protocol analysis: Pain Disability Index: A: 34.3 (SD 15.6); B:37.5 (SD 15.2), p=0.051; SF-36 General Health: “no difference” Quebec Back Pain Disability: “no difference”
Hyup Lee, 2013[88] 29 days Subacute, chronic *Good*	A. Extended-release tramadol HCl 75 mg/acetaminophen 650 mg fixed-combination tablet (n=125) Max dose=4 tabs/day=300 mg tramadol B. Placebo (n=120)	A. vs. B. Mean age: 59.9 vs. 60.4 years Female sex: 75% vs. 74%	A. vs. B. Pain intensity change ≥30%, full analysis set: 57.7% (49/85) vs. 41.1% (37/90); p=0.037 Pain intensity change ≥30%, per protocol: 63% (46/73) vs. 44.9% (35/78); p=0.027 Pain intensity change ≥50%, full analysis set: 31.8% vs. 20.0%; p=0.075 Pain intensity change ≥50%, per protocol: 34.3% vs. 21.8%; p=0.088	A. vs. B. Korean SF-36: patients in the intervention group had significant improvements in role-physical, general health, and reported health transition domains, and a tendency (p=0.052) toward improvement in vitality Korean ODI: patients in the intervention group had significant functional improvement in the personal care section (p=0.045) and a tendency (p=0.053) toward improvement in total ODI scores

Rauck, 2014[89] 12 weeks Chronic *Poor*	A. Extended-release hydrocodone in 10, 20, 30, 40, and 50 mg capsules (n=151) Mean dose=119 mg/day Max dose=200 mg/day B. Placebo (n=151)	A. vs. B. Mean age: 50.4 vs. 50.8 years Female sex: 62% vs. 49%; p=0.028 Mean pain score before titration (NRS 0-10): 6.9 vs. 6.9 Mean pain score after titration (NRS 0-10): 3.1 vs. 3.1	A. vs. B. Change from baseline in mean daily pain intensity score: 0.48 vs. 0.96; p=0.008	
Schiphorst Preuper, 2014[90] 2 weeks Chronic *Fair*	A. tramadol 37.5 mg/acetaminophen 325 mg fixed-combination capsule (n=25) Max dose tramadol=225 mg/d B. Placebo (n=25)	A. vs. B. Mean age: 42 vs. 44 years Female sex: 72% vs. 64% Mean duration of pain: 18 vs. 24 months Mean pain score (VAS 0-10): 6.1 vs. 4.7	A. vs. B. VAS (0-10) current pain, baseline-followup: 6.1-5.1 vs. 4.7-4.5; change -1 vs. -0.2VAS (0-10), maximum pain, baseline-followup: 7.3-7.4 vs. 7.1-7.7; change 0.1 vs. 0.6 VAS (0-10), minimum pain, baseline-followup: 4.4-3.8 vs. 2.0-2.6; change -0.6 vs. 0.6 Pain relief: 42% (10/24) vs. 4% (1/25); RR 10.42 (95% CI 1.44 to 75.29) Same pain or worsened: 58% (14/24) vs. 96% (24/25); RR 0.61 (95% CI 0.43 to 0.86)	A. vs. B. Lifting (kg), baseline-followup: 18-19 vs. 20-17 kg; change 1 vs. -3 kg Carrying (kg), baseline-followup: 24-20 vs. 24-21 kg; change -4 vs. -3 Static bending (seconds), baseline-followup: 119-143 vs. 158-192.5; change 24 vs. 34.5 s Dynamic bending (seconds/rep), baseline-followup: 2.7-2.8 vs. 2.7-3.0; change 0.1 vs. 0.3 Roland Morris Disability Questionnaire (0-24), baseline-followup: 13.0-11.5 vs. 13.0-13.0; change -1.5 vs. 0

ITT = intention to treat; Mg = milligrams; NRS = numeric rating scale; ODI = Oswestry Disability Index; SF-36 = 36 item short form; RR = relative risk

Table 5. Characteristics and conclusions of included skeletal muscle relaxant trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Pareek, 2009[126] 7 days Acute *Fair*	A. Tizanidine 2 mg + aceclofenac 100 mg twice daily for 7 days (n=101)B. Aceclofenac 100 mg twice daily for 7 days (n=96)	A. vs. B Mean age: 62 vs. 58 years Female:39% vs. 40% Baseline pain, function not reported	A. vs. B. Pain at rest, mean change from baseline day 3: -3.01 vs. -1.90, p=0.0001; day 7 -5.88 vs. -4.35, p=0.0001 Pain with movement, mean change from baseline day 3: -2.94 vs. -1.81, p=0.0001; day 7 -6.09 vs. -3.98, p=0.0001	A. vs. B. Global improvement, proportion of patients reporting good or excellent response: 75% (71/94) vs. 34% (31/94); RR 1.28 (95% CI 1.07 to 1.52)
Ralph, 2008[127] 7 days Acute *Fair*	A. Carisoprodol 250 mg three times daily for 7 days (n=277) B. Placebo three times daily for 7 days (n=285)	A. vs. B. Mean age: 39 vs. 42 years Female:49% vs. 55% Baseline pain severity: mild 0.4% vs. 0.4%; moderate 74% vs. 74%; severe 25% vs. 26% Baseline RDQ 10 vs. 10	A. vs. B. Pain, patient-rated impression of pain relief, mean change from baseline day 3 (scale 0-4; higher score = greater pain relief): 1.8 vs. 1.1, p<0.0001; day 7 between-group difference p<0.0001 (data not shown)	A. vs. B. Global improvement, patient-rated impression of change, mean change from baseline at day 3 (scale 0-4; higher score = greater improvement); 2.3 vs. 1.7, p<0.0001; day 7 between-group difference p<0.0001 (data not shown)

LBP=low back pain, mg = milligrams; RDQ = Roland-Morris Disability Questionnaire; RR=relative risk

Table 6. Characteristics and conclusions of included benzodiapine trials

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Brotz, 2010[135] 1 year LBP duration not specified *Good*	A: Diazepam: 5 mg twice daily x 5 days, then tapered (tapering regimen not specified) (n=30) B: Placebo (n=30)	A. vs. B. Mean age: 43 vs. 42 years Female: 37% vs. 50% Baseline pain (median, 0-10 VAS): 8 vs. 8 Baseline RDQ (median, 0-24): 14 vs. 14	A. vs. B. Pain improved ≥50%: 41% (12/29) vs. 79% (23/29) at 1 week, RR 0.5 (95% CI 0.3 to 0.8);	A. vs. B. Duration of inability to work (median, days): 26 vs. 15 (p=0.73) RDQ (median improvement, 0-24): 3.0 vs. 5.0 at 1 week (p=0.67) RDQ (median, 0-24): 2 vs. 1 at 1 year Diclofenac consumption (median, mg): 750 vs. 750 at 1 week (p=0.78) Sensory loss improved: 83% (15/18) vs. 86% (19/22) at 1 week, RR 1.0 (95% 0.7 to 1.3) Sensory loss: 43% (9/21) vs. 44% (10/23) at 1 year Reduction of paresis: 22% (6/27) vs. 28% (8/28) at 1 week, RR 0.8 (95% CI 0.3 to 2.0) Paresis: 14% (3/21) vs. 13% (3/23) at 1 year Inability to work beyond day 28: 55% (16/29) vs. 41% (12/29) at 1 week, RR 1.3 (95% CI 0.7 to 2.2) Request for additional analgesics: 51% (15/29) vs. 41% (12/29) at 1 week, RR 1.3 (95% CI 0.7 to 2.3) Underwent surgery: 7 vs. 6 at 6 week, 8 vs. 7 at 1 year

CI = confidence interval; LBP=low back pain; RDQ= Roland-Morris Disability Questionnaire; RR=relative risk; VAS=visual analogue scale

Table 7. Characteristics and conclusions of included antidepressant trials

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention**	**Population**	**Pain Outcomes**	**Other Outcomes**
Farajirad, 2013[150] 8 weeks Chronic *Poor*	A. Amitriptyline 25 mg daily titrated to 150 mg daily (maximum) by week 2 (n=NR) B. Sustained-release bupropion 150 mg daily titrated to 300 mg daily by week 2 (n=NR)	A. vs. B. Mean age 37 vs. 34 years No other demographic or clinical characteristics reported	A. vs. B. No data shown Pain: No significant difference between groups	Not reported
Mazza, 2010[151] 13 weeks Chronic *Fair*	A. Escitalopram 20 mg daily (n=41) B. Duloxetine 60 mg daily (n=44)	A. vs. B. Mean age 52 vs. 54 years 56% vs. 57% female Race not reported Pain, mean VAS (scale 0-10) 6.3 vs. 6.4 Function, mean CGI-S score (scale 0-10) 3.6 vs. 3.5	A. vs. B. Pain, VAS (0-10) mean change from baseline: -2.3 vs. -2.45; p=0.74	A. vs. B. Function, CGI-S mean change from baseline: -0.92 vs. -0.69; p=0.21 Quality of life, mean change SF-36 subscales: no significant difference between groups for any subscale

Skljarevski, 2009[152] 13 weeks Chronic *Good*	A. Duloxetine 20 mg daily (n=59) B. Duloxetine 60 mg daily (n=116) C. Duloxetine 120 mg daily (n=112) D. Placebo (n=117)	A. vs. B. vs. C. vs. D. Mean age 53 vs. 53 vs. 55 vs. 54 years 61% vs. 58% vs. 58% vs. 55% female Race: 78% vs. 78% vs. 82% vs. 80% white; 22% vs. 22% vs. 18% vs. 20% other Pain, mean BPI 6.4 vs. 6.2 vs. 6.1 vs. 6.2 Function, mean CGI-S score 4.1 vs. 3.5 vs. 3.6 vs. 3.7	A. vs. B. vs. C. vs. D. Pain, mean change from baseline: -1.77 vs. -2.46 vs. -2.40 vs. -2.10; no significant differences among groups Pain, BPI-S mean change from baseline: -1.79 vs. -2.50 vs. -2.45 vs. -1.87; B vs. D: $p<0.05$	A. vs. B. vs. C. vs. D. Function, BPI-I average mean change from baseline: -1.84 vs. -2.40 vs. -1.92 vs. -1.61; B vs. D: $p<0.05$ Quality of life, mean change SF-36 subscales: -Bodily pain: 1.51 vs. 1.95 vs. 2.11 vs. 1.36; B vs. D, C vs. D: $p<0.05$ No significant difference among groups for other subscales Quality of life, EuroQoL 5D US Index score mean change from baseline: 0.04 vs. 0.07 vs. 0.08 vs. 0.05; no significant differences among groups
Skljarevski, 2009[152] 13 weeks Chronic *Good*				Global improvement, CGI-S mean change from baseline: -0.53 vs. -0.94 vs. -1.06 vs. -0.53; B vs. D, C vs. D: $p<0.05$

Skljarevski, 2010[153] 12 weeks Chronic *Fair*	A. Duloxetine 60 mg daily (n=198) B. Placebo (n=203)	A. vs. B. Mean age 55 vs. 53 years 60% vs. 63% female Race: 96% vs. 95% white, 3% vs. 3% African, 2% vs. 3% other Pain, mean BPI 5.8 vs. 5.8 Function, mean CGI-S 3.5 vs. 3.3 Function, mean RDQ 9.6 vs. 9.3	A. vs. B. Pain, BPI-S mean change from baseline: -2.25 vs. -1.65; p=0.002 Pain, BPI 24-hour Average Pain Score, proportion of patients with 30% improvement in score: 57% (111/195) vs. 49% (97/199); p=0.11; 50% improvement in score: 49% (95/195) vs. 35% (69/199); p=0.005	A. vs. B. Function, BPI-I scale, mean change from baseline: -2.01 vs. -1.43; p≤0.001 Function, RDQ mean change from baseline: -2.69 vs. -2.22; p=0.26 Quality of life, Profile of Mood states total mood disturbance mean change from baseline: -6.77 vs. -2.77; p≤0.001 Global improvement, CGI-S mean change from baseline: -0.95 vs. -0.79; p=0.08 Global improvement, Patients' Global Impressions score, mean change from baseline: 2.88 vs. 3.19; p=0.01
Skljarevski, 2010[154] 13 weeks Chronic *Fair*	A. Duloxetine 60 mg daily; titrated to 120 mg daily in nonresponders after week 7 (n=115) B. Placebo; sham titration in nonresponders after week 7 (n=121)	A. vs. B. Mean age 52 vs. 51 years 62% vs. 60% female Race: 74% vs. 75% white, 20% vs. 17% Hispanic, 6% vs. 7% other Pain, mean BPI 5.9 vs. 6.0 Function, mean CGI-S 3.2 vs. 3.2	A. vs. B. Pain, BPI-S mean change from baseline: -2.66 vs. -1.90; p<0.05 Pain, BPI 24-hour Average Pain Score mean change from baseline: -2.08 vs. -1.30; p≤0.01	A. vs. B. Function, BPI-I, mean change from baseline: -1.92 vs. -1.18; p≤0.01 Quality of life, Athens Insomnia Scale mean change from baseline: -2.07 vs. -1.49; p=0.38 Quality of life, SF-36 mean between group difference significant for bodily pain (p=0.04), general health (p=0.04) and vitality (p=0.04) subscales favoring duloxetine; no difference for other subscales (data not shown)

Skljarevski, 2010[154] 13 weeks Chronic *Fair*				Return to work, mean between-group difference significant for WPAI measure of health outcomes subscale (p=0.002) favoring duloxetine; no difference for other subscales (data not shown) Global improvement, CGI-S mean change from baseline: -0.98 vs. -0.77; p=0.14

BPI=Brief Pain Inventory; BPI-I=Brief Pain Inventory Interference scale; BPI-S=Brief Pain Inventory Severity scale; CGI-S=Clinical Global Impressions of Severity scale; mg = milligram; NR=not reported, QOL = quality of life; RDQ=Roland Morris Disability Questionnaire; SF-36 = 36 item short form health survey; VAS=visual analogue scale; WPAI=work productivity and activity impairment.

Table 8. Characteristics and conclusions of included antiseizure trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Baron, 2010[160] 5 weeks Subacute, chronic *Fair*	Placebo run-in period for 7 days, then pregabalin run-in for 28 days, then: A: Pregabalin: Optimal dose from run-in period (mean 410 mg) x 5 weeks, then 1 week taper (n=110) B: Placebo: Pregabalin taper x 1 week, then placebo x 4 weeks, then taper x 1 week (n=108)	A. vs. B. Mean age: 52 vs.53 years Female: 49% vs. 55% Baseline pain (mean, 0-10 VAS): 6.36 vs. 6.39 Baseline function: Not reported	A. vs. B. Pain (mean change from baseline, 0-10 VAS): -0.16 vs. 0.05 (p=0.33) Pain ≥7/10 (days): 7.1% (8/108) vs. 6.4% (7/107) at 5 w	A. vs. B. Loss of response (≥1 point increase in weekly mean pain score or use of rescue medication): 27.8% vs. 28.0% at 5 weeks, HR 0.87 (95% CI 0.52 to 1.47) Medical Outcome Study Sleep Scale sleep disturbance (mean change, 0-100): 2.26 vs. 6.86 (p=0.03) Medical Outcome Study Sleep Scale sleep quantity (mean change, hours): 0 vs. -0.43 (p=0.004)No differences on other Sleep Scale subscales HADS anxiety (mean change, 0-21): -0.19 vs. 0.82 at 5 weeks (p=0.01) HADS depression (mean change, 0-21): -0.57 vs. 0.56 at 5 weeks (p=0.0006) EuroQOL, RDQ: No differences, data not reported
Baron, 2014[161] 9-10 weeks Subacute, chronic *Fair*	Washout for 3-14 days, then tapentadol PR run-in for 3 weeks, then: A: Pregabalin + tapentadol PR: Pregabalin 150 mg/day x 1 week, 300 mg/day x 7 weeks + tapentadol PR 300 mg/day (n=157) B: Tapentadol PR: Tapentadol 300 mg/day + 100 mg/day x 1 week, tapentadol 300 mg/day + 200 mg/day x 7 weeks (n=152)	A. vs. B. Mean age: 56 vs.58 years Female: 54% vs. 62% Baseline pain: 5.9 vs. 5.9 (at randomization) Baseline function: Not reported	A. vs. B. Pain (mean change from baseline, 0-10 VAS): -1.6 vs. -1.7 at 9-10 w (p>0.05)	A. vs. B. Leg pain (mean change from baseline, 0-10 VAS): -1.6 vs. -1.9 at 9-10 w Patient satisfaction good, very good, or excellent: 73% (114/157) vs. 67% (102/152) at 9-10 w “Minimally”, “much”, or “very much” improved: 82% (129/157) vs. 81% (123/152) at 9-10 w SF-12: No difference on any subscale at 9-10 w EuroQOL (mean, 0-10): 0.60 vs. 0.61 at 9-10 w HADS anxiety (mean): 5.8 vs. 6.0 at 9-10 w HADS depression (mean): 5.4 vs. 6.2 at 9-10 w

Kalita, 2014[162] 14 weeks Chronic *Poor*	A: Pregabalin: 75 mg twice daily x 2 weeks, 150 mg twice daily x 2 weeks, 300 mg twice daily, then increased if tolerated and needed (mean dose ~430 mg/day) (n=97) B: Amitriptyline: 12.5 nightly x 2 weeks, 25 mg nightly x 4 weeks, then 50 mg nightly, then increased if tolerated and needed (mean dose 38 mg/day) (n=103)	A. vs. B. Mean age: 42 vs.42 years Female: Not reported Baseline pain: 6.7 vs. 6.7 Baseline ODI: 42 vs. 42 Radiculopathy: 47% Spinal stenosis: 6%	A. vs. B. Pain (mean, 0-10 VAS): 6.7 vs. 6.7 at baseline, 4.2 vs. 3.9 at 4 w, 3.8 vs. 2.8 at 16 weeks (estimated from graph; p>0.05 at all time points) Pain improved by ≥50%: 39% (38/97) vs. 57% (59/103), RR 0.68 (95% CI 0.51 to 0.92) Findings for dichotomous outcomes similar for patients with nonradicular back pain and radiculopathy; with or without neurological deficit	A. vs. B. ODI (mean, 0-100): 42 vs. 42 at baseline, 30 vs. 26 at 4 weeks, 22 vs. 17 at 16 weeks (estimated from graph; p>0.05 at all time points) ODI improved >20%: 50% (48/97) vs. 65% (67/103), RR 0.76 (955 CI 0.59 to 0.97) Findings for dichotomous outcomes similar for patients with nonradicular back pain and radiculopathy; with or without neurological deficit
Markman, 2014[163] 10 days Subacute, chronic *Fair*	A: Pregabalin: 75 mg twice daily x 3 days, 150 mg twice daily x 7 days, 75 mg twice daily x 4 days (n=14) B: Placebo: Diphenhydramine 6.25 mg twice daily x 3 days, 12.5 mg twice daily x 7 days, 6.25 mg twice daily x 4 days (n=12) Each treatment for 2 weeks, with 1 week washout	A. vs. B. Mean age: 71 vs.69 years Female: 29% vs. 33% Baseline pain with ambulation (mean, 0-10 NRS): 7.7 vs. 7.1 Baseline RDQ (mean, 0-24): 13 vs. 14	A. vs. B. Pain with ambulation (mean, 0-10 NRS): 7.22 vs. 6.97 at 2 weeks (p=0.46) Brief Pain Inventory-Short Form, interference (mean, 0-10): 3.7 vs. 3.58 at 2 weeks (p=0.68) BPI-SF, pain intensity (mean, 0-10): 4.4 vs. 4.5 at 2 weeks (p=0.68)	A. vs. B. Walking distance (mean, m): 237 vs. 261 at 2 weeks (p=0.35) RDQ (mean, 0-24): 13 vs. 11 at 2 weeks (p=0.01) ODI (mean, 0-100): 38 vs. 36 at 2 weeks (p=0.36) Swiss Spinal Stenosis Questionnaire, symptom severity (mean): 3.09 vs. 2.94 at 2 weeks (p=0.07) Swiss Spinal Stenosis Questionnaire, physical function (mean): 2.40 vs. 2.45 at 2 weeks (p=0.57)

Pota, 2012[164] 3 weeks Chronic *Fair*	Buprenorphine run-in period for 3 weeks, then: A: Pregabalin 300 mg/day + transdermal buprenorphine 35 mcg/hour x 3 weeks (n=22) B: Placebo + transdermal buprenorphine 35 mcg/hour x 3 weeks (n=22)	A. vs. B. Mean age: 56 years (overall) Female: 50% (overall) Baseline pain (mean, 0-100 VAS): 35 vs. 32 Baseline function: Not reported	A. vs. B. Pain (mean, 0-100 VAS): 9.5 vs. 32.8 at 1 week, 6.1 vs. 32.8 at 2 week, 5.7 vs. 33.3 ($p<0.05$) at 3 week MPQ-SF Pain Rating Index (mean, 0-15): 9.2 vs. 16.5 at 1 week, 4.6 vs. 16.6 at 2 weeks, 3.7 vs. 16.2 at 3 weeks ($p<0.05$) MPQ-SF Present Pain Intensity (mean, 0-5): 0.4 vs. 1.7 at 1 week, 0.3 vs. 1.8 at 2 weeks, 0.3 vs. 2.0 at 3 weeks	A. vs. B. Sleep interference (mean, 0-10): 0.2 vs. 2.3 at 1 week, 0.7 vs. 1.8 at 2 weeks, 0.6 vs. 1.9 at 3 weeks ($p>0.05$) Acetaminophen use (mean, mg): 46 vs. 636 at week 3 ($p<0.05$)
Romano, 2009[165] 4 weeks Chronic *Fair*	A: Pregabalin ~1 mg/kg/day x 1 week, then 2-4 mg/kg/day (mean 2.1 mg/kg/day) (n=12) B: Celecoxib ~3-6 mg/kg/day (mean 4.2 mg/kg/d) (n=12) C: Pregabalin + celecoxib (mean 1.78 and 3.75 mg/kg/day) (n=12) Each treatment for 4 weeks, with 1 week washout prior to crossover	A. vs. B. vs. C. Mean age: 53 years (overall) Female: 56% (overall) Baseline pain: Not reported for initial intervention (mean 45-48) Baseline function: Not reported for initial intervention Disc prolapse: 47% Lumbar spondylosis: 39% Spinal stenosis: 19%	A. vs. B. vs. C. Pain (mean, 0-100 VAS): 43 vs. 40 vs. 29 at 4 weeks ($p=0.0001$ for A. vs. C. and $p=0.001$ for B vs. C) Pain reduction: 10% vs. 12% vs. 38% at 4 weeks Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) score <12 Pain (mean, 0-100 VAS): 50.7 vs. 32.5 vs. 32.9 at 4 weeks ($p=0.0002$ for A. vs. C. and $p=0.9$ for B vs. C) Pain reduction (estimated from graph): -2.5% vs. 26% vs. 27% at 4 weeks LANSS score >12 Pain (mean, 0-100 VAS): 36.3 vs. 32.5 vs. 23.1 ($p=0.01$ for A. vs. C. and $p=0.0001$ for B vs. C) Pain reduction (estimated from graph): 23% vs. 2% vs. 52%	NR

Yaksi, 2007[166] 4 months LBP duration not specified Poor	A: Gabapentin: initial dose 300 mg/day, titrated up to 2400 mg/day (mean not reported) (n=28) B: No gabapentin (n=27) Both groups also received exercise, lumbar corset, and NSAIDS; duration of treatment 4 months	A. vs. B. Mean age: 51 vs.51 years Female: 79% vs. 56% Baseline pain (mean, 0-10 VAS): 7.0 vs. 6.7 Baseline function: Not reported	A. vs. B. Pain (mean, 0-10 VAS): 5.1 vs. 5.6 at 1 m (p=0.40), 4.3 vs. 5.0 at 2 m (p=0.12), 3.6 vs. 4.8 at 3 m (p=0.04), 2.9 vs. 4.7 at 4 m (p=0.006)	A. vs. B. Walking distance >1000 m (estimated from graph): 65% vs. 21% at 4 m (p=0.001) Sensory deficit: 32% (9/28) vs. 63% (17/27)

BPI-SF = Brief Pain Inventory-Short Form; HADS = The Hospital Anxiety and Depression Scale; kg = kilogram; LANSS = Leeds Assessment of Neuropathic Symptoms and Signs; mg = milligrams; MPQ-SF = McGill Pain Questionnaire; NRS = numeric rating scale; ODI = Oswestry Disability Index; QOL = quality of life; RDQ=Roland Morris Disability Questionnaire; RR = relative risk; SF-12 = 12 item short form health survey; VAS=visual analogue scale

Table 9. Characteristics and conclusions of included corticosteroid trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Eskin, 2014[172] 5-7 days Acute *Fair*	A: Prednisone: 50 mg once daily x 5 days (n=32) B: Placebo (n=35)	A. vs. B. Mean age: 39 vs. 41 years Female: 33% vs. 27% Baseline pain (mean, 0-10 VAS): 8.0 vs. 8.0 Baseline function: Not reported	A. vs. B. Pain (mean, 0-3 VRS): 1.3 vs. 1.1 at 5-7 days (difference 0.2, 95% CI -0.2 to 0.6) No or mild pain: 56% vs. 69% (difference -13%, 95% -36% to 10%)	A. vs. B. Days of work lost (mean): 2.1 vs. 1.3 (p=0.06) Sought further care: 40% vs. 18% (difference 22%, 95% CI 0% to 43%)
Friedman, 2008[173] 1 month Acute *Good*	A: Methylprednisolone: 160 mg IM x 1 (n=37) B: Placebo (n=41)	A. vs. B. Mean age: 39 vs. 37 years Female: 54% vs. 51% Baseline pain (0-10 VAS): 8.9 vs. 9.1 Baseline function: Not reported	A. vs. B. Improvement in pain (mean, 0-10 VAS): difference 1.1 (95% CI -0.5 to 2.8) at 1 week; 7.1 vs. 5.8 at 1 month, difference 1.3 (95% CI -0.2 to 2.7) Back pain in prior 24 hours: 46% vs. 61% at 1 month, OR 0.54 (95% CI 0.22 to 1.3)	A. vs. B. Analgesic use in past 24 hours: 22% vs. 43% at 1 m, OR 0.39 (95% CI 0.14 to 1.1) RDQ18 (median, 0-18): 0 vs. 0 (p=0.009) RDQ18 1 or higher: 42% vs. 46% at 1 w; 19% vs. 49% at 1 m, OR 0.25 (95 5CI 0.09 to 0.7) Not resumed usual activities: 14% vs. 23% at 1 m, OR 0.56 (95% CI 0.17 to 1.9) Not resumed work (among full-time workers): 8% (2/24) vs. 13% (3/24) at 1 m, OR 0.64 (95% CI 0.10 to 4.2) Did not seek additional health care: 67% vs. 59% at 1 m, difference 8% (95% CI -14% to 30%)
Hedeboe, 1982[176] 3 month LBP duration not specified *Fair*	A: Dexamethasone: 4 mg/ml, 16 mg IM three times daily x 1 day, 8 mg three times daily x 1 day, 8 mg three times daily x 1 day, 4 mg three times daily x 1 day, 4 mg twice daily on x 3 days (N=19) B: Placebo (n=20)	A. vs. B. Mean age: 44 vs. 40 years Female: 47% vs. 25% Baseline pain: Not reported Baseline function: Not reported		A. vs. B. Clear improvement (not otherwise defined): 68% (13/19) vs. 35% (7/20) at 9 d, RR 1.95, 95% CI 1.0 to 3.82; 32% (6/19) vs. 25% (5/20) at 3 m, RR 1.26, 95% CI 0.46 to 3.46

Holve, 2008[174] 6 months Acute *Poor*	A: Prednisone: 60 mg po once daily x 3 d, 40 mg po once daily x 3 d, 20 mg po once daily x 3 d (n=13) B: Placebo (n=14)	A. vs. B. Mean age: 39 vs. 46 years Female: 37% (overall) Baseline Roland Morris pain (mean, 0-5 VRS): 3.8 vs. 3.1 Baseline RDQ (mean, 0-24): 16 vs. 16	A. vs. B. RDQ Pain (mean, 0-5 RDQ pain, estimated from graph): 2.5 vs. 2.6 at 1 week, 1.8 vs. 2.1 at 2 weeks, 1.6 vs. 1.6 at 4 weeks, 1.5 vs. 1.0 at 3 months, 0.4 vs. 1.6 at 6 months (p>0.05)	A. vs. B. RDQ (mean, 0-24): 13 vs. 16 at 1 week, 8 vs. 13 at 2 weeks, 8 vs. 9 at 4 weeks, 3 vs. 2 at 3 months, 1 vs. 2 at 6 months (p>0.05) Return to baseline work hours: ~60% in each group by 2 m (p>0.05) NSAID and opioid use: No differences, data not provided Epidural injections: 15% (2/13) vs. 43% (6/14), RR 0.36 (95% CI 0.9 to 1.47)
Rodrigues, 2014[175] 12 weeks LBP duration not specified *Fair*	A: Prednisone 1 mg/kg/day, reduced by 1/3 per week (n=31) B: Placebo (n=30)	A. vs. B. Mean age: 39 vs. 46 years Female: 37% (overall) Baseline RDQ pain (mean, 0-5 VRS): 3.8 vs. 3.1 Baseline RDQ (mean, 0-24): 16 vs. 16	A. vs. B. Pain (mean, 0-10 VAS): 7.68 vs. 7.07 at baseline, 5.68 vs. 5.50 at 3 weeks, 6.71 vs. 5.17 at 6 weeks, 6.61 vs. 5.97 at 12 weeks (p=0.02 at 6 weeks, otherwise p>0.05)	A. vs. B. RDQ (mean 0-24): 16.16 vs. 15.27 at baseline, 12.77 vs. 14.73 at 3 weeks, 14.71 vs. 13.80 at 6 weeks, 14.81 vs. 13.80 at 12 weeks (p>0.05 at all time points) SF-36: No differences on any subscale Acetaminophen use: 19.42 vs. 19.6 (units unclear), p>0.05

CI = confidence interval; IM = intramuscular; LBP = low back pain; Mg = milligrams; NSAID = Nonsteroidal anti-inflammatory drugs; OR = odds ratio; RDQ=Roland Morris Disability Questionnaire; RR = relative risk; SF-36 = 36 item short form; VAS = visual analogue scale

Table 10. Summary of systematic reviews of nonpharmacological treatments for low back pain

Treatment	Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Acupuncture	Lee, 2013[364]	11 RCTs, Acute to subacute LBP (<12 weeks), 1139 patients (approximately 50 per arm), 5 low risk of bias	A. Acupuncture (n=3, 74 patients) B. sham (n=3, 74 patients) C. Acupuncture (n=7, 500 patients) D. conventional treatment (i.e., Meds) (n=7, 466 patients) E. Acupuncture + meds (n=1, 24 patients) F. meds alone (n=1, 25 patients)	Moderate evidence of benefit in global improvement with acupuncture compared with NSAIDs, but the effect is very small. Inconsistent benefit of acupuncture compared with NSAIDs in terms of pain relief. Real acupuncture may be more effective than sham at reducing acute pain, but the effect is small and there appears to be no benefit in terms of function. Acupuncture in addition to medication appears more effective for pain relief and function than medication alone, but these differences are small.
	Lam, 2013[365]	32 studies SR, 25 meta (n=6266 patients); 7 low risk of bias, duration of LBP: 4 trials Subacute to chronic LBP (>6 weeks) 28 trials chronic (>3 months), duration of followup 0-48 months	A. acupuncture (n=5,1735 patients) B. no treatment (n=5, 1596 patients) C. acupuncture (n=3, 75 patients) D. medication (n=3, 80 patients) E. acupuncture (n=3, 68 patients) F. TENS, (n=3 studies, 72 patients) G. acupuncture (n=4, 447 patients) H. sham (n=4, 452 patients) acupuncture, I. acupuncture in addition to usual care (n=4, 139 patients) J. self-care or usual care, (n=4, 139 patients) K. electroacupuncture (n=6, 156 patients) L. usual care.(n=6, 162 patients)	Acupuncture improved pain and function immediately post intervention more than no treatment, sham acupuncture or medications such as NSAIDs, muscle relaxants or analgesics, but these differences were small. Patients who received acupuncture in addition to usual care had greater pain relief and improved function immediately postintervention and at followup compared with those who received usual care alone. Patients who received electroacupuncture reported significantly less pain and levels of activity limitation than the control group immediately postintervention and at followup. There was no evidence that acupuncture was better than TENS.

Exercise	Bystrom, 2013186	16 RCTs (1 with 2 arms) (n=1933) 80% with chronic LBP; included studies of subacute if duration >6 months; define sub acute as 4-12 weeks short (6 weeks–4 months), intermediate (4–8 months) and long term (8-15 months) followup	1) A: MCE versus B: general exercise (n=741; 7 trials [1 with 2 arms]) 2) A: MCE versus C: minimal intervention (n=541; 3 trials) 3) A: MCE versus D: multimodal physical therapy (n=499; 4 trials) 4) A: MCE as part of multimodal intervention versus E: other components of that intervention (n=152; 2 trials)	For chronic low back pain, MCE was associated with lower pain intensity versus general exercise: Short term (6 trials, WMD −7.80 on 0 to 100 scale, 95% CI −10.95 to −4.65) Intermediate term (3 trials, WMD −6.06, 95% CI −10.94 to −1.18) Effects were smaller and not statistically significant at long term (4 trials, WMD −3.10, 95% CI −7.03 to 0.83) MCE was also associated with better function: Short term (6 trials, WMD −4.65 on 0 to 100 scale, 95% CI −6.20 to −3.11) Long term (3 trials, WMD −4.72, 95% CI −8.81 to −0.63). For chronic low back pain, MCE was associated with lower pain scores versus minimal intervention: Short term (WMD −12.48 on a 0 to 100 scale, 95% CI−19.04 to −5.93) Intermediate term (WMD −10.18, 95% CI −16.64 to −3.72) Long term (WMD −13.32 95% CI −19.75 to −6.90) MCE was also associated with better function: Short term (3 trials WMD -9.00 on 0 to 100 scale, 95% CI −15.28 to −2.73) Intermediate term (2 trials WMD -5.62, 95% CI−10.46 to −0.77) Long term (2 trials, WMD −6.64, 95% CI −11.72 to −1.57)
	Oesch, 2010[188]	23 RCTs (n=4138) (20 with data for meta-analysis, 17 comparisons of exercise vs. usual care and 11 comparisons of two different exercise) nonacute nonspecific LBP, duration ≥ weeks	A: Exercise versus B: usual care	No effects on work disability at short-term (~4 weeks) or intermediate-term (~6 months) followup, based on pooled analyses of high-quality studies (6 comparisons in 5 trials, OR 0.80, 95% CI 0.51 to 1.25 and 5 comparisons in 4 trials, OR 0.78, 95% CI 0.45 to 1.34, respectively).[188] Exercise, was associated with lower likelihood of work disability at long-term (~12 months) followup (10 comparisons in 8 trials, OR 0.66, 95% CI 0.48 to 0.92).

Exercise	van Middelkoop, 2010[187]	37 RCTs (N=3957) chronic (≥12 weeks) nonspecific LBP post-treatment, short, intermediate, and long-term followup (not defined)	1) A: Exercise versus B:wait list/no treatment (8 trials) 2) A: Exercise versus C: usual care (6 trials) 3) A: Exercise versus D: back school/ education (3 trials) 4) A: Exercise versus E: other forms of exercise therapy (11 trials)	Exercise therapy was associated with decreased pain intensity (3 trials, WMD −9.23, 95% CI –16.02 to –2.43)[193, 200, 210] and better function (3 RCTs, WMD −12.35 on a 0 to 100 scale, 95% CI –23.0 to –1.69)[193, 200, 210] versus usual care at the end of treatment. Effects on function were smaller but remained statistically significant at intermediate- and long-term followup (mean differences -5.23 and -3.17). Effects on pain were also smaller, and no longer statistically significant at long-term followup (mean difference -4.94, 95% CI -10.45 to 0.58).[193, 203, 214]
Lumbar Supports	van Duijvenbode, 2011[573]	8 RCTs; 7 English-language, 1 German language Chronic p 23 RCTs (n=4138) (20 with data for meta-analysis, 17 comparisons of exercise vs. usual care and 11 comparisons of two different exercise) nonacute nonspecific LBP, duration ≥ weeks ain (3 trials), mixed acute, subacute and chronic pain (4 trials); duration of pain not reported in 1 trial	A. Lumbar supports (n=418) B. Other active interventions (spinal manipulation therapy, n=186; other physiotherapy, n=114; massage, n=37; TENS, n=28; exercise [strength training], n=21; analgesics, n=113; nonsupportive corset, n=10) C. No support (n=309) *One trial that randomized 79 participants to support or no support did not report number in each treatment group*	Moderate evidence of no benefit with use of lumbar support compared with no support; evidence on use of lumbar support in combination with another treatment was limited and mixed.

Massage	Furlan, 2010[405]	13 RCTs (n=39 to 262, total 1596) Duration of followup: Immediately after sessions to 52 weeks (42 weeks after completion of therapy) Duration of low back pain: acute (1 RCT), subacute to chronic (4 RCTs), chronic (8 RCTs)	A: Massage (n=111) B: Sham/placebo massage (2 RCTs, n=111) C: Massage (n=1026) D: Other treatments (manipulation [1 RCT, n=67)], exercise [1 RCT, n=47)], relaxation therapy [3 RCTs, n=297)], acupuncture [1 RCT, n=172)], physiotherapy [2 RCTs, n=275]), self-care education [1 RCT, n=168)] E: Massage + other intervention F: Other intervention (exercise and education [1 RCT, n=47], exercise [2 RCTs, n=290], usual care [2 RCTs, n=183]) without massage G: Swedish massage H: Acupuncture massage (1 RCT, n=190) or traditional Thai massage (1 RCT, n=180)	Moderate evidence of short and long (up to 1 year) term improvement of pain and function with massage as compared with sham/placebo or other treatments, but the differences in improvement are small. Massage appears to be most beneficial when added to exercise and/or education. One RCT suggests acupuncture massage is superior to Swedish massage, otherwise there appears to be no difference between massage techniques, although evidence is limited.

Multidisciplinary Rehabilitation	Kamper, 2014[348] (Cochrane)	41 RCTs; all chronic low back pain; MBR vs. usual care: 16 trials; MBR vs. physical treatment: 19 trials; MBR vs. waitlist: 4 trials	1. MBR vs. usual care a. Short-term pain outcomes, 9 trials, 879 patients) b. Long-term pain outcomes, 7 trials, 821 patients) c. Short-term disability outcomes, 9 trials, 939 patients. d. Long-term disability outcomes, 6 trials, 722 patients e. Short-term work outcomes, 2 trials, 373 patients f. Long-term work outcomes, 7 trials, 1360 patients 2. MBR vs. physical treatment a. Short-term pain outcomes, 12 trials, 1661 patients b. Long-term pain outcomes, 9 trials, 872 patients c. Short-term disability outcomes, 13 trials, 1878 patients d. Long-term disability outcomes 10 trials, 1169 patients e. Short-term work outcomes, 3 trials, 379 patients f. Long-term work outcomes 8 trials, 1006 patients 3. MBR vs. waitlist a. Short-term pain outcomes, 3 trials, 213 patients b. Short-term disability outcomes, 3 trials, 213 patients	1. There is evidence that MBR improves pain and disability more than usual care in the short and long term, but no evidence that it improves work outcomes in the short or long term. There is evidence that MBR improves pain and disability more than no MBR in the short term. There is evidence that MBR improves pain, disability, and work outcomes more than physical treatments in the short and long term.
	Guzman, 2001[345]	10 RCTs (476 patients), chronic low back pain	High intensity multidisciplinary rehab (4 trials) Low intensity multidisciplinary rehab (4 trials) Other (3 trials)	Intensive (>100 hour) daily interdisciplinary therapy is more effective than usual care or less intensive therapy for function. Less intensive (<30 hour) interdisciplinary therapy is no more effective than usual care or nonmultidisciplinary therapy.

Pilates	Wells, 2014[286]	14 RCTS chronic LBP of > 3months duration; if studies included acute or subacute LPB with chronic LBP, were included, Pilates vs. standard care and physical activity; Pilates vs. massage; Pilates vs. other exercise	A. Pilates (14 studies) B Standard care and physical activity; vs. massage; vs. other exercise	Pilates was associated with small (mean difference -1.6 to -4.1 points) or no clear effects on pain at the end of treatment versus usual care plus physical activity and no clear effects on function
Psychological Therapies	Henschke, 2010[313] (Cochrane)	28 RCTs Chronic LBP: 28 trials Subacute, acute LBP: 0 trials Psychological therapy vs. waiting list: 12 trials Psychological therapy vs. other noninvasive interventions: 7 trials One psychological therapy vs. another: 10 trials Psychological therapy plus other intervention vs. other intervention alone: 9 trials	A. Psychological therapy vs. waiting list (12 trials total) 1. Respondent therapy (relaxation training) vs. wait list: n=74 (3 trials) 2. Respondent therapy (EMG biofeedback) vs. wait list: n=108 (4 trials) 3. Operant therapy vs. wait list: n=243 (4 trials) 4. Cognitive therapy vs. wait list: n=68 (2 trials) 5. Combined psychological therapies (including CBT) vs. wait list: n=239 (5 trials) B. Psychological therapy vs. other intervention (7 trials total): 1. Psychological therapy vs. usual care: n=330 (2 trials) 2. Psychological therapy vs. group exercise : n=146 (2 trials) 3. Psychological therapy vs. guideline-based care: n=114 (1 trial) 4. Psychological therapy vs. Back education: n=36 (1 trial) 5. Psychological therapy vs. hypnosis: n=15 (1 trial)	Moderate evidence of post-treatment pain relief benefit with operant therapy versus waiting list, and with psychological therapy versus usual care. Moderate evidence that there is no benefit of one type of psychological therapy over another in pain relief through six months. Moderate evidence of no benefit of psychological therapy over group exercise for pain relief or depression through twelve months. Otherwise, there was only low or very low evidence available for other comparisons and/or outcomes. All conclusions are for the chronic low back pain patient population.

Psychological Therapies	Henschke, 2010[313] (Cochrane)		C. One psychological therapy vs. another (10 trials total): 1. Respondent (EMG biofeedback) vs. respondent (relaxation therapy) therapy: n=24 (1 trial) 2. Cognitive vs. operant therapy: n=93 (2 trials) 3. Cognitive vs. respondent therapy: n=93 (1 trial) 4. Combined psychological therapies vs. cognitive therapy: n=61 (2 trials) 5. Combined psychological therapies vs. operant therapy: n=278 (4 trials) 6. Combined psychological therapies vs. respondent therapy: n=97 (4 trials) D. Psychological therapy plus other intervention vs. other intervention alone (9 trials total): 1. Physiotherapy with or without psychological therapy: n=59 (2 trials) 2. Exercise with or without psychological therapy: n=262 (3 trials) 3. Inpatient rehabilitation with or without psychological therapy: n=435 (3 trials) 4. Education booklet/audio cassette with or without psychological therapy: n=234 (1 trial) N=3090 total	

Spinal Manipulation	Rubinstein, 2012[437]	20 RCTs: 9 acute LBP; 4 mixed acute and subacute LBP; 6 any LBP Duration of followup <3 months to > 12 months. More than half of the studies limited followup to short-term measurements only (that is < 3 months) including, in particular, one study that measured the effect two days post-treatment only (Sutlive 2009). Five studies measured the long-term (that is > 12 months) effects of the treatments.	A. Any SMT (n=20) A1. Thrust SMT (n=13) A2. Combination mobilization, manipulation or both SMT (n=4) or unclear (n=3) B. Other active interventions (exercise; physical therapy; massage; standard care; back school; n=8) C. Sham SMT (n=1) D. Inert interventions (education; ultrasound alone; ultrasound + cold; ultrasound; short-wave diathermy; anti-edema gel; bed rest; n=7)	Low to very low-quality evidence of no difference in effect of SMT compared with inert interventions, sham SMT, or when added to another intervention, in terms of pain, function, QOL, work, global improvement. with the exception of moderate short-term effect of SMT on functional status when added to another intervention.
	Rubinstein, 2011[438]	26 total studies with wide variety of comparisons, 9 with low risk of bias, LBP >12 weeks, 18+ years old, outcomes short, intermediate and long term (>12 months)	A. Any SMT (n=26) B. Inert interventions ((i.e., detuned short-wave diathermy and detuned ultrasound; n=4) C. Other active interventions (exercise; physical therapy; massage; standard care; back school; n=15) D. Sham SMT (n=3)	SMT has statistically significant short-term effect on pain and function compared with other interventions; varying quality that SMT has a statistically significant short-term effect on pain and function when SMT is added to another intervention. Effect sizes were small - not clinically relevant. Very low-quality evidence that SMT is no more effective than inert interventions or sham SMT for short-term pain relief or functional status.

Superficial Heat-Cold	French, 2006[511] updated in French, 2011[537]	9 studies: 5 RCTs, 1 CCT, 3 crossover studies Acute pain (1 trial), mixed acute and subacute pain (4 trials), chronic pain (3 trials), mixed acute, subacute and chronic pain (1 trial) Heat vs. placebo (4 trials), heat vs. cold (2 trials), heat vs. other interventions (4 trials), cold vs. other interventions (1 trial) (some trials evaluated multiple comparisons)	A. Heat (hot pack or heated wrap; n=446) B. Cold (cold pack or ice massage; n=94) C. Other active interventions (NSAID, n=238; exercise, n=25; lumbar support, n=38; heat + other intervention, n=24) D. No heat/cold (n=216)	Moderate evidence of benefit on pain relief with use of heat (with or without exercise) in patients with acute or subacute low back pain. No clear evidence in patients with chronic low back pain, or with use of cold treatment in any population.
TENS	van Middelkoop, 2011[512]	6 RCTs, all chronic pain Duration of followup 2-16 weeks	A. TENS B. Other active intervention C. Sham TENS Total n=699	No difference between TENS and sham for pain (4 trials; WMD -4.47, 95% CI -12.84 to 3.89) or function (2 trials; WMD -1.36, 95% CI -4.38 to 1.66). When TENS was compared with other treatments there was also no difference in pain or functional outcomes.
Traction	Wegner, 2013[581]	32 RCTs Chronic LBP: 10 trials Subacute LBP: 1 trial Mixed acute, subacute and chronic: 17 trials Unspecified duration of LBP: 5 trials Traction vs. sham, placebo or no treatment: 13 trials Traction vs. other treatments: 15 trials Traction vs. traction: 5 trials	A. Traction A1. Traction + physiotherapy B. Sham, placebo or no treatment B1. Physiotherapy alone C. Other interventions (exercise, interferential therapy, massage, balneotherapy) Total n=2,762	Regardless of duration of low back pain, there was no strong evidence that use of traction (either alone or in combination with another treatment) has a consistent, positive effect on pain, function, global improvement or return to work.

Ultrasound	Ebadi, 2014[497]	7 RCTs (n=15 to 120) Duration of followup: At end of treatment in all trials except for two trials that evaluated patients 4 weeks and 6 months after end of treatment All trials enrolled patients with chronic low back pain	A: Ultrasound (n=65) B: Sham ultrasound (n=66) C: Ultrasound (n=39) D: No ultrasound (n=40) E: Ultrasound (n=95) F: Other interventions (electrical stimulation, phonophoresis, manipulation (n=96) Exercise therapy in all groups in all trials except for one (n=10)	For chronic low back pain, there was no difference between ultrasound versus sham ultrasound in pain at the end of treatment (3 trials, mean difference -7.12 on 0 to 100 scale, 95% CI -18.0 to 3.75, I2=77%) For chronic low back pain, there were no differences between ultrasound versus no ultrasound in pain (2 trials, mean difference -2.16, 95% CI -4.66 to 0.34, I2=0%) or back-specific function (2 trials, mean difference -0.41, 95% CI -3.14 to 2.32), but estimates were imprecise.
Yoga	Cramer, 2013300	10 RCTs in qualitative synthesis; Two citations with different outcomes from same trial, treated as single study 8 included in quantitative synthesis; 9/10 studies included CLBP patients; 1 included acute, subacute or chronic	A. Yoga B. Usual care C. Education D. Exercise TOTAL n for each intervention unclear across all studies; Total N for all studies=1067	For chronic low back pain, yoga was associated with lower pain intensity and better function versus exercise in most trials, though effects were small and differences were not always statistically significant For chronic low back pain, yoga was associated with: Lower short-term pain intensity versus education (5 trials, SMD -0.45, - 95% CI -0.63 to -0.26; I2=0%) Effects were smaller and not statistically significant at longer-term followup (4 trials, SMD -0.28, 95% CI-0.58 to -0.02' I2=47%) Yoga was also associated with better function: Short-term (5 trials, SMD 0.45, 95% CI-0.65 to -0.25; I2=8%) Long term followup (4 trials, SMD 0.39, 95% CI -0.66 to -0.11; I2=40%)

CBT = cognitive behavioral therapy; CCT = controlled clinical trial; CI = confidence interval; EMG = electromyography; LBP = Low back pain; MBR = Multidisciplinary biopsychosocial rehab; MCE = Motor control exercises; NSAIDs = Nonsteroidal anti-inflammatory drugs; OR = odds ratio; RCTs = Randomized controlled trials; SF-12 = 12 item short form health survey; SMD = standardized mean difference; SMT = spinal manipulation therapy; SR = systematic reviews; TENS = Transcutaneous Electrical Nerve Stimulation; VAS=visual analogue scale; WMD = weighted mean difference

Table 11. Characteristics and conclusions of included exercise trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Albaladejo, 2010[239] 26 weeks Subacute, chronic *Fair*	A. Education + 4 sessions of physiotherapy (n=100) B. Education (n=139) C. Usual care (n=109)	A. vs. B. vs. C. Median age: 51 vs. 51 vs. 53 Female: 68% vs. 63% vs. 72% Median pain intensity: 7.5 vs. 8 vs. 8 Median RDQ: 9.5 vs. 9.0 vs. 7.5 Median CSQ: 7.0 vs. 8.0 vs. 6.0 Median SF-12 PCS: 34.8 vs. 35.8 vs. 36.5 Median SF-12 MCS: 44.6 vs. 50.1 vs. 49.8	A. vs. B. vs. C. Change in median VAS (0-10), low back pain: -2.0 vs. -2.0 vs. 0 Change in median VAS (0-10), referred pain: -2.0 vs. -2.0 vs. -0.5	A. vs. B. vs. C. Improvement in RDQ: 2.0 vs. 1.6 vs. -0.3 Change in CSQ: -1.0 vs. -1.0 vs. 2.0 Change in SF-12 PCS: -3.2 vs. -2.4 vs. 0.6 Change in SF-12 MCS: -2.8 vs. -1.8 vs. 6.1

Albert, 2012[240] 12 months Acute, subacute, chronic *Fair*	A: Symptom-guided exercises (n=95). Directional end-range exercises and postural instructions guided by the individual patient's directional preference (based on the McKenzie method); stabilizing exercises for the transverse abdominis and multifidus muscles and dynamic exercises for the outer layers of the abdominal wall and back extensors; all patients received home exercise programs B: Sham exercises (n=96). Optional exercises that were not back related but were low-dose exercises to simulate an increase in systemic blood circulation. Both groups received identical information and advice and optional paracetamol and/or NSAIDs. Treatment lasted for 8 weeks with a minimum of 4 and a maximum of 8 treatments. Patients were discouraged from receiving any additional treatment of their sciatica.	A. vs. B. Mean age: 46 vs. 44 Female: 43% vs. 53% Baseline Current leg pain (LBPRS): 4.3 ± 2.3 vs. 4.5 ± 2.5 Total leg pain, median (IQR): 18 (15–21) vs. 18 (12–21); p=NS Disability (RDQ), median (IQR): 16 (11–18) vs. 15 (12–18) Quality of Life: 0.62 ± 0.18 vs. 0.62 ± 0.62	A. vs. B. Current leg pain (LBPRS) (mean, SD) 8 weeks (end of treatment): 1.5 ± 2.1 vs. 2.3 ± 2.7; p=0.06 EPC calculation of test mean diff -0.8 (95% CI -0.09 to -1.15) 12 months: 1.5 ± 2.1 vs. 1.4 ± 2.4; p=NS Total leg pain (LBPRS) (median, IQR) 8 weeks: 4 (0–9) vs. 4 (0–12); p=NS 12 months: 3 (0–10) vs. 2 (0–8); p=NS	A. vs. B. Disability (RDQ) (median, IQR) 8 weeks: 6 (2–12) vs. 6 (2–12); p=NS 12 months: 3.5 (1–10) vs. 3.5 (1–10); p=NS ≥30% improvement from baseline: 73% vs. 77.5%; p=NS Quality of Life EQ-5D (mean, SD) 12 months: 0.82 ± 0.21 vs. 0.79 ± 0.24; p=NS Global improvement 8 weeks Much better: 80% vs. 60% Some better: 14% vs. 26% 12 months: Much better: 84% vs. 76% Some better: 16% vs.18% Group A significantly (p<0.008) more improved (better or much better) compared with group B at both time points Patient satisfaction: 93.5% vs. 90.5%; p=NS
Bronfort, 2011[241] 52 weeks Chronic *Good*	A. Supervised exercise therapy for 12 weeks (n=100) B. Chiropractic spinal manipulation for 12 weeks (n=100) C. Home exercise and advice for 12 weeks (n=101)	A. vs. B. vs. C. Mean age: 44.5 vs. 45.2 vs. 45.6 years Female: 57% vs. 66% vs. 58% Mean pain severity score (0-10): 5.1 vs. 5.4 vs. 5.2 Roland-Morris disability score (0-23): 8.4 vs. 8.7 vs. 8.7		Only significant between-group differences in patient-reported outcomes were for satisfaction (favoring A, p<0.01 at 12 weeks and p<0.001 at 52 weeks) Overall treatment effect was significant for endurance (p<0.05) and strength (p<0.05) but not range of motion (also favoring A).

Garcia, 2013[242] 1, 3, 6 months Acute, subacute, chronic *Good*	A: McKenzie method (n=74). Exercises and progression tailored to the individual. Included a basic educational component and guidance on completing the exercises at home. Patients with a direction preference for extension were instructed to use a back roll while sitting. B: Back school (n=74). New exercises were prescribed and progressed following the sequence proposed by the program (i.e., not tailor to the individual). Educational component and theoretical and practical information given. All sessions except for the first were conducted in a group setting. All patients received 4 one-hour sessions over 4 weeks. In all patients, directional preference was assessed at baseline and the treating therapist was informed before the randomization. All patients received information in order to maintain lordosis while sitting without exacerbating their symptoms	A. vs. B. Mean age: 53.7 vs. 54.2 years Female: 78.4% vs. 68.9% Duration of LBP: 21 vs. 24 months Recent episode of LBP: 62.2% vs. 63.5% Pain intensity (NRS, 0-10): 6.77 ± 2.12 vs. 6.41 ± 2.54 Disability (RDQ, 0-24): 11.32 ± 4.95 vs. 11.08 ± 5.84 Quality of life (WHOQOL-BREF, 0-100) Physical domain: 51.64 ± 14.49 vs. 51.49 ± 17.05 Psychological domain: 62.88 ± 15.86 vs. 60.11 ± 15.86 Social domain: 63.62 ± 18.27 vs. 63.15 ± 18.96 Environmental domain: 55.40 ± 13.66 vs. 54.74 ± 16.09	A. vs. B. Unadjusted mean difference ± SD for A. vs. B.; adjusted mean difference (95% CI) for B – A Pain intensity (NRS, 0–10) 1 month: 4.14 ± 2.87 vs. 4.39 ± 2.73; 0.66 (–0.29 to 1.62), p=0.17 3 months: 5.18 ± 2.61 vs. 5.53 ± 2.78; 0.71 (–0.23 to 1.67), p=0.14 6 months: 5.09 ± 2.89 vs. 5.19 ± 3.08; 0.48 (–0.47 to 1.43), p=0.32	A. vs. B.:Unadjusted mean difference ± SD for A. vs. B.; adjusted mean difference (95% CI) for B – A Disability (RDQ, 0–24) 1 month: 6.20 ± 5.06 vs. 8.15 ± 5.79; 2.37 (0.76 to 3.99), p=0.004 3 months: 7.12 ± 5.67 vs. 8.39 ± 6.30; 1.51 (–0.09 to 3.11), p=0.06 6 months: 6.77 ± 6.02 vs. 8.12 ± 6.45; 1.55 (–0.05 to 3.16), p=0.06 Achievement of clinically important difference (5-point improvement): 53% (39/74) vs. 30% (22/73), p=0.01; RR 1.8, 95% CI 1.2 to 2.7 (calculated by EPC) Quality of Life (WHOQOL-BREF, 0-100) Physical domain: 1 month: 62.45 ± 16.94 vs. 59.27 ± 16.88; –3.65 (–8.26 to 0.96), p=0.12 3 months: 62.25 ± 15.37 vs. 57.43 ± 17.76; –4.67 (–9.26 to –0.07), p=0.04 6 months: 61.48 ± 16.12 vs. 60.76 ± 18.87; –0.44 (–5.04 to 4.16), p=0.85 Psychological domain:1 month: 67.68 ± 15.15 vs. 65.12 ± 13.98; –0.18 (–4.17 to 3.80), p=0.92 3 months: 67.62 ± 16.07 vs. 65.14 ± 14.14; 0.14 (–3.82 to 4.11), p=0.94 6 months: 68.00 ± 14.18 vs. 66.72 ± 14.15; 1.50 (–2.48 to 5.47), p=0.46 Social domain:1 month: 67.45 ± 18.00 vs. 67.24 ± 15.96; –0.47 (–5.50 to 4.56), p=0.85 3 months: 69.03 ± 16.11 vs. 65.76 ± 16.00; –3.15 (–8.16 to 1.85), p=0.21 6 months: 66.00 ± 18.74 vs. 66.09 ± 15.00; 0.26 (–4.75 to 5.28), p=0.91 Environmental domain:1 month: 58.57 ± 14.82 vs. 57.62 ± 16.48; –0.51 (–4.06 to 3.03), p=0.77 3 months: 58.23 ± 14.65 vs. 56.16 ± 14.75; –1.41 (–4.94 to 2.12), p=0.43 6 months: 57.84 ± 14.61 vs. 57.44 ± 15.00; 0.29 (–3.24 to 3.83), p=0.87

George, 2008[243] 6 months Acute, subacute *Poor*	A: TBC + GX (n=33). Fearful activities assessed; top 2 most feared activities implemented under this protocol using progression based on 0-10 NRS fear rating and performed under supervision of physical therapy and clinical staff. Also received patient education materials focused on biopsychosocial model. B: TBC + GA (n=35). Parameters (duration, intensity, and frequency) used to reach pain tolerance were then established as the activity quota; graded activity principles were used to progress exercise during subsequent treatment sessions. Also received patient education materials focused on biopsychosocial model C: Physical therapy based on the treatment-based classification (TBC) system (Delitto et al.) (n=34). Also received educational materials that were anatomically focused.	A. vs. B. vs. C. Mean age: 40.1 vs. 37.6 vs. 34.9 years Female: 64% vs. 69% vs. 68% Baseline Pain (NRS, 0-10): 4.7 ± 2.1 vs. 5.2 ± 1.8 vs. 4.3 ± 2.0 Function (PIS): 3.1 ± 1.6 vs. 3.6 ± 2.1 vs. 2.9 ± 1.7 Disability (ODI): 30.7 ± 15.6 vs. 31.1 ± 15.8 vs. 29.2 ± 15.7	A. vs. B. vs. C. Pain intensity (NRS, 0–10) High fear Baseline: 5.1 ± 2.1 vs. 5.1 ± 1.9 vs. 5.1 ± 1.8 4 weeks: 2.1 ± 2.0 vs. 2.3 ± 2.1 vs. 2.0 ± 1.6 6 months: 2.1 ± 2.3 vs. 1.5 ± 2.1 vs.1.6 ± 1.3 Low fear Baseline: 3.9 ± 1.5 vs. 4.9 ± 2.1 vs. 3.1 ± 2.1 4 weeks: 1.7 ± 0.9 vs. 2.1 ± 2.1 vs. 1.8 ± 1.9 6 months: 1.0 ± 1.0 vs. 2.3 ± 1.7 vs. 1.0 ± 1.2 Effect sizes Pain intensity (NRS, 0-10) 4 weeks A. vs. B.: 0.11 A. vs. C: –0.05 B vs. C: –0.16 6 months A. vs. B.: –0.32 A. vs. C: –0.26 B vs. C: 0.01 p=NS for all comparisons. These post hoc effect sizes suggest that for the primary comparisons of interest (GX vs. GA and GX vs. TBC) total sample sizes needed to detect these magnitudes of differences would range from 114 to over 700.	A. vs. B. vs. C. Disability (ODI, 0–100) High fear Baseline: 32.3 ± 16.3 vs. 29.9 ± 18.4 vs. 32.9 ± 16.1 4 weeks: 16.5 ± 12.1 vs. 11.5 ± 11.8 vs.16.4 ± 14.9 6 months: 16.7 ± 17.6 vs. 11.3 ± 14.2 vs.11.4 ± 11.5 Low fear Baseline: 20.4 ± 13.1 vs. 30.4 ± 13.3 vs. 23.0 ± 15.5 4 weeks: 11.4 ± 11.6 vs. 16.7 ± 11.9 vs. 12.0 ± 11.5 6 months: 9.7 ± 8.2 vs. 15.8 ± 11.1 vs. 5.8 ± 7.1 Effect sizes Disability (ODI, 0-100) 4 weeks A. vs. B.: –0.40 A. vs. C: –0.02 B vs. C: 0.39 6 months A. vs. B.: –0.38 A. vs. C: –0.37 B vs. C: 0.01 p=NS for all comparisons. These post hoc effect sizes suggest that for the primary comparisons of interest (GX vs. GA and GX vs. TBC) total sample sizes needed to detect these magnitudes of differences would range from 114 to over 700. Proportion of Success vs. Failure (ODI >10 point change, NRS >2 point change) at 6 months NRS 46% vs. 43% vs. 41% ODI 43% 41%, 56% p=0.70

Hagen, 2010[244] 24 months LBP duration not reported *Fair*	A: Standardized physical exercise program (n=124). Aim was to re-educate the trunk muscle to its normal stabilizing role and to improve balance, muscle coordination, and proprioception; program included warm-up (8 minutes), circuit training (34 minutes), stretching (13 minutes), and relaxation (5 minutes); duration 1 hour, 3x/week for 8 weeks. B: No treatment (n=122). Received a brief intervention program before randomization.	A. vs. B. Mean age: 40.7 vs. 41.6 years Female: 52% vs. 50%	A. vs. B No statistically significant difference between groups at any followup time point - 6, 12, 18 or 24 months – for Pain intensity.	A. vs. B. Only statistically significant difference found was for the sock test (physical function), which was more improved in Group A. vs. B.: mean difference –0.34; 95% CI –0.66 to –0.01; p=0.041 (time point NR). No statistically significant difference between groups at any followup time point - 6, 12, 18 or 24 months - for the following (no data provided): Functional tests (pick-up test, loaded reach test, 15 meter walk, fingertip-to-floor test, static balance test) Physical activity Walking distance Disability (RDQ) Subjective health complaints Psychological distress (HSCL-25) Return to work
Hartvigsen, 2010[245] 52 weeks Acute, subacute, chronic *Fair*	A. Supervised Nordic walking in groups twice/week for 8 weeks (n=45) B. Nordic walking instruction for 1 hour, with instruction to continue independently (n=46) C. Active living and exercise information (n=45)	A. vs. B. vs. C. Mean age: 49.2 vs. 45.4 vs. 45.5 years Female: 76% vs. 69% vs. 68% LBP rating scale (0-100), pain: 46.1 vs. 50.7 vs. 47.3 LBP rating scale (0-100), function: 44.4 vs. 47.3 vs. 48.9 Patient-specific function scale (0-100): 18.4 vs. 20.1 vs. 17.3 EQ-5D (0-100): 67.5 vs. 62.7 vs. 63.9	A. vs. B. vs. C. Mean improvement at 8 weeks in LBP rating scale, pain: 8.8 vs. 3.4 vs. 4.8; significant at all time-points for group A, significant only at 8 and 26 weeks for group B, significant only at 8 weeks for group C; no significant between-group differences at any point	A. vs. B. vs. C. Mean improvement at 8 weeks in LBP rating scale, function: 7.4 vs. 3.2 vs. 3.8; significant at all time-points for group A, never significant for group B, and significant only at 8 and 26 weeks in group C; no significant between-group differences at any point Patient-specific function scale: all groups improved significantly from baseline, but there were no between-group differences EQ-5D: very small and similar changes in all groups

Helmhout, 2008[246] 62 weeks Acute, subacute, chronic Poor	A: Lumbar extensor strength training program (n=71). Standardized, progressive resistance training of the isolated lumbar extensor muscle groups aimed at both strength and endurance gain; duration 10 weeks, 14 sessions 2x/wk and 3 isometric back strength tests (in weeks 1, 5, and 10). Training sessions were carried out on a Total Trunk Rehab machine. Patients were not allowed to undergo cotreatments during the treatment period. B: Regular physical therapy program (n=56). Regular physical therapy for 10 weeks, or less when the patient was free of complaints; could include hands-on treatment (e.g., passive mobilizing and pain cushioning techniques, manual therapy) and/or hands-off treatment (e.g., exercise therapy, individual education, instruction on the back function) (in the Dutch army, active therapy forms are favored); no cotreatments allowed, nor exercise on equipment that mimicked the specific components of the lower back machine	A. vs. B. Mean age: 37 vs. 35 years Female: 3% vs. 4% Baseline Function (PSFS): 178 ± 65 vs. 178 ± 52 Disability (RDQ): 8.3 ± 4.8 vs. 7.9 ± 4.4 Back extension strength (NMT): 214 ± 64 vs. 212 ± 65	A. vs. B. (mean ± SD; between group difference, 95% CI) LBP episodes 6 months (back pain in 1st half of year after the end of the treatment period?) (A, n=56; B, n=40): No, not at all: 9% vs. 18% Yes, incidentally: 57% vs. 63% Yes, monthly: 11% vs. 3% Yes, weekly: 23% vs. 18% 12 months (back pain in 2nd half of year after the end of the treatment period?) (A, n=61; B, n=46): No, not at all: 25% vs. 22% Yes, incidentally: 55% vs. 50% Yes, monthly: 2% vs. 11% Yes, weekly: 18% vs. 17%	A. vs. B. (mean ± SD; between group difference, 95% CI) Function (PSFS, score 0–300) 5 weeks: 119 ± 70 (n=64) vs. 116 ± 67 (n=46) 10 weeks: 85 ± 72 (n=59) vs. 97 ± 74 (n=47); –0.608 (–2.693 to 1.477), p=0.57 36 weeks: 74 ± 72 (n=57) vs. 64 ± 59 (n=37) 62 weeks: 69 ± 71 (n=61) vs. 65 ± 69 (n=45); –0.136 (–0.344 to 0.616), p=0.58 Disability (RDQ, score 0–24) 5 weeks: 5.8 ± 4.8 (n=64) vs. 4.2 ± 4.2 (n=46) 10 weeks: 3.4 ± 4.6 (n=59) vs. 3.5 ± 4.2 (n=47); –0.025 (–0.134 to 0.085), p=0.66 36 weeks: 3.2 ± 4.3 (n=57) vs. 2.7 ± 3.8 (n=37) 62 weeks: 2.6 ± 4.4 (n=61) vs. 2.5 ± 3.9 (n=45); 0.000 (– 0.025 to 0.026), p=0.99 Global perceived effect (GPE) 5 weeks: no data 10 weeks: 2.4 ± 0.8 (n=59) vs. 2.4 ± 0.7 (n=47) 36 weeks: 2.5 ± 1.0 (n=57) vs. 2.3 ± 0.9 (n=37) 62 weeks: 2.2 ± 1.0 (n=61) vs. 2.3 ± 1.0 (n=45); –0.002 (–0.010 to 0.006), p=0.66 Patient satisfaction (very satisfied; final degree of satisfaction at end of treatment program): 89% (n=56) vs. 89% (n=46) Back extension strength (NMT) 5 weeks: 23 ± 62 (n=64) vs. 246 ± 74 (n=46) 10 weeks: 244 ± 66 (n=59) vs. 247 ± 73 (n=47) 36 weeks: 264 ± 64 (n=57) vs. 254± 73 (n=37) 62 weeks: 267 ± 62 (n=61) vs. 249 ± 74 (n=45) p=NS for all time points

Henchoz, 2010[256] 52 weeks Subacute, chronic *Poor*	A. Functional multidisciplinary rehabilitation, followed by a 12-week exercise program (n=56) B. Functional multidisciplinary rehabilitation, followed by usual care (n=49)	A. vs. B. Mean age: 41 vs. 39 years Female: 34% vs. 45% Mean VAS (0-100): 5.3 vs. 5.1	A. vs. B. VAS (0-100): 3.8-3.8 (p=0.521) vs. 3.6-3.8 (p=0.995)	A. vs. B. ODI: 30.2-25.3 (p<0.001) vs. 30.5-27.2 (p=0.059) SFS: 66.1-89.8 (p<0.05) vs. 65.5-78.8 (p=0.653) Sorensen test (s): 64.8-81.6 (p<0.05) vs. 67.1-63.9 (p=0.249) MMS test, flexion (cm): 5.65-5.15 (p=0.368) vs. 5.27-5.19 (p=0.561) MMS test, extension (cm): -1.63 to -1.61 (p=0.138) vs. -1.46 to -1.64 (p=0.353) Fingertip-floor distance (cm): 126.5-135.7 (p=0.076) vs. 129.1-136.0 (p=0.470) Shirado test (seconds): 11.3-8.0 (p=0.063) vs. 17.3-10.0 (p<0.001) Modified Bruce test (minutes): 11.2-8.4 (p<0.001) vs. 11.2-8.7 (p<0.001)

Hofstee, 2002[248] 6 months Acute *Poor*	A: Physiotherapy (n=83). The protocol consisted of instructions and advice, segmental mobilization, disc unloading and loading exercises, depending on patients' conditions, and hydrotherapy; 2x/week for at least 4 to 8 weeks; asked to perform daily exercises at home. B: Bed rest (at home or in hospital) (n=84). Instructed to stay in bed for 7 days; only allowed out of bed to use the bathroom and shower. After this period, patients supposed to rest as much as possible when in pain. C: Continuation of ADLs (control group) (n=83). Continue jobs, household activities, studies, or hobbies to the best of the patients' abilities; advised to adjust the intensity, duration, and frequency of their activities according to the pain they experienced. All patients received a brochure with instructions and advice regarding their respective treatment; were allowed to use analgesic medication and to call the investigator for help if they had problems or questions. When patients called, they were reassured and urged to comply with their assigned treatment; if necessary, they were seen at the outpatient clinic.	A. vs. B. vs. C. Mean age: 38 vs. 38 vs. 41.9 years; p=0.02 Female: 37% vs. 32% vs. 31% Baseline Pain (VAS, 0-100): 60.9 ± 20.1 vs. 65.5 ± 18.5 vs. 60.7 ± 21.4 Disability (QDS): 56.0 ± 17.6 vs. 58.6 ± 14.6 vs. 57.4 ± 16.3	A. vs. B. vs. C. Mean improvement in scores from baseline Pain (VAS, 0–100) 1 month (mean): 24.2 (n=80) vs. 25.9 (n=84) vs. 23.4 (n=83) 1 month differences (95% CI) A. vs. B.: –1.7 (NR) A. vs. C: 0.8 (–8.2 to 9.8) 2 months (mean): 37.0 (n=77) vs. 38.1 (n=82) vs. 37.3 (n=79) 2 months difference (95% CI) A. vs. B.: –1.1 (NR) A. vs. C: –0.3 (–9.4 to 10.0) 6 months (mean): 46.8 (n=72) vs. 48.2 (n=78) vs. 47.8 (n=75) 6 months difference (95% CI) A. vs. B.: –1.4 (NR) A. vs. C: –1.0 (–10.0 to 8.0)	A. vs. B. vs. C. Mean improvement in scores from baseline Disability (QDS, 0–100) 1 month (mean): 15.7 (n=80) vs. 11.4 (n=84) vs. 16.2 (n=83) 1 month differences (95% CI) A. vs. B.: 4.3 (NR) A. vs. C: –0.5 (–6.3 to 5.3) 2 months (mean): 26.3 (n=77) vs. 23.5 (n=82) vs. 26.3 (n=79) 2 months difference (95% CI) A. vs. B.: 2.8 (NR) A. vs. C: 0.0 (–7.2 to 7.3) 6 months (mean): 34.6 (n=72) vs. 32.7 (n=78) vs. 35.4 (n=75) 6 months difference (95% CI) A. vs. B.: 1.9 (NR) A. vs. C: –0.7 (–8.4 to 6.9) Cumulative No. of patients, A. vs. B. vs. C; OR (95% CI) Treatment failure 1 month: 2% (n=2) vs. 6% (n=5) vs. 7% (n=6); A. vs. C: 0.3 (0.1–1.6); A. vs. B.: NR 2 months: 13% (n=11) vs. 19% (n=16) vs. 12% (n=10); A. vs. C: 1.1 (0.7–2.8); A. vs. B.: NR 6 months: 23% (n=19) vs. 25% (n=21) vs. 17% (n=14); A. vs. C: 1.5 (0.7–3.2); A. vs. B.: NR Surgery 1 month: 2% (n=2) vs. 5% (n=4) vs. 6% (n=5); A. vs. C: 0.4 (0.1–2.0); A. vs. B: NR 2 months: 12% (n=10) vs. 13% (n=11) vs. 11% (n=9); A. vs. C: 1.1 (0.4–2.9); A. vs. B.: NR 6 months: 16% (n=13) vs. 19% (n=16) vs. 13% (n=11); A. vs. C: 1.2 (0.5–2.9); A. vs. B.: NR

Hurley, 2015[249] 52 weeks Chronic *Fair*	A. Exercise class for 8 weeks (n=83) B. Walking program for 8 weeks (n=82) C. Usual physiotherapy for 8 weeks (n=81)	A. vs. B. vs. C. Mean age: 45.8 vs. 46.2 vs. 44.2 years Female: 71% vs. 71% vs. 62% Mean pain over past week, NRS (0-10): 5.6 vs. 5.5 vs. 6.0 ODI: 38 vs. 35 vs. 33 EQ-5D: 0.52 vs. 0.57 vs. 0.51	A. vs. B. vs. C. Average pain, NRS (0-10): 5.1 vs. 4.2 vs. 4.1; p=0.15	A. vs. B. vs. C. ODI: 27 vs. 27 vs. 27; p=0.37 EQ-5D: 0.62 vs. 0.63 vs. 0.62; p=0.72
Inani, 2013[279] 3 months LBP duration not specified *Poor*	A: MCE; phase 1, patient taught to cognitively perform skilled activation of deep muscle while relaxing superficial muscle; phase 2, improve precision of task including coordinating with breathing, progression to static function position, progression to light dynamic task; phase 3, coordinate the activity of deep and superficial muscles without the global muscle taking over using closed and open chain activities; phase 4 function re-education, subject specific; exercises included transversus abdominus and lumbar multifidus exercises, slow curl-ups, sit-ups, oblique plan/side bridge, and bird-dog exercises.(n=15) B: Conventional exercise; stretching, isometric exercises of spine (hollowing in abdominals, isometric for back extensors), bridging exercises, graded active flexion and extension exercises of spine (n=15) For both groups: 4 weeks regular continuous monitoring in OPD followed by successive followup 3x/week for remaining 2 months; ergonomic advice given	A. vs. B. Mean age (years): 27.8 vs. 32.9 Female: 40.0% vs. 26.7% Baseline Pain intensity (VAS 0-10): 6.3 ± 1.8 vs. 7.0 ± 1.6 Function/disability (modified ODI): 19.0 ± 6.4 vs. 21.4 ± 5.4 Disability (%): 38.0 ± 13.0% vs. 42.9 ± 11.0%	A. vs. B. (mean ± SD, t-test) VAS pain (0–10 cm): 1.4 ± 0.9 vs. 2.3 ± 1.1, t=2.273, p=0.031	A. vs. B. (mean ± SD, t-test) Modified ODI: 4.4 ± 2.3 vs. 8.0 ± 3.2, t=3.443, p=0.002 Disability (%): 8.8 ± 4.7% vs. 16.0 ± 6.5%, t=3.443, p=0.002

Jensen, 2012[250] 52 weeks Acute, subacute, chronic *Good*	A. Rest, avoiding hard physical activity and rest twice daily for one hour over 10 weeks (n=50) B. Exercise for 10 weeks (n=50)	A. vs. B. Mean age: 47 vs. 45 years Female: 67% vs. 69% Mean pain, NRS (0-10): 5.6 vs. 5.1 Mean RDQ: 12.0 vs. 13.3 Mean EQ-5D: 0.68 vs. 0.62 Mean BDI: 10.7 vs. 9.6	A. vs. B. (adjusted differences for intervention group) Post treatment Pain: 5.0 vs. 4.5; adjusted difference -0.07 (95% CI -0.9 to 0.7) One-year followup Pain: 4.8 vs. 4.3; adjusted difference -0.3 (95% CI -1.3 to 0.6)	A. vs. B. (adjusted differences for intervention group) Post treatment) RDQ: 11.0 vs. 11.1; adjusted difference -0.6 (95% CI -2.2 to 1.0) EQ-5D: 0.7 vs. 0.7; adjusted difference 0.04 (95% CI -0.007 to 0.09) BDI: 8.6 vs. 7.9; adjusted difference 0.67 (95% CI -0.99 to 2.3) vs. 0.08 (95% CI -0.3 to 0.4) One-year followup RDQ: 10.7 vs. 10.7; adjusted difference -1.2 (95% CI -3.3 to 1.0) EQ-5D: 0.7 vs. 0.7; adjusted difference 0.06 (95% CI -0.008 to 0.14) BDI: 9.5 vs. 8.0; adjusted difference -0.92 (95% CI -2.8 to 0.97) vs. -0.17 (95% CI -0.6 to 0.22)
Kell, 2011[251] 13 weeks Subacute, chronic *Poor*	A. PMR training four days per week with 1,563 repetitions each week (n=60) B. PMR training three days per week with 1,344 repetition each week (n=60) C. PMR training twice per week with 564 repetitions per week (n=60) D. No training (n=60)	A. vs. B. vs. C. vs. D. Mean age: 42.4 ± 5.6 vs. 41.7 ± 6.1 vs. 42.8 ± 6.3 vs. 43.2 ± 5.9 Female: 30% vs. 37% vs. 33% vs. 38.3%	A. vs. B. vs. C. vs. D. VAS pain (0-10): 4.35 ± 0.95 vs. 4.77 ± 1.00 vs. 4.96 ± 1.03 vs. 5.70 ± 0.86 p≤0.05 difference A. vs. B., C, and D p≤0.05 difference B and C vs. D	A. vs. B. vs. C. vs. D. Bench press (function): 79.3 ± 9.7 vs. 70.4 ± 9.1 vs. 68.2 ± 9.7 vs. 53.3 ± 9.3 p≤0.05 difference A. vs. B., C, and D Lat pull down (function): 75.3 ± 7.1 vs. 70.1 ± 7.7 vs. 67.2 ± 7.4 vs. 56.0 ± 6.1 p≤0.05 difference A. vs. B., C, and D p≤0.05 difference B and C Leg press (function): 237.2 ± 29.0 vs. 201.7 ± 30.8 vs. 184.2 ± 29.5 vs. 139.9 ± 28.9 p≤0.05 difference A. vs. B., C, and D p≤0.05 difference B and C ODI: 27.1 ± 10.7 vs. 31.6 ± 11.1 vs. 31.8 ± 10.9 vs. 39.1 ± 10.1 p≤0.05 difference A. vs. B., C, and D p≤0.05 difference B and C vs. D PCS: 55.7 ± 7.8 vs. 50.4 ± 8.0 vs. 50.2 ± 8.7 vs. 45.0 ± 8.0 p≤0.05 difference A. vs. B., C, and D p≤0.05 difference B and C vs. D MCS: 57.7 ± 8.2 vs. 52.6 ± 7.8 vs. 53.1 ± 8.3 vs. 46.0 ± 8.2 p≤0.05 difference A. vs. B., C, and D p≤0.05 difference B and C vs. D

Little, 2008[252] 52 weeks Subacute, chronic *Good*	A. Exercise + 24 lessons in Alexander technique (n=71) B. Exercise + 6 lessons in Alexander technique (n=71) C. Exercise + massage (n=72) D. Exercise (n=72) E. 24 lessons in Alexander technique (n=73) F. 6 lessons in Alexander technique (n=73) G. Massage (n=75) H. Usual care (n=72)	A. vs. B. vs. C. vs. D. vs. E. vs. F. vs. G. vs. H. Mean age: 46 vs. 46 vs. 45 vs. 45 vs. 45 vs. 46 years Female sex: 73% vs. 78% vs. 63% vs. 64% vs. 68% vs. 71%	A. vs. B. vs. C. vs. D. vs. E. vs. F. vs. G. vs. H. Number of days of pain in previous 4 months vs. usual care: -20 (p=0.001) vs. -13 (p=0.031) vs. -11 vs. -11 vs. -20 (p=0.001) vs. -13 (p=0.034) vs. -8 vs. 0 (ref)	A. vs. B. vs. C. vs. D. vs. E. vs. F. vs. G.vs. H. Roland disability score vs. usual care: -4.22 (p=0.002) vs. -2.98 (p=0.002) vs. -2.37 (p=0.015) vs. -1.65 vs. -4.14 (p<0.001) vs. -1.44 vs. -0.45 vs. 0 (ref) SF-36 PCS vs. usual care: 9.43 (p=0.015) vs. 8.53 (p=0.029) vs. 3.63 vs. -2.08 vs. 11.83 (p=0.002) vs. 2.04 vs. -1.45 vs. 0 (ref) SF-36 MCS vs. usual care: 4.99 vs. 0.64 vs. 2.73 vs. 0.72 vs. 3.74 vs. 4.10 vs. -2.11 vs. 0 (ref)s
Macedo, 2012[253] 12 months Subacute, chronic *Fair*	A: MCE; stage 1 = retraining program to improve activity of muscles assessed to have poor control and reduce activity of any muscle identified to be overactive; taught how to contract trunk muscles in a specific manner and progress until able to maintain isolated contractions of the target muscles for 10 reps of 10 seconds each while maintaining normal respiration (feedback available to enhance learning); additional exercises for breathing control, spinal posture, and lower limb and trunk movement were performed; stage 2 = progression toward more functional activities, first using static and then dynamic tasks; motor control exercise guided by pain, and exercises were mostly pain-free. (n=86)	A. vs. B. Mean age: 48.7 vs. 49.6 years Female: 66.3% vs. 52.3% Baseline Pain intensity (NRS 0-10): 6.1 vs. 6.1 Function (PSFS): 3.7 vs. 3.6 Disability (RDQ-24): 11.4 vs. 11.2 Quality of Life (SF-36 PCS and MCS): 43.9 vs. 43.8 and 52.9 vs. 54.7 Global impression of change (GPE): –1.4 vs. –1.6	A. vs. B. (mean ± SD; adjusted treatment effect (95% CI)) Pain intensity (NRS 0-10) baseline: 6.1 ± 1.9 vs. 6.1 ± 2.1 (NS) 2 months: 4.1 ± 2.5 vs. 4.1 ± 2.5, 0.0 (–0.7 to 0.8), p=0.94 6 months: 4.1 ± 2.5 vs. 4.1 ± 2.7, 0.0 (–0.8 to 0.8), p=0.99 12 months: 3.7 ± 2.7 vs. 3.7 ± 2.6, 0.1 (–0.7 to 0.9), p=0.83	A. vs. B. (mean ± SD; adjusted treatment effect (95% CI)) Function (PSFS) baseline: 3.7 ± 1.6 vs. 3.6 ± 1.6 (NS) 2 months: 5.9 ± 2.1 vs. 5.5 ± 2.4, 0.2 (–0.5 to 0.9), p=0.53 6 months: 5.7 ± 2.3 vs. 5.7 ± 2.4, –0.2 (–0.9 to 0.5), p=0.53 12 months: 5.9 ± 2.2 vs. 6.1 ± 2.3, –0.4 (–1.1 to 0.3), p=0.25 Disability (RDQ-24) baseline: 11.4 ± 4.8 vs. 11.2 ± 5.3 (NS) 2 months: 7.5 ± 6.4 vs. 8.0 ± 6.5, –0.8 (–2.2 to 0.7), p=0.30 6 months: 8.0 ± 7.1 vs. 8.6 ± 6.8, –0.8 (–2.3 to 0.6), p=0.26 12 months: 7.4 ± 6.7 vs. 8.0 ± 6.9, –0.6 (–2.0 to 0.9), p=0.45 Quality of Life, SF-36 PCS baseline: 43.9 ± 10.8 vs. 43.8 ± 10.3 (NS) 2 months: 51.6 ± 12.0 vs. 51.6 ± 13.4, –0.2 (–13.7 to 3.2), p=0.89

Macedo, 2012[253] 12 months Subacute, chronic *Fair*	B: Graded activity; increase activity tolerance by performing individualized and submaximal exercises (based on activities that each participant identified as problematic/could not perform due to pain), in addition to ignoring illness behaviors and reinforcing wellness behaviors; activities progressed in a time-contingent manner; patients received daily quotas and instructed to only perform the agreed amount. (n=86) Both groups to receive 14 individually supervised sessions of approximately 1 hour (12 initial treatment sessions over an 8-week period [2x wk for first 4 weeks then 1x/week for next 4 weeks] and 2 booster sessions at 4 and 10 months following randomization; advised to do home exercises (type, intensity, number at discretion of physical therapy) for 30 minutes/week in first month and 1 hr/week in second month.			6 months: 52.6 ± 13.0 vs. 51.2 ± 13.8, 1.1 (–2.4 to 4.6), p=0.54 12 months: 53.8 ± 12.7 vs. 53.3 ± 14.0, –0.3 (–3.8 to 3.3), p=0.88 Quality of Life, SF-36 MCS baseline: 52.9 ± 10.5 vs. 54.7 ± 11.5 (NS) 2 months: 56.0 ± 10.9 vs. 55.8 ± 13.0, 2.3 (–0.7 to 5.3), p=0.14 6 months: 54.9 ± 10.4 vs. 56.9 ± 11.8, 0.1 (–3.0 to 3.1), p=0.97 12 months: 57.0 ± 10.1 vs. 58.2 ± 10.8, 0.8 (–2.3 to 3.9), p=0.62 Global impression of change (GPE) baseline: –1.4 ± 2.3 vs. –1.6 ± 2.6 (NS) 2 months: 2.0 ± 1.9 vs. 2.0 ± 1.9, –0.1 (–1.0 to 0.7), p=0.74 6 months: 1.6 ± 2.4 vs. 1.5 ± 2.5, 0.0 (–0.9 to 0.8), p=0.91 12 months: 1.8 ± 2.5 vs. 1.5 ± 2.5, 0.2 (–0.6 to 1.0), p=0.62

Machado, 2010[254] 3 months Acute *Fair*	A: McKenzie method + first-line care (n=73). Number of treatment sessions at discretion of the physical therapy, with a max of 6 session over 3 weeks; encouraged to perform the prescribed exercises at home and to follow physical therapists' postural advice at all times; some participants received lumbar support (93%, original McKenzie lumbar roll). B: First-line care only (n=73). Consisted of advice to remain active and to avoid bed rest, reassurance of the favorable prognosis of acute LBP and instructions to take acetaminophen (paracetamol) on a time-contingent basis (NSAIDs not prescribed however those already on them were allow to remain on them); 3 weeks, return for followup as needed during that time	A. vs. B. Mean age: 47.5 vs. 45.9 years Female: 52% vs. 48% Baseline Pain (NRS 0-10): 6.6 ± 1.8 vs. 6.3 ± 1.9 Function (PSFS): 3.7 ± 1.6 vs. 3.4 ± 1.8 Disability (RDQ): 13.7 ± 5.5 vs. 13.5 ± 5.3	A. vs. B. (treatment effects [95% CI] are model-based adjusted differences in outcomes between groups) Pain (NRS 0-10) 1 week: –0.4 (–0.8 to –0.1); p=0.02 (A, n=70; B, n=69) 3 weeks: –0.7 (–1.2 to –0.1); p=0.02 (A, n=70; B, n=68) Mean pain over first 7 days: –0.3 (–0.5 to –0.0); p=0.02 (A, n=70; B, n=69)	A. vs. B. (treatment effects [95% CI] are model-based adjusted differences in outcomes between groups) Function (PSFS) 1 week: 0.0 (–0.4 to 0.5); p=0.90 (A, n=70; B, n=68) 3 weeks: 0.0 (–0.7 to 0.8); p=0.90 (A, n=70; B, n=69) Disability (RDQ) 1 week: –0.2 (–1.5 to 1.0); p=0.74 (A, n=70; B, n=68) 3 weeks: –0.3 (–2.3 to 1.6); p=0.74 (A, n=70; B, n=69) Global perceived effect 1 week: 0.5 (–0.0 to 1.1); p=0.07 (A, n=70; B, n=68) 3 weeks: 0.3 (–0.3 to 0.8); p=0.33 (A, n=70; B, n=69) Development of persistent LBP: 53% (37/70) vs. 47% (32/68); RR 1.1, 95% CI 0.8 to 1.6, p=0.49 Sought additional health care for LBP complaints: 7% (5/70) vs. 26% (18/68); RR 0.27, 95% CI 0.1 to 0.7, p=0.002
Pengel, 2007[255] 12 months Acute, subacute *Fair*	A: Exercise and advice (n=63). B: Sham exercise and advice (n=63). C: Exercise and sham advice (n=65). D: Sham exercise and sham advice (n=68). **Exercise**: Based on program described by Lindstrom and colleagues, to improve the abilities of participants to complete functional activities that they specified as being difficult to perform because of low back pain and includes: aerobic exercise (for example, a walking or cycling	A. vs. B. vs. C. vs. D. Mean age (years): 50.1 vs. 51.2 vs. 48.0 vs. 50.0 Female: 46% vs. 44% vs. 46% vs. 54% Baseline Pain (NRS 0-10): 5.4 ± 2.2 vs. 5.5 ± 2.1 vs. 5.4 ± 1.9 vs. 5.3 ± 1.7 Function (PSFS): 3.8 ± 1.9 vs. 3.8 ± 1.8 vs. 3.7 ± 2.0 vs. 4.0 ± 1.7	A. vs. B. vs. C. vs. D. adjusted multivariable mixed model, relative change (95% CI) <u>Exercise vs. No Exercise</u> Pain (NRS 0-10) 6 weeks: –0.8 (–1.3 to –0.3), p=0.004 3 months: –0.5 (–1.1 to 0.1), p=0.092 12 months: –0.5 (–1.1 to 0.2), p=0.138	A. vs. B. vs. C. vs. D. adjusted multivariable mixed model, relative change (95% CI) <u>Exercise vs. No Exercise</u> Function (PSFS) 6 weeks: 0.4 (–0.2 to 1.0), p=0.174 3 months: 0.5 (0.0 to 1.1), p=0.063 12 months: 0.5 (–0.1 to 1.0), p=0.094 Disability (RDQ): 6 weeks: –0.8 (–1.8 to 0.3), p=0.141 3 months: –0.1 (–1.2 to 1.1), p=0.901 12 months: –0.3 (–1.6 to 0.9), p=0.597

Pengel, 2007[255] 12 months Acute, subacute *Fair*	program), stretches, functional activities, activities to build speed, endurance, and coordination, and trunk- and limb-strengthening exercises. Physical therapists used principles of cognitive-behavioral therapy and provided individualized home exercise programs. **Sham exercise**: Sham pulsed ultrasonography (5 minutes) and sham pulsed short-wave diathermy (20 minutes). Advice: Based on the program by Indahl and colleagues and aimed to encourage a graded return to normal activities. Physical therapists explained the benign nature of LBP, addressed any unhelpful beliefs about back pain, and emphasized that being overly careful and avoiding light activity would delay recovery. **Sham advice**: Participants could talk about their LBP and any other problems, physical therapist responded in a warm and empathic manner, displaying genuine interest, but did not give advice about the LBP. .	Disability (RDQ): 9.1 ± 4.8 vs. 8.2 ± 4.4 vs. 8.3 ± 5.0 vs. 8.1 ± 5.6 Global perceived effect: –0.4 ± 2.3 vs. 0.2 ± 2.3 vs. –0.3 ± 2.6 vs. 0.5 ± 2.3 Depression (DASS): 7.3 ± 8.8 vs. 7.4 ± 7.7 vs. 7.1 ± 7.8 vs. 7.1 ± 7.6 Anxiety (DASS): 4.7 ± 6.7 vs. 5.2 ± 7.4) vs. 6.2 ± 7.6 vs. 5.4 ± 6.9 Stress (DASS): 10.1 ± 9.0 vs. 11.7 ± 8.7 vs. 12.6 ± 9.1 vs. 11.7 ± 10.0	<u>Exercise + Advice vs. No Exercise or Advice</u> Pain (NRS 0-10) 6 weeks: –1.5 (–2.2 to –0.7) ,p<0.001 3 months: –1.1 (–2.0 to –0.3), p=0.009 12 months: –0.8 (–1.7 to 0.1),p=0.069	Global perceived effect 6 weeks: 0.5 (0.1 to 1.0), p=0.017 3 months: 0.5 (0.1 to 1.0), p=0.030 12 months: 0.4 (–0.1 to 1.0), p=0.134 Depression (DASS) 6 weeks: –0.7 (–2.5 to 1.2), p=0.47 3 months: –0.3 (–2.1 to 1.6), p=0.78 12 months: –0.6 (–2.6 to 1.3), p=0.51 <u>Exercise + Advice vs. No Exercise or Advice</u> Function (PSFS) 6 weeks: 1.1 (0.3 to 1.9), p=0.006 3 months: 1.3 (0.6 to 2.1), p=0.001 12 months: 1.1 (0.3 to 1.8), p=0.005 Disability (RDQ): 6 weeks: –1.3 (–2.7 to 0.2), p=0.085 3 months: –1.0 (–2.6 to 0.6), p=0.20 12 months: –0.9 (–2.7 to 0.8), p=0.29 Global perceived effect 6 weeks: 1.3 (0.7 to 1.9), p<0.001 3 months: 0.8 (0.2 to 1.5), p=0.017 12 months: 0.8 (0.0 to 1.6), p=0.059 Depression (DASS) 6 weeks: 0.2 (–2.5 to 2.8), p=0.91 3 months: 0.2 (–2.4 to 2.7), p=0.91 12 months: –0.4 (–3.1 to 2.3), p=0.76

Pengel, 2007[255] 12 months Acute, subacute *Fair*	The 12 exercise or sham exercise sessions were delivered over 6 weeks: 3 sessions per week in weeks 1 and 2, 2 sessions per week in weeks 3 and 4, and 1 session per week in weeks 5 and 6. In weeks 1, 2, and 4, participants also received advice or sham advice			

ADL = activities of daily living; BDI = Beck Depression Inventory; CM = centimeter; CSQ = coping strategies questionnaire; DASS = Depression Anxiety Stress Scales; EPC = evidence-based practice center; LBP=low back pain; GA=graded activity; GPE = Global Perceived Effect scale; GX=graded exposure; HSCL-25 = Hopkin's Symptom Check list; IQR = interquartile range; LBPRS = low back pain rating scale; MCE = Motor control exercises; MCS = Mental component score of the SF-36; NMT = measure of back extension strength; NRS = numeric rating scale; NS = non-significant; NSAIDs = Nonsteroidal anti-inflammatory drugs; ODI = Oswestry Disability Index; PCS = Pain Catastrophizing Scale; PMR= Periodized musculoskeletal rehabilitation; PSFS = patient-specific functional scale; RDQ=Roland Morris Disability Questionnaire; RR = relative risk; SD = Standard deviation; SF-12 = 12 item short form health survey; TBC=treatment-based classification system; VAS=visual analogue scale; WHOQOL = World Health Organization Quality of Life

Table 12. Characteristics and conclusions of included tai chi trials

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Hall, 2011[285] 10 weeks Subacute, chronic *Fair*	A. Tai chi, 18 sessions over 10 weeks (n=80) B. Waitlist (n=80)	A. vs. B. Mean age: 43 vs. 44 years Female: 79% vs. 70%	A. vs. B. Pain, NRS (0-10): 4.4-3.4 vs. 4.4-4.7; mean between-group difference 1.3 (95% CI 0.7 to 1.9) <u>Proportion achieving ≥30% improvement</u> Pain, NRS (0-10): 46.3% vs. 15%; NNT 4	A. vs. B. Bothersomeness, NRS (0-10): 5.0-3.7 vs. 4.5-4.9; mean between-group difference 1.7 (95% CI 0.9 to 2.5) PDI: 22.7-17.0 vs. 23.9-23.8; mean between-group difference 5.7 (95% CI 1.8 to 9.6) RDQ: 10.2-7.0 vs. 9.1-8.1; mean between-group difference 2.6 (95% CI 1.1 to 3.7) QBPDS: 29.2-22.0 vs. 30.2-29.6; mean between-group difference 6.6 (95% CI 2.4 to 10.7) PSFS: 3.5-4.7 vs. 4.0-4.1; mean between-group difference -1.0 (95% CI -1.7 to -0.4) GPE: 0.4-1.6 vs. -0.1-0.4: mean between-group difference -0.8 (95% CI -1.5 to -0.0); p=0.05 <u>Proportion achieving ≥30% improvement</u> Bothersomeness, NRS: 50% vs. 17.5%; NNT 4 PDI, 45% vs. 17.5%; NNT 4 RDQ: 50% vs. 23.8%; NNT 4 QBPDS: 40% vs. 7.5%; NNT 4 PSFS: 43.8% vs. 16.3%; NNT 4

Weifen, 2013[299] 26 weeks Chronic Fair	A. Tai chi chuan (n=141) B. Backward walking (n=47) C. Jogging (n=47) D. Swimming (n=38) E. No exercise (n=47)	A. vs. B. vs. C. vs. D. vs. E. Mean age: 37.5 vs. 38.2 vs. 37.2 vs. 37.5 vs. 38.1 years Female: 39% vs. 45% vs. 40% vs. 45% vs. 40% Mean VAS (0-100): 5.3 vs. 5.2 vs. 5.0 vs. 5.2 vs. 5.1	A. vs. B. vs. C. vs. D. vs. E. VAS (0-100), 3 months: 2.7 vs. 3.3 vs. 3.4 vs. 2.8 vs. 3.6; $p<0.05$ for A. vs. all other groups except D VAS (0-100), 6 months: 2.3 vs. 2.9 vs. 3.1 vs. 2.4 vs. 3.2; $p<0.05$ for A. vs. all other groups except D	

CI = confidence interval; GPE = Global Perceived Effect scale; LBP = low back pain; NNT = Number needed to treat; NRS = numeric rating scale; PDI = Pain Disability Index; PSFS = patient-specific functional scale; RDQ = Roland Morris Disability Questionnaire; QBPDS = Quebec Back Pain Disability Scale; VAS = visual analogue scale

Table 13. Characteristics and conclusions of included yoga trials

Author, Year **Duration of Followup** **LBP Duration** *Quality*	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Nambi, 2014[307] 6 months Subacute, chronic *Fair*	A: 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 (n=30) B: 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 (n=30)	A. vs. B. Mean age: 44.26 vs. 43.66 Female: 63.34% vs. 43.34% 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	A. vs. B. Pain intensity (10 cm VAS, mean): 4 weeks 3.8 vs. 5.3; 6 months 1.8 vs. 3.8, % improvement 72.81% vs. 42.5%, p=0.001; SMD[a] 4 weeks (-1.66, 95% CI -2.24 to -1.07); 6 months (-2.17, 95% CI -2.81 to -1.53)	A. vs. B. Physically unhealthy days (mean): 4 weeks 7.7 vs. 12.0; 6 months 2.6 vs. 6.9, % improvement 85.61% vs. 61.0%, p=0.001; Mentally unhealthy days (mean): 4 weeks 8.4 vs. 10.5; 6 months 2.6 vs. 6.9, % improvement 87.53% vs. 71.37%, p=0.001; Activity limitation days (mean): 4 weeks 7.5 vs. 12.0; 6 months 2.0 vs. 5.0, % improvement 87.83% vs. 70.59%, p=0.001;
Saper, 2013[308] 12 weeks Chronic *Fair*	A: 75 minute Hatha Yoga class once per week + recommended 30 minute home practice (n=49) B: 75 minute Hatha Yoga class twice per week + recommended 30 minute home practice (n=46) 12 weeks	A. vs. B. Mean age: 46.4 vs. 48.7 years Female: 71% vs. 80% Baseline pain (mean, low back pain intensity, 11 point numeric scale) 7.1 vs. 6.7	A. vs. B. Change from baseline, *between group difference* in means:	A. vs. B. Change from baseline, between group difference in means: RDQ: 6 weeks −0.6 (−2.7 to 1.6), p-0.62; 12 weeks, −0.1 (−1.4 to 1.2), p=0.83 RDQ proportion experiencing ≥30% improvement from baseline: 57% (27/47) vs. 66%(29/44), p=0.41, RR 0.87 (95% CI 0.63 to 1.21): proportion experiencing ≥50% improvement from baseline: 47% (22/47) vs. 50% (22/44), p=0.76, RR 0.94 (95% CI 0.61 to 1.43)

Saper, 2013[308] 12 weeks Chronic *Fair*		Back-specific function: (mean Roland-Morris Disability Questionnaire (RDQ)) 13.7 vs. 13.6 SF-26 Physical: 37.5 vs. 37.4; Mental 44.8 vs.44.	Pain: 6 weeks, −0.3 (−1.1 to 0.6), p=0.49; 12 weeks, 0.3 (−0.2 to 0.8), p=0.62 Pain: proportion experiencing ≥30% improvement from baseline: 29% (23/47) vs. 59%(26/44), p=0.33, RR 0.83 (95% CI 0.57 to 1.12): proportion experiencing ≥50% improvement from baseline: 57% (27/47) vs. 66% (29/44), p=0.41, RR 1.14 (95% CI 0.64 to 2.02;	Change from baseline, between group difference in means SF-36 Physical: 6 weeks 1.6 (95% CI -1.6 to 4.9) p=0.33; 12 weeks 0.2 (-3.4 to 3.7) p=0.93; SF-36 Mental 6 weeks 2.2 (-1.9 to 6.3) p=0.29; 12 weeks 1.5 (-2.6 to 5.6) p=0.47. Overall improvement scores: Same for A and B (mean 4.5, median 5) Satisfaction scores: mean 1.3 vs. 1.5, median 1 for both Medication use: Use of any pain medication decrease at 6 weeks (27% vs. 35%) and remained similar at 12 weeks, but NS difference in use of any pain medication or specific analgesic categories. Per protocol analyses did not reveal any statistical differences between groups for any outcome; Dose-response: Substantial variability in data; authors report potential for a “modest” dose-response” relationship with decrease in relationship slope for change in pain at approximately 12 class and approximately 9 classes for RDQ -figure provided, but not detailed data -Authors indicated that conclusions regarding the causality of the association are not possible. Adherence: Class attendance: 65% (32/47) vs. 44% (20/44), p=0.04; weekly amount of home practice 93 vs. 97 minutes; home practice for both groups a median of 4 days/week; Hours of class + home 37 vs. 29, p=0.037

CDC HRQOL = Centers for Disease Control and Prevention’s Health related quality of life questionnaire; CI = confidence interval; NR = not reported; RDQ = Roland-Morris Disability Questionnaire; RR = relative risk; SF-36 = 36 item short form; SMD = standardized mean difference; VAS = visual analogue scale

[a]SMD calculated from means and SD based on sample before attrition

Table 14. Characteristics and conclusions of included psychological therapy trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Khan, 2014[314] Post-treatment Sub-acute, chronic *Fair*	A: Behavioral therapy plus exercise (n=27). Physical-therapist guided sessions 3 times per week for 12 weeks; patients instructed to continue exercises at home twice a day at least 5 times a week. Cognitive behavioral therapy aimed to guide patients to achieve their daily life goals, consisting of operant behavioral graded activity and problem solving training. B: Exercise (n=27). Physical-therapist guided sessions 3 times per week for 12 weeks; patients instructed to continue exercises at home twice a day at least 5 times a week. Graded activity led by physical therapist that focused on gradual increase or pacing of activities important for individual patients with general exercises.	A. vs. B. Mean age: 40 years Female: 54% Baseline pain (0-10 VAS): 6.5 vs. 7.0 (mean) (p=0.1877) Baseline function (0-24 RDQ):13.8 vs. 12.9 (mean) (p=0.1842)	A. vs. B. Pain (mean 0-10 VAS): 6.5 vs. 7.0 at baseline; 2.7 vs. 5.3 post-treatment (p<0.0001)	A. vs. B. Function (mean 0-24 RDQ): 13.8 vs. 12.9 at baseline; 5.3 vs. 9.9 post-treatment (p<0.0001)

Lamb, 2010[315]/2012[316] 3, 6, 12 months, and at a mean of 34 months Subacute to chronic *Fair*	A. Group cognitive behavioral therapy plus active management advisory consult (n=468) B. Active management advisory consult alone (patients free to seek additional care) (n=233) Treatment protocols: CBT (group A): 7x90 minute sessions; treatment duration not reported Active management advisory consult (both groups): 1x15 minute session	A. vs. B. Mean age 53 vs. 54 years 59% vs. 61% female Pain (Van Korf pain): 59 vs. 59 Function (RDQ): 9 vs. 9 Function (Von Korff disability): 49 vs. 46 Quality of life (EQ-5D): not reported Quality of life (SF-12 physical): 37 vs. 38 Quality of life (SF-12 mental): 45 vs. 46 Pain Self-efficacy: 40 vs. 41 Fear avoidance beliefs (Fear avoidance beliefs questionnaire): 14 vs. 14	A. vs. B. Pain (mean change from baseline, 0-100% Von Korff pain): 12.2 vs. 5.4 at 3 months (p<0.0001), 13.7 vs. 5.7 at 6 months (p<0.0001),13.4 v. 6.4 at 12 months (p<0.0001), 17.4 vs. 12.8 at 34 months (p=0.107) Pain self-efficacy (mean change from baseline 0-60 Pain Self Efficacy): -2.4 vs. 0.9 at 3 months (p<0.0001), -2.6 vs. 1.5 at 6 months (p<0.0001), -3.0 vs. 0.8 at 12 months (p<0.0001)	A. vs. B. Function (mean change from baseline, 0-24 RDQ): 2.0 vs. 1.1 at 3 months (p=0.0021), 2.5 vs. 1.0 at 6 months (p=0.0002), 2.4 vs. 1.1 at 12 months (p=0.0008), 2.9 vs. 1.6 at 34 months (p=0.013) Function (mean change from baseline, 0-100% Von Korff disability): 13.2 vs. 8.9 at 3 months (p=0.0316), 13.9 vs. 5.7 at 6 months (p<0.0001),13.8 vs. 5.4 at 12 months (p<0.0001), 16.7 vs. 11.2 at 34 months (p=0.039) Quality of life (mean change from baseline, -0.59 to 1 EQ-5D): -0.06 vs. 0.01 at 3 months (p=0.007), -0.05 vs. -0.03 at 6 months (p=0.382), -0.06 vs. -0.0003 at 12 months (p=0.027), -0.07 vs. -0.04 at 34 months (p=0.387) Quality of life (mean change from baseline, 0-100 SF-12 physical): -3.7 vs. -1.5 at 3 months (p=0.0031), -3.6 vs. -1.8 at 6 months (p=0.0144), -4.9 vs. -0.8 at 12 months (p<0.0001) Quality of life (mean change from baseline 0-100 SF-12 mental): -1.3 vs. 0 at 3 months (p=0.1276), -2.5 vs. 0.09 at 6 months (p=0.0035), -0.9 vs. -0.7 at 12 months (p=0.8323) Treatment benefit (% patients who considered themselves recovered): 59% (235/395) vs. 31% (62/197) at 12 months (p<0.0001) Treatment satisfaction (% patients satisfied with treatment): 65% (212/328) vs. 28% (43/151) at 12 months (p=0.463) Fear avoidance beliefs (mean change from baseline 0-24 Fear Avoidance Beliefs Questionnaire): 3.4 vs. 0.7 at 3 months (p=0.0004), 3.0 vs. -0.1 at 6 months (p<0.0001), 3.4 vs. 0.5 at 12 months (p<0.0001)

Siemonsma, 2013[317] Post-treatment Chronic *Fair*	A. Cognitive treatment of illness perceptions (n=104) B. Wait list control (no interventions, could be treated as group A at end of 18 weeks) (n=52) Treatment protocol (group A): 10-14x60 minute sessions over 18 weeks	A. vs. B. Mean age 45 vs. 47 years 51% vs. 60% female Activity-specific pain (PSC): ~76 vs. ~70 (estimated from graph) Function (QBPDS): 40.4 vs. 40.3 Illness perception (IPQ timeline/duration scale): 23.6 vs. 23.3 Illness perception (IPQ, time line cyclical nature scale): 13.6 vs. 13.0 Illness perception (IPQ, consequences scale): 19.0 vs. 18.2 Illness perception (IPQ, personal control scale): 19.1 vs. 19.2 Illness perception (IPQ, treatment control scale): 17.1 vs. 17.1 Illness perception (IPQ, coherence scale): 14.3 vs. 13.7 Illness perception (IPQ, emotional response scale): 16.9 vs. 17.5	A. vs. B. Activity-specific pain (mean 0 to 100 PSC): ~44 vs. ~64 post-treatment (estimated from graph) Activity-specific pain (mean change from baseline, 0 to 100 PSC): -19.1 (95% CI -24.3 to -13.9) vs. -5.2 (95% CI -14.7 to 4.2) (p=0.018) post-treatment Activity-specific pain (% of patients with clinically relevant change, defined as decrease of 18 to 24 mm): 49% (46/93) vs. 26% (12/46) post-treatment (OR 2.77 (95% CI 1.28 to 6.01))	A. vs. B. Function (mean 0-100 QBPDS): 36.9 vs. 38.7 post-treatment (p=0.27)

Vong, 2011[318] 1 month Chronic *Fair*	A. Motivational enhancement treatment during physical therapy (n=45) B. Physical therapy (n=20) Treatment protocol: 10x30 minute sessions over 8 weeks	A. vs. B. Mean age 45 vs. 45 years 58% vs. 68% female Pain (0-10 VAS): 5.3 vs. 5.3 Pain self-efficacy (PSEQ): 39.5 vs. 40.5 at baseline Pain (SF-36 bodily pain): 41 vs. 49 (p=0.047) Function (RDQ) (mean): 10.0 vs. 10.0 Function (mean 0-100 SF-36 physical function): 67 vs. 63 Quality of life (SF-36 role-physical): 22 vs. 30 Quality of life (SF-36 general health): 41 vs. 49	A. vs. B. Pain (mean 0-10 VAS): 3.1 vs. 3.9 at 1 month (p>0.05) Pain self-efficacy (mean 0-60 PSEQ): 45.4 vs. 45.6 at 1 month (p>0.05) Pain (mean 0-100 SF-36 bodily pain): p> 0.05 at 1 month (data not reported)	A. vs. B. Function (mean 0-24 RDQ): 5.6 vs. 7.6 at 1 month (p>0.05) Function (mean 0-100 SF-36 physical function): p> 0.05 at 1 month (data not reported) Quality of life (mean 0-100 SF-36 role-physical and general health scales): p> 0.05 at 1 month (data not reported)

CBT = cognitive behavioral therapy; EQ-5D = Euro Quality of Life; IPQ = Illness Perception Questionnaire; LBP = low back pain; PSC = Patient Specific Complaints; PSEQ = Chronic Pain Self Efficacy Scale; QBPDS = Quebec Back Pain Disability Scale; RDQ = Roland-Morris Disability Questionnaire; SF-12 = 12 item short form health survey; SF-36 = 36 item short form; VAS = visual analogue scale

Table 15. Characteristics and conclusions of included multidisciplinary rehabilitation trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Eisenberg, 2012[349] 2, 5, 12, and 26 weeks LBP duration not specified *Good*	A Integrative Care (acupuncture, chiropractic, internal med consult, massage, occupational therapy, physical therapy, mind-body techniques, neuro consult, nutrition counseling, ortho consult, psych and rheum consult as needed) + usual care B. Usual care (medical care) 12 weeks	A. vs. B. Mean age: 47 vs. 48 years Female: 50% vs. 67% Average Pain (0-10): 4.8 vs. 5.7 Modified RDQ: 15.7 vs. 16	A. vs. B. Pain (0-10 scale) Week 2: 3.6 vs. 4.8 (p=0.62) Week 5: 1.9 vs. 5.5 (p=0.05) Week 12: 0.6 vs. 5.0 (p=0.005) Week 26: 1.0 vs. 4.7 (p=0.04)	A. vs. B. RDQ mean differences, A. vs. B. Week 2: 12 vs. 11.3 (p=0.87) Week 5: 8.5 vs. 13 (p=0.26) Week 12: 3.9 vs. 11 (p=0.08) Week 26: 4.3 vs. 10.7 (p=0.10) SF-12 physical Week 2: 35 vs. 41 (p=0.90) Week 5: 42 vs. 42 (p=0.38) Week 12: 49 vs. 43 (p=0.06) Week 26: 51 vs. 44 (p=0.03) SF-12 mental Week 2: 47 vs. 51 (p=0.26) Week 5: 51 vs. 50 (p=0.59) Week 12: 501 vs. 51 (p=0.48) Week 26: 54 vs. 51 (p=1.00) Days in bed, days at home and reduced activity days NS Regression showed positive differences significant for RDQ, pain, and bothersomeness at 12 weeks, but not at 26 weeks
Gatchel, 2003[350] 3,6,9,12 months Acute *Fair*	A. Intensive Multidisciplinary rehabilitation (physician evaluation, psychology, physical therapy, biofeedback, case management, occupational therapy) B. Usual care	Mean age: 38 years Female: 35% Baseline pain: not reported Baseline function: not reported	A. vs. B. Average self-rated pain over last 3 months: 27 vs. 43, p=0.001	A. vs. B. Return to work at 12 months: 91% vs. 69%, OR 4.55 (p=0.027) Average number of disability days due to back pain: 38 vs. 102, p=0.001 Taking opioid analgesics: 27% vs. 44%, OR 0.44, p=0.020 Cost: $12,721 vs. $21,843, p<0.05

Monticone, 2014[351] 0, 8 weeks; 3 months Chronic *Good*	A. Multidisciplinary rehabilitation of 2 months duration (physiatry, psychology, occupational therapy, and physiotherapy) providing spinal stabilization and cognitive behavioral therapy to address fear avoidance B. Usual care = passive spinal mobilization, stretching, muscle strengthening, and posture control	A. vs. B. Mean age: 59 vs. 57 years Female: 70% vs. 40% Baseline pain: not reported BMI: 27 vs. 25		A. vs. B. Baseline ODI 26 vs. 24 (p=0.43) TSK 29 vs. 27 (p=0.55) NRS (0-10) 5 vs. 4 (p=0.67) PCS 25 vs. 23 (0.43) SF-36 Physical Activity 41 vs. 43 (p=0.55) 6 minute walk test 1.17 m/s vs. 1.26 m/s (p=0.29) 8 weeks ODI 10 vs. 8 (p=0.03) TSK 29 vs. 27 (p=0.01) NRS (0-10) 5 vs. 4 (p=1.0) PCS 25 vs. 23 (p=0.006) SF-36 Physical Activity 41 vs. 43 (p=0.001) 6 minute walk test 1.17 m/s vs. 1.26 m/s (p=0.478) 3 months ODI 8 vs. 15 TSK 15 vs. 27 NRS (0-10) 2 vs. 3 PCS 9 vs. 18 SF-36 Physical Activity 84 vs. 67 6 minute walk test 1.53 vs. 1.42

LBP = low back pain; NRS = numeric rating scale; NS = non-significant; ODI = Oswestry Disability Index; OR = odds ratio; PCS = Pain Catastrophizing Scale; RDQ = Roland-Morris Disability Questionnaire; SF-12 = 12 item short form health survey; SF-36 = 36 item short form health survey; TSK = Tampa Scale of Kinesiophobia

Table 16. Characteristics and conclusions of included acupuncture trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Cho, 2013[391] Primary: 8 weeks FU to 6 months Chronic *Good*	A: Acupuncture (n=65) B: Sham acupuncture (n=65) Treatment protocol: 2x weekly x 6 weeks	A. vs. B. Mean age 42 vs. 42 83% vs. 86% female Race not reported Pain, VAS (0-10) 6.5 vs. 6.4 Disability, ODI: 28.2 vs. 24.2	A. vs. B. Pain, bothersomeness (primary) mean change from baseline (0-10 VAS): -3.4 vs. -2.3 ($p<0.05$) Pain intensity mean change from baseline (0-10 VAS): -3.5 vs. -2.3 ($p=0.008$)	A. vs. B.(to primary endpoint) Disability, Proportion of ODI improvement from baseline: -0.42 vs. 0.29 (NS)
Hasegawa, 2014[389] 28 days Acute *Good*	A. Scalp acupuncture +diclofenac (n=40) B. Sham scalp acupuncture +diclofenac (n=40) Treatment protocol: 5 30 min sessions (unclear time period)	A. vs. B. Mean age 47 vs. 44 years 63% vs. 65% female 63% vs. 55% Caucasian Pain, VAS (0-10): 6.6 vs. 6.7 Disability, RDQ: 14.9 vs. 14.6	A. vs. B.: Acute LBP Pain, VAS(0-10) mean change from baseline: -4.6 vs. -3.3; $p=0.005$	A. vs. B. Disability, RDQ mean change from baseline: -10.8 vs. -8.6; $p=0.002$
Vas, 2012[390] Primary: 3 weeks FU to 48 weeks Acute *Good*	A. True acupuncture (n=68) B. Sham acupuncture (n=68) C. Placebo acupuncture (n=69) D. Control group (n-70) Treatment protocol: 5 20 min sessions over 2 weeks	A. vs. B. vs. C. vs. D Mean age 42 vs. 44 vs. 44 vs. 41 63% vs. 57% vs. 49% vs. 64% female Race not reported (Spain)	A. vs. B. vs. C. vs. D Pain VAS not reported Continuing pain and recurrence of pain reported only	A. vs. B. vs. C. vs. D Disability (Proportion achieving 35% improvement in RDQ (0-24) at 3 weeks): 74% vs. 75% vs. 65% vs. 44% ($p<0.05$ for A. vs. C. and A. vs. D)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention Treatment Protocol**	**Population**	**Pain Outcomes**	**Other Outcomes**
Weiss, 2013[393] 3 months after end of treatment Chronic *Poor*[a]	A. Acupuncture plus intensive rehab (n=74) B. Intensive inpatient rehab only (n=69) Treatment protocol: Daily acupuncture for 21 days of inpatient rehab	A. vs. B. Mean age 49.8 vs. 51.7 27% vs. 39.1% female Race not reported (Germany) Bodily Pain, SF-36 41.2 vs. 36.0 Physical function, SF-36 71.2 vs. 69.8	A. vs. B. Bodily pain, SF-36 mean change from baseline to 3 months post treatment 8.3 vs. 3.8 p=0.28 (p<0.05) Bodily pain, SF-36 mean change from baseline to end of treatment 24.5 vs. 22.6 p=0.56	A. vs. B. Physical function, SF-36 mean change from baseline to 3 months post treatment -3.6 vs. -11.8 p=0.0.02 Physical function, SF-36 mean change from baseline to end of treatment 9.8 vs. 6.4 p=0.20
Yun, 2012[392] Chronic 24 weeks *Fair*	A. Back-pain-acupuncture (n=80) B. Standard acupuncture (n=82) C. Usual care (n=74) Treatment protocol: 14 daily treatments	A. vs. B. vs. C Mean age 33 vs. 34 vs. 31 33% vs. 27% vs. 31%female Race not reported (China) Pain, (0-10 VAS): 6.1 vs. 6.1 vs. 6.1 Disability, RDQ: 11.8 vs. 12 vs. 11.8	A. vs. B. vs. C Pain, bothersomeness (primary) mean change from baseline 24 weeks (0-10 VAS): 2.5 vs. 2.0 vs. 1.2 (p<0.0001)	A. vs. B. vs. C RDQ mean change from baseline: 6.2 vs. 5.3 vs. 4.1 (p<0.0001)

LBP = low back pain; NS = non-significant; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; SF-36 = 36 item short form health survey; VAS = visual analogue scale

[a]▲VAS for bothersomeness (at the end of treatments)=absolute value of [VAS for bothersomeness (baseline) − VAS for bothersomeness (end of treatments)] / VAS for bothersomeness (baseline) significances by 2-sample t test.

Table 17. Characteristics and conclusions of included massage trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Ajimsha, 2014[411] 12 weeks Subacute, chronic *Fair*	A. Myofascial release+ specific back exercise (n=38) B. Sham myofascial release + specific back exercise (n=36) Treatment given 3 times weekly for 8 weeks	A. vs. B. Mean age: 35.8 vs. 34.2 Female: 76% vs. 78% Baseline pain: not reported Baseline function: not reported	A. vs. B. Mean differences, B vs. A: MPQ, week 8: 4.813, p=0.000 MPQ, week 12: 3.25, p=0.000	A. vs. B. Mean differences, B vs. A: QBPDS, 8 weeks: 3.413, p=0.000 QBPDS, 12 weeks: 2.023, p=0.000
Borges, 2014[412] 6 weeks LBP duration: not reported *Fair*	A. Massage by accupressure (n=14) B. Laser applied but turned off (placebo) (n=15) C. No treatment (n=14)	A. vs. B. vs. C. Mean age: 39.6 overall Female: 92.9% vs. 73.3% vs. 64.3 Pain score: of 7: 64.3% vs. 26.7% vs. 21.4% Baseline function: not reported	A. vs. B. vs. C. Pain scores, baseline vs. 3 weeks vs. 6 weeks: A: 6.4 vs. 3.4 vs. 0.9, p<0.001 B: 5.7 vs. 4.8 vs. 4.7, p>0.05 C: 5.0 vs. 5.3 vs. 5.9, p>0.05	
Cherkin, 2011[406] 1 month and 3 months >12 weeks Chronic *Good*	A. Structural massage (n=132) B. Relaxation massage (n=136) C. Usual care (n=133) Treatment protocol: 10 weekly treatments, with first visits lasting 75 to 90 minutes and followup visits lasting 50 to 60 minutes	A. vs. B. vs. C. 46 vs. 47 vs. 48 Mean age 66% vs. 65% vs. 62% female 86% vs. 87% vs. 86% white LBP Bothersomeness, VAS (0-10): 5.6 vs. 5.6 vs. 5.8 Disability, RDQ: 10.1 vs. 11.6 vs. 10.5	A. vs. B. LBP bothersomeness, VAS (0-10) mean change from baseline (10 weeks): A. vs. C: –1.4 (–1.9 to –0.8) B vs. C: –1.7 (–2.2 to –1.2) A. vs. B.: 0.3 (–0.2 to 0.8) P<0.05 but not reported separately	Disability, RDQ mean change from baseline (10 weeks): A. vs. C: –2.5 (–3.5 to –1.4) B vs. C: –2.9 (–4.0 to –1.8) A. vs. B.: 0.5 (–0.5 to 1.5) P<0.05 but not reported separately
Kong, 2012[407] 2 months Acute and chronic *Good*	A: Chinese massage with herbal ointment (n=55) B: Standard massage (n=55) Treatment protocol: 2 30 minute sessions per week x 4 weeks	A. vs. B. Mean age 21 vs. 20 (male athletes) 26/55 vs. 27/55 female Race not reported (Shanghai) Pain, 5.4 vs. 5.4 Disability, not reported	A. vs. B. Pain mean change from baseline (0-10 VAS): (− 0.64 points [95% CI − 1.04 to − 0.24]; p=0. 002	Disability not reported C-SFMPQ scores favored A. vs. B.

Romanowski, 2012[408] 10 days FU to 48 weeks Chronic *Poor*	A. Therapeutic massage (n=13) B. Deep tissue massage (n=13) Treatment protocol: 10 daily 30 min sessions	A. vs. B. Not described except to say there were no differences in age and sex	A. vs. B. Mean change in (0-10 VAS): 13.54 ± 7.75 vs. 4.92 ± 13.55 p<0.001	A. vs. B. Mean change in ODI 9.46 ± 11.22 vs. 16.38 ± 11.68, p<0.001
Sritoomma, 2014[409] 15 weeks Chronic *Fair*	A. Swedish massage with ginger oil (n=70) B. Thai massage (n=70) Treatment protocol: 10 30 min sessions over a 5 week period	A. vs. B. Mean age not described (60 and older) 77% vs. 83% female Race not described (Thailand) Pain, VAS (0-10): 66.66 vs. 63.27 Disability, ODI: 26.9 vs. 29.5	A. vs. B. Pain, VAS (0-10) mean change from baseline: −6.37 (−12.58, −0.17) 0.044 (15 weeks)	A. vs. B. Disability, RDQ mean change from baseline: - −3.66 (−7.17, −0.14) 0.042
Zhang, 2015[413] 1 year Duration of LBP: not reported *Fair*	A. Chinese massage + core stabilization exercises B. Chinese massage only	A. vs. B. Mean age: 48.71 vs. 51.62 years Female: 37% vs. 33% Baseline pain: not reported Baseline function: not reported Duration of pain: ≥12 weeks: 43% vs. 37%	A. vs. B. VAS (0-100), 2 weeks: 3.88±1.31 vs. 4.12±1.33, p>0.05 VAS (0-100), 8 weeks: 1.46±0.76 vs. 2.85±1.58, p<0.05	A. vs. B. ODI, 2 weeks: 21.58±6.34 vs. 23.41±7.43, p>0.05 ODI, 8 weeks: 13.20±2.42 vs. 18.39±3.67, p<0.05
Zheng, 2012[410] 3 weeks, Subacute, chronic *Fair*	A. Massage + traction (n=32) B. Traction alone (n=32)	A. vs. B. Mean age: 43 vs. 42 years Female: 44% vs. 50% Baseline pain: not reported Baseline function: not reported	A. vs. B. Mean difference in pain VAS (0-10) 1.9±0.9 vs. 1.4±0.8 p<0.05	

CSFMPQ = Chinese Short Form McGill Pain Questionnaire; LBP = low back pain; MPQ = McGill Pain Questionnaire; ODI = Oswestry Disability Index; QBPDS = Quebec Back Pain Disability Scale; RDQ = Roland-Morris Disability Questionnaire; VAS = visual analogue scale;

Table 18. Characteristics and conclusions of included spinal manipulation trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Balthazard, 2012[476] 6 months Chronic *Fair*	A. HVLA + 5-10 min active exercises (n=22) B. Detuned ultrasound (sham) + 5-10 min active exercises (n=20) Treatment protocol: 8 sessions over 4-8 weeks (unclear duration)	A. vs. B. Mean age 44 vs. 42 years 36% vs. 30% female Race not reported Pain VAS (0-10) 53 vs. 65 ODI: 30 vs. 32	A. vs. B. Pain, VAS (0-10)-pain mean group difference: -1.24; 95% CI: -2.37 to − 0.30; p=0.032, statistically not significant at the 0.025 level.	A. vs. B. ODI mean group difference: -7.14; 95% CI: -12.8 to − 1.52; p=0.013
Bicalho, 2010[477] Immediate Chronic Fair	A. HVLA (n=20) B. Control (side lying) (n=20) Treatment protocol: single session	A. vs. B. Mean age 30 vs. 27 ODI: 14.6 vs. 16.6 Race not reported (Brazil)	A. vs. B. Pain VAS mean group difference (0-100): -11 vs. -2.2, no CI provided, p=0.04)	A. vs. B. Finger to floor, EMG flex-ext reported (favored SMT), ODI measured but not reported
Bronfort, 2004[487] 52 weeks Subacute or Chronic *Poor*	A. Chiropractic (n=11) B. Epidural steroid injection (n=11) C. Self-care education (n=10)	A. vs. B. vs. C Mean Age: 44 vs. 52 vs. 52 Female=45% v 36% v 50%	Results were combined; no group specific results were reported. 3 weeks vs. 12 weeks vs. 52 weeks: Leg Pain: 1.8 vs. 2.9 vs. 2.3 Low back pain: 0.9 vs. 1.7 vs. 1.9	Results were combined; no group specific results were reported. 3 weeks vs. 12 weeks vs. 52 weeks: RDQ: 13.7 vs. 22.7 vs. 19.6 Oswestry disability questionnaire: 11 vs. 22.9 vs. 15.6
Bronfort, 2011 52 weeks Chronic *Good*	A. Supervised exercise therapy for 12 weeks (n=100) B. Chiropractic spinal manipulation for 12 weeks (n=100) C. Home exercise and advice for 12 weeks (n=101)	A. vs. B. vs. C Mean age: 44.5 vs. 45.2 vs. 45.6 years Female: 57% vs. 66% vs. 58% Mean pain severity score (0-10): 5.1 vs. 5.4 vs. 5.2 Roland-Morris disability score (0-23): 8.4 vs. 8.7 vs. 8.7		Only significant between-group differences in patient-reported outcomes were for satisfaction (favoring A, p<0.01 at 12 weeks and p<0.001 at 52 weeks) Overall treatment effect was significant for endurance (p<0.05) and strength (p<0.05) but not range of motion (also favoring A).

Bronfort, 2014[486] 52 weeks Acute, subacute, chronic *Fair*	A. SMT plus HEA (home exercise with advice) B. HEA	A. vs. B. Mean age: 57 vs. 58 years Female: 59% vs. 68% Mean NRS (0-10) leg pain: 5.4 vs. 5.4 Mean RDQ: 10.2 vs. 10.2	A. vs. B. Leg Pain 12 weeks: -1.0 (-1.9 to -0.2), p=0.008 Leg Pain 52 weeks: -0.7 (-1.5 to 0.2), p=0.15 LBP 12 weeks: -0.9 (-1.6 to -0.3), p=0.005 LBP 52 weeks: -0.3 (-1.0 to 0.4) p=0.4	
Burton, 2000[488] 12 months Chronic *Poor*	A. Osteopathic manipulation (15 min treatment sessions over 12 weeks) (n=20) B. Chemonucleolysis (control) (n=20)	Mean Age 42 53% female Mean duration of symptoms: 30 weeks vs. 32 weeks	A. vs. B. Leg Pain, baseline: 4 vs. 3.7; 2 weeks: 3.2 vs. 3.3; 6 weeks: 2.7 vs. 2.7; 12 months: 2.1 vs. 2.3 Back pain, baseline: 3.8 vs. 4.1; 2 weeks: 3.2 vs. 4; 6 weeks: 2.7 vs. 3.6; 12 months: 2.3 vs. 2.9	RDQ, baseline: 11.9 vs. 12; 2 weeks: 10.2 vs. 13.9; 6 weeks: 7.8 vs. 11; 12 months: 5.9 vs. 7.3
Cecchi, 2010[478] 12 months Chronic *Fair*	A. Back school (n=70) B. Physical therapy (n=70) C. SMT (n=70) Treatment protocol: Back school and individual physical therapy: 15 1-hour-sessions for 3 weeks. SMT: 4-6 20 min sessions once a week	A. vs. B. vs. C. Mean age 58 vs. 61 vs. 58 49% vs. 43% vs. 48% female Race not reported (Italy) Pain, (mean): 2 vs. 2 vs. 2.2 RDQ (0-24) (mean): 9.5 vs. 9.7 vs. 8.5 (sick leave due to LBP higher in A. vs. B. A. vs. B and C – p=0.001)	A. vs. B. vs. C. Mean differences not reported – will need to calculate Back Pain 12 month mean change from baseline (0.7 vs. 0.4 vs. 1.5) C improved to greater degree than B or A at 12 months in terms of pain (but small, clinically insignificant)	A. vs. B. vs. C. RDQ mean (SD) reduction from baseline to 12 months: 4.2+/- 4.8 vs. 4.0+/-5.1 vs. 5.9+/-4.6 C improved to greater degree than B or A at 12 months in terms of disability (but small, clinically insignificant)
De Oliviera, 2013[479] immediate Chronic *Good*	A: HVLA – region specific (n=74) B: HVLA nonspecific (n=74) Treatment protocol: single treatment	A. vs. B. Mean age 46 vs. 46 80% vs. 68% female Race not reported Pain, NPRS 6.1 vs. 6.0 Disability, RDQ: 11.3 vs. 9.3	A. vs. B. Pain, intensity mean group difference: 0.50 (-0.10 to 1.10), p=0.10	A. vs. B. Pressure pain thresholds measured, no difference between groups

Goertz, 2013[483] 4 weeks Acute *Fair*	A: HVLA + standard medical care (n=45) B: Standard medical care (n=46) Treatment protocol: 2 visits weekly x 4 weeks	A. vs. B. Mean age 25 vs. 26 15% vs. 14% female 73% vs. 52% White, more missing in SMC Pain, NPRS 5.8 vs. 5.8 Disability, RDQ: 11 vs. 12.7	A. vs. B. Pain, intensity (NRS 0-10) mean group difference: 1.2 (0.2, 2.3) p=0.02	A. vs. B. Disability (RDQ): 4.0 (1.3, 6.7), p=0.004
Haas, 2014[480] 1 year Chronic *Good*	A: Massage (n=100) B. Massage + 6 SMT (n=100) C. Massage + 12 SMT (n=100) D. Massage + 18 SMT (n=100) Treatment protocol: 15 min sessions (18 total, unclear duration); 5 min hot pack, 5 min SMT or massage + 5 min sham ultrasound	A. vs. B. vs. C. vs. D. Mean age 41 vs. 41 vs. 42 vs. 41 49% vs. 49% vs. 49% vs. 52% female Nonwhite: 14% vs. 18% vs. 11% vs. 16% Pain, VAS (0-100) 52.2 vs. 51.0 vs. 51.6 vs. 51.5	A. vs. D. Pain intensity, percentage responders (>50%) at 52 weeks 10.6 (-3.2, 24.4), NS NS differences in A. vs. B., A. vs. C Only sig diff in 12 week A. vs. C. 21.1 (7.7, 34.6), p<0.025	Disability score calculated, but unclear what measure
Paatelma, 2008[466] 1 year Acute to chronic *Fair*	A. SMT (n=45) B. McKenzie (n=52), C. “advice only to be active” (n=37) Treatment protocol: A and B: 3-7 sessions (mean 6) A. C. one 45-60 min session	A. vs. B. vs. C. Mean age 44 vs. 44 vs. 44 42% vs. 29% vs. 35% female Race not reported (Finland) Pain, VAS (0-10) (median): 20 vs. 16 vs. 16 RDQ (0-24) (median): 9 vs. 9 vs. 8	A. vs. C. (12 months) Pain, intensity (VAS 0-10) mean group difference: –4 (–17 to 9) p=0.714 B vs. C Pain, intensity (VAS 0-10) mean group difference: –10 (–23 to 2) p=0.144	A. vs. C. (12 months) Disability (RDQ): –3 (–6 to 0) p=0.068 B vs. C Disability (RDQ): –3 (–6 to 0) 0.028
Petersen, 2011[481] 12 months Chronic *Good*	A. McKenzie exercise (n=175) B. SMT (n=175) Treatment Protocol: Max 15 sessions over 12 weeks (variable)	A. vs. B. Mean age 38 vs. 37 59% vs. 53% female Race not reported (Denmark) Pain (3 0-10 scales), 30/60 vs. 29/30 Disability, RDQ: 13 vs. 13	A. vs. B. Pain, intensity mean group difference: 2.8 (− 0.2 to 5.8) p=0.063 (12 months)	A. vs. B. Disability (RDQ): 1.5 (0.2 to 2.9) p=0.030 (12 months, favoring A)

Santilli, 2006[489] 180 days Acute *Good*	A. Active manipulation 5 days/ week (n=53) B. Control (simulated manipulation) (n=49)	Mean age <40 Female 30% vs. 45% Pain 6.4 vs. 6.4 Radiating Pain 5.3 vs. 5.1	Patients with reduction of local pain: 98% vs. 94% (NS) Patients with reduction of radiating pain 100% vs. 83% (p<0.01)	NS difference between SF-36 results
Schneider, 2015[484] 6 months Acute, subacute *Good*	A. manual thrust SMT B. mechanical assisted SMT C. usual care	A. vs. B. vs. C. Mean age: 41 vs. 41 vs. 40 years Female: not reported Pain: 5.7 vs. 5.5 vs. 6.0 ODI: 33.9 vs. 33.1 vs. 34.6	A. vs. B. vs. C. adjusted group differences, mean (95% CI) Pain: -1.2 (-3.2 to 0.7) vs. -0.9 (-2.9 to 1.1) vs. 0.3 (-1.6 to 2.3)	A. vs. B. vs. C. adjusted group differences, mean (95% CI) ODI: 0.4 (-10.2 to 11.0) vs. 1.4 (-9.1 to 12.0) vs. 1.0 (-9.6 to 11.6)
Senna, 2011[482] 10 months Chronic *Fair*	A. sham SMT (12 sessions over 1 month) (n=40) B. SMT (12 sessions over 1 month) (n=27) C. SMT (12 sessions over 1 month + every 2 weeks x 9 months) (n=27) Treatment protocol: 12 sessions over 1 month for initial treatments	A. vs. B. vs. C. Mean age 42 vs. 40 vs. 42 24% vs. 27% vs. 24% female Race not reported (Egypt) Pain, VAS (0-10) 41 vs. 42 vs. 43 ODI: 38 vs. 39 vs. 40	A. vs. B. vs. C. Pain, intensity mean group difference: A. vs. B. Unadjusted mean difference in VAS (0-10) at 1 month 4; at 10 months 0 A. vs. C. Unadjusted mean difference at 1 month 6, at 10 months 17 Results not reported as group mean differences – will need to calculate these; overall B and C improved to similar degree compared with A at 1 month, group C maintained the improvement through 10 months whereas B returned to baseline for both pain and function	A. vs. B. vs. C. Disability (ODI):

Von Heymann, 2013[485] 12 weeks Acute *Fair*	A. SMT and placebo-diclofenac (n=37) B. Sham SMT and diclofenac (n=38) C. Sham SMT and placebo diclofenac. (n=25)	A. vs. B. vs. C. Mean age 34 vs. 38 vs. 39 36% vs. 38% vs. 46% female Race not reported (Germany) Pain, VAS (0-10) 41 vs. 42 vs. 43 ODI: 38 vs. 39 vs. 40	A. vs. B. vs. C. (only reported to 9 days) Pain VAS (0-10) – unable to calculate group mean differences based on the way presented (graphs) And only A. vs. B. was presented, not A. vs. B. vs. C	A. vs. B. vs. C. A. vs. B.: Unadjusted mean difference in RDQ at 12 weeks: 3.0 RDQ - unable to calculate group mean differences based on the way presented (graphs)

HVLA = High-Velocity Low-Amplitude; NPRS = Numerical pain rating scale; NRS = numerical rating scale; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SMT = spinal manipulation therapy; VAS = visual analogue scale

Table 19. Characteristics and conclusions of included ultrasound trials

Author, Year Duration of Followup LBP Duration *Quality*	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Fiore, 2011[504] 3 weeks Acute, subacute, chronic *Fair*	A: Ultrasound 2 W/cm2 at 1 MHz; fifteen 10 minutes sessions over 3 weeks (n=15) B: Low level laser therapy with Nd:YAG laser pulsated waveform, 1 KW, wavelength 1064 nm, maximum energy for single impulse 150 mJ, average power 6 W, fluency 760 mJ/cm2, duration of single impulse <150 ms applied in 3 phases, total 10 minutes and 2,600 J, fifteen sessions over 3 weeks (n=15)	A. vs. B. Mean age: 51 years Female: 63% Pain intensity (median, 0-10 VAS): 7 vs. 7 ODI (median, 0-100): 28 vs. 28	A. vs. B. Pain (median, 0-10 VAS): 4 vs. 3 at 3 w (p=0.009)	A. vs. B. ODI (median, 0-100): 16 vs. 12 at 3 w (p=0.006)

Goren, 2010[505] 3 weeks Subacute, chronic *Fair*	A: Ultrasound 1.5 W/cm2 at 1 MHz; fifteen 10 minutes sessions over 3 weeks + exercise therapy with stretching and strengthening for 20 minutes, and low-intensity cycling for 15 minutes (n=15) B: Sham ultrasound + exercise therapy (n=15) C: No ultrasound or exercise (n=15)	A. vs. B. vs. C. Mean age: 57 vs. 49 vs. 53 years Female: 53% vs. 87% vs. 73% Back pain (mean, 0-10 VAS): 5.5 vs. 6.2 vs. 5.3 Leg pain (mean, 0-10 VAS): 5.8 vs. 6.3 vs. 6.6 ODI (mean, 0-100): 25 vs. 27 vs. 32 Central stenosis: 100% vs. 93% vs. 93% Lateral stenosis: 13% vs. 13% vs. 13%	A. vs. B. vs. C. Back pain (mean, 0-10 VAS): 3.33 vs. 4.26 vs. 5.66 at 3 w (p=0.10) Leg pain (mean, 0-10 VAS): 4.33 vs. 3.86 vs. 7.13 at 3 w (p=0.007 for A. vs. C, p=0.006 for B vs. C)	A. vs. B. vs. C. ODI (mean, 0-100): 22 vs. 19 vs. 29 at 3 w (p=0.01 for A. vs. C, p=0.01 for B vs. C) Paracetamol tablet use (mean): 8.33 vs. 16.0 vs. 31 at 3 w (p=0.02 for A. vs. C)
Licciardone, 2013[503] 12 weeks Subacute, chronic *Good*	A: Ultrasound 1.2 W/cm2 at 1 MHz; six 10 minute treatments over 8 weeks (n=233) B: Sham ultrasound, at 0.1 W/cm2, treatment otherwise identical to A (n=222) Factorial design, patients also randomized to osteopathic manual treatment vs. sham treatment; no interaction between treatments	A. vs. B. Mean age: 38 vs. 43 years Female: 58% vs. 68% Pain intensity (median, 0-100 VAS): 44 vs. 44 RDQ (median, 0-24): 5 vs. 5 SF-36 general health (median, 0-100): 72 vs. 67	A. vs. B. ≥30% improvement in pain: RR 1.02 (95% CI 0.86 to 1.20) at week 12 ≥50% improvement in pain: RR 1.09 (95% CI 0.88 to 1.35) at week 12 RDQ (median, 0-24): 4 vs. 4 at week 4 (p=0.99), 3 vs. 4 at week 8 (p=0.76), 3 vs. 3 at week 12 (p=0.93)	A. vs. B. SF-36 general health (median, 0-100): 72 vs. 72 at week 4 (p=0.73), 72 vs. 72 at week 8 (p=0.53), 72 vs. 74 at w 12 (p=0.66) Lost 1 or more days work in past 4 weeks because of low back pain: 16% vs. 7% (p=0.04) at week 4, 17% vs. 8% at week 8 (p=0.54), 13% vs. 6% at week 12 (p=0.11) Very satisfied with back care: 41% vs. 45% at week 4 (p=0.44), 49% vs. 51% at week 8 (p=0.77), 55% vs. 55% at week 12 (p=0.99)

Unlu, 2008[506] 3 months Acute *Poor*	A: Ultrasound 1.5 W/cm2 at 1 MHz; 15 sessions over 3 weeks (n=20) B: Lumbar traction: Motorized traction system (Tru-trac 401), 15 minutes per session (hold for 30 seconds and rest for 10 seconds), traction forced increased as tolerated from minimum traction force 35% to maximum 50% of body weight; 90 degree hip and knee flexion C: Low-level laser: Gal-Al-As diode laser at 50 mV and wavelength 830 nm, diameter 1 mm, 4 minute application over both sides of disc spaces where herniation detected, dose 1 J at each point	A. vs. B. vs. C. Mean age: 48 vs. 42 vs. 43 years Female: 65% vs. 80% vs. 65% Pain intensity, leg (mean, 0-100 VAS): 56 vs. 60 vs. 53 RDQ (mean, 0-24): 13 vs. 14 vs. 12 Modified ODI (mean, 0-50): 20 vs. 15 vs. 18	A. vs. B. vs. C. Pain intensity, low back (0-100 VAS): 30 vs. 30 vs. 34 at end of treatment, 27 vs. 26 vs. 31 1 month after end of treatment, 27 vs. 31 vs. 30 3 months after end of treatment Pain intensity, leg (0-100 VAS): 29 vs. 28 vs. 33 at end of treatment, 27 vs. 22 vs. 26 1 month after end of treatment, 25 vs. 30 vs. 24 3 months after end of treatment RDQ (0-24): 9.3 vs. 9.8 vs. 9.9 at end of treatment, 8.2 vs. 8.5 vs. 7.3 1 months after end of treatment, 8.6 vs. 8.9 vs. 6.7 3 months after end of treatment Modified ODI (0-50): 14 vs. 15 vs. 15 at end of treatment, 14 vs. 14 vs. 14 1 month after end of treatment, 14 vs. 15 vs. 14 3 months after end of treatment	

LBP = low back pain; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; RR = relative risk; SF-36 = 36 item short form health survey; VAS = visual analogue scale

Table 20. Characteristics and conclusions of included transcutaneous electrical nerve stimulation (TENS) trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Buchmuller, 2012[517] 3 months Chronic *Fair*	A. Active TENS 4 1-hour sessions per day (n=117) B. Sham TENS 4 1-hour sessions per day (n=119)	A. vs. B. Mean age: 53 vs. 53 years Female:62% vs. 64% LBP alone: 39% vs. 43%; LBP + radicular pain: 61% vs. 57% VAS (0-100): 63 vs. 66 Roland-Morris disability score: 15 vs. 15	A. vs. B. Improvement of ≥50% in lumbar pain VAS (0-100) from baseline: 25% (26/104) vs. 7% (7/104); RR 3.71 (95% CI 1.69 to 8.18) Improvement of ≥50% in radicular pain VAS (0-100) from baseline: 34% (22/65) vs. 15% (9/60); RR 2.26 (95% CI 1.13 to 4.51)	Improvement on Roland-Morris disability questionnaire at 6 weeks: 30% (32/107) vs. 24% (28/115); RR 1.23 (95% CI 0.80 to 1.89) Improvement on Roland-Morris disability questionnaire at 3 months: 26% (29/110) vs. 25% (28/112); RR 1.05 (95% CI 0.67 to 1.65) Dallas functional repercussion of pain score, everyday activities: 69 vs. 69; p=0.84 Dallas functional repercussion of pain score, professional and leisure activities: 70 vs. 70; p=0.98 Dallas functional repercussion of pain score, anxiety and depression: 43 vs. 43; p=0.95 Dallas functional repercussion of pain score, sociability: 30 vs. 35; p=0.80 SF-36 physical dimensions score: 35.3 vs. 34.4; p=0.22 SF-36 psychological dimensions score: 39.3 vs. 39.1; p=0.96 Patient satisfaction scale >50% at 6 weeks: 53% (51/96) vs. 57% (55/96); RR 0.93 (95% CI 0.72 to 1.20) Patient satisfaction scale >50% at 3 months: 62% (53/86) vs. 57% (43/75); RR 1.07 (95% CI 0.83 to 1.39)

Facci, 2011[519] 2 weeks Subacute *Good*	A. TENS 10 30-minutes sessions over 2 weeks (n=50) B. Interferential therapy 10 30-minutes sessions over 2 weeks (n=50) C. No treatment (n=50)	A. vs. B. vs. C. Mean age: 50 vs. 45 vs. 47 Female: 70% vs. 74% vs. 74% LBP alone: 78% vs. 78% vs. 70%; LBP + sciatica 22% vs. 22% vs. 30% Use of pharmacologic treatments: 65% vs. 69% vs. 67%	A. vs. B. vs. C. VAS (0-100), mean change from baseline: -3.91 vs. -4.48 vs. -0.85; A. vs. B., p=NS; A. vs. C. and B vs. C. p>0.05 McGill pain intensity index, mean change from baseline: -1.45 vs. -1.41 vs. -0.66; A. vs. B., p=NS; A. vs. C. and B vs. C. p>0.05 McGill pain rating index, mean change from baseline: -17.66 vs. -25.34 vs. -3.53; A. vs. B. p>0.05; A. vs. C. and B vs. C. p>0.05	McGill number of words describing pain, mean change from baseline: -6.80 vs. -8.30 vs. -0.12; A. vs. B., p=NS; A. vs. C. and B vs. C. p>0.05 RDQ, mean change from baseline (scores approximated based on graphic description): -6.26 vs. -7.42 vs. -0.91; A. vs. B., p=NS; A. vs. C. and B vs. C. p>0.05
Shimoji, 2007[518] 6 weeks Acute Fair	A. Active TENS + massage twice a week for 5 weeks (n=11) B. Sham TENS + massage twice a week for 5 weeks (n=10)	A. vs. B. Mean age: 62 vs. 64 years Female:18% vs. 20% Spondylosis deformans: 82% vs. 80% Mean NRS (0-10): 4.5 vs. 5.0	A. vs. B. Pain, mean change from baseline: -1.4 vs. -1.1; p=0.4	
Tsukayama, 2002[520] 2 weeks Chronic Fair	A. TENS twice a week for 2 weeks (n=10) B. Electroacupuncture twice a week for 2 weeks (n=10)	A. vs. B. 43 vs. 47 years Female:80% vs. 89% Japanese Orthopedic Pain score: 15.6 vs. 16.3 Baseline function: not reported	A. vs. B. VAS (0-100), mean during intervention period: 86mm vs. 65mm VAS (0-100), difference between groups: 21mm, 95% CI 4.126 to 37.953, p=0.02 JOA, mean change from baseline: -0.802 vs. -2.222, p=0.24	

CI = confidence interval; JOI = Japanese Orthopedic Association; LBP = low back pain; NRS = numeric rating scale; NS = non-significant; RR = relative risk; SF-36 = 36 item short form health survey; TENS = Transcutaneous Electrical Nerve Stimulation; VAS = visual analogue scale

Table 21. Characteristics and conclusions of included electrical muscle stimulation trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Durmus, 2010[499] 6 weeks Chronic *Poor*	A: Electrical muscle stimulation + exercise: Applied at L2-L4 levels over erector spinae muscles bulks motor points when prone (15 minutes), symmetric biphasic wave at 50 Hz and 50 ms phase time, intensity increased until apparent muscle contraction established (60-130 mA), applied for 10 s of contraction and 10 s of relaxation; 15 minutes 3 times weekly for 6 weeks + exercise (see below) (n=20) B: Ultrasound + exercise: 1 MHz at 1 W/cm2, applied for 10 minutes 3 times a week for 6 week + exercise (see below) (n=19) C: Exercise: 45 minute back and abdominal exercises and 5 minute stretching 3 times a week for 6 weeks; also given an exercise program consisting of four exercises (n=20)	A. vs. B. vs. C. Mean age: 49 vs. 48 vs. 47 years Female: 100% vs. 100% vs. 100% Pain intensity (median, 0-10 VAS): 4.9 vs. 3.9 vs. 2.4 ODI (mean, 0-100): 28 vs. 26 vs. 26	A. vs. B. vs. C. Pain (mean, 0-10 VAS, estimated from graph): 2.9 vs. 2.9 vs. 3.9 at 3 weeks, 0.4 vs. 0.9 vs. 2.4 at 6 weeks ($p<0.05$ for A or B vs. C) ODI (mean, 0-100): 6.80 vs. 8.69 vs. 8.40 at 6 weeks (p=0.07) Pain Disability Index (median, 0-50): 5.15 vs. 6.21 vs. 6.50 at 6 weeks (p=0.62) SF-36 Pain (median): 88.0 vs. 88.0 vs. 77.0 at 6 weeks (p=0.28)	A. vs. B. vs. C. Beck Depression Inventory (mean, 0-63): 3.35 vs. 3.94 vs. 4.85 at 6 weeks (p=0.37) SF-36 Physical Function (mean, 0-100): 97.5 vs. 90.0 vs. 90.0 at 6 weeks (p=0.009) SF-36 Mental Health (mean): 78.7 vs. 73.0 vs. 71.8 at 6 weeks (p=0.17) SF-36 General health (mean): 70.4 vs. 65.5 vs. 64.2 at 6 weeks (p=0.23) SF-36 Social function (median): 88.0 vs. 77.0 vs. 77.0 at 6 weeks (p=0.02) SF-36 Physical role limitations (median): 100 vs. 100 vs. 100 at 6 weeks (p=0.30) SF-36 Emotional role limitations (median): 100 vs. 100 vs. 100 at 6 weeks (p=0.58) SF-36 Energy (median): 83.8 vs. 68.7 vs. 67.8 at 6 weeks (p=0.001)

Durmus, 2009[524] 8 weeks Chronic *Poor*	A: Electrical muscle stimulation + exercise: Applied at L2-L4 levels over erector spinae muscles bulks motor points when prone (15 minutes) and obliquus externus abdominus muscles motor points when supine (15 minutes), symmetric biphasic wave at 50 Hz and 50 ms phase time, intensity increased until apparent muscle contraction established (70-120 mA), applied for 10 s of contraction and 10 s of relaxation; 30 minutes 3 times weekly for 8 weeks plus exercise (see below) (n=21) B: Exercise: Group exercise 20 minute back and abdominal exercises and 5 minute stretching 3 times a week for 8 weeks; also given an exercise program consisting of six exercises (n=20)	A. vs. B. Mean age: 47 vs. 43 years Female: 100 vs. 100% Pain intensity (mean, 0-10 VAS): 7.9 vs. 7.5 ODI (mean, 0-100): 37 vs. 37	A. vs. B. Pain (mean, 0-10 VAS, estimated from graph): 4.9 vs. 5.8 at 2 weeks, 2.9 vs. 4.8 at 4 w, 0.9 vs. 3.8 at 8 weeks (p not reported and not estimable) ODI (mean, 0-100): 6.6 vs. 19.2 at 8 w (p=0.001) Pain Disability Index (median, 0-50): 4 vs. 9.5 at 8 weeks (p=0.01) SF-36 Pain (mean): 87 vs. 64 at 8 weeks (p=0.001)	A. vs. B. Beck Depression Inventory (mean, 0-63): 2.8 vs. 3.3 at 8 weeks (p>0.05) SF-36 Physical Function (mean, 0-100): 92 vs. 73 at 8 weeks (p=0.001) SF-36 Mental Health (mean): 82 vs. 70 at 8 weeks (p=0.006) SF-36 General health (mean): 76 vs. 64 at 8 weeks (p=0.01) SF-36 Social function (median): 55 vs. 44 at 8 weeks (p>0.05) SF-36 Physical role limitations (median): 100 vs. 65 at 8 weeks (p=0.001) SF-36 Emotional role limitations (median): 100 vs. 82 at 8 weeks (p=0.01) SF-36 Energy (median): 85 vs. 70 at 8 weeks (p=0.001)
Glaser, 2001[525] 6 months Chronic *Poor*	A: Electrical muscle stimulation + exercise: Placed on lower back, parameters not reported + exercise (see below), 30 minutes 2 times daily for 2 months (n=32) B: Sham stimulation + exercise: Group instruction on strength and flexibility exercises, 3 sessions once weekly for 3 weeks and instructed to perform home exercises for 6 months (n=23)	A. vs. B. Mean age: 51 vs. 53 years Female: 62 vs. 52% Pain: Not reported Back-specific function: Not reported	None	A. vs. B. Low Back Pain Outcome Instrument Job Exertion (mean, 1-6): 2.69 vs. 2.83 at 2 months, 2.74 vs. 2.89 at 6 months LBPOI Job Stress/Satisfaction (mean, 1-6): 3.20 vs. 2.25 at 2 months, 3.02 vs. 2.44 at 6 months LBPOI Back Pain/Disability (mean, 1-6): 2.36 vs. 2.13 at 2 months, 2.45 vs. 2.30 at 6 months LBPOI Neurogenic Symptoms (mean, 1-6): 1.92 vs. 1.87 at 2 months, 2.17 vs. 1.89 at 6 months LBPOI Expectations Met (mean, 1-6): 4.21 vs. 3.79 at 2 months, 4.02 vs. 3.72 at 6 months SF-36 Mental health (mean, 0-100): 70 .2 vs. 80.0 at 2 months, 67.9 vs. 76.2 at 6 months

Moore, 1997[526] 2 days after each intervention Chronic *Poor*	A: Electrical muscle stimulation: Location not specified, symmetric biphasic wave at 70 Hz and 200 ms pulse width, amplitude adjustable from 0 to 100 mA to produce muscle contractions, cycle on-time 5 seconds and off-time 15 seconds; three 10 minute periods of stimulation alternating with 130 minute periods of no treatment B: TENS: Asymmetrical biphasic square pulse, 100 Hz and 100 ms pulse width, amplitude 0 to 60 mA C: Electrical muscle stimulation + TENS: Alternating one 10 minute and one 20 minute period of electrical muscle stimulation with 3 periods of TENS stimulation D: Sham TENS Crossover design (n=24), each intervention 5 hours/day for 2 days, with 2 day hiatus between interventions	A. vs. B. vs. C. vs. D. Mean age: 52 years Female: 67% Pain intensity: 49 vs. 46 vs. 48 vs. 51 Back-specific function: Not reported Conditions: 9 bulging disc, 7 postlaminectomy, 5 spinal stenosis, 1 spondylolisthesis; 15 low back pain, 3 middle back pain 4 upper back pain, 2 diffuse back pain	A. vs. B. vs. C. vs. D. Pain (mean, 0-100 VAS): 39.7 vs. 40.6 vs. 36.3 vs. 44.8 ($p>0.05$ for overall effect, but $p=0.02$ for C vs. D) Present Pain Intensity (mean, 0-4): 2.21 vs. 2.27 vs. 1.94 vs. 2.42 ($p=0.03$ for overall effect, $p<0.02$ for C vs. A, B, or D)	

Pope, 1994[492] 3 weeks Acute, subacute *Fair*	A: Electrical muscle stimulation: Applied to painful back on back, symmetric biphasic wave at 37 Hz and 225 ms pulse width, amplitude adjustable from 0 to 91 mA to produce muscle contractions, pulse ramped up for 2 seconds, held for 6 seconds, ramped off for 2 seconds, 6 second pause; used for at least 8 hours per day for 3 weeks (n=28) B: Manipulation: Dynamic short lever, high velocity, low amplitude thrust exerting force on the lumbar spine and/or sacroiliac joint, unilaterally or bilaterally as determined by treating physicians, 3 sessions per week for 3 weeks (n=70) C: Massage: Effleurage massage for up to 15 minutes, 3 sessions per week for 3 weeks (n=37) D: Lumbar support: Freeman Lumbosacral Corset to be worn during waking hours except while bathing, could be removed up to 10 minutes up to 3 times daily (n=29)	A. vs. B. vs. C. vs. D. Mean Age: Not reported Female: Not reported Pain intensity: States no statistically significant differences, data not reported Back-specific function: Not reported	A. vs. B. vs. C. vs. D. Pain (mean change from baseline, 0-100 VAS): -9.6 vs. -24 vs. -17 vs. -16 ($p>0.05$ for all between-group comparisons)	

LBP = low back pain; LBPOI = Low Back Pain Outcome Instrument; ODI = Oswestry Disability Index; SF-36 = 36 item short form health survey; TENS = Transcutaneous Electrical Nerve Stimulation; VAS = visual analogue scale

Table 22. Characteristics and conclusions of included percutaneous electrical nerve stimulation (PENS) trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Hamza, 1999[531] 2 weeks Chronic *Poor*	A: PENS: 10 32-gauge needles placed into low back pain to depth of 2-4 cm in a dermatomal (or sclerotomal) distribution of pain for 60 minutes; connected to bipolar leads at alternating frequency of 15 and 30 Hz for 45 minutes (maximum amplitude 25 mA using unipolar square-wave pattern and pulse width of 0.5 ms) B: PENS: Stimulation for 30 minutes C: PENS: Stimulation for 15 minutes D: PENS: Stimulation for 0 minutes Crossover design, each intervention administered 3 times a week for 2 weeks, with 1 week between treatments (total 11 weeks)	A. vs. B. vs. C. vs. D. Mean age: 43 years (overall) Female: not reported Baseline pain (mean, 0-10 VAS): 6.3 vs. 6.4 vs. 6.8 vs. 6.2 Baseline function: Not reported Prior surgery: 42% (overall)	A. vs. B. vs. C. vs. D. Pain (mean, 0-10 VAS): 1.5 vs. 1.6 vs. 2.0 vs. 5.4 at 2 weeks Pain (percent improvement from baseline, 0-10 VAS): 40% vs. 46% vs. 22% vs. 10% ($p<0.01$ for A or B vs. D. and $p<0.05$ for C vs. D)	SF-36 Physical component summary (mean improvement, 0-100): +7.1 vs. +7.4 vs. +5.4 vs. not reported ($p<0.001$ for A or B vs. D. and $p<0.01$ for C vs. D) SF-36 Mental component summary (mean improvement, 0-100): +2.9 vs. +3.1 vs. +2.1 vs. not reported ($p<0.001$ for A or B vs. D. and $p<0.01$ for C vs. D) Physical activity (percent improvement from baseline, 0-10 VAS): 50% vs. 53% vs. 28% vs. 8% ($p<0.01$ for A or B vs. D, $p<0.05$ for C vs. D) Sleep quality (percent improvement from baseline, 0-10 VAS): 40% vs. 44% vs. 25% vs. 5% ($p<0.01$ for A or B vs. D, $p<0.05$ for C vs. D) Use of nonopioid analgesics (percent decreased in pills per day): 35% vs. 38% vs. 21% vs. 8% ($p<0.01$ for A or B vs. D, $p<0.05$ for C vs. D)

Pérez-Palomares, 2010[530] 3 weeks Acute to chronic; 84% vs. 74% <3 months *Poor*	A: PENS: Eight 0.3 x 25 mm needles placed into low back pain to depth of 2-2.5 cm 8 in a dermatomal distribution, 0.3 ms impulse duration, for 30 minutes (n not reported) B: Dry needling: 0.30 x 40 mm needles inserted into trigger points using fast-in and fast-out Hong's technique, followed by spray and stretch technique (n not reported) 3 sessions weekly for total of 9 sessions over 3 weeks	A. vs. B. Mean age: Not reported, 34% vs. 50% <40 years of age Female: 81% vs. 67% Baseline pain (mean, 0-10 VAS): 6.27 vs. 6.04 Baseline function: Not reported	A. vs. B. Pain (mean difference from baseline, 0-10 VAS): 2.38 vs. 2.35 (p=0.94) >40% improvement in pain: 54% (28/52) vs. 46% (24/52), RR 1.17 (95% CI 0.79 to 1.72)	Sleep quality (mean difference from baseline, 0-10 VAS): 1.72 vs. 1.85 (p=0.68) ODI Personal care (median difference from baseline, 0-1): 0.38 vs. 0.34 (p=0.94) ODI Lifting weight: 0.59 vs. 0.06 (p=0.03) ODI Walking: 0.17 vs. 0.15 (p=0.86) ODI Sitting: 0.21 vs. 0.33 (p=0.51) ODI Standing: 0.25 vs. 0.41 (p=0.26) ODI Social life: 0.72 vs. 0.72 (p=0.18)
Weiner, 2008[532] 6 months Chronic Fair	A. PENS: Ten 32 gauge 40 mm needles placed at 15 mm depth placed bilaterally at levels corresponding to T12, L3, L5, and S2, and the motor point for the piriformis muscle, for 30 minutes, frequency based on algorithm; also two needles placed at T12 level with transient high frequency stimulation (control PENS procedure) (n=47) B. PENS + exercise: Supervised strength, flexibility, and aerobic exercise, sessions 60 minutes, plus home exercise (flexibility and graded walking) three times a week for 6 weeks (n=45)	A. vs. B. vs. C. vs. D. Mean age: 74 vs. 74 vs. 73 vs. 74 years Female: 58% vs. 56% vs. 60% vs. 54% Baseline pain (0-10): 2.5 vs. 2.4 vs. 2.4 vs. 2.3 Baseline RDQ: 10.5 vs. 10.2 vs. 11.0 vs. 10.5	A vs. B vs. C vs. D (mean change from baseline) McGill Pain Questionnaire (0 to 78 scale): -2.9 vs. -4.1 vs. -3.1 vs. -2.3 at 6 w, -3.4 vs. -3.8 vs. -3.1 vs. -3.3 at 6 m Average pain last week (0 to 10): -0.7 vs. -0.7 vs. -0.6 vs. -0.6 at 6 w, -0.5 vs. -0.6 vs. -0.5 vs. -0.6 at 6 m p>0.05 for all outcomes at both time points for A vs. D, B vs. C, B vs. A, and C vs. D	A vs. B vs. C vs. D (mean change from baseline) RDQ (0 to 24): -2.6 vs. -2.6 vs. -3.0 vs. -2.7 at 6 w, -2.1 vs. -2.1 vs. -2.8 vs. -3.0 at 6 m Geriatric Depression Scale: 0.3 vs. -0.4 vs. -0.3 vs. -0.2 at 6 w, 0.5 vs. -0.1 vs. -0.1 vs. -0.4 at 6 m SF-36 composite mental health (0 to 100): 1.5 vs. -0.3 vs. 2.8 vs. -0.1 at 6 w, -1.8 vs. -0.2 vs. 1.5 vs. 1.2 at 6 m SF-36 composite physical health: -1.1 vs. 3.9 vs. 6.9 vs. 5.9 at 6 w, -0.4 vs. 0.1 vs. -0.6 vs. -0.4 at 6 m Pittsburgh sleep score: -0.2 vs. 0.002 vs. -0.7 vs. 0.0 at 6 w, -0.4 vs. 0.1 vs. -0.6 vs. -0.4 at 6 m Moderate or major global improvement: 58% vs. 58% vs. 66% vs. 56% at 6 w, 40% vs. 55% vs. 50% vs. 44% at 6 m p>0.05 for all outcomes at both time points for A vs. D, B vs. C, B vs. A, and C vs. D

Weiner, 2008[532] 6 months Chronic Fair	C. Control PENS + exercise (n=44) D. Control PENS: Needles placed as for PENS, but stimulation (transient high frequency stimulation) only applied to needles at T12 level (n=48) 2 sessions weekly for total of 12 sessions over 6 weeks			

LBP = low back pain; ODI = Oswestry Disability Index; PENS = Percutaneous Electrical Nerve Stimulation; RDQ = Roland-Morris Disability Questionnaire; SF-36 = 36 item short form health survey; VAS = visual analogue scale

Table 23. Characteristics and conclusions of included interferential therapy trials

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Lara-Palomo, 2013[536] 10 weeks Subacute, chronic Fair	A: Interferential therapy: Bipolar current, carrier frequency 4000 Hz at constant voltage and amplitude modulation 80 Hz, applied to lumbar area for 30 minutes at 30-50 mA, 20 sessions over 10 weeks (n=31) B: Superficial massage: Effleurage, superficial pressure, and skin rolling on the lower back for 20 minutes, 20 sessions over 10 weeks (n=31)	A. vs. B. Mean age: 50 vs.47 years Female: 70% vs. 65% Baseline pain (mean, 0-10 VAS): 6.67 vs. 6.52 Baseline ODI (mean, 0-100): 36.07 vs. 37.94	A. vs. B., mean difference in change from baseline at 10 weeks Pain (0-10 VAS): -1.06 (95% CI -1.91 to -0.22)	A. vs. B., mean difference in change from baseline at 10 weeks ODI (0-100): -5.20 (95% CI -10.82 to 0.42) RDQ (0-24): -3.01 (95% CI -4.53 to -1.47) SF-36 Physical function (0-100): 5.57 (95% CI -2.27 to 13.41) SF-36 Physical role (0-100): 7.02 (95% CI 1.05 to 12.98) SF-36 Body pain (0-100): 4.72 (95% CI -0.28 to 9.71) SF-36 General health (0-100): 1.09 (95% CI -3.22 to 5.41) SF-36 Vitality (0-100): 2.04 (95% CI -3.36 to 7.43) SF-36 Social functioning (0-100): 1.14 (95% CI -3.88 to 6.15) SF-36 Mental health (0-100): 2.37 (95% CI -3.39 to 8.14) SF-36 Emotional role (0-100): 3.27 (95% CI -1.58 to 8.12) RDQ worsened by >2.5 points: 10% (3/30) vs. 13% (4/31), RR 0.78 (95% CI 0.19 to 3.18)

CI = confidence interval; LBP = low back pain; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; SF-36 = 36 item short form health survey; VAS = visual analogue scale

Table 24. Characteristics and conclusions of included superficial heat or cold trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Dehghan, 2014[548] 15 days Acute *Fair*	A: Hot water bottle 20 minutes twice a day for 1 week + naproxen 500 mg po bid B: Ice 20 minutes twice daily for 1 week + naproxen 500 mg po bid C: Naproxen 500 mg po bid	A. vs. B. vs. C. Mean age: 34 vs.33 vs.36 years Female: not reported Mean McGill Pain Questionnaire (overall, 0 to 78): 12.1 vs. 12.1 vs. 13.0 Baseline function: Not reported	A. vs. B. vs. C. McGill Pain Questionnaire, overall pain (method for scoring unclear): 12.1 vs. 12.1 vs. 13.0 at baseline, 7.3 vs. 9.3 vs. 9.9 on day 3, 3.7 vs. 5.1 vs. 7.7 on day 8, 0.76 vs. 2.2 vs. 5.6 on day 15 (p<0.005 for between group differences on days 3, 8, and 15)	A. vs. B. vs. C. McGill Pain Questionnaire, “affective dimension” (method for scoring unclear): 7.5 vs. 7.4 vs. 8.2 at baseline, 4.8 vs. 4.9 vs. 6.6 on day 3, 2.0 vs. 2.3 vs. 4.9 on day 8, 0.68 vs. 1.2 vs. 3.8 on day 15 (p<0.005 for between group differences on days 3, 8, and 15)
Kettenmann, 2007[546] 5 days Acute *Fair*	A. Continuous low-level heat wrap (ThermaCare®) 4 hours/day for 4 days (n=15) B. No heat wrap (oral NSAIDs allowed as needed but there was no formal protocol for their use) (n=15)	A. vs. B. Mean age: 56 vs. 58 years Female: 53% vs. 80% Mean pain (0-100 VAS): 4.1 vs. 3.9	A. vs. B. Pain, patient assessed severity (no pain to very severe pain, VAS scale 0-100) day 1: 40 vs. 52; p=NS; day 2: 30 vs. 44; p=NS; day 3: 31 vs. 57; p=0.02; day 4: 27 vs. 47; p=0.04 (pain values presented graphically)	A. vs. B. Function, proportion of patients woken from sleep due to pain: significantly lower proportion with heat wrap use at days 2 (p=0.16), 3 (p=0.002) and 4 (p=0.001)
Stark, 2014[547] 8 hours Acute *Fair*	A: Heat wrap (ThermaCare Lower Back/Hip HeatWrap), applied for 8 hours B: Oral placebo Acetaminophen 500 mg x 2 permitted for rescue analgesia 10 subjects randomized to sham wrap or oral ibuprofen but not included in analyses	A. vs. B. Mean age: 30 vs. 29 years Female: 42% vs. 60% Mean pain (VAS 0-100): 4.1 vs. 3.9 Pain moderate (2 on 0 to 5 scale): 73% vs. 80% Pain moderately severe or severe (3 or 4 on 0 to 5 scale): 27% vs. 20% Baseline function: Not reported	A. vs. B. Pain relief (mean, 0=no relief to 5=complete relief): 2.1 vs. 1.2 at 2 hours (p<0.05), 3.0 vs. 1.5 at 8 hours (p<0.001)	A. vs. B. Global evaluation of treatment 4 or 5 on 0 to 5 scale (0=very poor, 5=excellent): 84% (22/26) vs. 16% (4/25), RR 5.29 (95% CI 2.12 to 13.18)

Tao, 2005[549] 4 and 14 days from treatment initiation Acute *Poor*	A: Heat-wrap during daytime hours for 3 days plus education (written material) (n=25) B: Education only (n=18)	A. vs. B. Mean age: 35 vs. 36 years Female: 84% vs. 83% Baseline pain intensity: Not reported Baseline function: Not reported	A. vs. B. Pain intensity (mean difference in change from baseline, 0 to 10 scale): -1.01 (95% -2.08 to 0.06) at day 1, -2.05 (95% CI -3.34 to -0.76) at day 3, -1.66 (95% CI -2.97 to -0.37) at day 7, -1.63 (95% CI -2.92 to -0.34) at day 14 Pain relief (mean difference in change from baseline, 0 to 5 scale): 1.33 (95% CI 0.52 to 2.12) at day 1, 1.53 (95% CI 0.76 to 2.30) at day 3, 0.98 (95% CI 0.08 to 1.87) at day 7, 1.21 (0.26 to 2.14) at day 14	A. vs. B. RDQ (mean difference in change from baseline, 0 to 24): -2.38 (95% CI -5.62 to 0.85) at day 4, -4.60 (95% CI -8.27 to -0.94) at day 7, -4.02 (95% CI -7.82 to -0.24) at day 14

CI = confidence interval; LBP = low back pain; NS = non-significant; NSAIDs = Nonsteroidal anti-inflammatory drugs; RDQ = Roland-Morris Disability Questionnaire; RR = relative risk; VAS = visual analogue scale

Table 25. Characteristics and conclusions of included low-level laser therapy trials

Author, Year Duration of Followup LBP Duration Quality	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Ay, 2010[561] 3 weeks Subacute and chronic *Good*	Subacute LBP A. GaAlAs laser, 850 nm + heat (n=20) B. Sham laser + heat (n=20) Chronic LBP A. GaAlAs laser, 850 nm + heat (n=20) B. Sham laser + heat (n=20) Treatment protocol: 5 times/week for 3 weeks	A. vs. B.: Acute LBP Mean age 48 vs. 45 years 30% vs. 40% female Pain, VAS (0-10): 6.7 vs. 6.15 Pain, patient global assessment: 6.45 vs. 5.0 Pain, physician global assessment: 6.6 vs. 6.15 Disability, RDQ: 13.2 vs. 12.6 Disability, Modified ODI: 19.8 vs. 20.8 A. vs. B.: Chronic LBP Mean age 52 vs. 55 years 55% vs. 45% female Pain, VAS (0-10): 6.0 vs. 6.6 Pain, patient global assessment: 5.65 vs. 6.05 Pain, physician global assessment: 5.8 vs. 6.3 Disability, RDQ: 15.1 vs. 15.6 Disability, Modified ODI: 23.9 vs. 24.65	A. vs. B.: Acute LBP Pain, VAS (0-10) mean change from baseline: -4.0 vs. -4.15; p=0.07 Pain, patient global assessment mean change from baseline: -3.9 vs. -4.7; p=0.006 Pain, physician global assessment mean change from baseline: -4.1 vs. -4.2; p=-0.71 A. vs. B.: Chronic LBP Pain, VAS (0-10) mean change from baseline: -3.35 vs. -3.95; p=0.03 Pain, patient global assessment mean change from baseline: -3.3 vs. -3.9; p=0.11 Pain, physician global assessment mean change from baseline: -3.15 vs. -4.05; p=0.01	A. vs. B.: Acute LBP Disability, RDQ mean change from baseline: -6.0 vs. -5.65; p=0.39 Disability, Modified ODI mean change from baseline: -8.2 vs. -8.7; p=0.15 A. vs. B.: Chronic LBP Disability, RDQ mean change from baseline: -6.7 vs. -4.65; p p>0.05 Disability, Modified ODI mean change from baseline: -9.6 vs. -6.2; p>0.05

Djavid, 2007[558] 12 weeks Chronic *Fair*	A. GaAlAs laser, 810 nm (n=16) B. GaAlAs laser, 810 nm + exercise (n=19) C. Sham laser + exercise (n=18) Treatment protocol: laser, 2 times/week for 6 weeks; exercise, not reported	A. vs. B. vs. C. Mean age 40 vs. 38 vs. 36 years 56% vs. 37% vs. 17% female Race not reported Duration of pain 29 vs. 29 vs. 25 months Pain, VAS (0-10) 7.3 vs. 6.2 vs. 6.3 Disability, ODI 33.0 vs. 34.0 vs. 31.8	A. vs. B. vs. C. Pain (VAS 0-10): 4.4 vs. 2.4 vs. 4.3; A. vs. B., p=0.002; A. vs. C, p=0.87; B vs. C, p=0.0005; mean change from baseline -2.9 vs. -3.8 vs. -2.0	A. vs. B. vs. C. Disability (ODI 0-50): 20.8 vs. 16.8 vs. 24.1; A. vs. B., p=0.006; A. vs. C, p=0.06; B vs. C, p=0.0001
Hsieh, 2014[559] 2 weeks Subacute, chronic *Fair*	A: GaAlAs, 890 nm laser with 780 mW power (total 83.2 J/cm2), 40 minutes three times a week for 2 weeks (n=33) B: Sham laser, 40 minutes three times a week for 2 weeks (n=27)	A. vs. B. Mean age: 60 vs. 58 years Female: 58% vs. 70% Pain, VAS (0-10): 7.9 vs. 7.9 Disability, ODI: 2.3 vs. 2.6 Radiation in lower limb: 70% vs. 78%	A. vs. B. Pain (mean, 0-10 VAS): 7.8 vs. 7.9 at baseline, mean change 0.73 vs. 0.4 at 2 weeks, difference -0.3 (95% CI -1.0 to 0.3)	A. vs. B. ODI (mean, scale unclear): 2.3 vs. 2.6 at baseline, mean change -0.4 vs. -0.1 at 2 weeks, difference -0.3 (95% CI -0.6 to -0.1) Frenchay Activities Index (mean, 0 to 45): 32.2 vs. 33.5 at baseline, mean change 1.9 vs. 1.5 at 2 weeks, difference -0.4 (95% CI -3.4 to 2.6) Osteoarthritis Quality of Life Questionnaire (mean, scale not reported): 3.8 vs. 5.9 at baseline, mean change -0.5 vs. -0.6 at 2 weeks, difference -0.1 (95% CI -1.4 to 1.1) Multidimensional Fatigue Inventory: No differences on any subscale
Jovicic, 2012562 2 weeks Acute Fair	A. 904 nm laser, 0.1 joule per point (0.4 points/day; n=22) B. 904 nm laser, 1.0 joule per point (4.0 points/day; n=22) C. 904 nm laser, 4.0 joules per point (16.0 points/day; n=22) Treatment protocol: 5 times/week for 2 weeks	A. vs. B. vs. C. Mean age 47 vs. 44 vs. 45 years Sex, race not reported Lumbar pain, VAS (0-10): 7 vs. 7 vs. 6.5	A. vs. B. vs. C. Lumbar pain, VAS (0-10 mean change (results depicted graphically): -3 vs. -3 vs. -3.5; p>0.05	A. vs. B. vs. C. Function, Activities of Daily Life: walking, mean change from baseline in proportion able to complete activity - all outcomes A or B vs. C. p=0.007 Function, Activities of Daily Living: sitting, mean change from baseline in proportion able to complete activity - all outcomes A or B vs. C. p=0.005 Function, Activities of Daily Living: standing, mean change from baseline in proportion able to complete activity - all outcomes A or B vs. C. p=0.013

Konstantinovic, 2010560a 3 weeks Acute Good	A. 904 nm laser + nimesulide 200 mg/day (n=182) B. Sham laser + nimesulide 200 mg/day (n=182) C. Nimesulide 200 mg/day (n=182) Treatment protocol: laser 5 times/week for 3 weeks; nimesulide 15 consecutive days	A. vs. B. vs. C. Mean age 44 vs. 42 vs. 45 years 59% vs. 58% vs. 57% female Race not reported Lumbar pain, VAS (0-100): 66 vs. 65 vs. 67 Disability, ODI: 32 vs. 32 vs. 31 Quality of life, SF-36 PCS: 10 vs. 10 vs. 10 Quality of life, SF-36 MCS: 12 vs. 12 vs. 12	A. vs. B. vs. C. Lumbar pain, VAS (0-100) mean change: -30.0 vs. -15.7 vs. -20.8; A. vs. B., p<0.001; A. vs. C, p<0.001; B vs. C, p<0.001	A. vs. B. vs. C. Disability, ODI mean change: -12 vs. -6.5 vs. -10; A. vs. B., p<0.001; A. vs. C, p<0.001; B vs. C, p<0.001 Disability, ODI proportion improved (defined as change from moderate to minimal disability category): 72% (151/182) vs. 54% (98/182) vs. 18% (33/182); A. vs. B., RR 1.54 (95% CI 1.33 to 1.79); A. vs. C, RR 4.58 (95% CI 3.34 to 6.27); B vs. C, RR 2.97 (95% CI 2.12 to 4.16) Quality of life, SF-36 PCS: -4 vs. -2 vs. -3; A. vs. B., A. vs. C. p<0.01; B vs. C. p=0.06 Quality of life, SF-36 MCS: -6 vs. -3 vs. -4; A. vs. B., p<0.001; A. vs. C, p<0.001; B vs. C, p<0.001
Vallone, 2014563 3 weeks Chronic Fair	A: GaAlAs, 980 nm laser, 1 minute per spot, total 1200 J per spot for 1 m at each spot 3 times a week for 3 weeks, applied to 6 spots + exercise (stretching, strengthening) (n=50) B: Sham laser as above + exercise (n=50)	A. vs. B. Mean age: 68 years overall Female: 57% overall Pain (0-10 VAS): 6.64 vs. 6.36 Baseline function: not reported	A. vs. B. Pain (mean, 0-10 VAS): 6.64 vs. 6.36 at baseline, 2.68 vs. 4.08 at 3 w, change from baseline 3.96 vs. 2.32 (p<0.01) Complete pain relief: 10% (5/50) vs. 2.0% (1/50), RR 5.0 (95% CI 0.61 to 41.3)	

[a]Population characteristics for entire study population, including 74 participants with chronic cervical and extremity pain.
LBP = low back pain; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; SF-36 = 36 item short form health survey; VAS = visual analogue scale

Table 26. Characteristics and conclusions of included diathermy trials

Author, Year Duration of Followup LBP Duration Quality	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Ahmed, 2009[566] 6 weeks Subacute *Poor*	A: Short wave diathermy (n=47) B: Detuned (sham) diathermy (n=50) 15 minute sessions, 3 times a week for six weeks	A. vs. B. Mean age: 40 years (overall) Female: Not reported Baseline pain (mean, 0-34 [Lattinen's score plus tenderness score plus 0-10 VAS]): 20.4 vs. 20.1 Back-specific function: Not reported	A. vs. B. Pain (mean, 0-34 [Lattinen's score (0-20) plus tenderness score (0-4) plus 0-10 VAS]): 17.8 vs. 18.8 at w 1 (p=0.14), 15.3 vs. 17.6 at w 2 (p=0.01), 11.1 vs. 15.0 at w 4 (p<0.05), 6.4 vs. 13.4 at w 6 (p<0.05)	
Shakoor, 2008[567] 6 weeks *Poor*	A: Short wave diathermy: 27.33 MHz, wavelength 11 m (n=50) B: Detuned (sham) diathermy (n=52) 15 minute sessions, 3 times a week for six weeks Both groups also underwent extension and strengthening exercises (10 repetitions twice daily for 6 weeks) and received Naprosyn 250 mg po twice daily	A. vs. B. Mean age: 44.5 vs. 40.0 years Female: 59% (overall) Baseline pain (mean, 0-34 [Lattinen's score plus tenderness score plus 0-10 VAS]): 15.2 vs. 15.6 Back-specific function: Not reported	A. vs. B. Pain (mean, 0-34 [Lattinen's score (0-20) plus tenderness score (0-4) plus 0-10 VAS]): 13.9 vs. 14.5 at w 1 (p=0.31), 11.9 vs. 12.4 at w 2 (p=0.33), 10.3 vs. 11.8 at w 4 (p=0.02), 9.66 vs. 11.6 at w 6 (p<0.05)	

LBP = low back pain; VAS = visual analogue scale

Table 27. Characteristics and conclusions of included lumbar support trials

Author, Year Duration of Followup LBP Duration Quality	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Calmels, 2009[576] 3 months Acute *Fair*	A. Lumbar support (n=102) 5-8 hours/day, 3-5 days/week (varied according to study time point; hours of use/ week decreased over time) B. No lumbar support (n=95)	A. vs. B. Mean age: 43 years Female: 45% Mean pain (VAS, scale 0-100): 60.9 vs. 59.7 Mean function (EIFEL score, scale 0-24; higher score=more disability): 10.3 vs. 10.1	A. vs. B. Pain, mean change in VAS (0-100), day 30: -26.8 (SD 18.2) vs. -21.3 (SD 18.7); p=0.04 Pain, mean change in VAS (0-100), day 90: -41.5 (SD 21.5) vs. -32.0 (SD 20.0); p=0.002 Function, mean change in EIFEL score, day 30: -5.4 (SD 4.1) vs. -4.0 (SD 4.3); p=0.02 Function, mean change in EIFEL score, day 90: -7.6 (SD 4.4) vs. -6.1 (SD 4.7); p=0.02	A. vs. B. Function, mean change in EIFEL score, day 30: -5.4 (SD 4.1) vs. -4.0 (SD 4.3); p=0.02 Function, mean change in EIFEL score, day 90: -7.6 (SD 4.4) vs. -6.1 (SD 4.7); p=0.02
Morrisette, 2014578 2 weeks Mixed LBP duration, mean 14 vs. 18 vs. 10 weeks *Fair*	A. Inextensible lumbar support, number of hours per day not specified (mean 5.0 hours/day) (n=37) + standard care B. Extensible lumbar support, mean 4.8 hours/day (n=32) + standard care C. Standard care (n=29) All interventions administered for 2 weeks, standard care consisted of physician advice and medication and physical therapy including exercise, manual therapy, electrical stimulation, traction, cold/heat, and ultrasound	A. vs. B. vs. C. Mean age: 50 vs. 49 vs. 45 years Female: 54% vs. 69% vs. 62% Mean pain (0-10): 7.6 vs. 7.6 vs. 7.6 Mean ODI (0-100): 40 vs. 36 vs. 34	A vs. B vs. C. (mean difference from baseline) Pain (0-10 NRS): 3.3 (95% CI 2.3-4.3) vs. 3.3 (95% CI 2.2-4.4) vs. 2.4 (95% CI 1.4-3.5) at 2 w; p>0.05 for all comparisons Pain improved >2.4 points: 70% (26/37) vs. 75% (24/32) vs. 55% (16/29); RR 0.94 (95% CI 0.70 to 1.25) for A vs. B, RR 1.27 (95% CI 0.86 to 1.88) for A vs. C, RR 1.36 (95% CI 0.93 to 2.00) for B vs. C	A vs. B vs. C. (mean difference from baseline) ODI (0-100): 14.0 (95% CI 8.2-19.8) vs. 8.1 (95% CI 2.8-13.4) vs. 2.4 (95% CI -2.2-7.1) at 2 w; p=0.01 for A vs. C Patient Specific Activity Scale (0-10): -1.8 (95% CI -2.5 to -1.0) vs. -1.2 (95% CI -1.9 to -0.5) vs. -0.4 (95 %CI -1.3 to -0.4) at 2 w; p=0.01 for A vs. C ODI improved >50%: 35% (13/37) vs. 16% (5/32) vs. 10% (3/29); RR 2.25 (95% CI 0.90 to 5.62) for A vs. B, RR 3.40 (95% CI 1.07 to 10.8) for A vs. C, RR 1.51 (95% CI 0.40 to 5.77) for B vs. C ODI improved >6 points: 65% (24/37) vs. 59% (19/32) vs. 38% (11/29); RR 1.09 (95% CI 0.75 to 1.58) for A vs. B, RR 1.71 (95% CI 1.01 to 2.88) for A vs. C, RR 1.57 (95% CI 0.91 to 2.70) for B vs. C Patient Specific Activity Scale improved >2 points: 35% (13/37) vs. 31% (10/32) vs. 21% (6/29); RR 1.12 (95% CI 0.57 to 2.21) for A vs. B, RR 1.70 (95% CI 0.74 to 3.92) for A vs. C, RR 1.51 (95% CI 0.63 to 3.64) for B vs. C

Oleske, 2007[579] 1 year Acute *Fair*	A. Lumbar support + education (n=222), timing of support use not reported B. Education only (n=211)	A. vs. B. Mean age: 46 vs. 40 years Female: 17% vs. 24% Onset of LBP <2 weeks prior to study entry: 67% vs. 69% Mean pain (VAS, scale 0-10): 4.09 vs. 4.18 Mean function (Oswestry, scale 0-100; higher score=more disability): 24.4 vs. 24.5	A. vs. B. Pain, coefficient of change (group A=reference group): -0.248 days; p=0.3	Function, coefficient of change (group A=reference group): -0.298 days; p=0.8 Overall conclusion: no difference between treatment groups for pain or function outcomes
Sato, 2012[577] 6 months Subacute, chronic *Fair*	A. Lumbar support (corset; n=not reported) worn during all waking hours for 6 months except during bathing B. No lumbar support (n=not reported)	A. vs. B. Mean age: Mean age not reported; range 30 to 78 years Female: 50% Mean pain and function score not reported	A. vs. B. Function, Japanese Orthopedic Association (JOA) criteria (includes patient-assessment of pain and function), 1 month: significant difference in JOA score, favoring lumbar support: p<0.01 (no data shown); no significant difference between groups at 3 and 6 months	

CI = confidence interval; EIFEL = French translation of Roland-Morris Disability Questionnaire; JOI = Japanese Orthopedic Association; LBP = low back pain; NRS = numeric rating scale; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; RR = relative risk; SD = standard deviation; VAS = visual analogue scale

Table 28. Characteristics and conclusions of included traction trials

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Diab, 2012[584]; Diab, 2013[585] 6 months Subacute, chronic *Fair*	A. Traction, radiation and stretching 3 times/week for 10 weeks (n=40) B. Radiation and stretching 3 times/ week for 10 weeks (n=40)	A. vs. B. Mean age: 46 vs. 46 years Female: 45% vs. 43% Prior LBP treatment: 100% vs. 100% Pain, VAS (0-10): 6.0 vs. 5.5 Disability, ODI: 32.4 vs. 31.1	A. vs. B. Pain, VAS (0-10) at 10 weeks: 3.2 (SD 1.4) vs. 3.5 (SD 1.2); mean difference -0.30 (95% CI -0.88 to 0.28) Pain, VAS (0-10) at 6 months: 2.6 (SD 1.1) vs. 3.5 (SD 1.2); mean difference -0.90 (95% CI -1.41 to -0.39)	A. vs. B. Disability, ODI at 10 weeks: 21.8 (SD 3.1) vs. 23.4 (SD 3.4); mean difference -1.60 (95% CI -3.05 to -0.15) Disability, ODI at 6 months: 23.8 (SD 2.7) vs. 27.1 (SD 3.0); mean difference -3.30 (95% CI -4.57 to -2.03)
Moustafa, 2013[586] 6 months Subacute, chronic *Fair*	A. Traction, hot packs and interferential therapy 3 times/week for 10 weeks (n=32) B. Hot packs and interferential therapy 3 times/week for 10 weeks (n=32)	A. vs. B. Mean age: 44 vs. 43 years Female: 41% vs. 47% Using medication for LBP treatment: 38% vs. 44% Pain, VAS (0-10): 6.2 vs. 5.9 Disability, ODI: 32.4 vs. 31.7	A. vs. B. Pain, VAS (0-10) at 10 weeks: 2.3 (SD 1.6) vs. 3.5 (SD 1.04); mean difference -1.20 (95% CI -1.87 to -0.53) Pain, VAS (0-10) at 6 months: 2.4 (SD 0.9) vs. 4.6 (SD 1.3); mean difference -2.20 (95% CI -2.79 to -1.62)	A. vs. B. Disability, ODI at 10 weeks: 19.8 (SD 3.7) vs. 23.7 (SD 3.8); mean difference -3.90 (95% CI -5.77 to -2.03) Disability, ODI at 6 months: 23.1 (SD 2.8) vs. 31.2 (SD 2.9); mean difference -8.10 (95% CI -9.60 to -6.60)

Prasad, 2012[587] 6 weeks Acute, subacute *Poor*	A. Inversion traction 3 times/week for 4 weeks + physiotherapy (n=13) B. Physiotherapy alone (n=11)	A. vs. B. Mean age: 34 vs. 37 years Female: 46% vs. 64% Pain, VAS (0-10): 3.2 vs. 2.8 Disability, ODI: 50 vs. 48 Disability, RDQ: 12.5 vs. 10 Quality of life, SF36 physical function: 43.5 vs. 35.7	A. vs. B. Number analyzed for each outcome varied Pain, VAS (0-100: 0.9 (n=12) vs. 3.0 (n=7); p not reported (inadequate data provided to calculate)	A. vs. B. Disability, ODI: 31 (n=8) vs. 54 (n=3); p=0.3 Disability, RDQ: 7.5 (n=12) vs. 11 (n=7); p=0.55 Quality of life, SF-36 physical function mean change from baseline: 9.2 vs. 8.2; p=0.9; no significant difference between groups for other SF-36 measures including physical role, body pain, general health, vitality, social function, emotional role, mental health or change in health Need for surgery: 23% (3/13) vs. 82% (9/11); RR 0.28 (95% CI 0.10 to 0.79)

LBP = low back pain; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SF-36 = 36 item short form health survey; VAS = visual analogue scale

Table 29. Characteristics and conclusions of included taping trials

Author, Year Duration of Followup LBP Duration *Quality*	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Bae, 2013[592] 12 weeks Chronic *Fair*	A: Kinesio Taping® of lower back with tension, four "I" strips over area of maximum pain in star shape, 3 times per week for 12 weeks (n=10) B: Sham taping with one inelastic "I" strip transversely over lumbar area with maximum pain, 3 times per week for 12 weeks (n=10) All patients received hot pack (20 minutes), ultrasound (1.5 W/cm2 for 5 minutes), and TENS (4 pps, 15 minutes) to L1-2 and L4-5 areas (40 minutes); 3 times per week for 12 weeks	A. vs. B. Mean age: 54 vs. 51 years Female: 50% vs. 60% Pain intensity: 7.83 vs. 7.71 ODI: 16.3 vs. 15.4	A. vs. B. Pain (mean, 0-10 VAS): 7.83 vs. 7.71 at baseline, 5.07 vs. 5.14 at 12 weeks (p>0.05)	A. vs. B. ODI (mean, 0-100): mean 16.32 vs. 15.43 at baseline, 10.75 vs. 11.34 at 12 weeks (p>0.05)

Castro-Sanchez, 2012[593] 5 weeks Chronic Good	A: Kinesio Taping® of lower back with 25% tension in star shape overlying point of maximum pain, applied for 7 days (n=30) B: Sham taping with single transverse strip above point of maximal pain, applied for 7 days (n=30)	A. vs. B. Mean age: 50 vs. 47 years Female: 70% vs. 66% Pain intensity (0-10 VAS): 5.6 vs. 5.4 ODI (mean, 0-100): 28 vs. 29	A. vs. B. Pain (mean difference in change from baseline, 0-10): -1.1 (95% CI -1.9 to -0.3) at 1 week, -1.0 (95% CI -1.7 to -0.2) at 5 weeks	A. vs. B. ODI (mean difference in change from baseline, 0-100): -4 (95% CI -6 to -2) at 1 week, 1 (95% CI -1 to 3) at 5 weeks RDQ (mean difference in change from baseline, 0-24): -1.2 (95% CI -2.0 to -0.4) at 1 week, 0.1 (95% CI -1.0 to 1.3) at 5 weeks
Chen, 2012[594] 12 weeks Acute Fair	A: Functional Fascial Taping with tension applied in direction that resulted in maximal pain reduction on trunk flexion, applied in 3 directions, reapplied daily for 2 weeks (n=21) B: Sham taping without tension (n=22) All patients given instruction for home trunk flexion exercises	A. vs. B. Mean age: 46 vs. 40 years Female: 48% vs. 45% Average pain (mean, 0-100 VAS): 43 vs. 42 ODI (mean, 0-100): 31 vs. 24	A. vs. B. Average pain (mean difference in change from baseline, 0-100): -7.6 +/- 6.2 (p=0.23) at 2 weeks, -0.73 +/- 5.9 (p=0.90) at 6 weeks, -3.6 +/-6.9 (p=0.60) at 12 weeks Worst pain (mean difference in change from baseline, 0-100): -17.3 +/- 7.2 (p=0.02) at 2 weeks, -11.3 +/- 8.1 (p=0.17) at 6 weeks, -5.8 +/- 7.6 (p=0.45) at 12 weeks ODI (mean difference in change from baseline, 0-100): -5.5 +/- 2.8 (p=0.05) at 2 weeks, -3.4 +/- 3.1 (p=0.28) at 6 weeks, -3.1 +/- 3.1 (p=0.33) at 12 weeks Average pain improved >20 points: 57% (12/21) vs. 36% (8/14) at 2 weeks, 57% (12/21) vs. 59% (13/22) at 6 weeks, 71% (15/21) vs. 59% (13/22) at 12 weeks Worst pain improved >20 points: 81% (17/21) vs. 41% (9/22) at 2 weeks, 67% (14/21) vs. 68% (15/22) at 6 weeks, 76% (16/21) vs. 77% (17/22) at 12 weeks	A. vs. B. ODI improved >10 points: 81% (17/21) vs. 41% (9/22) at 2 weeks, 71% (15/21) vs. 55% (12/22) at 6 weeks, 62% (13/21) vs. 50% (11/22) at 12 weeks

Kachanathu, 2014595 4 weeks Chronic Poor	A: Kinesio Taping® with two strips from origin of lumbar erector spinae to insertion with slight traction with patient flexing + exercise therapy (stretching and strengthening three sessions/week for 4 weeks) (n=20) B: Exercise therapy without Kinesio Taping (n=20)	A. vs. B. Mean age: 35 years Female: 25% Pain intensity (mean , 0-10): 6.2 vs. 6.1 RDQ (mean 0-24): 10.3 vs. 1.8	A. vs. B. Pain (mean, 0-10): 2.9 vs. 3.7 at 4 weeks (p=0.57)	A. vs. B. RDQ (mean, 0-24): 4.7 vs. 7.0 at 4 weeks (p=0.67)
Paolini, 2011596 4 weeks Acute, subacute, chronic Fair	A: Kinesio Taping® of lower back with 3 vertical strips placed with patient bending forward to create tension, applied for 3 days at time over 4 weeks (n=13) B: Exercise therapy, 30 minutes three times/week with stretching, relaxation, and active exercises (n=13) C: Kinesio Taping + exercise (n=13)	A. vs. B. vs. C. Mean age: 63 vs. 63 vs. 62 years Female: 62% vs. 69% vs. 62% Pain intensity (mean, 0-10 VAS): 7.1 vs. 7.6 vs. 7.6 RDQ (mean, 0-24): 10.3 vs. 9.9 vs. 9.5	A. vs. B. vs. C. Pain (mean, 0-10): 3.1 vs. 3.5 vs. 3.7 at 3 weeks (p>0.05) RDQ (mean, 0-24): 9.5 vs. 5.4 vs. 7.3 at 3 weeks (p>0.05)	A. vs. B. vs. C. RDQ (mean, 0-24): 9.5 vs. 5.4 vs. 7.3 at 3 weeks (p>0.05)
Silva Parreira, 2014597 12 weeks Chronic Good	A: Kinesio Taping over erector spinae muscles parallel to the spinous processes starting near the posterior superior iliac crest with 10% to 15% tension to create convolutions in the skin, applied for 48 hours, twice weekly for 4 weeks (n=74) B: Sham taping without tension (0% tension), applied for 48 hours, twice weekly for 4 weeks (n=74)	A. vs. B. Mean age: 51 vs. 50 years Female: 76% vs. 80% Pain intensity (mean, 0-10 NRS): 7.0 vs. 6.8 RDQ (mean, 0-24): 11.5 vs. 10.4	A. vs. B. Pain (mean difference from baseline, 0-10 NRS): -0.4 (95% CI -1.3 to 0.4) at 4 weeks, -0.5 (95% CI -1.4 to 0.4) at 12 weeks	A. vs. B. RDQ (mean difference from baseline, 0-24): -0.3 (95% CI -1.9 to 1.3) at 4 weeks, 0.3 (95% CI -1.3 to 1.9) at 12 weeks Global Perceived Effect (mean difference from baseline, -5 to 5): 1.4 (95% CI 0.3 to 2.5) at 4 weeks, 0.4 (95% CI -0.7 to 1.5) at 12 weeks

CI = confidence interval; LBP = low back pain; NRS = numeric rating scale; ODI = Oswestry Disability Index; RDQ = Roland-Morris Disability Questionnaire; TENS = Transcutaneous Electrical Nerve Stimulation; VAS = visual analogue scale

Discussion

Key Findings and Strength of Evidence

The key findings or this review, including strength of evidence ratings are summarized in the summary of evidence table (Table 30); the factors used to determine the overall strength of evidence are summarized in Appendix H. This report updates a previous review that we conducted[15, 16] for the American College of Physicians and American Pain Society, expanding upon it with new evidence and evaluation of several additional interventions (e.g., tai chi, taping, electrical muscle stimulation). This report also incorporates evidence on new drugs within previously reviewed classes (e.g., the antidepressant duloxetine and the antiseizure medication pregabalin). Because of the large number of interventions addressed in this review, reviewing all of the primary literature was not feasible. Therefore, we used relevant, well-conducted systematic reviews when available, including updates of systematic reviews included in our prior report, and supplemented prior reviews with additional trials that were published subsequent to the reviews or not included for other reasons. All conclusions are based on the totality of evidence (i.e., studies included in systematic reviews plus additional primary studies). Across interventions, pain intensity was the most commonly reported outcome, followed by back-specific function (typically measured using the Roland-Morris Disability Questionnaire [RDQ] or the Oswestry Disability Index [ODI]). When present, observed benefits were generally in the small (5 to 10 points on a 100-point visual analogue scale [VAS] or equivalent or standardized mean difference [SMD] of 0.2 to 0.5) to moderate (10 to 20 points, or SMD of 0.5 to 0.8) range for pain. Effects on function were typically smaller than effects on pain; in some cases there were positive effects on pain but not on function, and fewer studies measured function than pain. Other outcomes (such as quality of life, mood, work, analgesic use, or utilization of resources) were generally reported inconsistently and data were too sparse to reach reliable conclusions.

New evidence affected conclusions for several classes of medications. For acetaminophen, the prior review concluded that acetaminophen was effective for acute low back pain, primarily based on indirect evidence from trials of acetaminophen for other conditions and trials of acetaminophen versus other analgesics. However, a recent, well-conducted trial—the first placebo-controlled trial in patients with acute low back pain—found acetaminophen to be no more than effective than placebo (strength of evidence [SOE]: low).[43] For antidepressant drugs, no studies in the prior review evaluated drugs in the serotonin norepinephrine reuptake inhibitor class. Evidence from several trials indicates that duloxetine is more effective than placebo for pain and function in patients with chronic low back pain (SOE: moderate).[152-154] However, effects were small (less than 1 point on a 0 to 10 scale) and all trials were funded by the manufacturer of duloxetine and led by the same researcher. For antiseizure medications, new evidence is available on pregabalin for radicular low back pain, but the studies had methodological shortcomings and were too inconsistent to reliably estimate effects (SOE: insufficient).[160, 163] The prior review found no studies on the effects of benzodiazepines for radiculopathy; one recent trial found that benzodiazepines were no more effective than placebo in for this condition (SOE: low).[135] The trial also found that for some outcomes, such as return to work, benzodiazepines were associated with worse outcomes versus placebo.

Main conclusions regarding the benefits and harms of pharmacological therapies for low back pain were otherwise relatively unchanged from the prior review. One area in which conclusions did change was related to effectiveness of tricyclic antidepressants. In our prior review, tricyclic antidepressants were found to be associated with small beneficial effects for chronic low back pain. However, evidence reviewed for this report suggests that tricyclic antidepressants are not effective versus placebo (4 trials; SMD −0.10, 95% CI −0.51 to 0.31; I2=32%) (SOE: moderate).[139] As noted above, duloxetine, a serotonin norepinephrine reuptake inhibitor that is not associated with the anticholinergic and cardiac side effects of tricyclics, is now available as a potential alternative antidepressant. Skeletal muscle relaxants appear to be effective for short-term pain relief in patients with acute low back pain, but are also associated with an increased risk of central nervous system adverse events (in particular, sedation) (SOE: moderate). Systemic corticosteroids do not appear to be effective versus placebo for either radicular or nonradicular low back pain (SOE: moderate) and evidence on the effectiveness of benzodiazepines versus placebo for nonradicular low back pain remains sparse (SOE: insufficient).[34]

Evidence on the effectiveness of opioids for low back pain remains limited to short-term trials showing modest effects versus placebo on short-term pain and function69 (SOE: moderate). Almost all trials of opioids enrolled patients with chronic low back pain, and no trial focused on patients with radicular symptoms. There remain no clear differences among different long-acting opioids or among long- versus short-acting opioids. Findings regarding the increased risk of opioids versus placebo for harms such as constipation, nausea, sedation, and dry mouth are also unchanged. Most trials of opioids used an enriched enrollment and withdrawal design; evidence from studies of chronic pain in general (not restricted to low back pain) suggest that estimates of harms are larger in trials that did not use such a design.[92] Trials of opioids for low back pain were not designed to assess risk of serious adverse events such as overdose, abuse or addiction, or accidental injuries, due to their relatively small samples and short duration of followup. In addition, trials of opioids typically excluded patients with risk factors for overdose, abuse, or addiction. Observational studies have shown an association between use of opioids for chronic pain and serious harms such as overdose that appears to be dose-dependent.[599] However, such studies did not meet inclusion criteria for this report because they were not restricted to patients with low back pain.

Relatively few studies directly compared the effectiveness of different medications for low back pain, or the effectiveness of a combination of medications versus one of the component medications of the combination alone. We found no clear differences between opioids versus nonsteroidal anti-inflammatory drugs (NSAIDs) in pain relief or function, and no clear differences between benzodiazepines versus skeletal muscle relaxants. As described above, there were no clear differences between acetaminophen versus NSAIDs in patients with chronic low back pain.

Serious harms were generally not observed in trials of nonopioid medications, though harms were generally not reported well. Like trials of opioids, trials of nonopioid medications were not designed to assess risk of serious, uncommon harms (e.g., liver toxicity with acetaminophen, bleeding with NSAIDs, fracture or infection with corticosteroids, or abuse or addiction with benzodiazepines).

The current report addresses several nonpharmacological therapies not addressed in the prior APS/ACP review. Evidence on taping (using techniques to increase skin tension) did not clearly show beneficial effects versus sham taping comparisons, though findings were limited by methodological shortcomings and inconsistency (SOE: insufficient to low). There was insufficient evidence to determine the effects of electrical muscle stimulation, due to methodological shortcomings in the trials and imprecision (SOE: insufficient). Two trials found that tai chi was more effective versus wait list control for pain intensity and function285 (SOE: low); effects appeared similar to those observed for other types of exercise and related interventions.

As in the APS/ACP review, we found little evidence to support the use of most passive physical modalities for low back pain. An exception was superficial heat, which was found to be more effective than a nonheated control for acute or subacute low back pain (SOE: moderate). There remains insufficient evidence to determine effects of superficial cold. There also remains insufficient evidence to determine the effectiveness of percutaneous electrical nerve stimulation, interferential therapy, short-wave diathermy, traction and lumbar supports versus sham or no treatment. Although evidence on effectiveness of ultrasound and transcutaneous electrical nerve stimulation (TENS) was previously classified as insufficient, additional evidence now supports the findings that ultrasound is not effective versus sham ultrasound[497] and that TENS is not effective versus sham TENS,[512] though the strength of evidence remains low due to methodological limitations in the trials and imprecision. Based on three trials,[550, 552, 553] low-level laser therapy was more effective than sham laser for pain, though methods for assessing pain and duration of followup varied; there was insufficient evidence from one trial to determine effects on function. Evidence to compare effects of one physical modality versus another, or a physical modality versus another active intervention, was generally too limited to reach reliable conclusions.

As in the APS/ACP review, we found evidence that psychological therapies (progressive relaxation, electromyography (EMG) biofeedback, operant therapy, combined psychological therapy [e.g., cognitive-behavioral therapy]) are associated with lower pain intensity (effects small to moderate) versus wait list control; effects of function were observed for progressive relaxation and combined psychological therapy only (SOE: low).[313] Multidisciplinary rehabilitation (consisting at a minimum of exercise therapy plus psychological therapy, with some coordination) was associated with moderately lower pain intensity versus usual care, with smaller effects on function and no clear effect on return to work (SOE: moderate).348 Psychological therapies and multidisciplinary rehabilitation were primarily evaluated for chronic low back pain, with insufficient evidence to determine effects in patients with acute low back pain or in those with radicular symptoms. Unlike the prior review, a stratified analysis reported in a systematic review found no association between the intensity of multidisciplinary rehabilitation and estimates of effectiveness,[313] though head-to-head comparisons of different intensities of multidisciplinary rehabilitation are not available. In head-to-head comparisons, there were no clear differences between psychological therapies versus exercise therapy, though multidisciplinary rehabilitation was moderately more effective than physical therapy not administered as part of a multidisciplinary program.

Our findings regarding the effectiveness of massage, acupuncture, and manipulation were generally consistent with the APS/ACP review in showing some beneficial, primarily short-term effects. These interventions were primarily evaluated for chronic low back pain, with few trials of patients with acute low back pain or specifically with radicular symptoms. Evidence was generally stronger for acupuncture[364, 365] and spinal manipulation[437, 438] than for massage,[405] which was evaluated in fewer trials, though the strength of evidence varied depending on the specific comparison evaluated (no SOE was rated above moderate). For all of these therapies, the evidence was characterized by marked heterogeneity in the interventions evaluated as well as in the intensity and number of sessions. Although some evidence suggested that massage is more effective versus other interventions considered active, it was not possible to draw strong conclusions due to methodological limitations and imprecision.[405] Although acupuncture was more effective than sham acupuncture for chronic low back pain,[365] sham acupuncture techniques varied among trials (superficial needling at acupuncture points, superficial needling at nonacupuncture points, nonpenetrating needles or pressure at acupuncture points) and there was inconsistency, with some trials showing no differences between acupuncture versus sham and effects were primarily observed immediately after treatment, with limited evidence of no effects at longer-term followup. Spinal manipulation was no more effective than sham manipulation for chronic low back pain, but manipulation was as effective as other interventions thought to be effective.[438] Therefore, there remains some uncertainty regarding the specific effects of these interventions, versus nonspecific effects related to needling, mobilization or manipulation, or other aspects of administering these treatments (e.g., attentional or placebo effects). Head-to-head trials that directly compared different massage, acupuncture, or spinal manipulation techniques generally found no clear differences.

Findings regarding the effectiveness of exercise therapies and related interventions were also consistent with the APS/ACP review. Most trials evaluated patients with chronic nonradicular low back pain. For yoga, newer trials strengthen conclusions regarding effectiveness, particularly for yoga versus educational interventions (SOE: moderate). Evidence on motor control exercises, which were not addressed in the APS/ACP review, was generally consistent with evidence for other types of exercise in showing small to moderate effects (SOE: low). Head-to-head trials of exercise programs generally found no clear differences in estimates of effectiveness.

Harms were not well-reported in trials of nonpharmacological therapies, though serious adverse events appear rare. For physical modalities, harms when reported were mostly related to superficial effects at the application site. Severe neurological complications were not reported in trials of lumbar spinal manipulation and serious infections, bleeding, or other complications were not reported in trials of acupuncture.

Findings in Relationship to What Is Already Known

Our findings are generally consistent with prior systematic reviews on noninvasive treatments for low back pain, in part because our report builds upon a prior review and used previously published, high-quality systematic reviews to inform its findings. However, our findings were also generally consistent with other recent systematic reviews that were not used in this report that found NSAIDs and opioids associated with small to moderate effects versus placebo for chronic low back pain, and tricyclic antidepressants associated with small effects that were

not statistically significant.[600, 601] Like other reviews, we only found evidence supporting short-term benefits of opioids. Although another review found no differences between opioids versus placebo for low back pain, searches were conducted through 2005 and its findings were based on only four trials, with a pooled estimate that slightly favored opioids (SMD −0.18, 95% CI −0.49 to 0.11).[602] As in other reviews, we found no randomized trials to determine long-term effectiveness of opioids for low back pain. In a recent review that we conducted on opioids for chronic pain in general, we also found no cohort studies to determine the long-term effectiveness of opioids versus no opioid therapy.[603] In that review, we found insufficient evidence from randomized trials to determine the risk of serious harms associated with opioids, due to small samples, inadequate length of followup, poorly standardized methods for assessing harms, and suboptimal harms reporting. In addition, trials typically excluded patients at higher risk for abuse or overdose, though evidence[604, 605] indicates that such patients are more likely to be prescribed opioids in clinical practice than people without risk factors.[600, 606]

Our finding that acetaminophen is not effective for acute low back pain is based on a recent, well-conducted randomized controlled trial (RCT)[43] and differs from our prior review, which concluded that there was good evidence of moderate effects. However, the prior conclusion was based on indirect evidence of acetaminophen for other pain conditions and effects of acetaminophen versus NSAIDs, which showed few differences. Another systematic review, noting the absence of placebo-controlled trials at the time and imprecision and methodological shortcomings in the available studies, rated the same evidence as insufficient.[607] Like our review, a recent systematic review found that acetaminophen was ineffective for low back pain, primarily based on the results of the new trial.[608]

Our prior report and other previous systematic reviews[137, 138] found tricyclic antidepressants associated with small beneficial effects for low back pain. However, the evidence reviewed for this report suggests that they are not effective versus placebo for pain relief (4 trials; SMD −0.10, 95% CI −0.51 to 0.31; I2=32%) or function.[139] One potential reason for the discrepancy between this finding and prior reviews are that some of the prior reviews did not conduct a meta-analysis.[136, 138] One positive review[137] did base findings on a meta-analysis. However, the study in the meta-analysis that reported the largest effect in favor of antidepressants did not report being randomized,[609] it did not include relevant studies that were in the more current review,[141, 146, 149] and it did not report methods for data imputation for two trials included in the meta-analysis.[140, 148]

Our findings regarding the small to moderate effectiveness of the antidepressant duloxetine are consistent with its recent approval by the US Food and Drug Administration for chronic musculoskeletal pain, including chronic low back pain.[610] Our conclusions were based on trials of duloxetine versus placebo. Although a systematic review found no differences between duloxetine versus other oral medications, its findings were based on a network analysis based on indirect comparisons.[611]

For nonpharmacological treatments, our findings are also generally consistent with other systematic reviews. Like other reviews, we found some evidence to support use of complementary and alternative medicine therapies such as acupuncture, spinal manipulation, and massage.[600, 612-616] Although acupuncture was no more effective than sham acupuncture in

some trials, other reviews have also found that the overall evidence (including pooled estimates) suggest beneficial effects on pain.[364, 365] As in prior reviews, we found no clear evidence to support one specific type of massage, manipulation, or acupuncture over another.[362, 404, 426, 617]

Findings regarding the effectiveness of exercise are similar to our prior review and other reviews.[618-620] Our findings are also consistent with more specific reviews that focused on specific types of exercise such as aquatic exercise,[621] sling exercise,[622] walking,[623] stability exercises,[624] and modifying patterns of movement.[625] Additional evidence published since our prior review strengthens conclusions that yoga is effective for low back pain,[626, 627] a finding consistent with other recent systematic reviews, and newer evidence supports the effectiveness of motor control exercises. Evidence on tai chi was previously unavailable, but recent randomized trials support its effectiveness. As in our prior review, evidence does not clearly demonstrate that one type of exercise therapy is superior to another. This is consistent with other systematic reviews that have evaluated specific exercise therapy comparisons (e.g., McKenzie versus other exercise methods).[183]

Our findings that psychological therapies and multidisciplinary rehabilitation were both effective are consistent with our prior review and other reviews.[628] Other reviews that focused on related interventions such as functional restoration or cognitive-behaviorally based physical therapy (in which the literature overlaps with that on multidisciplinary rehabilitation) have also reached positive conclusions.[606, 629, 630] Although there was insufficient evidence to determine which patients are most likely to benefit from psychological therapies and multidisciplinary rehabilitation, a recent randomized trial631 found that a stratified approach in which patients are assessed for risk factors for chronicity, and higher-risk patients receive more intensive cognitive-behavioral based physical therapy, is more effective than usual care without a stratified approach, suggesting that these therapies may be most effective in higher-risk people. Unlike our prior report, which found that higher-intensity multidisciplinary rehabilitation appeared more effective than lower-intensity programs, a stratified analysis based on currently available evidence348 indicated no clear difference in effects.

Like our prior review, we found that for most physical modalities, evidence was too weak to determine effectiveness. Although we previously found insufficient evidence to conclude that ultrasound and TENS are not effective, albeit with low strength of evidence. A recent assessment of TENS came to a similar conclusion.[632]

As in other reviews, we found that evidence the effectiveness of therapies for radicular low back pain was quite limited.[435, 633] Like other reviews, including our prior report, we found that systematic corticosteroids are not effective for radicular low back pain.[633, 634] Although duloxetine and other serotonin norepinephrine reuptake inhibitors and antiseizure medications such as gabapentin and pregabalin are increasingly being prescribed for low back pain, particularly when associated with radicular symptoms, evidence on the effectiveness of nonduloxetine serotonin norepinephrine reuptake inhibitors is not available and results of trials of pregabalin and gabapentin have been inconsistent or have not shown clear effects. Although a network meta-analysis has been performed on various treatments for radicular low back pain, the most commonly evaluated treatments were surgical and interventional, findings for noninvasive therapies were primarily based on indirect comparisons, and many estimates were imprecise.[635]

Applicability

A number of issues could impact the applicability of our findings. Some studies did not specifically enroll patients with acute, subacute, or chronic low back pain, but rather enrolled mixed populations or did not clearly describe the duration of symptoms, which could make it difficult to apply findings if benefits differ according to duration of symptoms. Relatively few studies enrolled patients specifically with radicular symptoms, and many studies did not specifically describe whether patients with radicular symptoms were excluded. Therefore, the degree to which it is possible to extrapolate evidence from studies of patients with primarily nonradicular symptoms to patients with radicular symptoms is uncertain. In addition, studies that focused on radicular pain evaluated clinically diverse populations. Some studies required imaging findings of disc herniation (typically involving younger individuals) or spinal stenosis (typically affecting older individuals), while others did not require imaging confirmation of radicular symptoms. Among studies of patients with nonradicular symptoms, most studies did not attempt to evaluate whether effectiveness varied in subgroups of patients defined by clinical, demographic, imaging, or other characteristics. It is not possible to determine whether effectiveness varies among groups with nonradicular pain based on these factors. For example, most trials of antidepressants excluded patients with depression or only included a small minority of such patients,[139] such that it is unclear whether antidepressants might have additional effects on mood in patients with low back pain and depression. Across interventions, few studies enrolled any or many older adults. Although trials of motor control exercise (MCE) generally selected patients on the basis of tests showing deficits in motor control, specific testing methods and criteria for inclusion varied, and it is unclear whether effects of MCE vary according to findings on motor control tests.[186]

For nonpharmacological treatments, the applicability of our findings is affected by the variability among trials in the interventions and comparators evaluated. For example, trials of acupuncture varied in the sites in which needles were applied, the length of acupuncture sessions, the number of sessions, and the time period over which the sessions were performed.[364, 365] In trials that evaluated "usual care" comparators, the components of usual care were often not well described or standardized, making it difficult to apply findings to clinical practice. Other factors that could impact the applicability of our findings regarding nonpharmacological interventions includes differences related to the setting in which the intervention was performed (e.g., United States versus another country, specialist versus primary care setting) or due to the training or skill of the person performing the intervention. For acupuncture, for example, some evidence suggests that patient expectations have an important influence on the effectiveness of treatment,[636, 637] such that results from countries in which acupuncture is widely practiced may not be applicable to settings in which it is considered an alternative practice. Another factor that could impact the effectiveness of interventions is the use of cointerventions, which varied across trials and was frequently not reported well. We separately analyzed comparisons that specifically involved the use of one intervention plus another intervention versus the other intervention alone. For example, spinal manipulation plus another intervention was more effective than the other intervention alone, suggesting potential additive effects.

To help interpret the results of the trials, we categorized the magnitude of effects for pain and function using the system in the APS/ACP review. Based on these categories, beneficial effects

when present were in the small or moderate range. However, effects that we classified as small (e.g., 5-10 points on a 0 to 100 scale for pain or function) are below some proposed thresholds for minimum clinically important differences (e.g., 15 points on a 0 to 100 VAS for pain, 2 points on a 0 to 10 NRS for pain or function, 5 points on the RDQ, and 10 points on the ODI; or a 30% change from baseline).[28] Nonetheless, our classification system provides some objective bench marks for assessing magnitude of effects, including the smaller effects typically observed in low back pain trials. We also evaluated the proportion of patients who experienced a clinically important improvement in pain or function (e.g., 50% improvement in pain or on the RDQ). However, many studies did not report such dichotomous outcomes, and among those that did, definitions for clinically important improvements varied. A factor that complicates interpretation of findings is that the magnitude of effects might vary depending on the baseline severity, with some evidence suggesting that treatment may be more effective in people with higher baseline symptom severity.[638] Also, the clinical relevance of the same absolute improvement in an outcome measure might differ in individual patients depending on the baseline score (e.g., a 1 point change on a 0- to 10-point NRS for pain might differ for someone with a baseline pain score of 4 versus 9). Most trials enrolled patients with pain symptoms of at least moderate intensity (e.g., >5 on a 0- to 10-point NRS for pain). When present, most beneficial effects were observed at shorter-term (e.g., <3 months) followup, with outcomes often assessed only through the end of the active treatment period, such that it was difficult to determine whether there were sustained benefits. When evidence on longer-term followup was available, effects were typically attenuated or no longer observed. Understanding long-term outcomes is particularly critical for chronic low back pain, given the persistent nature of symptoms.

Implications for Clinical and Policy Decisionmaking

Our findings have implications for clinical and policy decisionmaking. A number of pharmacological and nonpharmacological therapies are supported by some evidence of effectiveness in patients with acute (Tables 31, 32, 33, and 34) or chronic low back pain (Tables 35, 36, 37, and 38). Although clinical practice guidelines recommend acetaminophen as a first-line pharmacological therapy for acute and chronic low back pain,[14, 639] new evidence[43] that acetaminophen is ineffective for acute low back pain call into question its appropriateness as a recommended therapy, though findings are based on a single trial and other factors such as low cost, favorable side-effect profile, and effectiveness for other acute pain conditions could also impact decisions regarding its use.[640] Although tricyclic antidepressants have long been recommended as a secondary treatment option for chronic low back pain, duloxetine has specifically been approved by the US Food and Drug Administration for this condition and appears to be more effective than tricyclic antidepressants as well as associated with a more favorable safety profile, which could impact the selection of drugs within the antidepressant class.

The use of opioids for chronic pain has become an area of increasing concern, due to uncertain long-term effectiveness and marked increases in the number of accidental overdoses, as well as other harms related to their abuse potential.[603] Patients with low back pain are frequently prescribed opioids and account for a high proportion of the patients prescribed opioids. Decisions regarding the appropriate use of opioids for low back pain must weigh short-term, relatively

modest benefits against potential harms. Guidelines recommend risk assessment, careful patient selection, and close monitoring and followup in patients prescribed opioids.[641]

The continued paucity of evidence to determine effective treatments for radicular low back pain (Tables 39, 40, and 41) necessitates that most decisions are based on extrapolation of evidence on the effectiveness of treatments for nonradicular low back pain or other nonback-related neuropathic pain conditions. This could explain why antiseizure medications such as gabapentin and pregabalin are being prescribed more for radicular low back pain, despite the lack of evidence showing that they are effective. Systemic corticosteroids continue to be used for treatment of radicular back pain, despite trials showing that they are ineffective, presumably based upon their known anti-inflammatory properties and use in epidural injections.

Our review support clinical practice guidelines that found insufficient evidence to recommend most physical modalities, other than superficial heat. However, these therapies are still commonly used in clinical practice. Among nonpharmacological therapies that were found to be effective, there was insufficient evidence to determine which patients are most likely to benefit from specific therapies. However, a recent trial which found that a stratified approach (in which patients are assessed for risk factors for chronicity, and higher-risk patients receive more intensive cognitive-behavioral based physical therapy) is more effective than usual care without a stratified approach suggests that psychologically-based therapies and multidisciplinary rehabilitation may be most effective in higher-risk people.[631] Other factors that may impact decisions regarding which nonpharmacological therapies to use include cost, availability, and patient preferences. Some evidence suggests that greater patient expectations of benefit from a particular treatment are associated with greater benefits,[636, 637] suggesting that patient preferences should be considered in the selection of therapies. Potential barriers to use of some nonpharmacological therapies include variability in health insurance coverage (e.g., for complementary and alternative medicine therapies)[642] and nonavailability depending on locale or other factors (e.g., multidisciplinary rehabilitation).[643]

Limitations of the Review Process

We included previously published systematic reviews. The reliability of systematic reviews depends on the rigor with which they are conducted.[644] Therefore, we focused on higher-quality reviews. For a number of interventions addressed in this report, more than one higher-quality systematic review exists. In addition to quality, we therefore also selected systematic reviews for inclusion based on the closest relevance match based on the Key Questions and scope and how recently searches were conducted.[24] If two or more reviews were similar on these criteria, we prioritized inclusion of updates of reviews that were in the prior APS/ACP review. In some cases, the highest-quality systematic reviews did not provide all of the information necessary to assess findings. We only included such reviews if we could address any methodological limitations through review and assessment of the primary studies. Otherwise, such reviews were excluded.

We did not conduct meta-analyses or update meta-analyses included in prior systematic reviews. However, for comparisons without a meta-analysis, we synthesized results qualitatively, using the methods in the AHRQ methods guide. For comparisons for which pooled results were available from prior systematic reviews, we evaluated the consistency of results from new trials against the pooled estimates.

Other limitations of the review process are that we excluded non-English language articles and did not search for studies published only as abstracts. However, some systematic reviews included non-English language articles and abstracts, which did not materially impact conclusions. We were unable to assess for publication bias using graphical or statistical methods to detect small sample effects, methodological limitations in the trials, heterogeneity in the interventions, populations, and outcomes addressed, and small numbers of trials for many comparisons. However, based on searches of reference lists, clinical trials registries, and peer review suggestions, we did not find evidence to suggest that unpublished trials would impact conclusions.

There are other noninvasive interventions for low back pain that we did not address, including herbal medicines,[645] educational interventions,[646, 647] advice to remain active,[646, 648] mattresses, shoe insoles,[649] and others.[650, 651] We also did not include comparisons of noninvasive therapies versus surgery or interventional procedures, which were outside the scope of this review. We also excluded pain treatment trials that were not restricted to patients with low back pain. The applicability of such trials would depend in part on the proportion of patients with low back pain and what other pain conditions were present.

Limitations of the Evidence Base

The evidence base had a number of important limitations. As noted previously, evidence on the effectiveness of interventions for radicular low back pain was sparse. Most trials of nonpharmacological treatments focused on patients with chronic low back pain, with insufficient evidence to determine effects for acute low back pain, with the exception of superficial heat. This could be due in part because the natural history or acute low back pain is characterized by rapid improvement, such that nonpharmacological therapies are typically reserved for patients who do not improve in the initial period. A number of interventions were evaluated in small numbers of trials or in trials that primarily had important methodological limitations, precluding strong preclusions. In addition, there were relatively few head-to-head trials of different interventions, making it difficult to compare the effectiveness of one type of therapy versus another, particularly for comparisons of nonpharmacological versus pharmacological therapies.

Another limitation of the evidence base is that studies were frequently short term and often only evaluated patients at the end of a course of therapy, making it difficult to determine whether sustained benefits are present. In addition, many trials reported mean changes in outcome measures (typically pain and function), but did not report dichotomized outcomes (e.g., ≥30% or ≥50% pain relief or functional improvement). Assessment of outcomes based on continuous as well as dichotomized outcomes would provide a more complete assessment of treatment effects.[652]

Some limitations of the evidence were particularly relevant for trials of nonpharmacological interventions. Studies of nonpharmacological interventions were typically characterized by marked heterogeneity in the specific intervention techniques evaluated, as well as in the duration and intensity of treatments, which could attenuate treatment benefits if suboptimal treatment techniques or intensity of therapy was evaluated. In addition, a number of nonpharmacological therapies (e.g., psychological therapies, exercise therapy, massage, and spinal manipulation) are difficult to blind effectively. Therefore, observed benefits could be due in part to placebo,

attentional, or other nonspecific effects, and results are susceptible to performance and other biases, though it is not possible to reliably quantify the extent of such effects. Finally, trials of nonpharmacological therapies did not report harms well; this could be in part because serious harms are not expected with most of these treatments.

Research Gaps

A number of research gaps limit the full understanding of the effectiveness, comparative effectiveness, and harms of therapies for low back pain.[653-656] More research is needed to determine effective treatments for low back pain with radicular symptoms and in understudied populations such as older adults. Trials should be designed to not just evaluate patients immediately after they have completed therapy, but for at least several months after the completion of therapy, in order to help understand whether beneficial effects are sustained. Studies that use more pragmatic designs (e.g., more flexible dosing or use of cointerventions) might help improve patient recruitment and reduce attrition, which is high in long-term trials of low back pain. For nonpharmacological treatments, research to identify optimal treatment techniques and regimens (including intensity and duration of treatments) would be very helpful for defining more standardized interventions to be evaluated in trials.

Studies are needed to determine the long-term effectiveness and harms of opioids for chronic low back pain, including higher-risk patients like those commonly encountered in clinical practice. Studies that compare opioids versus nonopioid therapies that address the psychosocial factors often associated with chronic pain (e.g., interdisciplinary rehabilitation, exercise therapy, or psychological therapies) are needed. Observational studies that are designed to assess serious long-term harms provide some evidence regarding risks of opioids for chronic pain in general, but data specifically in patients with low back pain are lacking.[603] Although observational studies based on administrative databases can be helpful for evaluating risks of opioids, such studies are often limited in their ability to address important potential confounders, and should ideally be supplemented by clinical data, such as in well-designed clinical registries. For systemic corticosteroids, the largest trial to date was recently completed and should help further characterize the effectiveness (or lack thereof) of this treatment.[657]

More research is needed to help understand whether nonradicular low back pain can be reliably classified into clinically meaningful subgroups, and which patients or subgroups are most likely to benefit from specific therapies.[658-662] Trials are also needed to confirm whether effects of risk-stratified approaches are reproducible in the United States,[663, 664] and to optimize their implementation.[665] More research is needed to better understand whether combination therapy with different pharmacological or nonpharmacological treatments is associated with incremental benefits versus individual components of the combination therapy, and which combinations and sequences of therapy are the most effective.

Pain relief was the most commonly assessed outcome in trials of treatment for low back pain, followed by back-specific function. Trials should more consistently assess other outcomes related to return to work, quality of life, and health care utilization, in order to provide a more complete picture of treatment effects. Studies that evaluate the effectiveness of interventions for preventing future episodes of low back pain would also be very helpful, as low back pain can be a recurrent, episodic condition and these patients are likely to account for a high proportion

of resources. In addition, trials should evaluate the effectiveness of interventions for preventing the transition from acute to chronic low back pain. In order to provide balanced assessments of low back pain interventions, trials should more consistently and rigorously evaluate and report harms. Trials should routinely collect information on known or common harms associated with a particular intervention, and use more open-ended methods to identify unexpected or uncommon harms.

Table 30. Summary of evidence

Key Question	Intervention	Outcome	Strength of Evidence	Conclusion
Key Question 1. Pharmacological therapies	Acetaminophen	Acetaminophen vs. placebo, acute LBP: Pain and function	Low	One good-quality trial found no difference between acetaminophen vs. placebo in pain intensity or function through 3 weeks.
		Acetaminophen vs. NSAID, acute LBP: Pain and global improvement	Insufficient	A systematic review found no difference between acetaminophen vs. NSAIDs in pain intensity (3 trials; pooled SMD, 0.21; 95% CI, −0.02 to 0.43) or likelihood of experiencing global improvement (3 trials; RR, 0.81; 95% CI, 0.58 to 1.14) at ≤3 weeks, although estimates favored NSAIDs.
		Acetaminophen vs. placebo, chronic LBP	Insufficient	No study evaluated acetaminophen vs. placebo.
		Acetaminophen vs. NSAID, chronic LBP	Insufficient	There was insufficient evidence from 1 trial to determine effects of acetaminophen vs. NSAIDs.
		Acetaminophen vs. other interventions, acute LBP	Insufficient	There was insufficient evidence from 4 trials to determine effects of acetaminophen vs. other interventions.
		Acetaminophen vs. placebo: Adverse events (serious adverse events)	Moderate	One trial found no difference between scheduled acetaminophen, as-needed acetaminophen, or placebo in risk of serious adverse events (~1% in each group).
		Acetaminophen vs. NSAIDs: Adverse events	Moderate	A systematic review found that acetaminophen was associated with lower risk of side effects vs. NSAIDs.
		Acetaminophen vs placebo, NSAID, or other intervention, radicular LBP	Insufficient	No study evaluated acetaminophen for radicular low back pain.
	NSAIDs	NSAIDs vs. placebo, acute LBP: Pain and function	Moderate for pain, low for function	A systematic review found NSAIDs to be associated with greater improvement in pain intensity vs. placebo (4 studies; WMD, −8.39; 95% CI, −12.68 to −4.10; chi-square, 3.47; p >0.1), but 4 trials found no clear effects on the likelihood of achieving significant pain relief. One subsequent trial also found lower pain intensity after the first dose vs. placebo. One trial found NSAIDs to be associated with better function vs. placebo.
		NSAIDs vs. placebo, chronic LBP: Pain and function	Moderate for pain, low for function	A systematic review found NSAIDs to be associated with greater improvement in pain vs. placebo (4 trials; WMD, −12.40; 95% CI, −15.53 to −9.26; chi-square, 1.82; p >0.5); 2 trials found NSAIDs to be associated with greater improvement in function.

Key Question 1. Pharmacological therapies	NSAIDs	NSAIDs vs. placebo, radicular LBP: Pain	Low	A systematic review found no difference in pain intensity between NSAIDs vs. placebo (2 trials; WMD, −0.16; 95% CI, −11.92 to 11.59; chi-square, 7.25; p <0.01).
		NSAID plus another intervention vs. other intervention alone	Insufficient	There was insufficient evidence from 2 trials of an NSAID plus another intervention vs. the other intervention alone to determine effectiveness.
		NSAIDs vs. interventions other than acetaminophen and opioids	Insufficient	There was insufficient evidence from 2 trials to determine the effects of NSAIDs vs. interventions other than acetaminophen and opioids.
		NSAID vs. NSAID, acute or chronic LBP: Pain	Moderate	A systematic review found that most trials of 1 NSAID vs. another found no differences in pain relief in patients with acute LBP (15 of 21 trials) or chronic LBP (6 of 6 trials).
		NSAIDs vs. placebo: Adverse events	Moderate	A systematic review found NSAIDs to be associated with more side effects vs. placebo (10 trials; RR, 1.35; 95% CI, 1.09 to 1.68).
		COX-2-selective NSAIDs vs. nonselective NSAIDs: Adverse events	Moderate	COX-2-selective NSAIDs were associated with lower risk of side effects vs. nonselective NSAIDs (4 trials; RR, 0.83; 95% CI, 0.70 to 0.99).
	Opioids, tramadol, and tapentadol	Opioids vs. placebo, chronic LBP: Pain and function	Moderate	A systematic review found opioids to be associated with greater short-term improvement vs. placebo in pain scores (6 trials; SMD, −0.43; 95% CI, −0.52 to −0.33; I2 = 0.0%, for a mean difference of ~1 point on a 0–10 pain scale) and function (4 trials; SMD, −0.26; 95% CI, −0.37 to −0.15; I2 = 0.0%, for a mean difference of ~1 point on the RDQ); 3 additional trials reported results consistent with the systematic review.
		Tramadol vs. placebo, chronic LBP: Pain and function	Moderate	A systematic review found tramadol to be associated with greater short-term pain relief vs. placebo (5 trials; SMD, −0.55; 95% CI, −0.66 to −0.44; I2 = 86%, for a mean difference of 1 point or less on a 0–10 pain scale) and function (5 trials; SMD, −0.18; 95% CI, −0.29 to −0.07; I2 = 0%, for a mean difference of ~1 point on the RDQ); 2 trials not included in the systematic review reported results consistent with the systematic review findings.
		Buprenorphine patch vs. placebo, subacute or chronic LBP: Pain and function	Low for pain, insufficient for function	A systematic review included 2 trials that found buprenorphine patches to be associated with greater short-term improvement in pain vs. placebo patches; effects on function showed no clear effect or were unclearly reported.
		Opioids vs. NSAIDs, chronic LBP: Pain relief, function	Insufficient	Three trials reported inconsistent effects of opioids vs. NSAIDs for pain relief; 1 trial found no difference in function.

Key Question 1. Pharmacological therapies	Opioids, tramadol, and tapentadol	Opioids vs. acetaminophen, acute LBP: Days to return to work, pain	Insufficient	One trial found no significant differences between opioids vs. acetaminophen in days to return to work; pain was not reported.
		Long acting opioids vs. long-acting opioids: Pain and function	Moderate	Four trials found no clear differences among different long-acting opioids in pain or function.
		LongL-acting opioids vs. short-acting opioids: Pain	Low	Six trials found no clear differences between long-acting vs. short-acting opioids in pain relief. Although some trials found long-acting opioids to be associated with greater pain relief, patients randomized to long-acting opioids also received higher doses of opioids.
		Opioids vs. placebo: Adverse events	Moderate	Short-term use of opioids was associated with higher risk vs. placebo of nausea, dizziness, constipation, vomiting, somnolence, and dry mouth; risks of opioids were higher in trials that did not use an enriched enrollment and withdrawal design.
	Skeletal muscle relaxants	SMRs vs. placebo, acute LBP: Pain	Moderate	A systematic review found SMRs to be superior to placebo for short-term pain relief (≥2-point or 30% improvement on a 0–10 VAS pain scale) after 2 to 4 days (4 trials; RR, 1.25; 95% CI, 1.12 to 1.41; I2 = 0%) and 5 to 7 days (3 trials; RR, 1.72; 95% CI, 1.32 to 2.22; I2 = 0%); a more recent large (n = 562) trial was consistent with the systematic review.
		SMR plus NSAID vs. NSAID alone, acute LBP: Pain	Low	A systematic review found no difference between an SMR plus an NSAID vs. the NSAID alone in the likelihood of experiencing pain relief, although the estimate favored combination therapy (2 trials; RR, 1.56; 95% CI, 0.92 to 2.70; I2 = 84%); 1 other trial (n = 197) also reported results that favored combination therapy.
		SMR vs. placebo, chronic LBP: Pain	Insufficient	Evidence from 3 placebo-controlled trials was insufficient to determine effects due to imprecision and inconsistent results.
		SMR vs. SMR, acute or chronic LBP: Pain	Low	Three trials in a systematic review found no differences in any outcome among different SMRs for acute or chronic low back pain.
		SMR vs. placebo, acute LBP: Adverse events	Moderate	A systematic review found skeletal muscle relaxants for acute LBP to be associated with increased risk of any adverse event vs. placebo (8 trials; RR, 1.50; 95% CI, 1.14 to 1.98) and increased risk of central nervous system events, primarily sedation (8 trials; RR, 2.04; 95% CI, 1.23 to 3.37; I2 = 50%); 1 additional placebo-controlled trial was consistent with these findings.

Key Question 1. Pharmacological therapies	Benzodiazepines	Benzodiazepines vs. placebo, acute LBP: Pain and function	Insufficient	There was insufficient evidence from 2 trials with inconsistent results to determine effectiveness of benzodiazepines vs. placebo.
		Tetrazepam vs. placebo, chronic LBP: Pain, overall improvement	Low	A systematic review included 2 trials that found tetrazepam to be associated with lower likelihood of no improvement in pain at 5–7 days (RR, 0.82; 95% CI, 0.72 to 0.94) and at 10–14 days (RR, 0.71; 95% CI, 0.54 to 0.93) vs. placebo, and lower likelihood of no overall improvement at 10–14 days (RR, 0.63; 95% CI, 0.42 to 0.97).
		Diazepam vs. placebo, acute or subacute radicular pain: Pain and function	Low	One trial found no difference between diazepam 5 mg twice daily for 5 days vs. placebo in function at 1 week through 1 year or in other outcomes, including analgesic use, return to work, or likelihood of surgery through 1 year of followup. Diazepam was associated with lower likelihood of experiencing ≥50% improvement in pain at 1 week (41% vs. 79%; RR, 0.5; 95% CI, 0.3 to 0.8).
		Benzodiazepines vs. SMRs, chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 2 trials with inconsistent results to determine effects of benzodiazepines vs. SMRs.
		Diazepam vs. cyclobenzaprine, chronic LBP: Muscle spasms	Low	One trial found no difference between diazepam vs. cyclobenzaprine in outcomes related to muscle spasm.
		Benzodiazepines vs. placebo: Adverse events	Low	A systematic review found that central nervous system adverse events such as somnolence, fatigue, and lightheadedness were reported more frequently with benzodiazepines vs. placebo, although harms were not reported well; no trial was designed to evaluate risks with long-term use of benzodiazepines such as addiction, abuse, or overdose.
	Antidepressants	Tricyclic antidepressants or SSRIs vs. placebo, chronic LBP: Pain and function	Moderate for pain, low for function	A systematic review found no differences in pain between tricyclic antidepressants vs. placebo (4 trials; SMD, −0.10; 95% CI, −0.51 to 0.31; I2 = 32%) or SSRIs vs. placebo (3 trials; SMD, 0.11; 95% CI, −0.17 to 0.39; I2 = 0%); there was also no difference between antidepressants vs. placebo in function (2 trials; SMD, −0.06; 95% CI, −0.40 to 0.29; I2 = 0%).
		Duloxetine vs. placebo, chronic LBP: Pain and function	Moderate	Three trials found duloxetine to be associated with lower pain intensity (differences, 0.58 to 0.74 on a 0 to 10 scale) and better function (differences, 0.58 to 0.74 on the Brief Pain Inventory-Interference scale) vs. placebo.
		Duloxetine vs. tricyclic antidepressants	Insufficient	No study compared duloxetine vs. a tricyclic antidepressant.

Key Question 1. Pharmacological therapies	Antidepressants	Antidepressants vs. placebo: Adverse events, serious adverse events	Moderate	Antidepressants were associated with higher risk of any adverse events compared with placebo, with no difference in risk of serious adverse events.
	Antiseizure medications	Antiseizure medications, acute nonradicular LBP	Insufficient	No trial evaluated antiseizure medications for acute nonradicular LBP.
		Gabapentin vs. placebo, chronic nonradicular LBP	Insufficient	One trial found no difference between gabapentin (up to 3600 mg/day) vs. placebo but did not meet inclusion criteria because it was published only as an abstract.
		Gabapentin vs. placebo, chronic radicular LBP: Pain and function	Insufficient	There was insufficient evidence from 3 poor-quality trials with inconsistent findings to determine effects of gabapentin vs. placebo.
		Topiramate vs. placebo, chronic radicular or mixed radicular and nonradicular LBP: Pain	Insufficient	Two trials reported inconsistent results for effects of topiramate vs. placebo.
		Pregabalin vs. placebo, chronic radicular LBP: Pain and function	Insufficient	Two trials reported inconsistent effects of pregabalin vs. placebo for pain or function.
		Pregabalin vs. amitriptyline: Pain	Insufficient	There was insufficient evidence from 1 poor-quality trial to determine effects of pregabalin vs. amitriptyline.
		Pregabalin plus transdermal buprenorphine vs. transdermal buprenorphine, chronic nonradicular LBP: Pain	Insufficient	One small trial found that the addition of pregabalin 300 mg/day to transdermal buprenorphine was associated with substantially lower pain scores than transdermal buprenorphine alone at 3 weeks (difference, ~26 points on a 0 to 100 scale; $p < 0.05$), but the estimate was very imprecise.
		Pregabalin plus another analgesic vs. the other analgesic alone: Pain	Insufficient	One trial found pregabalin (mean, 2.1 mg/kg/day) plus celecoxib to be associated with lower pain scores than celecoxib alone (difference, 11 points on a 0–100 scale; $p = 0.001$) after 4 weeks, and 1 trial found no effects of adding pregabalin (titrated to 300 mg/day) to tapentadol prolonged release vs. tapentadol prolonged release alone on pain or the SF-12 after 8 weeks.
		Gabapentin vs. placebo: Adverse events	Low	Two trials of gabapentin vs. placebo reported no clear differences in risk of adverse events.

Key Question 1. Pharmacological therapies	Antiseizure medications	Topiramate vs. placebo: Withdrawal due to adverse events, sedation, diarrhea	Insufficient	Two trials of topiramate vs. placebo reported inconsistent effects on risk of withdrawal due to adverse events; 1 of the trials found topiramate to be associated with higher risk of sedation and diarrhea.
		Pregabalin vs. placebo: Withdrawal due to adverse events, somnolence, dizziness	Insufficient	Two trials of pregabalin vs. placebo reported inconsistent effects on risk of withdrawal due to adverse events, somnolence, and dizziness; 1 of the trials used an enrichment/withdrawal design
	Corticosteroids	Systemic corticosteroids vs. placebo, acute nonradicular LBP: Pain and function	Low	Two trials found no differences between a single intramuscular injection or a 5-day course of systemic corticosteroids vs. placebo for pain or function.
		Systemic corticosteroids vs. placebo, radicular LBP: Pain and function	Moderate	Five trials consistently found no differences between systemic corticosteroids (administered as a single bolus or as a short taper) vs. placebo in pain or function for acute or unspecified-duration LBP; 1 trial found no effect on need for spine surgery.
		Systemic corticosteroids vs. placebo, spinal stenosis: Pain and function	Low	One trial found no differences through 12 weeks of followup between a 3-week course of prednisone vs. placebo in pain intensity, the RDQ, or any SF-36 subscale.
		Systemic corticosteroids: Adverse events	Low	Trials of systemic corticosteroids did not report serious adverse events, including hyperglycemia requiring medical treatment, but adverse events were not reported well in some trials.
Key Question 2. Nonpharmacological noninvasive therapies	Exercise	Exercise vs. no exercise, acute to subacute LBP: Pain and function	Low	A systematic review found no differences between exercise therapy vs. no exercise in pain (3 trials; WMD, 0.59 at intermediate term on a 0 to 100 scale; 95% CI, −11.51 to 12.69) or function (3 trials; WMD at short term, −2.82; 95% CI, −15.35 to 9.71; WMD at intermediate term, 2.47; 95% CI, −0.26 to 5.21). For subacute LBP, there were also no differences in pain (5 trials; WMD, 1.89 on a 100-point scale; 95% CI, −1.13 to 4.91) or function (4 trials; WMD, 1.07; 95% CI, −3.18 to 5.32). Three subsequent trials for acute to subacute LBP reported inconsistent effects of exercise vs. usual care on pain and function
		Exercise vs. no exercise, chronic LBP: Pain and function	Moderate	A systematic review found exercise to be associated with greater pain relief vs. no exercise (19 trials; WMD, 10 on a 0 to 100 scale; 95% CI, 1.31 to 19.09), although the effect on function was small and not statistically significant (17 trials; WMD, 3.00 on a 0 to 100 scale; 95% CI, −0.53 to 6.48). Results from a more recent systematic review using more restrictive criteria and from additional trials not included in the systematic reviews were generally consistent with these findings.

Key Question 2. Nonpharmacological noninvasive therapies	Exercise	MCE vs. minimal intervention, chronic LBP: Pain and function	Low	A systematic review included 2 trials that found MCE to be associated with lower pain scores in the short term (WMD, −12.48 on a 0 to 100 scale; 95% CI, −19.04 to −5.93), intermediate term (WMD, −10.18; 95% CI, −16.64 to −3.72), and long term (WMD, −13.32; 95% CI, −19.75 to −6.90) vs. a minimal intervention. MCE was also associated with better function at short term (3 trials; WMD, −9.00 on 0 to 100 scale; 95% CI, −15.28 to −2.73), intermediate term (2 trials; WMD, −5.62; 95% CI, −10.46 to −0.77), and long term (2 trials; WMD, −6.64; 95% CI, −11.72 to −1.57).
		Exercise vs. usual care, nonacute LBP: Work disability	Moderate	A systematic review found no clear effects of exercise therapy versus usual care on likelihood of short- or intermediate-term (~6 months) disability, but exercise was associated with lower likelihood of work disability at long term (~12 months) followup (10 comparisons in 8 trials; OR, 0.66; 95% CI, 0.48 to 0.92).
		Exercise vs. usual care, radicular LBP: Pain and function	Low	Three trials not included in the systematic reviews found effects that favored exercise vs. usual care or no exercise in pain and function, although effects were small.
		MCE vs. general exercise, chronic LBP: Pain and function	Low	A systematic review found MCE to be associated with lower pain intensity at short term (6 trials; WMD, −7.80 on 0 to 100 scale; 95% CI, −10.95 to −4.65) and intermediate term (3 trials; WMD, −6.06; 95% CI, −10.94 to −1.18) vs. general exercise, but effects were smaller and no longer statistically significant at long term (4 trials; WMD, −3.10; 95% CI, −7.03 to 0.83). MCE was also associated with better function in the short term (6 trials; WMD, −4.65 on 0 to 100 scale; 95% CI, −6.20 to −3.11) and long term (3 trials; WMD, −4.72; 95% CI, −8.81 to −0.63). One of 2 subsequent trials found no effect on pain, although effects on function were consistent with the systematic review.
		Exercise vs. exercise, acute or chronic LBP	Moderate	For comparisons involving other types of exercise techniques, there were no clear differences in >20 head-to-head trials of patients with acute or chronic LBP.
		Exercise: Adverse events	Low	Harms were poorly reported in trials of exercise. When reported, harms were typically related to muscle soreness and increased pain, or no harms were reported; no serious harms were reported.
Key Question 2. Nonpharmacological noninvasive therapies	Pilates	Pilates vs. usual care plus physical activity, chronic LBP: Pain and function	Low	A systematic review included 7 trials that found Pilates to be associated with small (mean difference, −1.6 to −4.1 points) or no clear effects on pain at the end of treatment vs. usual care plus physical activity and no clear effects on function.
		Pilates vs. other exercise, chronic LBP: Pain and function	Low	Three trials found no clear differences between Pilates vs. other types of exercise in pain or function.

Key Question 2. Nonpharmacological noninvasive therapies	Tai chi	Tai chi vs. wait list or no tai chi, chronic LBP: Pain and function	Low	Two trials found tai chi to be associated with improved pain-related outcomes vs. wait list or no tai chi (mean differences, 0.9 and 1.3 on a 0 to 10 scale); 1 trial also found tai chi to be associated with better function (mean difference, 2.6 on the RDQ; 95% CI, 1.1 to 3.7).
		Tai chi vs. other exercise, chronic LBP: Pain	Low	One trial found tai chi to be associated with lower pain intensity vs. backward walking or jogging through 6 months (mean differences, −0.7 and −0.8), but there were no differences vs. swimming.
		Tai chi: Adverse events	Low	One trial of tai chi reported a small temporary increase in back pain symptoms, and 1 trial reported no harms.
	Yoga	Yoga vs. usual care, chronic LBP: Pain and function	Low	One trial found Iyengar yoga to be associated with lower pain scores (24 vs. 37 on a 0–100 VAS; $p < 0.001$) and better function (18 vs. 21 on the 0 to 100 ODI; $p < 0.01$, on a 0 to 100 scale) vs. usual care at 24 weeks.
		Yoga vs. exercise, chronic LBP: Pain and function	Low	A systematic review found yoga to be associated with lower pain intensity and better function vs. exercise in most trials, although effects were small and differences were not always statistically significant (5 trials).
		Yoga vs. education, chronic LBP: Pain and function	Moderate	Yoga was associated with lower short-term pain intensity vs. education (5 trials; SMD, −0.45; 95% CI, −0.63 to −0.26; I2 = 0%), but effects were smaller and not statistically significant at long term followup (4 trials; SMD, −0.28; 95% CI, −0.58 to −0.02; I2 = 47%); yoga was also associated with better function at short-term (5 trials; SMD, 0.45; 95% CI, −0.65 to −0.25; I2 = 8%) and long-term followup (4 trials; SMD, 0.39; 95% CI, −0.66 to −0.11; I2 = 40%).
		Yoga: Adverse events	Low	Reporting of harms was suboptimal, but adverse events, when reported, were almost all classified as mild to moderate.
	Psychological therapies	Progressive relaxation vs. wait-list control, chronic LBP: Pain and function	Low	A systematic review found progressive relaxation superior to wait-list control for post-treatment pain intensity (3 trials; mean difference, −19.77 on 0 to 100 VAS; 95% CI, −34 to −5.20; I2 = 57%) and functional status (3 trials; SMD, −0.88; 95% CI, −1.36 to −0.39; I2 = 0%).
		EMG biofeedback, chronic LBP: Pain and function	Low	A systematic review found EMG biofeedback to be associated with lower pain intensity at the end of treatment (3 trials; SMD, −0.80; 95% CI, −1.32 to −0.28; I2 = 0%), with no clear effect on function (3 trials).
		Operant therapy, chronic LBP: Pain and function	Low	A systematic review found operant therapy to be associated with lower pain intensity at the end of treatment (3 trials; SMD, −0.43; 95% CI, −0.75 to −0.1; I2 = 0%), with no clear effect on function (2 trials).
		Cognitive therapy vs. wait-list control, chronic LBP	Insufficient	There was insufficient evidence from 2 trials to determine effects of cognitive therapy vs. wait-list control due to inconsistency and imprecision.

Key Question 2. Nonpharmacological noninvasive therapies	Psychological therapies	Cognitive-behavioral and other combined therapy vs. wait-list control, chronic LBP: Pain and function	Low	A systematic review found cognitive-behavioral and other combined psychological therapy to be associated with greater improvements in post-treatment pain intensity compared with wait-list control (5 trials; SMD, −0.60; 95% CI, −0.97 to −0.22; I2 = 40%), but effects on function were smaller and not statistically significant (4 trials; SMD, −0.37; 95% CI, −0.87 to 0.13; I2 = 50%).
		Psychological therapies vs. exercise or physical therapy, chronic LBP: Pain and function	Low	A systematic review found no clear differences between psychological therapies vs. exercise therapy in pain intensity (2 trials) or between psychological therapies plus physiotherapy vs. physiotherapy alone (6 trials) in pain or function, although 1 small subsequent trial found combination therapy to be associated with greater improvements in pain and function immediately after treatment.
		Psychological therapies vs. psychological therapies: Pain and function	Moderate	Ten trials found no clear differences among different psychological therapies in pain or function.
		Psychological therapies: Adverse events	Low	Harms were not well reported, but no included trial reported any adverse events associated with psychological therapies.
	Multidisciplinary rehabilitation	Multidisciplinary rehabilitation vs. usual care, chronic LBP: Pain, function, return to work	Moderate	A systematic review found multidisciplinary rehabilitation, compared with usual care, to be associated with lower short-term pain intensity (9 trials; SMD, −0.55; 95% CI, −0.83 to −0.28; I2 = 72%, or ~1.4-point mean difference on a 0 to 10 point numeric rating scale) and disability (9 trials; SMD, −0.41; 95% CI, −0.62 to −0.19; I2 = 58%, or ~2.5-point mean difference on the RDQ); effects on long-term pain intensity and disability also favored multidisciplinary rehabilitation but were smaller (7 trials; SMD, −0.21; 95% CI, −0.37 to −0.04; I2 = 25% and 6 trials; SMD,−0.23; 95% CI, −0.40 to −0.06; I2 = 19%, respectively), with no difference in likelihood of return to work (7 trials; OR, 1.04; 95% CI, 0.73 to 1.47; I2 = 31%).
		Multidisciplinary rehabilitation vs. no multidisciplinary rehabilitation, chronic LBP: Pain and function	Low	A systematic review found multidisciplinary rehabilitation, compared with no multidisciplinary rehabilitation, to be associated with lower short-term pain intensity (3 trials; SMD, −0.73; 95% CI, −1.22 to −0.24; I2 = 64%, or ~1.7-point mean difference on a 0 to 10 numeric rating scale) and disability (3 trials; pooled SMD, −0.49; 95% CI, −0.76 to −0.22; I2 = 0%, or ~2.9-point mean difference on the RDQ); there was insufficient evidence to assess effects on long-term outcomes.

Key Question 2. Nonpharmacological noninvasive therapies	Multidisciplinary rehabilitation	Multidisciplinary rehabilitation vs. physical therapy, chronic LBP: Pain and function	Moderate	A systematic review found multidisciplinary rehabilitation, compared with nonmultidisciplinary physical therapy, to be associated with lower short-term pain intensity (12 trials; SMD, −0.30; 95% CI, −0.54 to −0.06; I2 = 80%, or an approximate 0.6-point mean difference on a 0 to 10 point numeric rating scale) and disability (13 trials; SMD, −0.39; 95% CI, −0.68 to −0.10; I2 = 88%, or an approximate 1.2-point mean difference on the RDQ); multidisciplinary rehabilitation was also associated with lower long-term pain intensity (9 trials; SMD, −0.51; 95% CI, −1.04 to 0.01; I2 = 92%) and function (10 trials; SMD, −0.68; 95% CI, −1.19 to −0.16; I2 = 94%) and greater likelihood for return to work (8 trials; OR, 1.87; 95% CI, 1.39 to 2.53; I2 = 0%).
		Multidisciplinary rehabilitation, acute LBP, radicular LBP	Insufficient	No study evaluated the effectiveness of multidisciplinary rehabilitation for acute LBP or for radicular LBP.
		Multidisciplinary rehabilitation: Adverse events	Low	Harms were poorly reported in trials of multidisciplinary rehabilitation, although no serious harms were reported.
	Acupuncture	Acupuncture vs. sham acupuncture, subacute LBP: Pain	Low	A systematic review found acupuncture to be associated with lower pain intensity vs. sham acupuncture using nonpenetrating needles (2 trials; mean difference, 9.38 on a 0 to 100 VAS; 95% CI, 1.76 to 17.0; I2 = 27%); 3 other trials reported effects consistent with these findings. One trial of sham acupuncture using penetrating needles to nonacupuncture points found no effect on pain. There were no clear effects on function in 5 trials.
		Acupuncture vs. sham acupuncture, chronic LBP: Pain and function	Moderate	A systematic review found acupuncture to be associated with lower pain intensity vs. sham acupuncture (superficial needling at acupuncture or nonacupuncture points or nonpenetrating pressure at acupuncture points) immediately at the end of treatment (4 trials; WMD, −16.76; 95% CI, −33.3 to −0.19; I2 = 90%) and at up to 12 weeks (3 trials; WMD, −9.55; 95% CI, −16.5 to −2.58; I2 = 40%), but there were no differences in function. Four additional trials reported results consistent with these findings.
		Acupuncture vs. no acupuncture, chronic LBP	Moderate	A systematic review found acupuncture to be associated with lower pain intensity (4 trials; SMD, −0.72; 95% CI, −0.94 to −0.49; I2 = 51%) and better function (3 trials; SMD, −0.94; 95% CI, −1.41 to −0.47; I2 = 78%) immediately after treatment vs. no acupuncture. Mean effects on pain ranged from 7 to 24 points on a 0 to 100 point scale; for function, 1 trial reported a difference of 8 points on a 0 to 100 scale and the other 2 trials showed small or no clear differences at long-term followup.
		Acupuncture vs. NSAIDs, acute LBP: Overall improvement	Low	A systematic review found acupuncture to be associated with slightly greater likelihood of overall improvement vs. NSAIDs at the end of treatment (5 trials; RR, 1.11; 95% CI, 1.06 to 1.16; I2 = 0%).

Key Question 2. Nonpharmacological noninvasive therapies	Acupuncture	Acupuncture vs. medications (NSAIDs, muscle relaxants and analgesics), chronic LBP: Pain and function	Low	A systematic review found acupuncture to be associated with better pain relief (3 trials; WMD, −10.56 on a 0 to 100 scale; 95% CI, −20.34 to −0.78; I 2 = 0%) and improvement in function (3 trials; SMD, −0.36; 95% CI, −0.67 to −0.04; I2 = 7%) immediately postintervention.
		Acupuncture: Adverse events	Low	Harms of acupuncture were poorly reported in the trials, although no serious adverse events were reported.
	Massage	Massage vs. sham massage, acute LBP: Pain and function	Low	A systematic review included 2 trials that found massage to be associated with greater short-term (1 week) improvement in pain (SMD, −0.92; 95% CI, −1.35 to −0.48) and function (SMD, −1.76; 95% CI, −3.19 to −0.32) vs. sham therapy, but there was no difference in pain or function at 5 weeks in 1 trial.
		Massage vs. usual care, chronic LBP: Pain and function	Low	One trial found no difference between foot reflexology vs. usual care in pain or function, and 1 trial found structural or relaxation massage to be associated with better function (mean, 2.5 to 2.9 points on the RDQ) vs. usual care at 10 weeks; effects were less pronounced at 52 weeks.
		Massage vs. other interventions, subacute to chronic LBP: Pain and function	Moderate	A systematic review found massage to be associated with better effects on short-term pain in 7 of 9 trials (mean differences, −0.6 to −0.94 points on a 0 to 10 scale) and better effects on short-term function in 3 of 4 trials.
		Massage plus another active intervention vs. the other intervention alone, subacute to chronic LBP: Pain and function	Low	A systematic review included 5 trials that generally found massage plus another intervention to be superior to the other intervention without massage for short-term pain, with effects somewhat stronger in trials in which massage was combined with exercise; few differences were observed for function or long-term pain. Two subsequent trials of massage plus exercise reported findings generally consistent with these findings.
		Massage vs. massage: Pain and function	Insufficient	Comparisons of different massage techniques were too heterogeneous and effects were too small from 6 trials to determine effects on pain and function.
		Massage: Adverse events	Low	Harms were not well reported in trials of massage, although no serious adverse events were reported; 2 trials reported soreness during or shortly after the treatment.
	Spinal manipulation	Spinal manipulation, acute LBP: Pain and function	Low for function, insufficient for pain	Two trials (1 included in a systematic review) found spinal manipulation to be associated with better effects on function vs. sham manipulation (statistically significant in 1 trial); in 1 trial, effects on pain favored manipulation but were small and not statistically significant (mean difference, −0.50; 95% CI, −1.39 to 0.39)

Key Question 2. Nonpharmacological noninvasive therapies	Spinal manipulation	Spinal manipulation vs. sham manipulation, chronic LBP: Pain and function	Low for pain, insufficient for function	A systematic review found spinal manipulation to be associated with small, statistically nonsignificant effects vs. sham manipulation on pain at 1 month (3 trials; WMD, −3.24; 95% CI, −13.62 to 7.15 on a 0 to 100 scale; I2 = 53%); 1 trial reported similar results for function (SMD, −0.45; 95% CI, −0.97 to 0.06); 1 trial not included in the systematic review reported generally consistent results.
		Spinal manipulation vs. inert treatment, acute LBP: Pain and function	Low	A systematic review found no differences between spinal manipulation vs. inert treatment in pain relief at 1 week (3 trials; WMD, 0.14 on a 0 to 10 scale; 95% CI, −0.69 to 0.96; I2 = 27%), although 1 trial found spinal manipulation to be associated with better long term pain relief (mean difference, −1.20 at 3 months; 95% CI, 2.11 to −0.29); there were no differences in function at 1 week (2 trials; SMD, −0.08; 95% CI, −0.37 to 0.21; I2 = 0%) or at 3 months (1 trial; SMD, −0.28; 95% CI, −0.59 to 0.02).
		Spinal manipulation vs. inert treatment, chronic LBP	Low	One trial with low risk of bias found spinal manipulation to be associated with greater improvement in the “main complaint” vs. an inert treatment (mean difference, 0.9 on a 0 to 10 scale; 95% CI, 0.1 to 1.7); results from 3 trials with high risk of bias and 3 additional trials not included in the systematic review were somewhat inconsistent, although some trials reported effects that favored manipulation.
		Spinal manipulation vs. other active interventions, acute LBP: Pain and function	Moderate	A systematic review found no difference between spinal manipulation vs. other active interventions in pain relief at 1 week (3 trials; WMD, 0.06 on a 0 to 10 scale; 95% CI, −0.53 to 0.65; I2 = 0%), 1 month (3 trials; WMD, −0.15; 95% CI, −0.49 to 0.18; I2 = 0%), 3 to 6 months (2 trials; WMD, −0.20; 95% CI, −1.13 to 0.73; I2 = 81%), or 1 year (1 trial; mean difference, 0.40; 95% CI, −0.08 to 0.88). Findings were similar for function, with no differences observed at any timepoint. A subsequent trial of patients with acute or subacute LBP found that spinal manipulation was associated with moderate effects vs. usual care on pain and small effects on function at short-term followup, but effects were smaller and no longer statistically significant at 3 and 6 months

Key Question 2. Nonpharmacological noninvasive therapies	Spinal manipulation	Spinal manipulation vs. other interventions, chronic LBP: Pain and function	Moderate	A systematic review found spinal manipulation to be associated with better short-term pain relief vs. other active interventions at 1 month (10 comparisons from 6 trials; WMD, −2.76 on a 0 to 100 scale; 95% CI, −5.19 to −0.32; I2 = 27%) and 6 months (7 comparisons from 4 trials; WMD, −3.07; 95% CI, −5.42 to −0.71; I2 = 0%), although the magnitude of effects was below the small/slight threshold. There was no difference at 12 months (3 trials; WMD, −0.76; 95% CI, −3.19 to 1.66; I2 = 0%). Manipulation was also associated with greater improvement in function vs. other active interventions at 1 month (10 comparisons from 6 trials; SMD, −0.17; 95% CI, −0.29 to −0.06; I2 = 3%); effects were smaller and no longer statistically significant at 6 and 12 months. Three trials not included in the systematic reviews reported results consistent with these findings.
		Spinal manipulation plus exercise or advice vs. exercise or advice alone, acute LBP: Function	Low	Four trials in a systematic review found spinal manipulation plus either exercise or advice to be associated with greater improvement in function at 1 week (SMD, −0.41; 95% CI, −0.73 to −0.10; I2 = 18%) vs. exercise or advice alone, but there were no differences at 1 month (3 trials; SMD, −0.09; 95% CI, −0.39 to 0.21; I2 = 37%) or 3 months (2 trials; SMD, −0.22; 95% CI, −0.61 to 0.16; I2 = 41%).
		Spinal manipulation plus another active treatment, chronic LBP: Pain and function	Low	A systematic review found spinal manipulation plus another active treatment to be associated with greater pain relief at 1 month (3 trials; WMD, −5.88 on a 0 to 100 scale; 95% CI, −10.85 to −0.90; I2 = 0%), 3 months (2 trials; mean difference, −7.23; 95% CI, −11.72 to −2.74; I2 = 43%), and 12 months (2 trials; mean difference, −3.31; 95% CI, −6.60 to −0.02; I2 = 12%) vs. the other treatment alone. Combination therapy was also associated with better function at 1 month, (2 trials; SMD, −0.40; 95% CI, −0.73 to −0.07; I2 = 0%), 3 months (2 trials; SMD, −0.22; 95% CI, −0.38 to −0.06; I2 = 33%), and 12 months (2 trials; SMD, −0.21; 95% CI, −0.34 to −0.09; I2 = 0%). One trial not included in the systematic review reported results consistent with these findings.
		Spinal manipulation plus home exercise and advice, radicular LBP	Low	One good-quality trial found spinal manipulation plus home exercise and advice to be associated with greater improvement in leg and back pain at 12 weeks vs. home exercise and advice alone (mean differences about 1 point on a 0 to 10 scale), but effects were smaller (0.3 to 0.7 points) and no longer statistically significant at 52 weeks.
		Spinal manipulation: Adverse events	Low	Harms were not reported well in most trials of spinal manipulation. No serious adverse events were reported, and most adverse events were related to muscle soreness or transient increases in pain.

Key Question 2. Nonpharmacological noninvasive therapies	Ultrasound	Ultrasound vs. sham ultrasound, chronic LBP: Pain and function	Low for pain, insufficient for function	A systematic review found no difference between ultrasound vs. sham ultrasound in pain at the end of treatment (3 trials; mean difference, −7.12 on 0 to 100 scale; 95% CI, −18.0 to 3.75; I2 = 77%), and 2 trials found no effects on pain 4 weeks after the end of treatment. Evidence from 5 trials was too inconsistent to determine effects on function, although a larger good-quality trial found no effect on the RDQ.
		Ultrasound vs. no ultrasound, chronic LBP: Pain and function	Low	A systematic review found no differences between ultrasound vs. no ultrasound in pain (2 trials; mean difference, −2.16; 95% CI, −4.66 to 0.34; I2 = 0%) or back-specific function (2 trials; mean difference, −0.41; 95% CI, −3.14 to 2.32), but estimates were imprecise.
		Ultrasound plus exercise vs. exercise, chronic LBP: Pain and function	Insufficient	Evidence from 3 trials was insufficient to determine effects of ultrasound plus exercise vs. exercise alone on pain or function due to imprecision and methodological shortcomings.
		Ultrasound plus exercise vs. exercise, radicular LBP: Back pain, leg pain	Insufficient	A small trial found no differences between ultrasound plus exercise vs. sham ultrasound plus exercise in back pain, leg pain, or the ODI after 3 weeks of therapy.
		Ultrasound vs. other interventions	Insufficient	There was insufficient evidence from 3 small trials with methodological shortcomings to determine effects of ultrasound vs. other interventions.
		Ultrasound vs. other interventions, radiculopathy	Insufficient	There was insufficient evidence from 2 small trials with methodological shortcomings to determine effects of ultrasound vs. other interventions.
		Ultrasound, acute nonradicular LBP	Insufficient	No study evaluated the effectiveness of ultrasound for acute nonradicular LBP.
		Ultrasound vs. sham ultrasound: Adverse events	Low	One trial found no differences between ultrasound vs. sham ultrasound in risk of any adverse event (6.0% vs. 5.9%; RR, 1.03; 95% CI, 0.49 to 2.13) or serious adverse events (1.3% vs. 2.7%; RR, 0.48; 95% CI, 0.12 to 1.88).

Key Question 2. Nonpharmacological noninvasive therapies	Transcutaneous electrical nerve stimulation	TENS vs. sham TENS, acute or subacute LBP: Pain and function	Insufficient	Evidence from single trials with methodological shortcomings was too limited to permit reliable conclusions regarding effectiveness.
		TENS vs. sham TENS, chronic LBP: Pain and function	Low	A systematic review found no differences between TENS vs. sham TENS in pain intensity (4 trials; WMD, −4.47 on a 0 to 100 scale; 95% CI, −12.84 to 3.89) or function (2 trials; WMD, −1.36 on a 0 to 100 scale; 95% CI, −4.38 to 1.66) at short-term followup; most trials found no effect on pain or function at the end of a course of treatment.
		TENS vs. acupuncture, chronic LBP: Pain	Low	A systematic review found no differences between TENS vs. acupuncture for short- (4 trials; SMD, 0.15; 95% CI, −0.33 to 0.63) or long-term pain (2 trials; SMD, 0.32; 95% CI, −0.33 to 0.96). Evidence for TENS vs. other interventions was too limited to permit reliable conclusions.
		TENS: Adverse events	Low	Evidence on harms associated with TENS was limited but suggests an increased risk of skin-site reactions without an increased risk of serious adverse events.
	Electrical muscle stimulation	EMS plus exercise vs. exercise, EMS vs. other interventions, acute or chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 5 RCTs to determine effects of EMS plus exercise vs. exercise alone or vs. other interventions due to methodological limitations and imprecision.
		EMS: Adverse events	Insufficient	There was insufficient evidence to determine harms of EMS.
	Percutaneous electrical nerve stimulation	PENS vs. sham PENS, PENS plus exercise vs. exercise, PENS vs. other interventions, chronic LBP (with or without radiculopathy)	Insufficient	There was insufficient evidence from 7 trials to determine effects of PENS vs. sham, PENS plus exercise vs. exercise alone, or PENS vs. other interventions due to methodological limitations, inconsistency, and imprecision.
		PENS: Adverse events	Insufficient	Harms were poorly reported in trials of PENS.
	Interferential therapy	IFT vs. other interventions, IFT plus another intervention vs. the other intervention, subacute to chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 4 trials to determine effects of IFT vs. other interventions or IFT plus another intervention vs. the other intervention alone, due to methodological limitations and imprecision.
		IFT: Adverse events	Insufficient	No study evaluated harms of IFT.

Key Question 2. Nonpharmacological noninvasive therapies	Superficial heat or cold	Heat wrap vs. placebo, acute or subacute LBP: Pain and function	Moderate	A systematic review found a heat wrap to be more effective than placebo for pain relief at 5 days (2 trials; mean difference, 1.06 on a 0 to 5 scale; 95% CI, 0.68 to 1.45) and disability at 4 days (mean difference, −2.10 on the RDQ; 95% CI, −3.19 to −1.01). Two subsequent trials also found a heat wrap to be associated with decreased pain intensity at 3 to 4 days (differences, 16 to 20 points on a 0 to 100 point VAS) or increased pain relief at 8 hours (difference, ~1.5 points on a 0 to 5 scale). Another trial found a heat wrap during emergency transport to be associated with substantially lower pain intensity vs, an unheated blanket on arrival to the hospital.
		Heat plus exercise vs. exercise alone, acute LBP: Pain and function	Low	One higher quality trial found heat plus exercise to be associated with greater pain relief (mean difference, 1.40 on 0 to 10 scale; 95% CI, 0.69 to 2.11) and higher function (mean RDQ difference, −3.20; 95% CI, −5.42 to −0) vs. exercise without heat at day 7.
		Heat plus NSAID vs. NSAID alone, acute LBP: Pain	Insufficient	One fair-quality trial found heat plus an NSAID to be associated with better pain scores versus an NSAID without heat at day 15 based on the McGill Pain Questionnaire (scoring methods unclear).
		Heat vs. simple analgesics, acute or subacute LBP: Pain and function	Low	A systematic review included 1 trial that found heat to be more effective for pain relief than acetaminophen (mean difference, 0.90 on a 0 to 10 scale; 95% CI, 0.50 to 1.30) or ibuprofen (0.65; 95% CI, 0.25 to 1.05) after 1 to 2 days of treatment; the heat wrap was also associated with greater improvement on the RDQ (mean differences, 2.00 on a 0 to 24 scale; 95% CI, 0.86 to 3.14, and 2.20; 95% CI, 1.11 to 3.29, respectively).
		Heat vs. exercise, acute LBP: Pain and function	Low	A systematic review included 1 trial that found no clear differences between heat vs. exercise in pain relief or function.
		Superficial cold vs. placebo	Insufficient	No study compared superficial cold vs. placebo or no cold treatment.
		Cold plus naproxen vs. naproxen alone, acute LBP: Pain	Insufficient	One small trial with methodological shortcomings found cold plus naproxen to be associated with better pain scores vs. naproxen alone based on the McGill Pain Questionnaire (scoring methods unclear)
		Heat vs. cold	Low	There was insufficient evidence from 3 trials to determine effects of heat vs. cold due to methodological limitations and imprecision.
		Heat vs. no heat or placebo: Adverse events, flushing	Insufficient	Heat was not associated with increased risk of skin flushing vs. no heat or placebo in 2 trials; no serious adverse events were reported with use of heat.

Key Question 2. Nonpharmacological noninvasive therapies	Low- level laser therapy	LLLT vs. sham laser, acute LBP	Insufficient	There was insufficient evidence from 1 trial to determine effectiveness of LLLT vs. sham laser due to serious methodological shortcomings and imprecision.
		LLLT vs. sham laser, chronic LBP: Pain and function	Low	Three of 4 trials found LLLT to be more effective than sham laser for pain, although methods for assessing pain and duration of followup varied; 2 trials found LLLT to be more effective than sham laser for function, with small magnitude of effect.
		LLLT plus NSAID vs. sham plus NSAID, acute or subacute LBP: Pain and function	Low	One trial found LLLT plus an NSAID to be associated with lower pain intensity vs. sham laser plus an NSAID or the NSAID alone (mean differences, 9 to 14 points on a 0 to 100 VAS); effects on the ODI also favored combination treatment but were smaller (differences <6 points).
		LLLT plus another intervention vs. the other intervention alone, chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 3 trials to determine effects of LLLT plus exercise vs. sham laser plus exercise alone due to methodological shortcomings and inconsistency.
		LLLT vs. another intervention: Pain and function	Insufficient	There was insufficient evidence to determine effects of LLLT vs. another intervention due to methodological shortcomings and imprecision.
		LLLT, differing wavelengths or doses	Insufficient	There was insufficient evidence to determine effects of different wavelengths or doses of LLLT due to methodological limitations and imprecision.
		LLLT: Adverse events	Low	Harms were not well reported in trials of LLLT, but no serious adverse events and no harms were reported.
	Short-wave diathermy	Short-wave diathermy vs. sham diathermy, mixed-duration LBP: Effectiveness and adverse events	Insufficient	There was insufficient evidence from 5 RCTs to determine effects of short-wave diathermy vs. sham diathermy due to methodological limitations and imprecision.
		Short-wave diathermy: Adverse events	Insufficient	No study evaluated harms of short-wave diathermy.

Key Question 2. Nonpharmacological noninvasive therapies	Lumbar supports	Lumbar supports vs. no lumbar supports or an inactive treatment, acute or subacute LBP: Pain and function	Insufficient	There was insufficient evidence from 5 trials to determine effects of lumbar supports vs. no lumbar supports or an inactive treatment due to methodological shortcomings and inconsistent results.
		Lumbar supports vs. no lumbar supports, chronic LBP	Insufficient	There was insufficient evidence from 2 trials to determine effects of lumbar supports vs. no lumbar supports due to methodological shortcomings and inconsistent results.
		Lumbar supports vs. no lumbar supports, mixed-duration LBP: Pain and function	Low	One trial found an inextensible, but not an extensible, lumbar supports to be associated with greater improvement in function vs. no lumbar support, but effects were small. There was no clear effect on function.
		Lumbar support plus education vs. education, acute or subacute LBP: Pain and function	Low	One trial found no differences between a lumbar support plus an education program vs. an education program alone in pain or function after 1 year
		Lumbar support plus exercise vs. exercise alone, chronic LBP: Pain and function	Low	One trial found no difference between a lumbar support plus exercise (muscle strengthening) vs. exercise alone in short-term (8 week) or long-term (6 month) pain or function.
		Lumbar support vs. other active treatments: Pain and function	Low	Three trials found no clear differences between lumbar supports vs. other active treatments in pain or function.
		Lumbar supports vs. lumbar supports: Pain and function	Insufficient	There was insufficient evidence from 2 trials to determine comparative effects of different types of lumbar supports for chronic LBP or back pain of mixed duration due to heterogeneous comparisons, methodological shortcomings, and imprecision.
		Lumbar supports: Adverse events	Low	Trials reported no harms associated with use of lumbar supports.
	Traction	Traction vs. placebo, sham, or no treatment, LBP with or without radicular symptoms: Pain, function, other outcomes	Insufficient	A systematic review included 13 trials that found no clear differences and inconsistent effects of traction vs. placebo, sham, or no treatment in pain, function, or other outcomes, although 2 trials reported favorable effects on pain in patients with radicular back pain.

Key Question 2. Nonpharmacological noninvasive therapies	Traction	Traction vs. physiotherapy, LBP with or without radicular symptoms	Low	A systematic review included 5 trials that found no clear differences between traction plus physiotherapy vs. physiotherapy alone.
		Traction vs. other interventions, LBP with or without radicular symptoms: Pain and function	Low	A systematic review included 15 trials of traction vs. other interventions that found no clear between traction vs. other active interventions in pain or function.
		Traction vs. traction	Low	A systematic review included 5 trials that found no clear differences among different types of traction.
		Traction: Adverse events	Low	Eleven trials of traction in a systematic review reported no adverse events or no difference in risk of adverse events vs. placebo or other interventions. Three subsequent trials reported findings consistent with the systematic review.
	Taping	Kinesio Taping® vs. sham taping, chronic LBP: Pain and function	Insufficient for pain, low for function	Two trials found no differences between Kinesio Taping vs. sham taping in back-specific function after 5 to 12 weeks; effects on pain were inconsistent.
		Functional Fascial Taping® plus exercise vs. sham taping plus exercise, chronic LBP: Pain and function	Insufficient	There was insufficient evidence from 1 trial to determine effects of Functional Fascial Taping plus exercise vs. sham taping plus exercise due to methodological limitations and imprecision.
		Kinesio Taping vs. exercise therapy, chronic LBP: Pain and function	Low	Two trials found no differences between Kinesio Taping vs. exercise therapy in pain or function.
		Taping: Adverse events	Insufficient	No trial of taping reported harms.

Table 31. Pharmacological therapies versus placebo for acute low back pain

Drug	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Acetaminophen	No effect	1 RCT	Low	No effect	1 RCT	Low
NSAIDs	Small (pain intensity); no effect (pain relief)	1 SR (4 RCTs)	Moderate	Small	2 RCTs	Low
Opioids (buprenorphine patch)	Small	2 RCTs	Low	No evidence	--	--
Skeletal muscle relaxants	Pain relief: RR, 1.72 (95% CI 1.32 to 2.22) at 5–7 days	1 SR (3 RCTs) + 1 RCT	Moderate	No evidence	--	--
Benzodiazepines	Unable to estimate	2 RCTs	Insufficient	Unable to estimate	2 RCTs	Insufficient
Antiseizure medications	No evidence	--	--	No evidence	--	--
Systemic corticosteroids	No effect	2 RCTs	Low	No effect	2 RCTs	Low

CI= confidence interval; NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized controlled trial; RR = relative risk; SOE = strength of evidence; SR = systematic review.

Table 32. Pharmacological therapies versus active comparators for acute low back pain

Drug	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE
Acetaminophen vs. NSAID	No effect	1 SR (3 RCTs) + 1 RCT	Low
NSAID vs. NSAID	No effect in 15 of 21 RCTs	1 SR (21 RCTs)	Moderate
COX-2 selective NSAID vs. traditional NSAID	No effect	1 SR (3 RCTs)	Low
Skeletal muscle relaxant + NSAID vs. NSAID alone	RR, 1.56 (95% CI, 0.92 to 2.70)	1 SR (2 RCTs) + 1 RCT	Low
Skeletal muscle relaxant vs. skeletal muscle relaxant	No effect	1 SR (2 RCTs)	Low

CI = confidence interval; NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized controlled trial; RR = relative risk; SOE = strength of evidence; SR = systematic review.

Table 33. Nonpharmacological treatments versus sham, no treatment, or usual care for acute or subacute low back pain

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Exercise vs. usual care	Moderate	1 SR (3 RCTs) + 3 RCTs	Low	Moderate	1 SR (3 RCTs) + 3 RCTs	Low
Acupuncture vs. sham	Small	2 RCTs	Low	No effect	5 RCTs	Low
Massage vs. sham	Moderate	1 SR (2 RCTs)	Low	Moderate	1 SR (2 RCTs)	Low

Massage vs. usual care	Small to no effect	2 RCTs	Low	Small to no effect	2 RCTs	Low
Spinal manipulation vs. sham	Small	2 RCTs	Low	No effect	1 SR (3 RCTs)	Low
Heat wrap vs. placebo	Moderate	1 SR (2 RCTs) + 2 RCTs	Moderate	Moderate	1 SR (2 RCTs)	Moderate
Low-level laser therapy plus NSAID vs. sham plus NSAID	Moderate	1 RCT	Low	Small	1 RCT	Low
Lumbar supports vs. no lumbar supports or inactive treatment	Unable to determine	5 RCTs	Insufficient	Unable to determine	5 RCTs	Insufficient

NSAID=nonsteroidal anti-inflammatory drug, RCT=randomized controlled trial, SOE=strength of evidence

Table 34. Nonpharmacological treatments versus active comparators for acute or subacute low back pain

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Exercise vs. exercise	No clear differences	> 20 RCTs	Moderate	--	--	--
Spinal manipulation vs. other active interventions	No clear differences at 1 week, 1 month, 3- 6 months, 1 year	1 SR (3 RCTs)	Moderate	No clear differences	1 SR (3 RCTs)	Moderate
Spinal manipulation plus exercise or advice vs. exercise or advice alone	--	--	--	Small, favors spinal manipulation at 1 week	1 SR (4 RCTs)	Low
Spinal manipulation plus exercise or advice vs. exercise or advice alone	--	--	--	No clear differences at 1, 3 months	1 SR (3 RCTs)	Low
Heat plus exercise vs. exercise alone	Moderate, favors heat	1 SR	Low	--	--	--
Heat vs. simple analgesics	Moderate, favors heat	1 SR	Low	--	--	--
Heat vs. exercise	No clear differences	1 RCT	Low	No clear differences	1 RCT	Low
Lumbar support plus education vs. education	No clear differences	1 RCT	Low	No clear differences	1 RCT	Low

RCT=randomized controlled trial, SOE=strength of evidence

Table 35. Pharmacological therapies versus placebo for chronic low back pain

Drug	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Acetaminophen	No evidence	--	--	No evidence	--	--
NSAIDs	Moderate	1 SR (4 RCTs)	Moderate	Small	1 SR (2 RCTs)	Low
Opioids	Small	1 SR (6 RCTs)	Moderate	Small	1 SR (4 RCTs)	Moderate
Skeletal muscle relaxants	Unable to estimate	3 RCTs	Insufficient	--	--	--
Tramadol	Moderate	1 SR (5 RCTs) + 2 RCTs	Moderate	Small	1 SR (5 RCTs) + 2 RCTs	Moderate
Benzodiazepines: tetrazepam	Failure to improve at 10–14 days: RR, 0.71 (95% CI, 0.54 to 0.93)	1 SR (2 RCTs)	Low	--	--	--
Tricyclic antidepressants	No effect	1 SR (4 RCTs)	Moderate	No effect	1 SR (2 RCTs)	Low
Antidepressants: SSRI	No effect	1 SR (3 RCTs)	Moderate	--	--	--
Antidepressants: duloxetine	Small	3 RCTs	Moderate	Small	3 RCTs	Moderate
Gabapentin/ pregabalin	Unable to estimate	2 RCTs	Insufficient	Unable to estimate	2 RCTs	Insufficient

NSAID=nonsteroidal anti-inflammatory drug, RCT=randomized controlled trial, SOE=strength of evidence, SSRI=selective serotonin reuptake inhibitor

Table 36. Pharmacological therapies versus active comparators for chronic low back pain

Drug	**Pain: Magnitude of Effect**	**Pain: Evidence**	**Pain: SOE**	**Function: Magnitude of Effect**	**Function: Evidence**	**Function: SOE**
Acetaminophen vs. NSAID	Unable to estimate	1 RCT	Insufficient	Unable to estimate	1 RCT	Insufficient
NSAID vs. NSAID	No difference	6 RCTs	Moderate	--	--	--
Opioid vs. NSAID	Unable to estimate (inconsistent)	3 RCTs	Insufficient	No difference	1 RCT	Insufficient

Long-acting opioid vs. long-acting opioid	No clear difference	4 RCTs	Moderate	No clear difference	4 RCTs	Moderate
Long-acting opioid vs. short-acting opioid	No clear difference*	6 RCTs	Low	--	--	--
Benzodiazepine (diazepam) vs. skeletal muscle relaxant	No difference	1 RCT	Low	--	--	--
Skeletal muscle relaxant vs. skeletal muscle relaxant	No clear difference	1 SR (2 RCTs)	Low	--	--	--

NSAID=nonsteroidal anti-inflammatory drug, RCT=randomized controlled trial, SOE=strength of evidence
*Although some RCTs found long-acting opioids associated with greater pain relief, patients randomized to long-acting opioids also received higher doses of opioids

Table 37. Nonpharmacological treatments versus sham, no treatment, or usual care for chronic low back pain

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Exercise vs. usual care	Small	1 SR (19 RCTs) + 1 SR	Moderate	Small	1 SR (17 RCTs) + 1 SR	Moderate
Motor control exercises vs. minimal intervention	Moderate (short to long term)	1 SR (2 RCTs)	Low	Small (short to long term)	1 SR (3 RCTs)	Low
Tai chi vs. wait list or no tai chi	Moderate	2 RCTs	Low	Small	1 RCT	Low
Yoga vs. usual care	Moderate	1 RCT	Low	Moderate	1 RCT	Low
Yoga vs. education	Small (short term) and no effect (long term)	5 RCTs (short term) + 4 RCTs (long term)	Low	Small (short term) and no effect (long term)	5 RCTs (short term) + 4 RCTs (long term)	Low
Progressive relaxation vs. wait-list control	Moderate	1 SR (3 RCTs)	Low	Moderate	1 SR (3 RCTs)	Low
EMG biofeedback vs. wait list or placebo	Moderate	1 SR (3 RCTs)	Low	No effect	1 SR (3 RCTs)	Low
Operant therapy vs. wait-list control	Small	1 SR (3 RCTs)	Low	No effect	1 SR (2 RCTs)	Low
Cognitive-behavioral therapy vs. wait-list control	Moderate	1 SR (5 RCTs)	Low	No effect	1 SR (4 RCTs)	Low

Multidisciplinary rehabilitation vs. no multidisciplinary rehabilitation	Moderate	1 SR (3 RCTs)	Low	Small	1 SR (3 RCTs)	Low
Multidisciplinary rehabilitation vs. usual care	Moderate (short term), small (long term), favors rehabilitation	1 SR (9 RCTs) (short term) + 1 SR (7 RCTs) (long term)	Moderate	Small (short and long term)	1 SR (9 RCTs) (short term) + 1 SR (7 RCTs) (long term)	Moderate
Acupuncture vs. sham acupuncture	Moderate	1 SR (4 RCTs) + 4 RCTs	Low	No effect	1 SR (4 RCTs) + 4 RCTs	Low
Acupuncture vs. no acupuncture	Moderate	1 SR (4 RCTs)	Moderate	Moderate	1 SR (3 RCTs)	Moderate
Spinal manipulation vs. sham manipulation	No effect	1 SR (3 RCTs) + 1 RCT	Low	Unable to estimate	1 RCT	--
Spinal manipulation vs. inert treatment	Small	7 RCTs	Low	--	--	--
Massage vs. usual care	No effect	1 RCT	Low	Unable to estimate	2 RCTs	Insufficient
Ultrasound vs. sham ultrasound	No effect	1 SR (3 RCTs)	Low	Unable to estimate	5 RCTs	Insufficient
Ultrasound vs. no ultrasound	No effect	1 SR (2 RCTs)	Low	No effect	1 SR (2 RCTs)	Low
TENS vs. sham TENS	No effect	1 SR (4 RCTs)	Low	No effect	1 SR (2 RCTs)	Low
PENS vs. sham PENS	Unable to estimate	2 RCTs	Insufficient	Unable to estimate	2 RCTs	Insufficient
Electrical muscle stimulation vs. sham, no stimulation, or usual care	No evidence	--	--	No evidence	--	--
Low-level laser therapy vs. sham laser	Small	3 RCTs	Low	Small	3 RCTs	Low
Lumbar supports vs. no lumbar supports	Unable to estimate	2 RCTs	Insufficient	Unable to estimate	2 RCTs	Insufficient
Traction vs. placebo, sham, or no traction	Unable to estimate	1 SR (13 RCTs)	Insufficient	Unable to estimate	1 SR (13 RCTs)	Insufficient
Kinesio taping® vs. sham taping	No effect	2 RCTs	Low	No effects	2 RCTs	Low

NSAID=nonsteroidal anti-inflammatory drug, PENS=percutaneous electrical nerve stimulation, RCT=randomized controlled trial, SOE=strength of evidence, TENS=transcutaneous electrical nerve stimulation

Table 38. Nonpharmacological treatments versus active comparators for chronic low back pain

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
MCE vs. general exercise (short term)	Small, favors MCE for short term	1 SR (6 RCTs)	Low	Small, favors MCE	1 SR (6 RCTs)	Low
MCE vs. general exercise (intermediate term)	Small, favors MCE for intermediate term	1 SR (3 RCTs)	Low	--	--	--
MCE vs. general exercise (long term)	Small, favors MCE for long term	1 SR (4 RCTs)	Low	Small, favors MCE	1 SR (3 RCTs)	Low
MCE vs. multimodal physical therapy (intermediate term)	Moderate, favors MCE	1 SR (4 RCTs)	Low	Moderate, favors MCE	1 SR (3 RCTs)	Low
MCE + exercise vs. exercise alone	No clear difference	2 RCTs	Low	--	--	--
Pilates vs. usual care + physical activity	No effect to small effect, favors Pilates	7 RCTs	Low	No clear difference	7 RCTs	Low
Pilates vs. other exercise	No clear difference	3 RCTs	Low	No clear difference	3 RCTs	Low
Tai chi vs. other exercise	Moderate, favors tai chi	1 RCT	Low	--	--	--
Yoga vs. exercise	Small, favors yoga	1 SR (5 RCTs)	Low	--	--	--
Psychological therapies vs. exercise or physical therapy	No clear difference	1 SR (6 RCTs)	Low	--	--	--
Psychological therapies vs. psychological therapies	No clear difference	10 RCTs	Moderate	No clear difference	10 RCTs	Moderate
Multidisciplinary rehabilitation vs. physical therapy (short term)	Small, favors multidisciplinary rehabilitation	1 SR (12 RCTs)	Moderate	Small, favors multidisciplinary rehabilitation	1 SR (13 RCTs)	Moderate
Multidisciplinary rehabilitation vs. physical therapy (long term)	Moderate, favors multidisciplinary rehabilitation	1 SR (9 RCTs)	Moderate	Moderate, favors multidisciplinary rehabilitation	1 SR (10 RCTs)	Moderate
Spinal manipulation vs. other active interventions (exercise, usual care, medications, massage)	No clear difference	1 SR (6 RCTs)	Moderate	No clear difference	1 SR (6 RCTs)	Moderate
Acupuncture vs. medications	Small, favors acupuncture	1 SR (3 RCTs)	Low	Small, favors acupuncture	1 SR (3 RCTs)	Low

MCE=motor control exercise, RCT=randomized controlled trial, SOE=strength of evidence

Table 39. Pharmacological therapies versus placebo for radicular low back pain

Drug	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
NSAIDs	Small	1 SR (2 RCTs)	Low	--	--	--
Benzodiazepines: diazepam	RR, 0.5 (95% CI, 0.3 to 0.8)	1 RCT	Low	No effect	1 RCT	Low
Systemic corticosteroids	No effect	5 RCTs	Moderate	No effect	5 RCTs	Moderate
Gabapentin/pregabalin	Unable to estimate	5 RCTs	Insufficient	Unable to estimate	5 RCTs	Insufficient

NSAID=nonsteroidal anti-inflammatory drug, RCT=randomized controlled trial, SOE=strength of evidence

Table 40. Nonpharmacological treatments versus sham, no treatment, or usual care for radicular low back pain

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of effect	Function: Evidence	Function: SOE
Exercise vs. usual care	Small, favors exercise	3 RCTs	Low	Small, favors exercise	3 RCTs	Low
Traction vs. placebo, sham, or no treatment (includes radicular and nonradicular patients)	Unable to estimate	1 SR (13 RCTs)	Insufficient	Unable to estimate	1 SR (13 RCTs)	Insufficient

RCT=randomized controlled trial, SOE=strength of evidence

Table 41. Nonpharmacological treatments versus active comparators for radicular low back pain

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Traction vs. physiotherapy (includes radicular and nonradicular pain patients)	No clear difference	1 SR (5 RCTs)	Low	--	--	--

RCT=randomized controlled trial, SOE=strength of evidence

Conclusions

A number of pharmacological and nonpharmacological noninvasive treatments for low back pain are associated with small to moderate, primarily short-term effects on pain versus placebo, sham, wait-list, or no treatment. Effects on function were generally smaller than effects on pain. More research is needed to understand optimal selection of treatments, effective combinations and sequencing of treatments, and effectiveness of treatments for radicular low back pain.

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Abbreviations

Abbreviation	Term
AHRQ	Agency for Healthcare Research and Quality
CER	Comparative Effectiveness Review
CGI-S	Clinical Global Impressions of Severity
CI	Confidence interval
DASS	Depression Anxiety Stress Scales
EMG	Electromyography
EMS	Electrical muscle stimulation
HADS	Hospital Anxiety and Depression Scale
HRQOL	Health-related quality of life
HVLA	High-velocity low-amplitude
IFT	Interferential therapy
JLEQ	Japan Low Back Pain Evaluation Questionnaire
LBP	Low back pain
LBPOI	Low Back Pain Outcome Instrument
LBRS	Low back pain rating scale
LLLT	Low-level laser therapy
MBR	Multidisciplinary biopsychosocial rehabilitation
MCE	Motor control exercise
MCS	Mental component score of the SF-36
MD	Mean difference
NRS	Numeric rating scale
NSAID	Nonsteroidal anti-inflammatory drug
ODI	Oswestry Disability Index
PCS scores	Pain Catastrophizing Scale
PICOTS	Population, intervention, comparator, outcomes, timing, settings, and study designs
QOL	Quality of life
RCT	Randomized controlled trial
RDQ	Roland-Morris Disability Questionnaire

RR	Relative risk
SARI	Serotonin antagonist and reuptake inhibitors
SF-36	Short Form-36
SMD	Standardized mean difference
SMT	Spinal manipulation therapy
SNRI	Serotonin-norepinephrine reuptake inhibitors
SOE	Strength of evidence
SSRI	Selective serotonin reuptake inhibitor
TENS	Transcutaneous electrical nerve stimulation
TEP	Technical Expert Panel
VAS	Visual analogue scale
WMD	Weighted mean difference

Appendix A. Search Strategies

Database: Ovid MEDLINE(R) Without Revisions 1996 to April Week 3 2015, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <April 27, 2015>

Population

1 Low Back Pain/
2 Spinal Stenosis/
3 Radiculopathy/
4 Back Injuries/
5 Spinal Injuries/
6 ("low back pain" or (spinal adj3 stenosis) or radiculopathy or radicular).ti,ab.
7 or/1-6

Pharmacologic interventions

8 nsaids.mp. or Anti-Inflammatory Agents, Non-Steroidal/
9 (acetaminophen or paracetamol or aspirin or diflunisal or "choline magnesium trisalicylate" or salsalate or naproxen or ibuprofen or ketoprofen or flurbiprofen or oxaprzin or diclofenac or etodolac or tolmetin of sulindac or meloxicam or piroxicam or meclofenamate or nabumetone or celecoxib).mp.
10 opioids.mp. or Analgesics, Opioid/
11 (alfentanil or alphaprodine or beta-casomorphin$ or buprenorphine or carfentanil or codeine or deltorphin or dextromethorphan or dezocine or dihydrocodeine or dihydromorphine or enkephalin$ or ethylketocyclazocine or ethylmorphine or etorphine or fentanyl or heroin or hydrocodone or hydromorphone or ketobemidone or levorphanol or lofentanil or meperidine or meptazinol or methadone or methadyl acetate or morphine or nalbuphine or opium or oxycodone or oxymorphone or pentazocine or phenazocine or phenoperidine or pirinitramide or promedol or propoxyphene or remifentanil or sufentanil or tilidine or tapentadol or tramadol).mp.
12 antidepressants.mp. or Antidepressive Agents/
13 Antidepressive Agents, Second-Generation/ or Antidepressive Agents, Tricyclic/
14 Serotonin Uptake Inhibitors/
15 (amitriptyline or clomipramine or desipramine or doxepin or imipramine or nortriptyline or citalopram or escitalopram or fluoxetine or paroxetine or sertraline or venlafaxine or duloxetine).mp.
16 skeletal muscle relaxants.mp. or Neuromuscular Agents/
17 (baclofen or carisoprodol or chlorzoxazone or cyclobenzaprine or dantrolene or metaxalone or methocarbamol or orphenadrine or tizanidine).mp.
18 corticosteroids.mp. or Adrenal Cortex Hormones/
19 (prednisone or prednisolone).mp.
20 anticonvulsants.mp. or Anticonvulsants/
21 (gabapentin or pregabalin).mp.

22 Anesthetics, Local/
23 (capsaisin or lidocaine).mp.
24 (22 or 23) and topical.mp.
25 or/8-21
26 24 or 25

Nonpharmacologic interventions
27 Rehabilitation/
28 Physical Therapy Modalities/
29 (rehabilitation adj3 multicomponent).mp.
30 (rehabilitation adj3 interdisciplinary).mp.
31 Cognitive Therapy/
32 exp Psychotherapy/
33 exercise therapy.mp. or Exercise Therapy/
34 exp Complementary Therapies/
35 yoga.mp. or Yoga/
36 tai chi.mp. or Tai Ji/
37 Acupuncture Therapy/ or Acupuncture/ or acupuncture.mp.
38 Massage/ or massage.mp.
39 spinal manipulation.mp. or Manipulation, Spinal/
40 tens.mp. or Transcutaneous Electric Nerve Stimulation/
41 Hot Temperature/tu
42 Cryotherapy/
43 Electric Stimulation Therapy/
44 Traction/ or traction.mp.
45 laser therapy.mp. or Laser Therapy/
46 orthotic devices/ or athletic tape/ or braces/
47 Patient Education as Topic/
48 47 and back pain/
49 "back school$".mp.
50 or/27-46
51 or/48-50
52 7 and (26 or 51)
53 limit 52 to yr="2007 - 2015"

Limit to RCTs
54 randomized controlled trial.mp. or exp Randomized Controlled Trial/
55 randomized controlled trial.pt.
56 controlled clinical trial.mp. or exp Controlled Clinical Trial/
57 controlled clinical trial.pt.
58 clinical trial.mp. or exp Clinical Trial/

59 clinical trial.pt.
60 or/54-59
61 limit 60 to humans

Limit to systematic reviews
62 53 and 61
63 meta-analysis.mp. or exp Meta-Analysis/
64 (cochrane or medline).tw.
65 search$.tw.
66 63 or 64 or 65
67 "Review Literature as Topic"/ or systematic review.mp.
68 66 or 67
69 53 and 68

Limit to controlled observational studies
70 53 and (cohort or control$).mp

Combined searches
71 62 or 69 or 70
72 limit 71 to english language
73 limit 71 to abstracts
74 72 or 73

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <March 2015>

Population
1 Low Back Pain/
2 Spinal Stenosis/
3 Radiculopathy/
4 Back Injuries/
5 Spinal Injuries/
6 ("low back pain" or (spinal adj3 stenosis) or radiculopathy or radicular).ti,ab.
7 or/1-6

Pharmacologic interventions
8 nsaids.mp. or Anti-Inflammatory Agents, Non-Steroidal/
9 (acetaminophen or paracetamol or aspirin or diflunisal or "choline magnesium trisalicylate" or salsalate or naproxen or ibuprofen or ketoprofen or flurbiprofen or oxaprzin or diclofenac or etodolac or tolmetin of sulindac or meloxicam or piroxicam or meclofenamate or nabumetone or celecoxib).mp.
10 opioids.mp. or Analgesics, Opioid/

11 (alfentanil or alphaprodine or beta-casomorphin$ or buprenorphine or carfentanil or codeine or deltorphin or dextromethorphan or dezocine or dihydrocodeine or dihydromorphine or enkephalin$ or ethylketocyclazocine or ethylmorphine or etorphine or fentanyl or heroin or hydrocodone or hydromorphone or ketobemidone or levorphanol or lofentanil or meperidine or meptazinol or methadone or methadyl acetate or morphine or nalbuphine or opium or oxycodone or oxymorphone or pentazocine or phenazocine or phenoperidine or pirinitramide or promedol or propoxyphene or remifentanil or sufentanil or tilidine or tapentadol or tramadol).mp.
12 antidepressants.mp. or Antidepressive Agents/
13 Antidepressive Agents, Second-Generation/ or Antidepressive Agents, Tricyclic/
14 Serotonin Uptake Inhibitors/
15 (amitriptyline or clomipramine or desipramine or doxepin or imipramine or nortriptyline or citalopram or escitalopram or fluoxetine or paroxetine or sertraline or venlafaxine or duloxetine).mp.
16 skeletal muscle relaxants.mp. or Neuromuscular Agents/
17 (baclofen or carisoprodol or chlorzoxazone or cyclobenzaprine or dantrolene or metaxalone or methocarbamol or orphenadrine or tizanidine).mp.
18 corticosteroids.mp. or Adrenal Cortex Hormones/
19 (prednisone or prednisolone).mp.
20 anticonvulsants.mp. or Anticonvulsants/
21 (gabapentin or pregabalin).mp.
22 Anesthetics, Local/
23 (capsaisin or lidocaine).mp.
24 (22 or 23) and topical.mp.
25 or/8-21
26 24 or 25

Nonpharmacologic interventions
27 Rehabilitation/
28 Physical Therapy Modalities/
29 (rehabilitation adj3 multicomponent).mp.
30 (rehabilitation adj3 interdisciplinary).mp.
31 Cognitive Therapy/
32 exp Psychotherapy/
33 exercise therapy.mp. or Exercise Therapy/
34 exp Complementary Therapies/
35 yoga.mp. or Yoga/
36 tai chi.mp. or Tai Ji/
37 Acupuncture Therapy/ or Acupuncture/ or acupuncture.mp.
38 Massage/ or massage.mp.
39 spinal manipulation.mp. or Manipulation, Spinal/
40 tens.mp. or Transcutaneous Electric Nerve Stimulation/

41 Hot Temperature/tu
42 Cryotherapy/
43 Electric Stimulation Therapy/
44 Traction/ or traction.mp.
45 laser therapy.mp. or Laser Therapy/
46 orthotic devices/ or athletic tape/ or braces/
47 Patient Education as Topic/
48 47 and back pain/
49 "back school$".mp.

Combined searches
50 or/27-46
51 or/48-50
52 7 and (26 or 51)
53 limit 52 to yr="2007 - 2015"

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to March 2015>

1 "low back pain".ti.
2 limit 1 to full systematic reviews

Appendix B. Inclusion and Exclusion Criteria

Table B. Inclusion and exclusion criteria

PICOTS	Include	Exclude
Population	Adults with acute, subacute, or chronic nonradicular low back pain, radicular low back pain, or symptomatic spinal stenosis.	Children, pregnant women Patients with low back pain related to cancer, infection, inflammatory arthropathy, high velocity trauma, fracture; or low back pain associated with severe or progressive neurological deficits
Interventions	KQ 1: Nonsteroidal anti-inflammatory drugs (NSAIDs) Nonopioid analgesics, such as acetaminophen Opioid analgesics, such as oxycodone, hydrocodone, hydromorphone, morphine, fentanyl Antidepressants, such as tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors (SNRIs), and selective serotonin-reuptake inhibitors (SSRIs), or serotonin antagonist and reuptake inhibitors (SARIs) Skeletal muscle relaxants, including benzodiazepines Corticosteroids, such as prednisone or prednisolone Anti-epileptic drugs, such as gabapentin or pregabalin Capsaicin or topical lidocaine	Parenterally administered medications
	KQ 2: Interdisciplinary or multicomponent rehabilitation Psychological therapies, such as cognitive behavioral therapy Exercise and related interventions, such as yoga or Tai Chi Complementary and alternative medicine therapies: spinal manipulation, acupuncture, massage Passive physical modalities: heat, cold, ultrasound, transcutaneous electrical nerve stimulation (TENS), electrical muscle stimulation (EMS), interferential therapy (IFT), traction, low level laser therapy, lumbar supports/braces Back schools Other noninvasive treatments, such as taping	Invasive, nonsurgical therapies (e.g., injections) and surgical therapies
Comparators	Any included intervention(s) versus any other included intervention(s); noninvasive, nonsurgical treatment options, alone or in combination (which may include both nonpharmacological and pharmacological) components. Other possible comparators include placebo (drug trials), sham (functionally-inert) treatments, or no treatment.	
Outcomes	Benefits (effectiveness): Reduction or elimination of low back pain, including related leg symptoms Improvement in back-specific and overall function Improvement in health-related quality of life (HRQOL) Reduction in work disability/return to work Global improvement Number of back pain episodes or time between episodes Patient satisfaction	

PICOTS	Include	Exclude
	Harms: Pharmaceutical: serious (anaphylaxis, death) and nonserious (mild allergic or untoward) drug reactions or effects; opioid addiction or overdose Nonpharmaceutical: serious (death, neurological including cauda equine syndrome, fracture, local skin burns, etc.) and nonserious (mild transient local or general soreness, stiffness, aching; local skin irritation, etc.)	
Timing	Duration of followup: short term (up to 6 months) and long term (at least 1 year)	
Setting	Any nonhospital setting or in self-directed care	

Appendix C. Included Studies

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Appendix D. Excluded Studies

Studies in an Included Systematic Review Not Directly Used in the Current Review

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Appendix E. Data Abstraction

Table E1. Data abstraction of systematic reviews of acetaminophen

Author, Year	Comparison	Databases Searched, Date of Last Search	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Roelofs, 2008	NSAIDs vs. placebo NSAID vs. NSAID NSAID vs. other active treatments	MEDLINE, EMBASE, Cochrane Library through 2007	65 trials (RCT and controlled clinical trials) NSAID vs. paracetamol or acetaminophen: 6 trials Other comparisons discussed in NSAIDs section of this report	A. NSAIDs (nonselective and selective) B. Other medications C. Other active interventions (i.e. passive physical modalities) D. Placebo Total n=11,237	Cochrane Back Review Group Criteria (2003)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Roelofs, 2008	Quantitative analysis of (weighted) mean difference used fixed effects model when possible; qualitative analysis for other outcomes	NSAIDs versus paracetamol or acetaminophen, acute LBP: Pain intensity: 3 studies, SMD -0.21, 95% CI -0.43 to 0.02 Global improvement: 3 studies, RR 1.23, 95% CI 0.88 to 1.73	Risk of side effects, NSAIDs versus paracetamol or acetaminophen, 3 studies: RR 1.76, 95% CI 1.12 to 2.76	Good

Please see Appendix C. Included Studies for full study references.

Table E2. Data abstraction of randomized controlled trials of acetaminophen

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Williams, 2014	Australia Multicenter	New episode of acute low back pain (<6 weeks duration with no pain in prior month) with or without leg pain of at least moderate intensity (based on item 7 of SF-12) Exclude: Suspected serious spinal pathology, use of full doses of an analgesic, spinal surgery in past 6 months, contraindication to acetaminophen, use of psychotropic drugs for a disorder judged to prevent reliable recording of study information, pregnant or planning pregnancy	Randomized: 1652 Analyzed: 1643 Attrition: 2.8% (46/1652)	A: Acetaminophen: 665 mg 2 tabs po q6-8 hours (6 tabs/day) + placebo 1-2 tabs po q4-6 hours prn (up to 8 tabs/day) (n=550) B: Acetaminophen: Placebo 2 tabs po q6-8 hours (6 tabs/day) + 500 mg 1-2 Tabs po q4-6 hours prn (up to 8 tabs/day) (n=546) C: Placebo: Placebo 2 tabs po q6-8 hours (6 tabs/day) + placebo 1-2 tabs po q4-6 hours prn (up to 8 tabs/day) (n=547) Medications taken until recovery or for 4 weeks	Mean age: 44 vs. 45 vs. 45 years Female: 48% vs. 47% vs. 45% Race: Not reported Baseline pain (mean, 0-10 NRS): 6.3 vs. 6.3 vs. 6.2 Baseline RDQ (mean, 0-24): 3.5 vs. 3.6 vs. 3.7 Pain below knee: 20% vs. 21% vs. 18%	<6 weeks; mean duration 10 vs. 10 vs. 10 days

Author, Year	Duration of Followup	Results (list results for acute, subacute, and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality
Williams, 2014	12 weeks	A vs. B vs. C Pain (mean, 0-10): 3.7 vs. 3.8 vs. 3.6 at w 1, 2.6 vs. 2.6 vs. 2.5 at w 2, 1.7 vs. 1.8 vs. 1.7 at w 4, 1.2 vs. 1.3 vs. 1.3 at w 12 RDQ (mean, 0-24): 7.7 vs. 8.0 vs. 8.3 at w 1, 5.2 vs. 5.4 vs. 5.3 at w 2, 3.2 vs. 3.5 vs. 3.3 at w 4, 2.4 vs. 2.6 vs. 2.4 at w 12 Patient Specific Functional Scale (mean, 0-10): 6.2 vs. 6.1 vs. 6.2 at w 1, 7.3 vs. 7.2 vs. 7.4 at w 2, 8.2 vs. 8.1 vs. 8.2 at w 4, 8.7 vs. 8.7 vs. 8.7 at w 12 Global change (mean, -5 to +5): 2.1 vs. 2.0 vs. 2.1 at w 1, 2.8 vs. 2.7 vs. 2.8 at w 2, 3.4 vs. 3.4 vs. 3.5 at w 4, 3.8 vs. 3.7 vs. 3.8 at w 12 Sleep quality "fairly bad" or "very bad": 28% (143/514) vs. 26% (129/501) vs. 26% (127/496) at w 1, 17% (85/508) vs. 18% (88/495) vs. 17% (85/497) at w 2, 12% (59/507) vs. 11% (57/500) vs. 10% (52/503) at w 4, 11% (54/506) vs. 11% (55/503) vs. 8.6% (44/514) at w 12 SF12 Physical score (mean, 0-100): 50 vs. 50 vs. 51 at w 4, 55 vs. 55 vs. 55 at w 12 SF12 Mental score (mean, 0-100): 44 vs. 44 vs. 44 at w 4, 46 vs. 46 vs. 45 at w 12 No differences in use of concomitant medications or health services or hours absent from work Days to recovery (median, days): 17 vs. 17 vs. 16 Satisfied with treatment: 76% (365/478) vs. 72% (342/472) vs. 73% (335/458)	A vs. B vs. C Serious adverse events: 1% (5/550) vs. 1% (4/546) vs. 1% (5/547)	National Health and Medical Research Council of Australia and GlaxoSmithKline	Good

Please see Appendix C. Included Studies for full study references.

Table E3. Data abstraction of systematic reviews of NSAIDs

Author, Year	Comparison	Databases Searched, Date of Last Search	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Roelofs, 2008	NSAIDs vs. placebo NSAID vs. NSAID NSAID vs. other active treatments	MEDLINE, EMBASE, Cochrane Library through 2007	65 trials (RCT and controlled clinical trials) NSAID vs. placebo (16 trials); NSAIDs vs. other medications (9 trials) or passive physical modalities (4 trials); NSAIDs vs. NSAIDs (33 trials); other studies included in other intervention sections (NSAIDs + SMR vs. NSAIDs, 3 trials; NSAIDs vs. acetaminophen, 7 trials); other studies outside the scope of this review (NSAIDs + B vitamins vs. NSAIDs alone, 3 trials) Acute low back pain (25 trials), chronic low back pain (9 trials) mixed or unclear low back pain population (31 trials)	A. NSAIDs (nonselective and selective) B. Other medications C. Other active interventions (i.e. passive physical modalities) D. Placebo Total n=11,237	Cochrane Back Review Group Criteria (2003)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Roelofs, 2008	Quantitative analysis of (weighted) mean difference used fixed effects model when possible; qualitative analysis for other outcomes	NSAIDs versus placebo, acute LBP: Pain: VAS (100 mm) ≤3 weeks: 4 studies, WMD -8.39, 95% CI -12.68 to -4.10 VAS (100 mm) from baseline: LBP without sciatica, 3 studies, WMD -7.69, 95% CI - 12.08 to -3.30 LBP with sciatica, 2 studies, WMD -0.16, 95% CI -11.92 to 11.59 Mixed population, 1 study, WMD -23.4, 95% CI -43.67 to -3.13 NSAIDs versus placebo, chronic LBP: Pain: VAS (100 mm) ≤12 weeks: 4 studies, WMD -12.40, 95% CI -15.53 to -9.26 COX-2 versus traditional NSAID, Acute LBP, VAS (100 mm): 3 studies, WMD -1.17, 95% CI -4.67 to 2.33 Chronic LBP, VAS (100 mm): 1 study, WMD 2.0, 95% CI -1.92 to 5.92	Proportion of patients experiencing side effects: NSAIDs versus placebo, acute LBP, followup ≤3 weeks: 10 studies, RR 1.35, 95% CI 1.09 to 1.68 NSAIDs versus placebo, chronic LBP, followup up ≤12 weeks: 4 studies, RR: 1.24, 95% CI 1.07 to 1.43 COX-2 versus traditional NSAID: Proportion of patients experiencing side effects: 4 studies, RR 0.83, 95% CI 0.70 to 0.99 Proportion of patients experiencing gastrointestinal side effects: 1 study, RR 0.88 95% CI 0.48 to 1.64	Good

Please see Appendix C. Included Studies for full study references.

Table E4. Data abstraction of randomized controlled trials of NSAIDs

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Herrmann, 2009	Germany Multicenter Outpatient	18-70 years, sciatica or lumbosciatica with onset within the last 72 hours with any previous attacks had to be resolved at least 3 months earlier.	Randomized: 171 Analyzed: 171 Attrition: 0	A: Lornoxicam 8mg tablets, with 16 mg loading dose on day 1, then 8mg after 8 hours; 8 mg twice per day on days 2-4; 8 mg on day 5 B: Diclofenac: 50 mg twice per day on days 1 and 5; 50mg three times per day on days 2-4. C: Placebo capsules in lornoxicam or diclofenac blister packs Day 5 treatment was optional	Mean age: 51.8 vs. 48.9 vs. 48.4 Gender, male: 56% vs. 53% vs. 58% Race, Caucasian: 91% vs. 93% vs. 98% Pain etiology: Sciatica or lumbosciatica	Acute pain, total duration of previous low back pain: 53.8 vs. 44.1 vs. 53.9 months
Majchrzycki, 2014	Poland Single center Outpatient clinic	40-60 years old, Pain lasting longer than 7 weeks, VAS1 and VAS2 scores ≥ 25mm of 100mm, no NSAID or strong analgesic therapy during the last 3 months	Randomized: 59 Analyzed: 54 Attrition: 5	A. Deep tissue massage + NSAID (n=26) B. Deep tissue massage (n=28)	Mean age: 50.8 vs. 52.6 Gender, female: 13/26 vs. 13/28 Race: NR Chronic pain: 100% Baseline pain: NR Baseline function: NR QOL: NR	Subacute duration, weeks: 11.9±3.9 vs. 10.8±2.4

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Herrmann, 2009	5 days	A vs. B vs. C Pain intensity difference, mm: 3 hours: -21.0 vs. -18.7 vs. -15.3, p≤0.05 for A vs. C 4 hours: -22.0 vs. -21.5 vs. -14.8, p≤0.05 for A vs. C 6 hours: -20.5 vs. -22.4 vs. -14.9, p≤0.05 for A vs. C 8 hours: -22.0 vs. -24.1 vs. -13.7, p≤0.05 for A vs. C Sum of time-weighted pain intensity difference, mm x minute: 0-4 hours: -4020 vs. -3879 vs. -2901, p≤0.05 for A vs. C 0-6 hours: -6486 vs. -6358 vs. -4713, p≤0.05 for A vs. C 0-8 hours: -9125 vs. -8833 vs. -6257, p≤0.05 for A vs. C Pain Relief (mm): 3 hours: 30.1 vs. 30.8 vs. 26.6 4 hours: 31.7 vs. 33.9 vs. 26.6 6 hours: 31.1 vs. 34.3 vs. 26.1 8 hours: 31.9 vs. 35.6 vs. 23.9, p≤0.05 for A vs. C Peak pain intensity difference, A vs. C: -27.9 mm vs. -19.9 mm, p=0.01 Time to peak pain intensity difference, A vs. C: 243 vs. 240 minutes, no difference Peak pain relief, A vs. C : 38.0 mm vs. 31.1 mm, p=0.05 Time to peak pain relief: no difference Start of peak pain relief: no difference End of peak pain relief: no difference Duration of peak pain relief: no difference	A vs. B vs. C Withdrawals: 4 vs. 2 vs. 1 Withdrawals due to AEs: 2 vs. 1 vs. 0 Serious AEs: 0 vs. 2 vs. 0 Nonserious AEs: 11 vs. 7 vs. 7	Nycomed Pharma Austria, Merckle GmbH Ulm, Germany	Fair
Majchrzycki, 2014	2 weeks	Difference scores, no significantly different results between groups on: Roland-Morris questionnaire: 21.2 vs. 16.1 Oswestry disability index: 24.7 vs. 19.6 VAS1: pain intensity during resting: 16.5 vs. 13.9 VAS2: pain intensity during motion: 3.2 vs. 3.4 VAS3: pain intensity during mobility of the aching area of the spine: 4.8 vs. 8.2	Withdrawals: 3 vs. 2 Withdrawals due to AEs: NR Serious AEs: NR Nonserious AEs: NR	Not reported	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Shirado, 2010	Japan Multicenter Orthopedic surgeon clinics	Age 20-64, nonspecific chronic low back pain of more than 3 months duration	Randomized: 201 Analyzed: 193 Attrition: 8	A: NSAIDs: loxoprofen sodium, 60 mg tablet 3 times daily; diclofenac sodium, 25 mg tablet 3 times daily; or zaltoprofen, 80 mg tablet 3 times daily B: Exercise: medical professionals at each clinic gave instruction of the exercise. 2 types of exercise: trunk strengthening and stretching. 2 sets of 10 repetitions of each exercise per day were encouraged.	Mean Age: 42.5 vs. 42.0 Female: 59% vs. 52% Race: NR Pain type: All chronic pain Baseline pain: VAS (0-10): 3.8 vs. 3.5 QOL scores: RDQ (0-24): 3.7 vs. 3.0 JLEQ score (0-120): 21.8 vs. 20.5	≥ Subacute duration, details not reported

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Shirado, 2010	12 months	Baseline to 8 week change ratio: Pain: VAS: -0.35 vs. -0.44, p=0.332 Function: Finger-floor distance: 0.00 vs. -0.09, p=0.112 RDQ: -0.47 vs. -0.72, p=0.023 JLEQ: -0.44 vs. -0.58, p=0.021	NR	No commercial sponsor	Good

Please see Appendix C. Included Studies for full study references.

Table E5. Study characteristics of systematic reviews of opioids

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies
Carson, 2011	1. Long acting opioids compared to each other 2. Long-acting opioids vs. short-acting opioids	MEDLINE, EMBASE, Cochrane library, reference lists for included studies	41 RCTs: 10 comparing long-acting with another long-acting; 3 were for low back pain. 27 trials comparing long-acting opioid to placebo; 4 for back pain 7 trials comparing long-acting vs. short-acting opioids; 5 for back pain	1. comparisons of long-acting opioids: total 1310 patients in trials for LBP 2. Comparisons of long vs. short acting opioids: 284 total patients in trials for LBP	USPSTF criteria	1. Qualitative summary

Author, Year	Results	Adverse Events	Number of Trials For Meta-analysis	Heterogeneity	Quality
Carson, 2011	1.insufficient evidence from 10 head-to-head trials to suggest that a long-acting opioid is superior to another in terms of efficacy in adult patients with chronic noncancer pain. 2. No useful indirect evidence for determining the comparative efficacy of long-acting opioids was found in 27 placebo-controlled trials. 3. In 7 fair-quality trials directly comparing a long-acting opioid to a short-acting opioid there was no good-quality evidence to suggest superior efficacy of long-acting opioids as a class over short-acting opioids.	1.Insufficent evidence from 10 head-to-head trials of long acting opioids that any drug safer than others. No trials adequately assessed addiction or abuse. There was insufficient evidence from 27 placebo-controlled trials to suggest that a long-acting opioid was superior in terms of adverse events to any other. 2.No convincing evidence from 7 randomized controlled trials to suggest lower adverse event rates with long-acting opioids as a class compared with short-acting opioids for all assessed adverse events. No data compared rates of addiction or abuse of long-acting and short-acting opioids.	No meta-analysis	Not formally assessed	Good, given quality of original studies

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies
Chaparro, 2014 Nalamachu, 2014	1. Strong opioids vs. placebo 2. Tramadol vs. placebo 3. Buprenorphine vs. placebo 4. Tramadol vs. celecoxib 5. Opioids vs. antidepressants	No language restriction MEDLINE, EMBASE, Cochrane Library, PsycINFO, CINAHL, all through October. 2012 Citation tracking of identified trials	≥ 50% of participants had chronic LBP, defined as ≥12 weeks Adults with or without leg pain Excluded intravenous or neuraxial administration; other routes included RCTs with blinded outcome assessment Outpatient treatment, opioid Rx ≥ 1 month Must have reported on pain, function, or global improvement	1. Strong opioids: 1154; Placebo: 733 2. Tramadol: 689; Placebo: 689 3. Buprenorphine: 312; Placebo: 341 4. Tramadol: 785; Celecoxib: 798 5. Opioids: 135; Antidepressants: 137	GRADE approach	Data pooled in meta-analysis, performed with both fixed-effect and random-effect models; more conservative result reported

Author, Year	Results	Adverse Events	Number of Trials For Meta-analysis	Heterogeneity	Quality
Chaparro, 2014 Nalamachu, 2014	1. Pain: moderate quality evidence that strong opioids are better than placebo; SMD 0.43 lower (95% CI 0.52 to 0.33); Function: Moderate quality evidence better than placebo in improving function (SMD 0.26 lower disability score (95% CI 0.37 to 0.15) 2. Pain: low quality evidence tramadol is better than placebo, SMD 0.55 lower, 95% CI 0.66 to 0.44 ; Function: Moderate evidence tramadol is better than placebo, SMD 0.18 lower (95% CI 0.29 to 0.07) 3. Pain: very low quality evidence that transdermal buprenorphine is better than placebo (MD 0.58 lower, 95%CI 0.61 to0.55; Function: very low quality evidence of no difference in function (MD 3 lower (95% CI 11.44 lower to 5.44 higher) 4. Pain: very low quality evidence that tramadol is better than celecoxib; RAD note: this seems to be a misprint; in fact, celecoxib appeared to be better than tramadol (at least 30% pain reduction: 63.7% with celecoxib; 52.5% with tramadol, OR 0.63 (95% CI 0.52, 0.77) 5. Pain: very low quality evidence that opioids and antidepressants do not differ (SMD 0.21, 95%CI -0.03 to 0.45); Function: very low quality evidence that that opioids and antidepressants do not differ (SMD -0.11, 95% CI -0.63 to 0.42) Post-hoc analysis: Overall: Pain NRS: A. Worse by 0.4 points, B: Worse by 1.2 points in placebo group, p<0.001 30% improvement in pain: A. 60.6%, B. 42.9% 50% improvement in pain: A. 42.4%, B. 24.1% Roland: at 12 weeks, 1 point better in group A, p<0.005 In comparing non-neuropathic to neuropathic, changes in pain score and Roland and global self-assessments were very similar	For strong opioids: Somnolence: 2.5% placebo; 8.6% opioids Nausea: 10.2% placebo; 22.3% opioids; Constipation: 3.6% placebo; 14.8% opioids, all statistically significant Post-hoc analysis: Overall: Withdrawals in double-blind phase: : 50.7%, Placebo: 67.2%, p<.01 Withdrawals due to AE: A: 5.2%; B: 2.2% Any AE in double-blind phase: A: 54.5%, B: 47.8% Serious AEs: A: 6 patients; Placebo: 4 patients AEs very similar for neuropathic and non-neuropathic subgroups.	1. 7 RCTs 2. 5 RCTs 3. 2 RCTs for pain; one for function 4. Only 1 RCT, no meta-analysis 5. 2 RCTs	1. $I^{2=}$0% for both pain and function 2. $I^{2=}$86% for pain, 0% for function 3. I^2 =99% for pain 4. Only 1 trial 5. I^2 for pain, 0%; only 1 trial for function	Good

Please see Appendix C. Included Studies for full study references.

Table E6. Data abstraction of randomized controlled trials of opioids

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Outcome Measures
Cloutier, 2013	Canada; 10 centers; setting unclear	Age>18 Back pain intensity ≥2 on a 0-4 scale (moderate or severe) Currently taking opioids Low back pain ≥3 mos. Must undergo 2-7 day washout of pre-study opioids Exclusions: psychological dependence on opioids or alcohol; major psychiatric disorder; litigation	Randomized: 83 Analyzed: 54 for per-protocol analysis (completed at least 2 weeks each of active therapy and placebo) Attrition: 29 (35%) The intention-to-treat analysis included all 83, who had at least one dose of medication and at least one post-randomization data point.	A. Oxycodone/ Naloxone, both controlled release, titrated dose of 10mg/5mg q 12h up to 40mg/20mg q 12 h B. placebo Crossover design: 4 weeks of each intervention	Due to crossover design, all patients received both A and B. Among the 54 analyzed: women=50% Mean age=50.6 Caucasian: 94.4% Baseline score on Pain and Disability Index was 42 on a 0-70 scale (70 worst) Among the full 83 enrolled, 39 men, 44 women; mean age 51.3; 91.6% Caucasian	Subacute or chronic	Pain ordinal scale, 0-4 (0=none, 4=excruciating); Pain VAS - 100mm; Pain & Sleep Questionnaire: each item on a 0-100 VAS; Pain Disability Index: overall score 0-70, with 70 worst; Quebec Back Pain Disability Questionnaire: 20 items on 0-5 ordinal scale; Bowel Function Index: 3 items on numerical analog scale, 0-100; General Health status scale from SF-36; Effectiveness of Treatment on 4-point scale; Global Impression of change on 7-point scale

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Cloutier, 2013	4 weeks each on active therapy and placebo	Intention-to-Treat Analysis (n=83): Pain VAS: A. 52.2 mm (SD 23.0; B: 57.8 mm (SD 24.2) (p=0.053) Ordinal pain score: A: 2.3 (SD 0.8); B: 2.5 (SD 0.9), (p=0.086) No other results for ITT analysis Per protocol analysis: Pain VAS: A. 48.6 mm (SD 23.1); B: 55.9 mm (SD 25.4) (p=0.03) Ordinal pain score: A: 2.1 (SD 0.8); B: 2.4 (SD 0.9), (p=0.042) Pain Disability Index: A: 34.3 (SD 15.6); B:37.5 (SD 15.2), p=0.051; SF-36 General Health: "no difference" Quebec Back Pain Disability: "no difference"	Withdrawals: 9 dropouts during active treatment; 11 during placebo treatment; Withdrawals due to AEs: 6 on active therapy, 5 on placebo Bowel Function Index and use of rescue laxatives: no significant differences Overall count of AEs: A. 48, B: 40, p=0.068 Serious AEs: 2 in each group; all judged not related to study meds. Somnolence: A: 5.4%; B: 0.0%, p=0.04 Other AEs (nausea, constipation, fatigue, vomiting, dizziness, abdominal pain): no significant differences	Purdue Pharma	Good	Main intent of oral naloxone was to reduce constipation side effects; there is very low systemic bioavailability due to first-pass metabolism by liver.

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Outcome Measures
Hyup Lee, 2013	15 centers South Korea	Age 25-75 years, able to walk, with moderate to severe LBP with average intensity ≥4 and duration ≥3 months requiring analgesics Exclude: recent back surgery or steroid injection, more severe pain in an area other than the back, or comorbid conditions that may interfere with assessment	248 randomized 196 completed (21% attrition)	A. Extended-release tramadol HCl 75 mg/acetaminophen 650 mg fixed-combination tablet (n=125) Max dose=4 tabs/d=300 mg tramadol B. Placebo (n=120)	A vs. B Mean age: 59.9 vs. 60.4 years Female sex: 75% vs. 74% Race: NR	Subacute or chronic	10-cm VAS, SF-36, ODI

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Hyup Lee, 2013	29 days	A vs. B Pain intensity change ≥30%, full analysis set: 57.7% (49/85) vs. 41.1% (37/90); p=0.037 Pain intensity change ≥30%, per protocol: 63% (46/73) vs. 44.9% (35/78); p=0.027 Pain intensity change ≥50%, full analysis set: 31.8% vs. 20.0%; p=0.075 Pain intensity change ≥50%, per protocol: 34.3% vs. 21.8%; p=0.088 Korean SF-36: patients in the intervention group had significant improvements in role-physical, general health, and reported health transition domains, and a tendency (p=0.052) toward improvement in vitality Korean ODI: patients in the intervention group had significant functional improvement in the personal care section (p=0.045) and a tendency (p=0.053) toward improvement in total ODI scores	A vs. B Any adverse event: 83.2% (104/125) vs. 54.2% (65/120); RR 1.54 (95% CI 1.28 to 1.84) Withdrawal due to adverse event: 19.2% (24/125) vs. 5.0% (6/120); RR 3.31 (95% CI 1.40 to 7.83)	Janssen Korea, Ltd.	Good	Also available: patient-reported efficacy, investigator-reported pain improvement, all subscores of SF-36 (Table 2) and ODI (Table 3), specific AEs

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Outcome Measures
Rauck, 2014	59 centers United States	Males and non-pregnant, non-lactating females age 18-75 years, with moderate-to-severe chronic LBP for ≥3 months, average pain score ≥4 Exclude: history of opioid or alcohol or illicit drug abuse in previous 5 years, history of intolerance to hydrocodone or acetaminophen N-acetyl-para-aminophenol, comorbid conditions that could interfere with pain assessment, uncontrolled blood pressure, BMI >45, or depression	302 randomized 183 completed (39% attrition)	A. Extended-release hydrocodone in 10-, 20-, 30-, 40-, and 50-mg capsules (n=151) Mean dose=119 mg/d Max dose=200 mg/d B. Placebo (n=151)	A vs. B Mean age: 50.4 vs. 50.8 years Female sex: 62% vs. 49%; p=0.028 Race: 82% White, 17% Black, 1% other vs. 80% White, 17% Black, 4% other Mean pre-study opioid usage: 76.8 vs. 79.2 mg/day MED Mean pain score before titration (NRS): 6.9 vs. 6.9 Mean pain score after titration (NRS): 3.1 vs. 3.1	Chronic	10-point NRS

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Rauck, 2014	12 weeks	A vs. B Change from baseline in mean daily pain intensity score: 0.48 vs. 0.96; p=0.008	A vs. B Withdrawal due to adverse event: 1.3% (2/151) vs. 3.3% (5/151); RR 0.40 (95% CI 0.08 to 2.03)	Zogenix, Inc.	Poor	Dosages, specific AEs EERW design

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Outcome Measures
Schiphorst Preuper, 2014	2 centers The Netherlands	Age ≥18 years, with chronic LBP lasting >3 months, a VAS score ≥4 Exclude: hypertension, mental or physical conditions leading to reduced functioning	50 randomized 43 completed (14% attrition)	A. tramadol 37.5 mg/acetaminophen 325 mg fixed-combination capsule (n=25) Max dose tramadol=225 mg/d B. Placebo (n=25)	A vs. B Mean age: 42 vs. 44 years Female sex: 72% vs. 64% Race: NR Mean duration of pain: 18 vs. 24 months Mean pain score (VAS): 6.1 vs. 4.7	Chronic	Lifting, carrying, and bending; 10-cm VAS; RDQ; global pain assessment

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Schiphorst Preuper, 2014	2 weeks	A vs. B Lifting (kg), baseline-followup: 18-19 vs. 20-17 kg; change 1 vs. -3 kg Carrying (kg), baseline-followup: 24-20 vs. 24-21 kg; change -4 vs. -3 Static bending (s), baseline-followup: 119-143 vs. 158-192.5; change 24 vs. 34.5 s Dynamic bending (s/rep), baseline-followup: 2.7-2.8 vs. 2.7-3.0; change 0.1 vs. 0.3 Roland Morris Disability Questionnaire (0-24), baseline-followup: 13.0-11.5 vs. 13.0-13.0; change -1.5 vs. 0 VAS current pain, baseline-followup: 6.1-5.1 vs. 4.7-4.5; change -1 vs. -0.2 VAS, maximum pain, baseline-followup: 7.3-7.4 vs. 7.1-7.7; change 0.1 vs. 0.6 VAS, minimum pain, baseline-followup: 4.4-3.8 vs. 2.0-2.6; change -0.6 vs. 0.6 Pain relief: 42% (10/24) vs. 4% (1/25); RR 10.42 (95% CI 1.44 to 75.29) Same pain or worsened: 58% (14/24) vs. 96% (24/25); RR 0.61 (95% CI 0.43 to 0.86)	A vs. B Withdrawal due to adverse event: 8% (2/25) vs. 0% (0/25)	Grunenthal BV and Stichting Beatrixoord	Fair	

Please see Appendix C. Included Studies for full study references.

Table E7. Data abstraction of randomized controlled trials of SMRs

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Pareek, 2009	India Multicenter	Age 18-70 with acute low back pain and VAS score ≥6 at baseline (scale 0-10) Excluded: sciatica or other underlying spinal disorder, malignancy, osteoporosis	Randomized: 197 Analyzed: 185 Attrition: 6% (12/197)	A. Tizanidine 2 mg + aceclofenac 100 mg bid for 7 days (n=101) B. Aceclofenac 100 mg bid for 7 days (n=96)	A vs. B Mean age 62 vs. 58 years 39% vs. 40% female Race not reported Baseline pain, function not reported	Acute/subacute; mean duration not reported but inclusion criteria required <30 days pain	7 days
Ralph, 2008	United States Multicenter	Age 18-65 years with moderate to severe acute low back pain ≤3 days Excluded: duration >3 days, sciatica, history of spinal pathology, neurologic symptoms, chronic low back pain, osteoporosis	Randomized: 562 Analyzed: 547 for efficacy, 561 for safety Attrition: efficacy 3% (15/547); safety 0.2% (1/561)	A. Carisoprodol 250 mg QID for 7 days (n=277) B. Placebo QID for 7 days (n=285	A vs. B Mean age 39 vs. 42 years 49% vs. 55% female Race: 74% vs. 77% Caucasian; 15% vs. 12% African; 10% vs. 10% Asian; 0.7% vs. 0.4% Native American; 0.4% vs. 0.4% other Baseline pain severity: mild 0.4% vs. 0.4%; moderate 74% vs. 74%; severe 25% vs. 26% Baseline RDQ 10 vs. 10	Acute; mean duration 2 vs. 2 days	7 days

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Pareek, 2009	A vs. B Pain at rest, mean change from baseline day 3: -3.01 vs. -1.90, p=0.0001; day 7 -5.88 vs. -4.35, p=0.0001 Pain with movement, mean change from baseline day 3: -2.94 vs. -1.81, p=0.0001; day 7 -6.09 vs. -3.98, p=0.0001 Global improvement, proportion of patients reporting good or excellent response: 75% (71/94) vs. 34% (31/94); RR 1.28 (95% CI 1.07 to 1.52)	A vs. B No serious adverse events in either group Vomiting: 5% (5/101) vs. 7% (7/96); RR 0.68 (95% CI 0.22 to 2.07) Dizziness: 5% (5/101) vs. 4% (4/96); RR 1.19 (95% CI 0.33 to 4.29)	Ipca Laboratories	Fair
Ralph, 2008	A vs. B Pain, patient-rated impression of pain relief, mean change from baseline day 3 (scale 0-4; higher score = greater pain relief): 1.8 vs. 1.1, p<0.0001; day 7 between-group difference p<0.0001 (data not shown) Global improvement, patient-rated impression of change, mean change from baseline at day 3 (scale 0-4; higher score = greater improvement); 2.3 vs. 1.7, p<0.0001; day 7 between-group difference p<0.0001 (data not shown)	A vs. B No serious adverse events in either group Withdrawals due to adverse events: 3% (8/277) vs. 2% (5/284); RR 1.64 (95% CI 0.54 to 4.95) Drowsiness: 13% (37/277) vs. 5% (13/284); RR 2.92 (95% CI 1.59 to 5.37) Dizziness: 10% (27/277) vs. 3% (9/284); RR 3.08 (95% CI 1.47 to 6.42) Headache: 4% (10/277) vs. 1% (4/284); RR 2.56 (95% CI 0.81 to 8.08)	MedPointe Pharmaceuticals	Fair

Please see Appendix C. Included Studies for full study references.

Table E8. Data abstraction of randomized controlled trials of benzodiazepines

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Brotz, 2010	Germany Single center	18 to 75 years of age, sciatica with or without neurological deficit due to lumbar disc prolapse, CT or MRI confirmation of lumbar disc prolapse, pain centralization within the first physical therapy session Exclude: bladder or bowel disturbance, acute (<24 h) development of paresis grade 1 or plegia; benzodiazepine in last 2 weeks, benzodiazepine intolerance, prior disc prolapse surgery, prior trauma to the vertebral column	Randomized: 60 (30 vs. 30) Analyzed: 60 Attrition: Reports none	A: Diazepam: 5 mg po bid x 5 d, then tapered (tapering regimen not specified) (n=30) B: Placebo (n=30)	Mean age: 43 vs. 42 years Female: 37% vs. 50% Race: Not reported Baseline pain (median, 0-10 VAS): 8 vs. 8 Baseline RDQ (median, 0-24): 14 vs. 14	Duration not specified, 93% <90 days

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Brotz, 2010	1 year (treatment 5 days)	A vs. B Duration of inability to work (median, days): 26 vs. 15 (p=0.73) RDQ (median improvement, 0-24): 3.0 vs. 5.0 at 1 w (p=0.67) RDQ (median, 0-24): 2 vs. 1 at 1 y Diclofenac consumption (median, mg): 750 vs. 750 at 1 w (p=0.78) Pain improved ≥50%: 41% (12/29) vs. 79% (23/29) at 1 w, RR 0.5 (95% CI 0.3 to 0.8); Sensory loss improved: 83% (15/18) vs. 86% (19/22) at 1 w, RR 1.0 (95% 0.7 to 1.3) Sensory loss: 43% (9/21) vs. 44% (10/23) at 1 y Reduction of paresis: 22% (6/27) vs. 28% (8/28) at 1 w, RR 0.8 (95% CI 0.3 to 2.0) Paresis: 14% (3/21) vs. 13% (3/23) at 1 y Inability to work beyond d 28: 55% (16/29) vs. 41% (12/29) at 1 w, RR 1.3 (95% CI 0.7 to 2.2) Request for additional analgesics: 51% (15/29) vs. 41% (12/29) at 1 w, RR 1.3 (95% CI 0.7 to 2.3) Underwent surgery: 7 vs. 6 at 6 w, 8 vs. 7 at 1 y	Not reported	University of Tubingen	Good

Please see Appendix C. Included Studies for full study references.

antidepressants

Table E9. Dat abstraction of systematic reviews of antidepressants for low back pain

Author, Year	Comparison	Databases Searched, Date of Last Search	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Urquhart, 2010	Antidepressant vs. placebo	MEDLINE, EMBASE, PsycINFO and CCRCT through November 2008	10 RCTs; 9 trials conducted in pts with chronic low back pain; 1 trial duration of low back pain not reported. Duration of followup 10 days to 12 weeks.	A. Antidepressants (n=315): paroxetine (3 studies); desipramine (3 studies); imipramine (2 studies); maprotiline (2 studies); fluoxetine (2 studies); bupropion, trazodone, amitriptyline, nortriptyline and clomipramine IV (1 study each) B. Placebo (n=252)	Cochrane Back Review Group criteria (2003)

antidepressants

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Urquhart, 2010	Random effects model assessing standardized mean differences (SMD)	A vs. B Pain (9 studies): SMD -0.04 (95% CI -0.25 to 0.17; I^2=0%) -Pain, SSRIs (3 studies): SMD 0.11 (95% CI -0.17 to 0.39; I^2=0%) -Pain, tricyclic antidepressants (4 studies): SMD -0.10 (95% CI -0.51 to 0.31; I^2-32%) Depression (2 studies): SMD 0.06 (95% CI -0.29 to 0.40) Functional status (2 studies): SMD -0.06 (95% CI -0.40 to 0.29)	Not reported	Good

Please see Appendix C. Included Studies for full study references.

Table E10. Data abstraction of randomized controlled trials of antidepressants

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Farajirad, 2013	Iran Single-center	Outpatient neurosurgery clinic patients age 18 to 70 years with chronic low back pain	Randomized: 60 Analyzed: unclear Attrition: unclear	A. Amitriptyline 25 mg/day titrated to 150 mg/day (maximum) by week 2 (n=NR) B. Sustained-release bupropion 150 mg/day titrated to 300 mg/day by week 2 (n=NR)	A vs. B Mean age 37 vs. 34 years No other demographic or clinical characteristics reported	Chronic; mean duration not reported	8 weeks
Mazza, 2010	Italy Number of centers not reported	Adults with low back pain (with or without sciatica) for ≤6 months Excluded: prior back surgery, regular use of antidepressants or diagnosis of depression	Randomized: 85 Analyzed: 80 Attrition: 6% (5/85)	A. Escitalopram 20 mg/day (n=41) B. Duloxetine 60 mg/day (n=44)	A vs. B Mean age 52 vs. 54 years 56% vs. 57% female Pain, mean VAS (scale 0-10) 6.3 vs. 6.4 Function, mean Clinical Global Impressions of Severity Scale (CGI-S) score (scale 0-10) 3.6 vs. 3.5	Chronic; mean duration A vs. B: 12.3 vs.13.4 years	13 weeks

Author, Year	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Farajirad, 2013	A vs. B No data shown Pain: No significant difference between groups	A vs. B Any adverse event (no details provided): 43% vs. 30%; p=0.3	Not reported	Poor	
Mazza, 2010	A vs. B Pain, VAS mean change from baseline: -2.3 vs. -2.45; p=0.74 Quality of life, mean change SF-36 subscales: no significant difference between groups for any subscale -Bodily pain: 1.94 vs. 1.99 -General health: 1.22 vs. 1.13 -Mental health: 0.99 vs. 0.87 -Physical function: 2.11 vs. 2.54 -Emotional role: 0.80 vs. 0.76 -Physical role: 0.54 vs. 0.58 -Social function: 0.06 vs. 0.05 -Vitality: 0.14 vs. 0.12 Global improvement, CGI-S mean change from baseline: -0.92 vs. -0.69; p=0.21	A vs. B No mortality and no serious adverse events in any group Nausea: 5% (2/39) vs. 7% (3/41); p=0.69 Dry mouth: 10% (4/39) vs. 10% (4/41); p=0.94 Headache: 3% (1/39) vs. 5% (2/41); p=0.59 Constipation: 3% (1/39) vs. 2% (1/41); p=0.97 Dizziness: 5% (2/39) vs. 2% (1/41); p=0.54 Decreased appetite: 3% (1/39) vs. 2% (1/41); p=0.97 Insomnia: 8% (3/39) vs. 7% (3/41); p=0.95	No external funding	Fair	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Skljarevski, 2009	United States Number of centers not reported	Adults with chronic low back pain (duration ≥6 months) with or without sciatica and mean pain scores ≥4 Excluded: radicular compression, spinal stenosis, spondylolisthesis grade 3-4, back surgery within 12 months of study, invasive treatment of low back pain within 1 month of study	Randomized: 404 Analyzed: 404 Attrition: 0%	A. Duloxetine 20 mg/day (n=59) B. Duloxetine 60 mg/day (n=116) C. Duloxetine 120 mg/day (n=112) D. Placebo (n=117)	A vs. B vs. C vs. D Mean age 53 vs. 53 vs. 55 vs. 54 years 61% vs. 58% vs. 58% vs. 55% female Race: 78% vs. 78% vs. 82% vs. 80% white; 22% vs. 22% vs. 18% vs. 20% other Pain, mean BPI 6.4 vs. 6.2 vs. 6.1 vs. 6.2 Global health assessment, mean CGI-S score 4.1 vs. 3.5 vs. 3.6 vs. 3.7	Chronic; mean duration A vs. B vs. C vs. D: 12.5 vs. 10.5 vs. 13.9 vs. 10.3 years	13 weeks

Author, Year	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Skljarevski, 2009	A vs. B vs. C vs. D Pain, weekly average (0-10 scale) mean change from baseline: -1.77 vs. -2.46 vs. -2.40 vs. -2.10; no significant differences between groups Pain, Brief Pain Inventory - Severity scale average pain mean change from baseline: -1.79 vs. -2.50 vs. -2.45 vs. -1.87; B vs. D: p<0.05 Function, Brief Pain Inventory - Interference scale, average interference mean change from baseline: -1.84 vs. -2.40 vs. -1.92 vs. -1.61; B vs. D: p<0.05 Quality of life, mean change SF-36 subscales: -Bodily pain: 1.51 vs. .1.95 vs. 2.11 vs. 1.36; B vs. D, C vs. D: p<0.05 No significant difference between groups for other subscales (general health, mental health, physical functioning, emotional role, physical role, social functioning, vitality) Quality of life, EuroQoL (EQ) 5D U.S. Index score mean change from baseline: 0.04 vs. 0.07 vs. 0.08 vs. 0.05; no significant differences between groups Global improvement, CGI-S mean change from baseline: -0.53 vs. -0.94 vs. -1.06 vs. -0.53; B vs. D, C vs. D: p<0.05	A vs. B vs. C vs. D No mortality in any group Serious adverse events: 1.7% (1/59) vs. 0.8% (1/116) vs. 2.7% (3/112) vs. 2.6% (3/117); no significant differences between groups Withdrawals due to adverse events: 15% (9/59) vs. 15% (17/116) vs. 24% (27/112) vs. 9% (10/117); C vs. D p<0.05 ≥1 adverse events: 64.4% (38/59) vs. 67.2% (78/116) vs. 72.3% (81/112) vs. 59.0% (69/117); C vs. D: p=0.04 Nausea, insomnia, dry mouth, constipation, somnolence and fatigue all significantly more likely with duloxetine use vs. placebo (p<0.05)	Eli Lilly	Good	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Skljarevski, 2010 Journal of Pain	Germany, Netherlands, Poland, Russia, Spain, United States Multicenter	Age ≥18 years with chronic low back pain duration ≥6 months and BPI ≥4 Excluded: radicular compression, spinal stenosis, spondylolisthesis grade 3-4, back surgery within 12 months of study, invasive treatment of low back pain within 1 month of study, previous participation in duloxetine study, major depressive disorder or other psychiatric disorder	Randomized: 401 Analyzed: 394 Attrition: 1.7% (7/401)	A. Duloxetine 60 mg/day (n=198) B. Placebo (n=203)	A vs. B Mean age 55 vs. 53 years 60% vs. 63% female Race: 96% vs. 95% white, 3% vs. 3% African, 2% vs. 3% other Pain, mean BPI 5.8 vs. 5.8 Function, mean RDQ 9.6 vs. 9.3 Global health assessment, mean CGI-S 3.5 vs. 3.3	Chronic; mean duration A vs. B 8.3 vs. 8.7 years	12 weeks

Author, Year	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Skljarevski, 2010 Journal of Pain	A vs. B Pain, BPI - Severity scale average pain mean change from baseline: -2.25 vs. -1.65; p=0.002 Pain, BPI 24-hour Average Pain Score, proportion of patients with 30% improvement in score: 57% (111/195) vs. 49% (97/199); p=0.11; 50% improvement in score: 49% (95/195) vs. 35% (69/199); p=0.005 Function, Brief Pain Inventory - Interference scale, average interference mean change from baseline: -2.01 vs. -1.43; p≤0.001 Function, RDQ mean change from baseline: -2.69 vs. -2.22; p=0.26 Quality of life, Profile of Mood states total mood disturbance mean change from baseline: -6.77 vs. -2.77; p≤0.001 Global improvement, CGI-S mean change from baseline: -0.95 vs. -0.79; p=0.08 Global improvement, Patients' Global Impressions score, mean change from baseline: 2.88 vs. 3.19; p=0.01	A vs. B No mortality in either group Serious adverse events: 3% (5/198) vs. 0% (0/203); p=0.25 Withdrawals due to adverse events: 15% (30/198) vs. 5% (11/203); p=0.002 Specific adverse events more likely to occur in duloxetine group: nausea (p<0.001), dry mouth (p=0.03), somnolence (p=0.34); no difference for headache, constipation, dizziness	Eli Lilly	Fair	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Skljarevski, 2010 Spine	Brazil, France, Germany, Mexico, The Netherlands Multicenter	Age ≥18 years with chronic low back pain duration ≥6 months and BPI ≥4 Excluded: radicular compression, spinal stenosis, spondylolisthesis grade 3-4, back surgery within 12 months of study, invasive treatment of low back pain within 1 month of study, previous participation in duloxetine study, major depressive disorder or other psychiatric disorder	Randomized: 236 Analyzed: 225 Attrition: 5% (11/236)	A. Duloxetine 60 mg/day; titrated to 120 mg/day in nonresponders after week 7 (n=115) B. Placebo; sham titration in nonresponders after week 7 (n=121)	A vs. B Mean age 52 vs. 51 years 62% vs. 60% female Race: 74% vs. 75% white, 20% vs. 17% Hispanic, 6% vs. 7% other Pain, mean BPI 5.9 vs. 6.0 Global health assessment, mean CGI-S 3.2 vs. 3.2	Chronic; mean duration 8.8 vs. 9.5 years	13 weeks

Author, Year	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Skljarevski, 2010 Spine	A vs. B Pain, BPI - Severity scale average worst pain mean change from baseline: -2.66 vs. -1.90; p<0.05 Pain, BPI 24-hour Average Pain Score mean change from baseline: -2.08 vs. -1.30; p≤0.01 Function, Brief Pain Inventory - Interference scale, average interference mean change from baseline: -1.92 vs. -1.18; p ≤0.01 Quality of life, Athens Insomnia Scale mean change from baseline: -2.07 vs. -1.49; p=0.38 Quality of life, SF-36 mean between group difference significant for bodily pain (p=0.04), general health (p=0.04) and vitality (p=0.04) subscales favoring duloxetine; no difference for other subscales (data not shown) Return to work, mean between-group difference significant for WPAI work activity impairment subscale (p=0.002) favoring duloxetine; no difference for other subscales (data not shown) Global improvement, CGI-S mean change from baseline: -0.98 vs. -0.77; p=0.14	A vs. B No mortality in either group Serious adverse events: 4% (4/115) vs. 0.8% (1/121); p=0.20 Withdrawals due to adverse events: 14% (16/115) vs. 6% (7/121); p=0.04 Any treatment-emergent adverse event: 57% (65/115) vs. 48% (58/121); p=0.19 Specific adverse events more likely to occur in duloxetine group: nausea (p=0.009), fatigue (p=0.02), hyperhidrosis (p=0.006); specific adverse events more likely to occur in placebo group: headache (p=0.04); no significant difference between groups in incidence of dry mouth, diarrhea, dizziness or constipation	Eli Lilly	Fair	

Please see Appendix C. Included Studies for full study references.

Table E11. Data abstraction of randomized controlled trials of antiseizure medications

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Baron, 2010	USA, Canada, and Europe Multicenter	≥18 years of age, pain consistent with chronic lumbosacral radiculopathy due to spinal stenosis, leg pain greater than back pain, pain present ≥3 months, stable for ≥4 weeks, mean weekly pain score >4; placebo nonresponder and pregabalin responder (including ≥30% improvement in pain) in run-in period Exclude: Radicular pain for >4 years, surgery for lumbosacral radiculopathy in last 6 months, more than one previous spinal surgery for L5-S1 pain/radiculopathy, epidural injection in last 6 weeks	Randomized: 218 (111 vs. 107) of 378 in run-in period Analyzed: 211 (110 vs. 108) Attrition: 14% (31/218)	Placebo run-in period for 7 days, then pregabalin run-in for 28 days, then: A: Pregabalin: Optimal dose from run-in period (mean 410 mg) x 5 w, then 1 w taper (n=110) B: Placebo: Pregabalin taper x 1 w, then placebo x 4 w, then taper x 1 w (n=108)	Mean age: 52 vs. 53 years Female: 49% vs. 55% Race: Not reported Baseline pain (mean, 0-10 VAS): 6.36 vs. 6.39 Baseline function: Not reported	Chronic (≥3 months); mean duration not reported

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Baron, 2010	5 weeks (at end of therapy)	A vs. B Pain (mean change from baseline, 0-10 VAS): -0.16 vs. 0.05 (p=0.33) Pain ≥7/10 (days): 7.1% (8/108) vs. 6.4% (7/107) at 5 w Loss of response (≥1 point increase in weekly mean pain score or use of rescue medication): 27.8% vs. 28.0% at 5 w, HR 0.87 (95% CI 0.52 to 1.47) Medical Outcome Study Sleep Scale sleep disturbance (mean change, 0-100): 2.26 vs. 6.86 (p=0.03) Medical Outcome Study Sleep Scale sleep quantity (mean change, hours): 0 vs. -0.43 (p=0.004) No differences on other MOS Sleep Scale subscales HADS anxiety (mean change, 0-21): -0.19 vs. 0.82 at 5 w (p=0.01) HADS depression (mean change, 0-21): -0.57 vs. 0.56 at 5 w (p=0.0006) EQ-5D, RDQ: No differences, data not reported	A vs. B Any adverse event: 40.9% (45/110) vs. 42.1% (45/107) Serious adverse event: 1.8% (2/110) vs. 0% (0/107) Dizziness: 3.6% (4/110) vs. 1.9% (2/107) Somnolence: 0.9% (1/110) vs. 0.9% (1/107) Edema: 4.5% (5/110) vs. 1.9% (2/107)	Pfizer Inc.	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Baron, 2014	Europe Multicenter	≥18 years of age, chronic (≥3 months) low back pain requiring a WHO step III analgesic (baseline pain thresholds specified for persons on step I or 2 analgesics), painDETECT score for neuropathic pain ≥13 (0 to 38 scale), tapentadol responder during run-in period Exclude: Pregnant, breastfeeding, back pain due to cancer, painful procedure planned, other pain condition, comorbid conditions, alcohol or drug abuse, allergy or sensitivity to study drugs	Randomized: 313 (159 vs. 154) of 313 in run-in period Analyzed: 309 (157 vs. 152) Attrition: 17% (56/313)	Washout for 3-14 days, then tapentadol PR run-in for 3 weeks, then: A: Pregabalin + tapentadol PR: Pregabalin 150 mg/day x 1 w, 300 mg/day x 7 w + tapentadol PR 300 mg/day (n=157) B: Tapentadol PR: Tapentadol 300 mg/day + 100 mg/day x 1 w, tapentadol 300 mg/day + 200 mg/day x 7 w (n=152)	Mean age: 56 vs. 58 years Female: 54% vs. 62% White: 99% vs. 100% Baseline pain: 5.9 vs. 5.9 (at randomization) Baseline function: Not reported	Chronic (≥ 3 months): mean 8.7 vs. 9.4 years
Kalita, 2014	India Single center	15 to 65 years of age, low back pain >3 months Exclude: Chronic low back pain due to a specific cause, immunosuppressant therapy, anticancer drugs, post-transplant, post-spinal surgery, pregnant or breastfeeding, severe neurological deficit due to radiculopathy or spinal stenosis	Randomized: 200 (97 vs, 193) Analyzed: 200 Attrition: 26% (53/200)	A: Pregabalin: 75 mg bid x 2 w, 150 mg bid x 2 w, 300 mg bid, then increased if tolerated and needed (mean dose ~430 mg/day) (n=97) B: Amitriptyline: 12.5 QHS x 2 w, 25 mg QHS x 4 w, then 50 mg QHS, then increased if tolerated and needed (mean dose 38 mg/day) (n=103)	Mean age: 42 vs. 42 years Sex: Not reported Race: Not reported Baseline pain: 6.7 vs. 6.7 Baseline ODI: 42 vs. 42 Radiculopathy: 47% Spinal stenosis: 6%	Chronic (≥ 3 months): mean 36 vs. 35 years

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Baron, 2014	9-10 weeks (1-2 weeks after end of therapy)	A vs. B Pain (mean change from baseline, 0-10 VAS): -1.6 vs. -1.7 at 9-10 w (p>0.05) Leg pain (mean change from baseline, 0-10 VAS): -1.6 vs. -1.9 at 9-10 w Patient satisfaction good, very good, or excellent: 73% (114/157) vs. 67% (102/152) at 9-10 w "Minimally", "much", or "very much" improved: 82% (129/157) vs. 81% (123/152) at 9-10 w SF-12: No difference on any subscale at 9-10 w EQ-5D (mean, 0-10): 0.60 vs. 0.61 at 9-10 w HADS anxiety (mean): 5.8 vs. 6.0 at 9-10 w HADS depression (mean): 5.4 vs. 6.2 at 9-10 w	A vs. B Any adverse events: 65% (103/159) vs. 64% (98/154) Discontinued due to adverse events: 7.5% (12/158) vs. 7.8% (12/154) Dizziness: 17.6% vs. 11.0% Somnolence: 11.9% vs. 8.4% Nausea: 9.4% vs. 10.4% Headache: 8.2% vs. 6.5% Constipation: 5.0% vs. 7.1% Dry mouth: 5.0% vs. 3.9%	Grunenthal GmbH	Fair
Kalita, 2014	14 weeks (at end of therapy)	A vs. B Pain (mean, 0-10 VAS): 6.7 vs. 6.7 at baseline, 4.2 vs. 3.9 at 4 w, 3.8 vs. 2.8 at 16 w (estimated from graph; p>0.05 at all time points) ODI (mean, 0-100): 42 vs. 42 at baseline, 30 vs. 26 at 4 w, 22 vs. 17 at 16 w (estimated from graph; p>0.05 at all time points) Pain improved by >=50%: 39% (38/97) vs. 57% (59/103), RR 0.68 (95% CI 0.51 to 0.92) ODI improved >20%: 50% (48/97) vs. 65% (67/103), RR 0.76 (955 CI 0.59 to 0.97) Findings for dichotomous outcomes similar for patients with non-radicular back pain and radiculopathy; with or without neurological deficit	A vs. B Any adverse event: 22% (29/97) vs. 17% (18/103) Sedation: 4.1% (4/97) vs. 9.7% (10/103) Unsteadiness: 0% (0/97) vs. 1.9% (2/103) Dry mouth: 1.0% (1/97) vs. 2.9% (3/103) Vertigo: 6.2% (6/97) vs. 1.9% (2/103)	Reports no funding	Poor

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Markman, 2014	USA Single center	≥50 years of age, radiographically confirmed lumbar spinal stenosis with neurogenic claudication for ≥3 months (inducible pain ≥4/10 within 15 minutes of treadmill ambulation) Exclude: Previous pregabalin, prior surgery for lumbar spinal stenosis, vascular disease, movement disorder, neurologic disease impacting ambulation, moderate or severe arthritis of knee or hip, serious medical comorbidities, allergy to diphenhydramine, severe psychiatric disorder	Randomized: 29 (14 vs. 15) Analyzed: 26 (14 vs. 12) Attrition: 10% (3/29)	A: Pregabalin: 75 mg po bid x 3 d, 150 mg bid x 7 d, 75 mg bid x 4 d (n=14) B: Placebo: Diphenhydramine 6.25 mg po bid x 3 d, 12.5 mg bid x 7 d, 6.25 mg bid x 4 d (n=12) Each treatment for 2 weeks, with 1 week washout	Mean age: 71 vs. 69 years Female: 29% vs. 33% White: 100% vs. 93% Baseline pain with ambulation (mean, 0-10 NRS): 7.7 vs. 7.1 Baseline RDQ (mean, 0-24): 13 vs. 14	Chronic (≥3 months): 84% vs. 93% >12 months

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Markman, 2014	10 days (prior to tapering of each treatment)	A vs. B Walking distance (mean, m): 237 vs. 261 at 2 w (p=0.35) Pain with ambulation (mean, 0-10 NRS): 7.22 vs. 6.97 at 2 w (p=0.46) RDQ (mean, 0-24): 13 vs. 11 at 2 w (p=0.01) Brief Pain Inventory-Short Form, interference (mean, 0-10): 3.7 vs. 3.58 at 2 w (p=0.68) BPI-SF, pain intensity (mean, 0-10): 4.4 vs. 4.5 at 2 w (p=0.68) ODI (mean, 0-100): 38 vs. 36 at 2 w (p=0.36) Swiss Spinal Stenosis Questionnaire, symptom severity (mean): 3.09 vs. 2.94 at 2 w (p=0.07) Swiss Spinal Stenosis Questionnaire, physical function (mean): 2.40 vs. 2.45 at 2 w (p=0.57)	A vs. B Any adverse events: 64% (19/28) vs. 35% (9/26) Serious adverse events: None Withdrawal due to adverse events: 7.1% (2/28) vs. 0% (0/26) Dizziness: 43% (12/28) vs. 3.8% (1/26) Diarrhea: 11% (3/28) vs. 7.7% (2/26) Somnolence: 18% (5/28) vs. 7.7% (2/26) Dry mouth: 14% (4/28) vs. 0% (0/26) Nausea: 11% (3/28) vs. 15% (4/26) Edema: 18% (5/28) VS. 7.7% (2/26)	Pfizer Inc.	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Pota, 2012	Italy Single center	35 to 80 years of age, chronic mechanical-degenerative back pain, symptoms began 12 to 60 months prior, pain ≥50 on 0-100 VAS and >20 on the Pain Rating Index of the Short-Form McGill Pain Questionnaire Exclude: Neurological and neuromuscular conditions, other comorbid conditions, hypersensitivity to study drugs, psychiatric disease, HIV infection or other immunodeficiency, skin conditions preventing patch application, cancer-related back pain, pregnant or lactating, renal or liver failure	Randomized: 44 (22 vs. 22) of 44 in run-in period Analyzed: 44 Attrition: 0%	Buprenorphine run-in period for 3 weeks, then: A: Pregabalin 300 mg/day + transdermal buprenorphine 35 mcg/h x 3 w (n=22) B: Placebo + transdermal buprenorphine 35 mcg/h x 3 w (n=22)	Mean age: 56 years (overall) Female: 50% (overall) Race: Not reported Baseline pain (mean, 0-100 VAS): 35 vs. 32 Baseline function: Not reported	Chronic (12 to 60 months); mean 15 months

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Pota, 2012	3 weeks (at end of therapy)	A vs. B Pain (mean, 0-100 VAS): 9.5 vs. 32.8 at 1 w, 6.1 vs. 32.8 at 2 w, 5.7 vs. 33.3 ($p<0.05$) at 3 w Short-Form McGill Pain Questionnaire Pain Rating Index (mean, 0-15): 9.2 vs. 16.5 at 1 w, 4.6 vs. 16.6 at 2 w, 3.7 vs. 16.2 at 3 w ($p<0.05$) SF-MPQ Present Pain Intensity (mean, 0-5): 0.4 vs. 1.7 at 1 w, 0.3 vs. 1.8 at 2 w, 0.3 vs. 2.0 at 3 w Sleep interference (mean, 0-10): 0.2 vs. 2.3 at 1 w, 0.7 vs. 1.8 at 2 w, 0.6 vs. 1.9 at 3 w ($p>0.05$) Acetaminophen use (mean, mg): 46 vs. 636 at w 3 ($p<0.05$)	A vs. B Withdrawal due to adverse events: None Constipation: 23% (5/22) vs. 14% (3/22) Nausea: 14% (3/22) vs. 14% (3/22) Dizziness: 0% (0/22) vs. 14% (3/22) Somnolence: 18% (4/22) vs. 23% (5/22)	Reports no funding	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Romano, 2009	Italy Single center	18 to 75 years of age; chronic (>6 months) low back pain due to disc prolapse, lumbar spondylosis, and/or spinal stenosis; pain VAS >40 Exclude: Prior back surgery, diabetes, neurological disease, cardio-renal disease history of gastric ulcers or gastrointestinal bleeding, allergy to study drugs, alcohol or drug abuse	Randomized: 42 Analyzed: 36 (12 vs. 12 vs. 12) Attrition: 14% (6/42)	A: Pregabalin ~1 mg/kg/d x 1 w, then 2-4 mg/kg/d (mean 2.1 mg/kg/d) (n=12) B: Celecoxib ~3-6 mg/kg/d (mean 4.2 mg/kg/d) (n=12) C: Pregabalin + celecoxib (mean 1.78 and 3.75 mg/kg/d) (n=12) Each treatment for 4 weeks, with 1 week washout prior to crossover	Mean age: 53 years (overall) Female: 56% (overall) Race: Not reported Baseline pain: Not reported for initial intervention (mean 45-48) Baseline function: Not reported for initial intervention Disc prolapse: 47% Lumbar spondylosis: 39% Spinal stenosis: 19%	Chronic (>6 months); mean duration not reported
Yaksi, 2007	Turkey Single center	Lumbar spinal stenosis (central or lateral recess) confirmed on CT or MRI Exclude: Other pain syndromes	Randomized: 55 (28 vs. 27) Analyzed: Unclear Attrition: Not reported	A: Gabapentin: initial dose 300 mg/day, titrated up to 2400 mg/day (mean not reported) (n=28) B: No gabapentin (n=27) Both groups also received exercise, lumbar corset, and NSAIDS; duration of treatment 4 months	Mean age: 51 vs. 51 years Female: 79% vs. 56% Race: Not reported Baseline pain (mean, 0-10 VAS): 7.0 vs. 6.7 Baseline function: Not reported	Duration not Specified

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Romano, 2009	4 weeks (at end of each treatment period)	A vs. B vs. C Pain (mean, 0-100 VAS): 43 vs. 40 vs. 29 at 4 w (p=0.0001 for A vs. C and p=0.001 for B vs. C) Pain reduction: 10% vs. 12% vs. 38% at 4 w Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) score <12 Pain (mean, 0-100 VAS): 50.7 vs. 32.5 vs. 32.9 at 4 w (p=0.0002 for A vs. C and p=0.9 for B vs. C) Pain reduction (estimated from graph): -2.5% vs. 26% vs. 27% at 4 w LANSS score >12 Pain (mean, 0-100 VAS): 36.3 vs. 32.5 vs. 23.1 (p=0.01 for A vs. C and p=0.0001 for B vs. C) Pain reduction (estimated from graph): 23% vs. 2% vs. 52%	A vs. B vs. C Withdrawal due to adverse events: 9% (4/42) overall (not reported by group) Side effects: 14% (5/36) vs. 11% (4/36) vs. 19% (7/36)	Not reported	Fair
Yaksi, 2007	4 months (at end of therapy)	A vs. B Pain (mean, 0-10 VAS): 5.1 vs. 5.6 at 1 month (p=0.40), 4.3 vs. 5.0 at 2 months (p=0.12), 3.6 vs. 4.8 at 3 months (p=0.04), 2.9 vs. 4.7 at 4 months (p=0.006) Walking distance >1000 meters (estimated from graph): 65% vs. 21% at 4 meters (p=0.001) Sensory deficit: 32% (9/28) vs. 63% (17/27)	A vs. B Withdrawal due to adverse events: None Ataxia: 7.1% (2/28) vs. not reported	Reports no Funding	Poor

Please see Appendix C. Included Studies for full study references.

Table E12. Data abstraction of randomized controlled trials of corticosteroids

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Eskin, 2014	USA Single center	18 to 55 years of age, musculoskeletal low back pain from bending or twisting within 48 hours, ≥5 on 0-10 VAS Exclude: Blunt trauma, neurological motor deficits, neoplastic disease, fever, pregnant, current use of steroids of other immunosuppressant, diabetes, uncontrolled hypertension, significant peptic ulcer disease, cataracts, urinary tract infection, allergy to prednisone, lactose intolerance, visits from occupational medicine program	Randomized: 79 (39 vs. 40) Analyzed: 67 (32 vs. 35) Attrition: 15% (12/79)	A: Prednisone: 50 mg po QD x 5 days (n=32) B: Placebo (n=35)	Mean age: 39 vs. 41 years Female: 33% vs. 27% Race: Not reported Baseline pain (mean, 0-10 VAS): 8.0 vs. 8.0 Baseline function: Not reported	Acute (<2 days)

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Eskin, 2014	5-7 days (treatment 5 days)	A vs. B vs. C Pain (mean, 0-3 VRS): 1.3 vs. 1.1 at 5-7 d (difference 0.2, 95% CI -0.2 to 0.6) No or mild pain: 56% vs. 69% (difference -13%, 95% -36% to 10%) Days of work lost (mean): 2.1 vs. 1.3 (p=0.06) Sought further care: 40% vs. 18% (difference 22%, 95% CI 0% to 43%)	"No significant side effects"	Emergency Medical Associates Research Foundation	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Friedman, 2008	USA Single center	21 to 50 years of age, non-radicular low back pain for ≤1 week Exclude: Back pain episode in last month, positive straight leg raise test, fever, cancer with metastatic risk, recent blunt trauma to back, chronic pain syndrome, history of spinal surgery, inflammatory arthritis, recent use of corticosteroids, use of pain medication daily or near daily, pregnant or lactating, allergy to study medications	Randomized: 82 (39 vs. 43) Analyzed: 78 (37 vs. 41) Attrition: 4.9% (4/82)	A: Methylprednisolone: 160 mg IM x 1 (n=37) B: Placebo (n=41)	Mean age: 39 vs. 37 years Female: 54% vs. 51% Hispanic/Latino: 69% vs. 67% African-American/Black: 22% vs. 21% White: 8% vs. 7% Baseline pain (0-10 VAS): 8.9 vs. 9.1 Baseline function: Not reported	Acute (<1 week), median 48 hours
Hedeboe, 1982	Denmark Single center	4 of the following: Radicular pain, paresthesia, paresis, sensory change, decreased tendon reflexes, positive straight leg raise Exclude: Psychiatric conditions, cardiac disease, hypertension, diabetes, prior spinal surgery	Randomized: 39 (19 vs. 20) Analyzed: 39 Attrition: Not reported	A: Dexamethasone: 4 mg/ml, 16 mg IM QID x 1 d, 8 mg QID x 1 d, 8 mg tid x 1 d, 4 mg tid x 1 d, 4 mg bid on x 3 d (N=19) B: Placebo (n=20)	Mean age: 44 vs. 40 years Female: 47% vs. 25% Race: Not reported Baseline pain: Not reported Baseline function: Not reported	Duration not specified

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Friedman, 2008	1 month (single treatment in ER)	A vs. B Improvement in pain (mean, 0-10 VAS): difference 1.1 (95% CI -0.5 to 2.8) at 1 w; 7.1 vs. 5.8 at 1 m, difference 1.3 (95% CI -0.2 to 2.7) Back pain in prior 24 hours: 46% vs. 61% at 1 m, OR 0.54 (95% CI 0.22 to 1.3) Analgesic use in past 24 hours: 22% vs. 43% at 1 m, OR 0.39 (95% CI 0.14 to 1.1) RDQ18 (median, 0-18): 0 vs. 0 (p=0.009) RDQ18 1 or higher: 42% vs. 46% at 1 w; 19% vs. 49% at 1 m, OR 0.25 (95 5CI 0.09 to 0.7) Not resumed usual activities: 14% vs. 23% at 1 m, OR 0.56 (95% CI 0.17 to 1.9) Not resumed work (among full-time workers): 8% (2/24) vs. 13% (3/24) at 1 m, OR 0.64 (95% CI 0.10 to 4.2) Did not seek additional health care: 67% vs. 59% at 1 m, difference 8% (95% CI -14% to 30%)	A vs. B Any adverse event: 32% vs. 24% at 1 w, difference 9% (95% CI -12% to 30%) No gastrointestinal bleeding, osteonecrosis, infection, hyperglycemia, need for additional treatment due to study drugs	Reports no funding	Good
Hedeboe, 1982	3 months (treatment 7 days)	A vs. B Clear improvement (not otherwise defined): 68% (13/19) vs. 35% (7/20) at 9 d, RR 1.95, 95% CI 1.0 to 3.82; 32% (6/19) vs. 25% (5/20) at 3 m, RR 1.26, 95% CI 0.46 to 3.46	A vs. B Withdrawal due to adverse events: 0% (0/19) vs. 0% (0/20) Any side effect: 32% (6/19) vs. 5.0% (1/20) at 1 w, RR 6.32, 95% CI 0.84 to 47.7	Not reported	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Holve, 2008	USA Single center	20 to 60 years of age, acute (<1 week) sciatica (unilateral leg pain extending below knee and positive straight leg raise) Exclude: Pregnant, diabetes, renal failure, upper gastrointestinal bleeding, major psychiatric disease, red flag symptoms	Randomized: 29 (15 vs. 14) Analyzed: 27 (13 vs. 14) Attrition: 6.9% (2/29)	A: Prednisone: 60 mg po QD x 3 d, 40 mg po QD x 3 d, 20 mg po QD x 3 d (n=13) B: Placebo (n=14)	Mean age: 39 vs. 46 years Female: 37% (overall) Race: Not reported Baseline Roland Morris pain (mean, 0-5 VRS): 3.8 vs. 3.1 Baseline RDQ (mean, 0-24): 16 vs. 16	Acute (<1 week)

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Holve, 2008	6 months (treatment 9 days)	A vs. B Roland Morris Pain (mean, 0-5 Rolad Morris pain, estimated from graph): 2.5 vs. 2.6 at 1 w, 1.8 vs. 2.1 at 2 w, 1.6 vs. 1.6 at 4 w, 1.5 vs. 1.0 at 3 m, 0.4 vs. 1.6 at 6 months (p>0.05) RDQ (mean, 0-24): 13 vs. 16 at 1 week, 8 vs. 13 at 2 weeks, 8 vs. 9 at 4 weeks, 3 vs. 2 at 3 months, 1 vs. 2 at 6 months (p>0.05) Return to baseline work hours: ~60% in each group by 2 months (p>0.05) NSAID and opioid use: No differences, data not provided Epidural injections: 15% (2/13) vs. 43% (6/14), RR 0.36 (95% CI 0.9 to 1.47)	Not reported	Kaiser Foundation Research Institute	Poor

Please see Appendix C. Included Studies for full study references.

Table E13. Study characteristics of systematic reviews of exercise

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Bystrom, 2013	1) MCE vs. general exercise; 2) MCE vs. minimal intervention (none, placebo or advice/ education); 3) MCE vs. multimodal physical therapy; 4) MCE as part of multimodal intervention vs. other components of that intervention	October 2012: PubMed, EMBASE, PEDro, and CINAHL databases; English only	16 RCTs (1 with 2 arms) (n=1933) 80% with CBLP; included studies of subacute if duration >6 months; (?they define sub acute as 4-12 weeks) short (6 weeks–4 months), intermediate (4–8 months) and long term (8-15 months) followup	1) A: MCE versus B: general exercise (n=741; 7 trials [1 with 2 arms]) 2) A: MCE versus C: minimal intervention (n=541; 3 trials) 3) A: MCE versus D: multimodal PT (n=499; 4 trials) 4) A: MCE as part of multimodal intervention versus E: other components of that intervention (n = 152; 2 trials)	10-point PEDro scale

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Bystrom, 2013	Random effects model (RevMan5) when data displayed statistical heterogeneity, fixed effects model (RevMan5) for homogenous data; heterogeneity assessed using I^2 statistic	A vs. B Pain, weighted mean difference (95% CI) Short-term (6 trials [1 with 2 arms], n=529): −7.80 (−10.95 to −4.65) Intermediate (3 trials, n=523): −6.06 (−10.94 to −1.18) Long-term (4 trials [1 with 2 arms], n=632): −3.10 (−7.03 to 0.83) Disability, weighted mean difference (95% CI) Short-term (6 trials [1 with 2 arms], n=529): −4.65 (−6.20 to −3.11) Intermediate (3 trials, n=523): −4.86 (−8.59 to −1.13) Long-term (3 trials, n=523): −4.72 (−8.81 to −0.63) A vs. C Pain, weighted mean difference (95% CI) Short-term (2 trials, n=500): −12.48 (−19.04 to −5.93 Intermediate (2 trials, n=500): −10.18 (−16.64 to −3.72) Long-term (2 trials, n=500): −13.32 (−19.75 to −6.90) Disability, weighted mean difference (95% CI) Short-term (3 trials, n=541): −9.00 (−15.28 to −2.73) Intermediate (2 trials, n=500): −5.62 (−10.46 to −0.77) Long-term (2 trials, n=500): −6.64 (−11.72 to −1.57) A vs. D Pain, weighted mean difference (95% CI) Short-term: lack of data Intermediate (4 trials, n=499): −14.20 (−21.23 to −7.16) Long-term: lack of data Disability, weighted mean difference (95% CI) Short-term: lack of data Intermediate (2 trials, n=256): −12.98 (−19.49 to −6.47) Long-term: lack of data A vs. E No pooled analysis, trials reported at different time points (Figure 5 individual study results)	NR	Fair

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Oesch, 2010	1) Exercise vs. usual care	August 2008: MEDLINE, EMBASE, PEDro, Cochrane Library databases, NIOSHTIC-2, and PsycINFO; English only	23 RCTs (n=4138) (20 with data for meta-analysis, 17 comparisons of exercise vs. usual care and 11 comparisons of two different exercise) nonacute nonspecific LBP, duration ≥ weeks	1) A: Exercise versus B: usual care	Criteria according to Juni et al.

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Oesch, 2010	Meta regression and random effects models (Stata); odds ratios (OR) calculated; heterogeneity assessed using I^2 statistic	A vs. B Work Disability Short term (closest to 4 weeks) (5 trials, 6 comparisons, n=1030) OR=0.80 (95% CI 0.51 to 1.25); addition of 1 low quality study: OR=0.68 (95% CI, 0.42 to 1.10) Intermediate (closest to 6 weeks) (4 trials, 5 comparisons, n=971) OR=0.78 (95% CI 0.45 to 1.34) Long term (closest to 12 months) (8 trials, 10 comparisons, n=1992) OR=0.66 (95% CI 0.48 to 0.92); addition of 2 low quality studies, OR=0.70 (95% CI 0.54 to 0.91) (favor exercise, reduced work disability) Influence of exercise (output individually designed) characteristics, long term (8 trials, n=1149 group A, n=843 group B) OR=0.59 (95% CI 0.45 to 0.78); I^2=60.4%; none of variables below were significant in meta-regression -delivery type (home-based exercises vs. supervised exercises), -dose (high- vs. low-dose exercise), -administration within a cognitive behavioral approach (yes/no), -work context (yes/no) Comparison of different exercise interventions (13 trials, 15 interventions) Effect of more contact hours: OR 1.07 (95% CI, 0.67 to 1.72) 3 trials applying exercise within behavioral approach: (OR 0.75, 95% CI 0.47 to 1.20) vs. trials without (OR 1.74, 95% CI 0.71 to 4.30) 1 trial on work-related exercise in inpatient (OR 0.53, 95% CI 0.30 to 0.93) compared with exercise not specifically designed to restore work-related physical capacity (OR 1.25, 95% CI 0.80 to 1.97)	NR	Fair

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
van Middelkoop, 2010	1) Exercise vs. wait list/no treatment; 2) Exercise vs. usual care; 3) Exercise vs. back school/education; 4) Exercise vs. other forms of exercise therapy	All trials of the Cochrane review (Hayden 2005) and updated search thru December 22, 2008: MEDLINE, EMBASE, CINAHL, CENTRAL and PEDro databases; language restriction NR	37 RCTs (N=3957) chronic (≥12 weeks) nonspecific LBP post-treatment, short, intermediate, and long-term followup (not defined)	1) A: Exercise versus B:wait list/no treatment (8 trials) 2) A: Exercise versus C: usual care (6 trials) 3) A: Exercise versus D: back school/education (3 trials) 4) A: Exercise versus E: other forms of exercise therapy (11 trials)	GRADE

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
van Middelkoop, 2010	NR	A vs. B Pain intensity, pooled mean differences (95% CI) Post-treatment (5 trials, n=268) : −4.51 (–9.49 to 0.47) Intermediate (2 trials, n=137) : −16.46 (–44.48 to 11.57) Long-term (1 trial, n=102): NS (no data reported) Disability, pooled mean differences (95% CI) Post-treatment (6 trials, n=331: −3.63 (–8.89 to 1.63) Intermediate (1 trial, n=102): NS (no data reported) Long-term (1 trial, n=102): NS (no data reported) A vs. C Pain intensity, weighted mean difference (95% CI) Post-treatment (2 trials, n=108) : −9.23 (–16.02 to –2.43) Long term (12 months) (3 trials, n=301): −4.94 (–10.45 to 0.58) Disability, weighted mean difference (95% CI) Post-treatment (3 trials, n=188): −12.35 (–23.00 to –1.69) Intermediate (2 trials, n=267): −5.23 (–9.54 to –1.32) Long term (12 months) (3 trials, n=301): −3.17 (–15.96 to –0.38) A vs. D Pain intensity, weighted mean difference (95% CI) Post-treatment (1 trial, n=NR): NS (no data reported) Short-term (3 months) (3 trials, n=200) : −7.63 (–17.20 to 1.93) Intermediate (6 months) (2 trials, n=141): −5.58 (–16.65 to 5.48) Long-term (1 trial, n=346): NS (no data reported) Disability, weighted mean difference (95% CI) Post-treatment (2 trials, n=139): −11.20 (–16.78 to –5.62) Short-term (3 months) (3 trials, n=200) : −2.55 (–10.07 to 4.97) Intermediate (6 months) (3 trials, n=241): −4.42 (–9.90 to 1.05) Long-term (1 trial, n=346): NS (no data reported)	NR	Fair

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
van Middelkoop, 2010 (cont.)		A vs. E (no pooling due to heterogeneity) Aerobic exercise training vs. lumbar flexion exercise program of 3 months (1 study) Pain intensity 3 months: statistically significant difference between groups (no data reported) General exercise program (strengthening and stretching) versus motor control exercise program (improving function of specific trunk muscles) of 12 weeks (1 study) Function 8 weeks: **mean adjusted between-group difference, 2.9 (favoring motor control exercise)** 6 and 12 months: "similar group outcomes" (no data reported) Global perceived effect 8 weeks: **mean adjusted between-group difference, 1.7 (favoring motor control exercise)** 6 and 12 months: "similar group outcomes" (no data reported) Yoga program vs. conventional exercise class program of 12 weeks (1 study) Back-related function 12 weeks: "superior in the yoga group" (no data reported) Various exercise interventions (9 studies) - no statistical differences		

Please see Appendix C. Included Studies for full study references.

Table E14. Data abstraction of randomized controlled trials of exercise

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Albaladejo, 2010	Spain 8 centers Primary care	Presenting for LBP with no "red flags" for systemic disease or referral for surgery Excluded: bedridden, physiotherapy in previous 12 months, inflammatory rheumatologic disease, fibromyalgia	69 randomized 69 completed 0% attrition *Randomization of physicians who recruited subjects (i.e., cluster randomized)*	A. Education + 4 sessions of physiotherapy (n=100) B. Education (n=139) C. Usual care (n=109)
Albert, 2012	Denmark Single center Secondary care facility (after unsuccessful treatment in primary care)	18 to 65 years of age, radicular pain of dermatomal distribution to the knee or below in 1 or both legs, leg pain > 3 on a 1- to 10-point scale at first visit to the clinic, and duration of sciatica between 2 weeks and 1 year. EXCLUSION cauda equina syndrome, pending worker's litigation, previous back surgery, spinal tumors, pregnancy, a language other than Danish as their first language, or an inability to follow the rehabilitation protocol due to concomitant disease such as depression or heart failure.	Randomized, N=181 Analyzed, N=181 Attrition, 7.2% (13/181)	A: Symptom-guided exercises (n=95). Directional end-range exercises and postural instructions guided by the individual patient's directional preference (based on the McKenzie method); stabilizing exercises for the transverse abdominis and multifidus muscles and dynamic exercises for the outer layers of the abdominal wall and back extensors; all patients received home exercise programs B: Sham exercises (n=96). Optional exercises that were not back related but were low-dose exercises to simulate an increase in systemic blood circulation. Both groups received identical information and advice and optional paracetamol and/or NSAIDs. Treatment lasted for 8 weeks with a minimum of 4 and a maximum of 8 treatments. Patients were discouraged from receiving any additional treatment of their sciatica.

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Albaladejo, 2010	A vs. B vs. C Median age: 51 vs. 51 vs. 53 Female sex: 68% vs. 63% vs. 72% Race: NR Duration of pain >3 months: 72% vs. 78% vs. 89% Median pain intensity: 7.5 vs. 8 vs. 8 Median RDQ: 9.5 vs. 9.0 vs. 7.5 Median CSQ: 7.0 vs. 8.0 vs. 6.0 Median SF-12 PCS: 34.8 vs. 35.8 vs. 36.5 Median SF-12 MCS: 44.6 vs. 50.1 vs. 49.8	Chronic (79.8% with pain >3 months, n=265)	26 weeks
Albert, 2012	A vs. B Mean age (years): 46 vs. 44 Female: 43% vs. 53% Race NR Pain etiology NR Mean number of treatments: 5 vs. 5 Baseline Current leg pain (LBPRS): 4.3 ± 2.3 vs. 4.5 ± 2.5 Total leg pain, median (IQR): 18 (15–21) vs. 18 (12–21); p=NS Disability (RDQ), median (IQR): 16 (11–18) vs. 15 (12–18) Quality of Life: 0.62 ± 0.18 vs. 0.62 ± 0.62	A vs. B 0–4 weeks: 25% vs. 18% 5–12 weeks: 59% vs. 63% 12–52 weeks: 16% vs. 19%	12 months

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Albaladejo, 2010	A vs. B vs. C Change in median VAS, low back pain: -2.0 vs. -2.0 vs. 0 Change in median VAS, referred pain: -2.0 vs. -2.0 vs. -0.5 Improvement in RDQ: 2.0 vs. 1.6 vs. -0.3 Change in CSQ: -1.0 vs. -1.0 vs. 2.0 Change in SF-12 PCS: -3.2 vs. -2.4 vs. 0.6 Change in SF-12 MCS: -2.8 vs. -1.8 vs. 6.1	NR	"Foundation and other funds were received"	Fair	Also self-reported satisfaction and interim time-point results; Results reporting is poor; not describe between group comparisons' stat tests
Albert, 2012	A vs. B Current leg pain (LBPRS) (mean, SD) 8 weeks (end of treatment): 1.5 ± 2.1 vs. 2.3 ± 2.7; p=0.06 EPC calc of test mean difference -0.8 (95% CI -0.09 to -1.15) 12 months: 1.5 ± 2.1 vs. 1.4 ± 2.4; p=NS Total leg pain (LBPRS) (median, IQR) 8 weeks: 4 (0–9) vs. 4 (0–12); p=NS 12 months: 3 (0–10) vs. 2 (0–8); p=NS Disability (RDQ) (median, IQR) 8 weeks: 6 (2–12) vs. 6 (2–12); p=NS 12 months: 3.5 (1–10) vs. 3.5 (1–10); p=NS ≥30% improvement from baseline: 73% vs. 77.5%; p=NS Quality of Life (EQ-5D (mean, SD) 12 months: 0.82 ± 0.21 vs. 0.79 ± 0.24; p=NS Global improvement 8 weeks Much better: 80% vs. 60% Some better: 14% vs. 26% 12 months: Much better: 84% vs. 76% Some better: 16% vs.18% Group A significantly (p<0.008) more improved (better or much better) compared with group B at both time points Patient satisfaction: 93.5% vs. 90.5%; p=NS	NR	Federal, institutional, and foundation funds	Fair	Global improvement estimated from figure 3 of article Do we care about nerve root compression signs and sick leave? They also report these outcomes

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Bronfort, 2011	United States Single center University research clinic	Age 18-65 years, primary complaint of mechanical LBP ≥6 weeks w/w/o radiating pain to the lower extremity Excluded: previous lumbar surgery, vascular disease, pain score <3	301 randomized 245 completed 19% attrition	A. Supervised exercise therapy for 12 weeks (n=100) B. Chiropractic spinal manipulation for 12 weeks (n=100) C. Home exercise and advice for 12 weeks (n=101)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Bronfort, 2011	A vs. B vs. C Mean age: 44.5 vs. 45.2 vs. 45.6 years Female sex: 57% vs. 66% vs. 58% Race: NR Duration of back pain: 4.8 vs. 5.0 vs. 5.0 years Mean pain severity score (0-10): 5.1 vs. 5.4 vs. 5.2 Roland-Morris disability score (0-23): 8.4 vs. 8.7 vs. 8.7	Chronic; median duration 4.8 to 5 (0-51) years	52 weeks

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Bronfort, 2011	Only significant between-group differences in patient-reported outcomes were for satisfaction (favoring A, p<0.01 at 12 weeks and p<0.001 at 52 weeks) Overall treatment effect was significant for endurance (p<0.05) and strength (p<0.05) but not range of motion (also favoring A).	A vs. B vs. C Nonserious adverse events: 1% (1/100) vs. 1% (1/100) vs. 4% (4/101) All adverse events were transient, required little to no change in activity level, and were considered non-serious	NR	Good	Large tables of data at each time point available

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Garcia, 2013	Brazil Single center Outpatient clinics	Age 18-80 years, nonspecific LBP ≥ 3 months' duration. Excluded: any contraindication to physical exercise, serious spinal pathology (e.g., tumors, fractures, inflammatory disease), previous spinal surgery, nerve root compromise, cardiorespiratory illnesses, pregnancy	Randomized, N=148 Analyzed, N=148 Attrition, 1.4% (2/148) at 1 month; 0% at 3 months; 0.7% (1/148) at 6 months	A: McKenzie method (n=74). Exercises and progression tailored to the individual. Included a basic educational component and guidance on completing the exercises at home. Patients with a direction preference for extension were instructed to use a back roll while sitting. B: Back school (n=74). New exercises were prescribed and progressed following the sequence proposed by the program (i.e., not tailor to the individual). Educational component and theorectical and practical information given. All sessions except for the first were conducted in a group setting. All patients received 4 one-hour sessions over 4 weeks. In all patients, directional preference was assessed at baseline and the treating therapist was informed before the randomization. All patients received information in order to maintain lordosis while sitting without exacerbating their symptoms

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Garcia, 2013	A vs. B Mean age: 53.7 vs. 54.2 years Female: 78.4% vs. 68.9% Race: NR Duration of LBP: 21 vs. 24 months Recent episode of LBP: 62.2% vs. 63.5% Pain intensity (NRS, 0-10): 6.77 ± 2.12 vs. 6.41 ± 2.54 Disability (RDQ, 0-24): 11.32 ± 4.95 vs. 11.08 ± 5.84 Quality of life (WHOQOL-BREF, 0-100) Physical domain: 51.64 ± 14.49 vs. 51.49 ± 17.05 Psychological domain: 62.88 ± 15.86 vs. 60.11 ± 15.86 Social domain: 63.62 ± 18.27 vs. 63.15 ± 18.96 Environmental domain: 55.40 ± 13.66 vs. 54.74 ± 16.09	Chronic (≥ 3 months) A vs. B duration of symptoms: 21 ± 28 vs. 24 ± 83 months	1, 3, 6 months

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Garcia, 2013	Unadjusted mean difference ± SD for A vs. B; adjusted mean difference (95% CI) for B – A **Pain intensity (NRS, 0–10)** 1 month: 4.14 ± 2.87 vs. 4.39 ± 2.73; 0.66 (–0.29 to 1.62), p=0.17 3 months: 5.18 ± 2.61 vs. 5.53 ± 2.78; 0.71 (–0.23 to 1.67), p=0.14 6 months: 5.09 ± 2.89 vs. 5.19 ± 3.08; 0.48 (–0.47 to 1.43), p=0.32 **Disability (RDQ, 0–24)** 1 month: 6.20 ± 5.06 vs. 8.15 ± 5.79; 2.37 (0.76 to 3.99), p=0.004 3 months: 7.12 ± 5.67 vs. 8.39 ± 6.30; 1.51 (–0.09 to 3.11), p=0.06 6 months: 6.77 ± 6.02 vs. 8.12 ± 6.45; 1.55 (–0.05 to 3.16), p=0.06 Achievement of MCID (5-point improvement): 53% (39/74) vs. 30% (22/73), p=0.01; RR 1.8, 95% CI 1.2 to 2.7* **Quality of Life (WHOQOL-BREF, 0-100)** **Physical domain** 1 month: 62.45 ± 16.94 vs. 59.27 ± 16.88; –3.65 (–8.26 to 0.96), p=0.12 3 months: 62.25 ± 15.37 vs. 57.43 ± 17.76; –4.67 (–9.26 to –0.07), p=0.04 6 months: 61.48 ± 16.12 vs. 60.76 ± 18.87; –0.44 (–5.04 to 4.16), p=0.85 **Psychological domain** 1 month: 67.68 ± 15.15 vs. 65.12 ± 13.98; –0.18 (–4.17 to 3.80), p=0.92 3 months: 67.62 ± 16.07 vs. 65.14 ± 14.14; 0.14 (–3.82 to 4.11), p=0.94 6 months: 68.00 ± 14.18 vs. 66.72 ± 14.15; 1.50 (–2.48 to 5.47), p=0.46	A vs. B 0% (0/74) vs. 1.4% (1/74) (temporary exacerbation of pain during the third session which has ceases by the 4th week)	the Fundacao de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP), Brazil.	Good	

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Garcia, 2013 (Cont.)	Social domain 1 month: 67.45 ± 18.00 vs. 67.24 ± 15.96; –0.47 (–5.50 to 4.56), p=0.85 3 months: 69.03 ± 16.11 vs. 65.76 ± 16.00; –3.15 (–8.16 to 1.85), p=0.21 6 months: 66.00 ± 18.74 vs. 66.09 ± 15.00; 0.26 (–4.75 to 5.28), p=0.91 Environmental domain 1 month: 58.57 ± 14.82 vs. 57.62 ± 16.48; –0.51 (–4.06 to 3.03), p=0.77 3 months: 58.23 ± 14.65 vs. 56.16 ± 14.75; –1.41 (–4.94 to 2.12), p=0.43 6 months: 57.84 ± 14.61 vs. 57.44 ± 15.00; 0.29 (–3.24 to 3.83), p=0.87 *RR (95% CI) calculated by EPC				

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
George, 2008	United States Multicenter (3) Outpatient clinics	Age 15 to 60 years, ability to read and speak English, QTFSD classification 1a or 1b (acute or sub acute LBP without radiation below the gluteal fold) or 2a or 2b (acute or sub-acute LBP with proximal radiation to the knee) or 3a or 3b (acute or sub-acute LBP with distal radiation below the knee). EXCLUSION any other QTFSD classification; pregnancy; osteoporosis	N=108 Analyzed, N=102 Attrition, 29.4% (30/102)	A: Treatment based classification + Graded Exposure (GX) (n=33). Fearful activities assessed; top 2 most feared activities implemented under this protocol using progression based on NRS fear rating and performed under supervision of PT and clinical staff. Also received patient education materials focused on biopsychosocial model. B: Treatment based classification + Graded Activity (GA) (n=35). Parameters (duration, intensity, and frequency) used to reach pain tolerance were then established as the activity quota; graded activity principles were used to progress exercise during subsequent treatment sessions. Also received patient education materials focused on biopsychosocial model C: Physical therapy based on the treatment-based classification system (Delitto et al.) (n=34). Also received educational materials that were anatomically focused.

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
George, 2008	A vs. B vs. C Mean age (years): 40.1 vs. 37.6 vs. 34.9 Female: 64% vs. 69% vs. 68% Race NR Pain etiology NR Prior history of LBP: 67% vs. 69% vs. 50% Referred leg pain: 42% vs. 49% vs. 38% Baseline Pain (NRS): 4.7 ± 2.1 vs. 5.2 ± 1.8 vs. 4.3 ± 2.0 Function (PIS): 3.1 ± 1.6 vs. 3.6 ± 2.1 vs. 2.9 ± 1.7 Disability (ODI): 30.7 ± 15.6 vs. 31.1 ± 15.8 vs. 29.2 ± 15.7	Acute and sub-acute; operationally defined as reporting current symptoms for 1–24 weeks A vs. B vs. C duration of current LBP episode (weeks): 9.8 vs. 5.8 vs. 6.7; p=0.015	6 months

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
George, 2008	A vs. B vs. C Pain intensity (NRS, 0–10) **High fear** Baseline: 5.1 ± 2.1 vs. 5.1 ± 1.9 vs. 5.1 ± 1.8 4 weeks: 2.1 ± 2.0 vs. 2.3 ± 2.1 vs. 2.0 ± 1.6 6 months: 2.1 ± 2.3 vs. 1.5 ± 2.1 vs.1.6 ± 1.3 **Low fear** Baseline: 3.9 ± 1.5 vs. 4.9 ± 2.1 vs. 3.1 ± 2.1 4 weeks: 1.7 ± 0.9 vs. 2.1 ± 2.1 vs. 1.8 ± 1.9 6 months: 1.0 ± 1.0 vs. 2.3 ± 1.7 vs. 1.0 ± 1.2 Disability (ODI, 0–100) **High fear** Baseline: 32.3 ± 16.3 vs. 29.9 ± 18.4 vs. 32.9 ± 16.1 4 weeks: 16.5 ± 12.1 vs. 11.5 ± 11.8 vs.16.4 ± 14.9 6 months: 16.7 ± 17.6 vs. 11.3 ± 14.2 vs.11.4 ± 11.5 **Low fear** Baseline: 20.4 ± 13.1 vs. 30.4 ± 13.3 vs. 23.0 ± 15.5 4 weeks: 11.4 ± 11.6 vs. 16.7 ± 11.9 vs. 12.0 ± 11.5 6 months: 9.7 ± 8.2 vs. 15.8 ± 11.1 vs. 5.8 ± 7.1 p=NS for all comparisons	No adverse events reported during followup	NIH-NIAMS Grant AR051128	Poor	

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
George, 2008 (cont.)	Effect sizes Pain intensity (NRS, 0-10) 4 weeks A vs. B: 0.11 A vs. C: –0.05 B vs. C: –0.16 6 months A vs. B: –0.32 A vs. C: –0.26 B vs. C: 0.01 Disability (ODI, 0-100) 4 weeks A vs. B: –0.40 A vs. C: –0.02 B vs. C: 0.39 6 months A vs. B: –0.38 A vs. C: –0.37 B vs. C: 0.01 p=NS for all comparisons. These post hoc effect sizes suggest that for the primary comparisons of interest (GX vs. GA and GX vs. treatment based classification) total sample sizes needed to detect these magnitudes of differences would range from 114 to over 700. Proportion of Success vs. Failure (ODI >10 point change, NRS >2 point change) at 6 months NRS 46% vs. 43% vs. 41% ODI 43%41%, 56% p=0.70				

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Hagen, 2010	Norway Single center Outpatient spine clinic	Age 18–60 years; sick listed (i.e., sick leave from work) for 8–12 weeks for LBP w/w/o sciatica EXCLUSION on sick leave >12 weeks, not sick listed, pregnancy, recent low back trauma, cauda equina symptoms, cancer, osteoporosis, rheumatic low back disease, ongoing treatment for LBP by another specialist, and information from the general practitioner on the sickness certificates indicating forthcoming return to work.	Randomized, N=246 Analyzed, N=246 Attrition, 3.3% (8/246)	A: Standardized physical exercise program (n=124). Aim was to re-educate the trunk muscle to its normal stabilizing role and to improve balance, muscle coordination, and proprioception; program included warm-up (8 minutes), circuit training (34 minutes), stretching (13 minutes), and relaxation (5 minutes); duration 1 hour, 3x/week for 8 weeks. B: No treatment (n=122). Received a brief intervention program before randomization.

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Hagen, 2010	A vs. B Mean age (years): 40.7 vs. 41.6 Female: 52% vs. 50% Race NR Pain etiology NR Previous sick leave for LBP: 72% vs. 75%	Unclear	24 months

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Hagen, 2010	Only statistically significant difference found was for the sock test (physical function), which was more improved in Group A vs. B: mean difference –0.34; 95% CI, –0.66 to –0.01; p=0.041 (time point NR). No statistically significant difference between groups at any followup time point - 6, 12, 18 or 24 months - for the following (no data provided): Pain intensity Functional tests (pick-up test, loaded reach test, 15 meter walk, fingertip-to-floor test, static balance test) Physical activity Walking distance Disability (RDQ) Subjective health complaints Psychological distress (HSCL-25) Return to work	NR	EXTRA funds from the Norwegian Foundation for Health and Rehabilitation, Grant No. Nkr 840 000 (Euro 105 000)	Fair	Percentage of patients that returned to work and self-reported physical activity are presented in Figures 2 and 3. Is it worth estimating from the graphs? Both groups increased return to work, reported less pain and better function, and reduced fear-avoidance beliefs for physical activity during the followup period; authors provide change score for all patients which I did not extract assuming it is not relevant/helpful

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Hartvigsen, 2010	Denmark Single center Outpatient back pain clinic	LBP with or without leg pain >8 weeks, average pain score >3 (on 11-point NRS) during previous 2 weeks, and had completed 4 weeks of previous treatment Excluded: unable to sit on a stationary bike for at least 30 minutes, other comorbidities preventing full participation	136 randomized 126 completed 7% attrition	A. Supervised Nordic walking in groups twice/week for 8 weeks (n=45) B. Nordic walking instruction for 1 hour, with instruction to continue independently (n=46) C. Active living and exercise information (n=45)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Hartvigsen, 2010	A vs. B vs. C Mean age: 49.2 vs. 45.4 vs. 45.5 years Female sex: 76% vs. 69% vs. 68% Race: NR LBP rating scale (0-100), pain: 46.1 vs. 50.7 vs. 47.3 LBP rating scale (0-100), function: 44.4 vs. 47.3 vs. 48.9 Patient-specific function scale (0-100): 18.4 vs. 20.1 vs. 17.3 EQ-5D (0-100): 67.5 vs. 62.7 vs. 63.9	Subacute/chronic: >8 weeks (mean duration NR)	52 weeks

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Hartvigsen, 2010	A vs. B vs. C Mean improvement at 8 weeks in LBP rating scale, pain: 8.8 vs. 3.4 vs. 4.8; significant at all time points for group A, significant only at 8 and 26 weeks for group B, significant only at 8 weeks for group C; no significant between-group differences at any point Mean improvement at 8 weeks in LBP rating scale, function: 7.4 vs. 3.2 vs. 3.8; significant at all time points for group A, never significant for group B, and significant only at 8 and 26 weeks in group C; no significant between-group differences at any point Patient-specific function scale: all groups improved significantly from baseline, but there were no between-group differences EQ-5D: very small and similar changes in all groups	NR	NR	Fair	Most data reported in figures

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Helmhout, 2008	Netherlands Muticenter (6) PT department in military primary care clinics	military employees of the Dutch army, age 18-54 years, ≥4 weeks of continuous or recurrent (at least 3 times a week) episodes of LBP, pain localized between posterior iliac crests and angulus inferior scapulae, with or without radiation in the legs, availability in duty time to visit the local military health center 2 times a week during 10 consecutive weeks, with no more than 2 sessions of absence because of job-related activities (e.g., military exercise, course, leave), and willingness to abandon other treatment interventions for the lower back during the intervention period.	Randomized, N=127 Analyzed, N=127 Attrition, 15.7% (20/127)	A: Lumbar extensor strength training program (n=71). Standardized, progressive resistance training of the isolated lumbar extensor muscle groups aimed at both strength and endurance gain; duration 10 weeks, 14 sessions 2x/w and 3 isometric back strength tests (in weeks 1, 5, and 10). Training sessions were carried out on a Total Trunk Rehab machine. Patients were not allowed to undergo cotreatments during the treatment period. B: Regular PT program (n=56). Regular PT for 10 weeks, or less when the patient was free of complaints; could include hands-on treatment (e.g., passive mobilizing and pain cushioning techniques, manual therapy) and/or hands-off treatment (e.g., exercise therapy, individual education, instruction on the back function) (in the Dutch army, active therapy forms are favored); no cotreatments allowed, nor exercise on equipment that mimicked the specific components of the lower back machine .

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Helmhout, 2008	A vs. B Mean age (years): 37 vs. 35 Female: 3% vs. 4% Race NR Pain etiology NR Prior LBP complaints: 76% vs. 74% Pain radiating to legs: 10% vs. 10% Work absenteeism in last year due to LBP: 10% vs. 8% Baseline Function (PSFS): 178 ± 65 vs. 178 ± 52 Disability (RDQ): 8.3 ± 4.8 vs. 7.9 ± 4.4 Back extension strength (NMT): 214 ± 64 vs. 212 ± 65	A vs. B <4 weeks: 0% vs. 2% 4–6 weeks: 8% vs. 16% 6–12 weeks: 20% vs. 27% 3–6 months: 20% vs. 9% 6–12 months: 15% vs. 7% ≥12 months: 36% vs. 39%	62 weeks

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Helmhout, 2008	A vs. B (mean ± SD; between group difference, 95% CI) Function (PSFS, score 0–300) 5 weeks: 119 ± 70 (n=64) vs. 116 ± 67 (n=46) 10 weeks: 85 ± 72 (n=59) vs. 97 ± 74 (n=47); –0.608 (–2.693 to 1.477), p=0.57 36 weeks: 74 ± 72 (n=57) vs. 64 ± 59 (n=37) 62 weeks: 69 ± 71 (n=61) vs. 65 ± 69 (n=45); –0.136 (–0.344 to 0.616), p=0.58 Disability (RDQ, score 0–24) 5 weeks: 5.8 ± 4.8 (n=64) vs. 4.2 ± 4.2 (n=46) 10 weeks: 3.4 ± 4.6 (n=59) vs. 3.5 ± 4.2 (n=47); –0.025 (–0.134 to 0.085), p=0.66 36 weeks: 3.2 ± 4.3 (n=57) vs. 2.7 ± 3.8 (n=37) 62 weeks: 2.6 ± 4.4 (n=61) vs. 2.5 ± 3.9 (n=45); 0.000 (– 0.025 to 0.026), p=0.99 Global perceived effect (GPE) 5 weeks: no data 10 weeks: 2.4 ± 0.8 (n=59) vs. 2.4 ± 0.7 (n=47) 36 weeks: 2.5 ± 1.0 (n=57) vs. 2.3 ± 0.9 (n=37) 62 weeks: 2.2 ± 1.0 (n=61) vs. 2.3 ± 1.0 (n=45); –0.002 (–0.010 to 0.006), p=0.66 LBP episodes 6 months (back pain in 1st half of year after the end of the treatment period?) (A, n=56; B, n=40): No, not at all: 9% vs. 18% Yes, incidentally: 57% vs. 63% Yes, monthly: 11% vs. 3% Yes, weekly: 23% vs. 18% 12 months (back pain in 2nd half of year after the end of the treatment period?) (A, n=61; B, n=46): No, not at all: 25% vs. 22% Yes, incidentally: 55% vs. 50% Yes, monthly: 2% vs. 11% Yes, weekly: 18% vs. 17%	A vs. B 1.4% (1/71; acute lumbago) vs. 0% (0/56)	NR	Poor	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Helmhout, 2008 (cont.)		EXCLUSION spinal surgery in the last 2 years; specific treatment for LBP in the last 4 weeks (e.g., PT, manual therapy); severe LBP that hindered performing maximal isometric strength efforts; and specific LBP, defined as herniated disk, ankylosing spondylitis, spondylolisthesis, or other relevant neurologic diseases		

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Helmhout, 2008 (cont.)	Patient satisfaction (very satisfied; final degree of satisfaction at end of treatment program): 89% (n = 56) vs. 89% (n=46) Back extension strength (NMT) 5 weeks: 23 ± 62 (n=64) vs. 246 ± 74 (n=46) 10 weeks: 244 ± 66 (n=59) vs. 247 ± 73 (n=47) 36 weeks: 264 ± 64 (n=57) vs. 254± 73 (n=37) 62 weeks: 267 ± 62 (n=61) vs. 249 ± 74 (n=45) p=NS for all timepoints				

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Henchoz, 2010	Switzerland Single center Spine unit	Age 18-60 years, subacute or chronic LBP, phases 2-6 of Krause classification, without neurologic deficit Excluded: phases 7-8 of Krause classification, total disability pension, sciatica, pregnancy, acute rheumatic disease, spinal fracture in previous 3 months, osteoporosis, tumor, heart or respiratory failure, drug addiction, psychiatric pathology	105 randomized 91 completed 13% attrition	A. Functional multidisciplinary rehabilitation, followed by a 12-week exercise program (n=56) B. Functional multidisciplinary rehabilitation, followed by usual care (n=49)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Henchoz, 2010	A vs. B Mean age: 41 vs. 39 years Female sex: 34% vs. 45% Race: NR Mean VAS: 5.3 vs. 5.1	Subacute/chronic (mean duration NR)	52 weeks

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Henchoz, 2010	A vs. B, end of functional multidisciplinary rehabilitation- 1 year ODI: 30.2-25.3 (p<0.001) vs. 30.5-27.2 (p=0.059) VAS: 3.8-3.8 (p=0.521) vs. 3.6-3.8 (p=0.995) PSFS: 66.1-89.8 (p<0.05) vs. 65.5-78.8 (p=0.653) Sorensen test (s): 64.8-81.6 (p<0.05) vs. 67.1-63.9 (p=0.249) MMS test, flexion (cm): 5.65-5.15 (p=0.368) vs. 5.27-5.19 (p=0.561) MMS test, extension (cm): -1.63 to -1.61 (p=0.138) vs. -1.46 to -1.64 (p=0.353) Fingertip-floor distance (cm): 126.5-135.7 (p=0.076) vs. 129.1-136.0 (p=0.470) Shirado test (s): 11.3-8.0 (p=0.063) vs. 17.3-10.0 (p<0.001) Modified Bruce test (min): 11.2-8.4 (p<0.001) vs. 11.2-8.7 (p<0.001)	NR	None	Poor	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Hofstee, 2002	Netherlands Single center Outpatient clinic	Age < 60 years, radicular pain <1 month's duration, available for 6 months of followup, and able to provide informed consent EXCLUSION cauda equina syndrome or severe weakness (Medical Research Council grade <3), previous bed rest or physiotherapy, or unwilling to comply with one of the three treatment strategies	Randomized, N=250 Analyzed, N=250 Attrition, 10% (25/250)	A: Physiotherapy (n=83). The protocol consisted of instructions and advice, segmental mobilization, disc unloading and loading exercises, depending on patients' conditions, and hydrotherapy; 2x/week for at least 4 to, at most, 8 weeks; asked to perform daily exercises at home. B: Bed rest (at home or in-hospital) (n=84). Instructed to stay in bed for 7 days; only allowed out of bed to use the bathroom and shower. After this period, patients supposed to rest as much as possible when in pain. C: Continuation of ADLs (control group) (n=83). Continue jobs, household activities, studies, or hobbies to the best of the patients' abilities; advised to adjust the intensity, duration, and frequency of their activities according to the pain they experienced. All patients received a brochure with instructions and advice regarding their respective treatment; were allowed to use analgesic medication and to call the investigator for help if they had problems or questions. When patients called, they were reassured and urged to comply with their assigned treatment; if necessary, they were seen at the outpatient clinic.

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Hofstee, 2002	A vs. B vs. C Mean age (years): 38 vs. 38 vs. 41.9; p=0.02 Female: 37% vs. 32% vs. 31% Race NR Pain etiology NR Previous LBP: 70% vs. 70% vs. 65% Previous sciatica: 32% vs. 34% vs. 25% Past lumbar surgery: 5% vs. 3% vs. 2% Root compression on CT: 60% vs. 63% vs. 58% Baseline Pain (VAS, 0-100): 60.9 ± 20.1 vs. 65.5 ± 18.5 vs. 60.7 ± 21.4 Disability (QDS): 56.0 ± 17.6 vs. 58.6 ± 14.6 vs. 57.4 ± 16.3	Mixed acute/subacute (radicular pain < 1 month)	6 months

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Hofstee, 2002	Mean improvement in scores from baseline, A vs. B, vs. C Pain (VAS, 0–100) 1 month (mean): 24.2 (n=80) vs. 25.9 (n=84) vs. 23.4 (n=83) 1 month differences (95% CI) A vs. B: –1.7 (NR) A vs. C: 0.8 (–8.2 to 9.8) 2 months (mean): 37.0 (n=77) vs. 38.1 (n=82) vs. 37.3 (n=79) 2 months difference (95% CI) A vs. B: –1.1 (NR) A vs. C: –0.3 (–9.4 to 10.0) 6 months (mean): 46.8 (n=72) vs. 48.2 (n=78) vs. 47.8 (n=75) 6 months difference (95% CI) A vs. B: –1.4 (NR) A vs. C: –1.0 (–10.0 to 8.0) Disability (QDS, 0–100) 1 month (mean): 15.7 (n=80) vs. 11.4 (n=84) vs. 16.2 (n=83) 1 month differences (95% CI) A vs. B: 4.3 (NR) A vs. C: –0.5 (–6.3 to 5.3) 2 months (mean): 26.3 (n=77) vs. 23.5 (n=82) vs. 26.3 (n=79) 2 months difference (95% CI) A vs. B: 2.8 (NR) A vs. C: 0.0 (–7.2 to 7.3) 6 months (mean): 34.6 (n=72) vs. 32.7 (n=78) vs. 35.4 (n=75) 6 months difference (95% CI) A vs. B: 1.9 (NR) A vs. C: –0.7 (–8.4 to 6.9)	New sciatica, 4% (10/250) Cauda equina syndrome, 0.4% (1/250) Pulmonary embolism, 0.4% (1/250) (this patient was in group B; 1.2% (1/84))	Hoelen Foundation	Poor	Confidence intervals could not be calculated for the difference between A vs. B at any timepoint because no SDs were provided. Unclear if the cauda equina syndrome was also in a patient from group B (bed rest)

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Hofstee, 2002 (cont.)	Cumulative No. of patients, A vs. B vs. C; OR (95% CI) Treatment failure 1 month: 2% (n=2) vs. 6% (n=5) vs. 7% (n=6); A vs. C: 0.3 (0.1–1.6); A vs. B: NR 2 months: 13% (n=11) vs. 19% (n=16) vs. 12% (n = 10); A vs. C: 1.1 (0.7–2.8); A vs. B: NR 6 months: 23% (n=19) vs. 25% (n=21) vs. 17% (n = 14); A vs. C: 1.5 (0.7–3.2); A vs. B: NR Surgery 1 month: 2% (n=2) vs. 5% (n=4) vs. 6% (n=5); A vs. C: 0.4 (0.1–2.0); A vs. B: NR 2 months: 12% (n=10) vs. 13% (n=11) vs. 11% (n = 9); A vs. C: 1.1 (0.4–2.9); A vs. B: NR 6 months: 16% (n=13) vs. 19% (n=16) vs. 13% (n = 11); A vs. C: 1.2 (0.5–2.9); A vs. B: NR				

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Hurley, 2015	Ireland 5 centers Acute public teaching hospital	Age 18-65 years, nonspecific LBP ≥3 months or ≥3 episodes in previous 12 months, no recent spinal injury, and low to moderate levels of physical activity Excluded: received treatment for LBP in previous 3 months, radicular pain indicative of nerve root compression, systemic inflammatory disease, severe spinal stenosis, fibromyalgia, neurological disorders, cancer, or acute or subacute LBP with <3 episodes in previous 12 months	246 randomized 110 completed 28% attrition	A. Exercise class for 8 weeks (n=83) B. Walking program for 8 weeks (n=82) C. Usual physiotherapy for 8 weeks (n=81)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Hurley, 2015	A vs. B vs. C Mean age: 45.8 vs. 46.2 vs. 44.2 years Female sex: 71% vs. 71% vs. 62% Race: NR Duration of LBP: 7.0 vs. 8.7 vs. 7.5 years Mean pain over past week, NRS: 5.6 vs. 5.5 vs. 6.0 ODI: 38 vs. 35 vs. 33 EQ-5D: 0.52 vs. 0.57 vs. 0.51 Low physical activity: 44% vs. 62% vs. 58% Moderate physical activity: 39% vs. 33% vs. 30%	Chronic: mean duration 7.0-8.7 years	52 weeks

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Hurley, 2015	A vs. B vs. C ODI: 27 vs. 27 vs. 27; p=0.37 Average pain, NRS: 5.1 vs. 4.2 vs. 4.1; p=0.15 EQ-5D: 0.62 vs. 0.63 vs. 0.62; p=0.72	A vs. B vs. C Withdrawal due to adverse events: 0% vs. 8.5% (7/82) vs. 0%	Health Research Board Project Grant	Fair	Other belief scales available (all nonsignificant), as well as other time points

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Jensen, 2012	Denmark Single center Outpatient back pain clinic	Age 18-60 years, persistent LBP with or without radiculopathy, pain ≥3 on 11-point NRS, duration of current symptoms 2-12 months, at least one modic change extending into the vertebral body, and previous unsuccessful primary care treatment	100 randomized 96 completed 4% attrition	A. Rest, avoiding hard physical activity and rest twice daily for one hour over 10 weeks (n=50) B. Exercise for 10 weeks (n=50)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Jensen, 2012	A vs. B Mean age: 47 vs. 45 years Female sex: 67% vs. 69% Race: NR Mean pain, NRS: 5.6 vs. 5.1 Mean RDQ: 12.0 vs. 13.3 Mean EQ-5D: 0.68 vs. 0.62 Mean BDI: 10.7 vs. 9.6	Subacute/chronic ("persistent", duration of current symptoms 2-12 months, mean duration NR)	52 weeks

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Jensen, 2012	A vs. B (adjusted differences for intervention group) Posttreatment Pain: 5.0 vs. 4.5; adjusted difference -0.07 (95% CI -0.9 to 0.7) RDQ: 11.0 vs. 11.1; adjusted difference -0.6 (95% CI -2.2 to 1.0) EQ-5D: 0.7 vs. 0.7; adjusted difference 0.04 (95% CI -0.007 to 0.09) BDI: 8.6 vs. 7.9; adjusted difference 0.67 (95% CI -0.99 to 2.3) vs. 0.08 (95% CI -0.3 to 0.4) One-year followup Pain: 4.8 vs. 4.3; adjusted difference -0.3 (95% CI -1.3 to 0.6) RDQ: 10.7 vs. 10.7; adjusted difference -1.2 (95% CI -3.3 to 1.0) EQ-5D: 0.7 vs. 0.7; adjusted difference 0.06 (95% CI -0.008 to 0.14) BDI: 9.5 vs. 8.0; adjusted difference -0.92 (95% CI -2.8 to 0.97) vs. -0.17 (95% CI -0.6 to 0.22)	No adverse events reported in any group	VELUX Foundation	Good	No differences in any outcome between groups

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Kell, 2011	Alberta Community setting	Men and women aged 18 - 50 years old with chronic (≥3 months, ≥3 days per week) nonspecific (soft tissue in origin) low back (lumbar 1–5) pain (visual analogue scale [VAS] ≥3). Excluded: pain below the knee, spinal stenosis, herniated or ruptured disc(s), spondylolisthesis, infection in the lumbosacral area, tumor(s), scoliosis, rheumatologic disorder, osteoporosis, previous back surgery, usage of any prescriptive or nonprescriptive pain medication, history of metabolic, endocrine, cardiovascular, or neurological disease.	240 randomized 207 completed 13.75% attrition	A. Periodized musculoskeletal rehabilitation (PMR) training four days per week with 1,563 repetitions each week (n=60) B. PMR training three days per week with 1,344 repetitions each week (n = 60) C. PMR training twice per week with 564 repetitions per week (n=60) D. No training (n=60)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Kell, 2011	A vs. B vs. C vs. D Mean age: 42.4 ± 5.6 vs. 41.7 ± 6.1 vs. 42.8 ± 6.3 vs. 43.2 ± 5.9 Female sex: 30% vs. 37% vs. 33% vs. 38.3% Race: NR Pain duration >3 months: 100% vs. 100% vs. 100% vs. 100%	Chronic (100% with pain > 3 months)	13 weeks

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Kell, 2011	A vs. B vs. C vs. D VAS pain: 4.35 ± 0.95 vs. 4.77 ± 1.00 vs. 4.96 ± 1.03 vs. 5.70 ± 0.86 p≤0.05 difference A vs. B, C, and D p≤0.05 difference B and C vs. D Bench press (function): 79.3 ± 9.7 vs. 70.4 ± 9.1 vs 68.2 ± 9.7 vs. 53.3 ± 9.3 p≤0.05 difference A vs. B, C, and D Lat pull down (function): 75.3 ± 7.1 vs. 70.1 ± 7.7 vs 67.2 ± 7.4 vs. 56.0 ± 6.1 p≤0.05 difference A vs. B, C, and D p≤0.05 difference B and C Leg press (function): 237.2 ± 29.0 vs. 201.7 ± 30.8 vs 184.2 ± 29.5 vs. 139.9 ± 28.9 p≤0.05 difference A vs. B, C, and D p≤0.05 difference B and C ODI: 27.1 ± 10.7 vs. 31.6 ± 11.1 vs. 31.8 ± 10.9 vs 39.1 ± 10.1 p≤0.05 difference A vs. B, C, and D p≤0.05 difference B and C vs. D PCS: 55.7 ± 7.8 vs. 50.4 ± 8.0 vs. 50.2 ± 8.7 vs. 45.0 ± 8.0 p≤0.05 difference A vs. B, C, and D p≤0.05 difference B and C vs. D MCS: 57.7 ± 8.2 vs. 52.6 ± 7.8 vs. 53.1 ± 8.3 vs. 46.0 ± 8.2 p≤0.05 difference A vs. B, C, and D p≤0.05 difference B and C vs. D	The authors report no occurrence of adverse events in treatment groups A and B. NR for treatment groups C and D.	The University of Alberta, Augustana Campus Research and Travel Grant.	Poor	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Little, 2008	England 64 centers General practice	Age 18-65 years, with LBP ≥3 months, score ≥4 on Roland disability scale, and current pain for ≥3 weeks Excluded: serious spinal disease, current nerve root pain, previous spinal surgery, inability to walk 100 m	579 randomized 463 completed 20% attrition	A. Exercise + 24 lessons in Alexander technique (n=71) B. Exercise + 6 lessons in Alexander technique (n=71) C. Exercise + massage (n=72) D. Exercise (n=72) E. 24 lessons in Alexander technique (n=73) F. 6 lessons in Alexander technique (n=73) G. Massage (n=75) H. Usual care (n=72)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Little, 2008	Alexander technique control vs. massage vs. 6 lessons vs. 24 lessons vs. exercise control vs. exercise Mean age: 46 vs. 46 vs. 45 vs. 45 vs. 45 vs. 46 years Female sex: 73% vs. 78% vs. 63% vs. 64% vs. 68% vs. 71% Race: NR Median number of days in pain in previous 4 weeks: 24.5 vs. 28 vs. 28 vs. 28 vs. 28 vs. 28	Chronic; >3 months, average 243 ± 131 days of pain in past 12 months	52 weeks

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Little, 2008	A vs. B vs. C vs. D vs. E vs. F vs. G vs. H Roland disability score vs. usual care: -4.22 (p=0.002) vs. -2.98 (p=0.002) vs. -2.37 (p=0.015) vs. -1.65 vs. -4.14 (p<0.001) vs. -1.44 vs. -0.45 vs. 0 (ref) Number of days of pain in previous 4 months vs. usual care: -20 (p=0.001) vs. -13 (p=0.031) vs. -11 vs. -11 vs. -20 (p=0.001) vs. -13 (p=0.034) vs. -8 vs. 0 (ref) SF-36 PCS vs. usual care: 9.43 (p=0.015) vs. 8.53 (p=0.029) vs. 3.63 vs. -2.08 vs. 11.83 (p=0.002) vs. 2.04 vs. -1.45 vs. 0 (ref) SF-36 MCS vs. usual care: 4.99 vs. 0.64 vs. 2.73 vs. 0.72 vs. 3.74 vs. 4.10 vs. -2.11 vs. 0 (ref)	One patient reported that massage made their back pain worse	Medical Research Council	Good	Deyo troublesomeness score, Von Korff score, back health transition, fear avoidance, and back health measures also reported, at one year and interim time points; although good quality, results are reported in a very confusing way; difficult to separate out exercise component

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Macedo, 2012	Australia, multicenter, primary care settings	chronic nonspecific LBP (3 months' duration) w/w/o leg pain; currently seeking care for LBP; 18-80 years of age; English speaker; patient suitable for active exercises; expected to continue residing in the Sydney or Brisbane region for the study duration; score of moderate or greater on question 7 or 8 of the SF-36. EXCLUDE: known or suspected serious pathology such as nerve root compromise (at least 2 of the following signs: weakness, reflex changes, or sensation loss, associated with the same spinal nerve); previous spinal surgery or scheduled for surgery during trial period; comorbid health conditions that would prevent active participation in exercise programs.	Randomized: N=172 Analyzed: 2 months, n=158; 6 and 12 months, n=155 Attrition: 9.9% (17/172)	A: MCE; stage 1=retraining program to improve activity of muscles assessed to have poor control and reduce activity of any muscle identified to be overactive; taught how to contract trunk muscles in a specific manner and progress until able to maintain isolated contractions of the target muscles for 10 reps of 10 seconds each while maintaining normal respiration (feedback available to enhance learning); additional exercises for breathing control, spinal posture, and lower limb and trunk movement were performed; stage 2 = progression toward more functional activities, first using static and then dynamic tasks; motor control exercise guided by pain, and exercises were mostly pain-free. (n = 86) B: Graded activity; increase activity tolerance by performing individualized and submaximal exercises (based on activities that each participant identified as problematic/could not perform due to pain), in addition to ignoring illness behaviors and reinforcing wellness behaviors; activities progressed in a time-contingent manner; patients received daily quotas and instructed to only perform the agreed amount. (n=86) Both groups to receive 14 individually supervised sessions of approximately 1 hour (12 initial treatment sessions over an 8-week period [2x week for first 4 weeks then 1x/week for next 4 weeks] and 2 booster sessions at 4 and 10 months following randomization; advised to do home exercises (type, intensity, number at discretion of PT) for 30 mins/week in first month and 1 hr/week in second month.

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Macedo, 2012	A vs. B Mean age (years): 48.7 vs. 49.6 Female: 66.3% vs. 52.3% Race: NR Baseline Pain intensity (NRS): 6.1 vs. 6.1 Function (PSFS): 3.7 vs. 3.6 Disability (RDQ-24): 11.4 vs. 11.2 Quality of Life (SF-36 PCS and MCS): 43.9 vs. 43.8 and 52.9 vs. 54.7 Global impression of change (GPE): –1.4 vs. –1.6	chronic/mixed subacute; mean LBP duration (mos) (A vs. B): 74.0 vs. 100.7	12 months

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Macedo, 2012	A vs. B (mean ± SD; adjusted treatment effect (95% CI)) Pain intensity (NRS) baseline: 6.1 ± 1.9 vs. 6.1 ± 2.1 (NS) 2 months: 4.1 ± 2.5 vs. 4.1 ± 2.5, 0.0 (–0.7 to 0.8), p=0.94 6 months: 4.1 ± 2.5 vs. 4.1 ± 2.7, 0.0 (–0.8 to 0.8), p=0.99 12 months: 3.7 ± 2.7 vs. 3.7 ± 2.6, 0.1 (–0.7 to 0.9), p=0.83 Function (PSFS) baseline: 3.7 ± 1.6 vs. 3.6 ± 1.6 (NS) 2 months: 5.9 ± 2.1 vs. 5.5 ± 2.4, 0.2 (–0.5 to 0.9), p=0.53 6 months: 5.7 ± 2.3 vs. 5.7 ± 2.4, –0.2 (–0.9 to 0.5), p=0.53 12 months: 5.9 ± 2.2 vs. 6.1 ± 2.3, –0.4 (–1.1 to 0.3), p=0.25 Disability (RDQ-24) baseline: 11.4 ± 4.8 vs. 11.2 ± 5.3 (NS) 2 months: 7.5 ± 6.4 vs. 8.0 ± 6.5, –0.8 (–2.2 to 0.7), p=0.30 6 months: 8.0 ± 7.1 vs. 8.6 ± 6.8, –0.8 (–2.3 to 0.6), p=0.26 12 months: 7.4 ± 6.7 vs. 8.0 ± 6.9, –0.6 (–2.0 to 0.9), p=0.45 Quality of Life, SF-36 PCS baseline: 43.9 ± 10.8 vs. 43.8 ± 10.3 (NS) 2 months: 51.6 ± 12.0 vs. 51.6 ± 13.4, –0.2 (–13.7 to 3.2), p=0.89 6 months: 52.6 ± 13.0 vs. 51.2 ± 13.8, 1.1 (–2.4 to 4.6), p=0.54 12 months: 53.8 ± 12.7 vs. 53.3 ± 14.0, –0.3 (–3.8 to 3.3), p=0.88	A vs. B Mild adverse effects: 22.1% (19/86) vs. 19.8% (17/86), RR=1.12 (95% CI, 0.62 to 2.00), including (not reported by A vs. B): temporary exacerbation of pain, n = 27; increased pain of preexisting musculoskeletal conditions, n=7; development of shin splints, n=1; hip bursitis, n=1 Withdrawals (by 12 months): 8.1% (7/86) vs. 2.3% (2/86), RR=3.50 (95% CI, 0.75 to 16.37) RRs calculated by EPC	Australia's National Health and Medical Research Council; the funding source had no role in the planning or conduct of the study.	Fair	MCE and graded activity have similar effects (no significant difference between groups for any outcome)

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Machado, 2010	Australia Multicenter (27) Primary care clinics	18 to 80 years old; present with a new episode of acute non-specific LBP; and be able and willing to visit one of the trial physical therapists for commencement of the McKenzie treatment program within 48 h of presentation to the physician. EXCLUSION nerve root compromise; 'red flags' for serious spinal pathology (for example, infection, fracture); spinal surgery in the past 6 months; pregnancy; severe cardiovascular or metabolic disease; or the inability to read and understand English.	Randomized, N=148 Analyzed, N=146 Attrition, 5.5% (8/146)	A: McKenzie method + first-line care (n=73). Number of treatment sessions at discretion of the PT, with a max of 6 session over 3 weeks; encouraged to perform the prescribed exercises at home and to follow PT's postural advice at all times; some participants received lumbar support (93%, original McKenzie lumbar roll). B: First-line care only (n=73). Consisted of advice to remain active and to avoid bed rest, reassurance of the favorable prognosis of acute LBP and instructions to take acetaminophen (paracetamol) on a time-contingent basis (NSAIDs not prescribed however those already on them were allow to remain on them); 3 weeks, return for followup as needed during that time

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Machado, 2010	A vs. B Mean age (years): 47.5 vs. 45.9 Female: 52% vs. 48% Race NR Pain etiology NR Referred pain to leg: 45% vs. 50% Previous LBP episode: 74% vs. 67% Baseline Pain (NRS): 6.6 ± 1.8 vs. 6.3 ± 1.9 Function (PSFS): 3.7 ± 1.6 vs. 3.4 ± 1.8 Disability (RDQ): 13.7 ± 5.5 vs. 13.5 ± 5.3	Acute (defined as pain in the area between the 12th rib and buttock crease, w/w/o leg pain, of < 6 weeks duration, preceded by a period of at least 1 month without LBP in which the patient did not consult a health care practitioner). A vs. B < 2 weeks: 66% vs. 67% 2–6 weeks: 34% vs. 33%	3 months

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Machado, 2010	A vs. B (treatment effects [95% CI] are model-based adjusted differences in outcomes between groups) Pain (NRS) **1 week: –0.4 (–0.8 to –0.1); p=0.02** (A, n=70; B, n=69) **3 weeks: –0.7 (–1.2 to –0.1); p=0.02** (A, n=70; B, n=68) **Mean pain over first 7 days: –0.3 (–0.5 to –0.0); p=0.02** (A, n=70; B, n=69) Function (PSFS) 1 week: 0.0 (–0.4 to 0.5); p=0.90 (A, n=70; B, n=68) 3 weeks: 0.0 (–0.7 to 0.8); p=0.90 (A, n=70; B, n=69) Disability (RDQ) 1 week: –0.2 (–1.5 to 1.0); p=0.74 (A, n=70; B, n=68) 3 weeks: –0.3 (–2.3 to 1.6); p=0.74 (A, n=70; B, n=69) Global perceived effect 1 week: 0.5 (–0.0 to 1.1); p=0.07 (A, n=70; B, n=68) 3 weeks: 0.3 (–0.3 to 0.8); p=0.33 (A, n=70; B, n=69) Development of persistent LBP: 53% (37/70) vs. 47% (32/68); RR 1.1, 95% CI 0.8 to 1.6, p=0.49 Sought additional health care for LBP complaints: 7% (5/70) vs. 26% (18/68); RR 0.27, 95% CI 0.1 to 0.7, p=0.002	NR	research and development grant from the University of Sydney, Australia.	Fair	For all outcomes except pain, the additional effects of the McKenzie method were near zero at all time points and not statistically significant. Authors' conclusions: A treatment program based on the McKenzie method does not produce appreciable improvements in pain, disability, function, global perceived effect or risk of developing persistent symptoms. Patients receiving only the recommended first-line care seek more additional health care than patients receiving the McKenzie method.

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Pengel, 2007	Australia, New Zealand Multicenter (7) PT clinics at University teach hospitals (6) and a primary care clinic (1)	18 to 80 years of age with nonspecific LBP lasting for at least 6 weeks but no longer than 12 weeks. EXCLUSION spinal surgery in the past 12 months, pregnancy, nerve root compromise, confirmed or suspected serious spinal abnormality (for example, infection, fracture, or the cauda equina syndrome), contraindications to exercise, and poor comprehension of the English language; participants who were receiving low back pain treatment other than spinal surgery were NOT excluded	Randomized, N=260 Analyzed, N=259 Attrition: 10.8% (28/259)	A: Exercise and advice (n=63). B: Sham exercise and advice (n=63). C: Exercise and sham advice (n=65). D: Sham exercise and sham advice (n=68). **Exercise**: Based on program described by Lindstrom and colleagues, to improve the abilities of participants to complete functional activities that they specified as being difficult to perform because of low back pain and includes: aerobic exercise (for example, a walking or cycling program), stretches, functional activities, activities to build speed, endurance, and coordination, and trunk- and limb-strengthening exercises. PTs used principles of cognitive-behavioral therapy and provided individualized home exercise programs; **Sham exercise:** Sham pulsed ultrasonography (5 minutes) and sham pulsed short-wave diathermy (20 minutes); **Advice:** Based on the program by Indahl and colleagues and aimed to encourage a graded return to normal activities. PTs explained the benign nature of LBP, addressed any unhelpful beliefs about back pain, and emphasized that being overly careful and avoiding light activity would delay recovery; **Sham advice:** Participants could talk about their LBP and any other problems, PT responded in a warm and empathic manner, displaying genuine interest, but did not give advice about the LBP. The 12 exercise or sham exercise sessions were delivered over 6 weeks: 3 sessions per week in weeks 1 and 2, 2 sessions per week in weeks 3 and 4, and 1 session per week in weeks 5 and 6. In weeks 1, 2, and 4, participants also received advice or sham advice.

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Pengel, 2007	A vs. B vs. C vs. D Mean age (years): 50.1 vs. 51.2 vs. 48.0 vs. 50.0 Female: 46% vs. 44% vs. 46% vs. 54% Race NR Pain etiology NR Previous episodes of LBP: 71% vs. 69% vs. 60% vs. 65% Referred pain to legs: 29% vs. 38%, vs. 31% vs. 29% Baseline Pain (NRS): 5.4 ± 2.2 vs. 5.5 ± 2.1 vs. 5.4 ± 1.9 vs. 5.3 ± 1.7 Function (PSFS): 3.8 ± 1.9 vs. 3.8 ± 1.8 vs. 3.7 ± 2.0 vs. 4.0 ± 1.7 Disability (RDQ): 9.1 ± 4.8 vs. 8.2 ± 4.4 vs. 8.3 ± 5.0 vs. 8.1 ± 5.6 Global perceived effect: –0.4 ± 2.3 vs. 0.2 ± 2.3 vs. –0.3 ± 2.6 vs. 0.5 ± 2.3 Depression (DASS): 7.3 ± 8.8 vs. 7.4 ± 7.7 vs. 7.1 ± 7.8 vs. 7.1 ± 7.6 Anxiety (DASS): 4.7 ± 6.7 vs. 5.2 ± 7.4) vs. 6.2 ± 7.6 vs. 5.4 ± 6.9 Stress (DASS): 10.1 ± 9.0 vs. 11.7 ± 8.7 vs. 12.6 ± 9.1 vs. 11.7 ± 10.0	Mixed acute/subacute A vs. B vs. C vs. D 6–8 weeks: 48% vs. 51% vs. 45% vs. 47 9–11 weeks: 34% vs. 41% vs. 38% vs. 37% 12 weeks: 18% vs. 8% vs. 17% vs. 16%	12 months

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Pengel, 2007	Adjusted multivariable mixed model, relative change (95% CI) Exercise vs. No Exercise Pain (NRS) **6 weeks: –0.8 (–1.3 to –0.3), p=0.004** 3 months: –0.5 (–1.1 to 0.1), p=0.092 12 months: –0.5 (–1.1 to 0.2), p=0.138 Function (PSFS) 6 weeks: 0.4 (–0.2 to 1.0), p=0.174 3 months: 0.5 (0.0 to 1.1), p=0.063 12 months: 0.5 (–0.1 to 1.0), p=0.094 Disability (RDQ): 6 weeks: –0.8 (–1.8 to 0.3), p=0.141 3 months: –0.1 (–1.2 to 1.1), p=0.901 12 months: –0.3 (–1.6 to 0.9), p=0.597 Global perceived effect **6 weeks: 0.5 (0.1 to 1.0), p=0.017** **3 months: 0.5 (0.1 to 1.0), p=0.030** 12 months: 0.4 (–0.1 to 1.0), p=0.134 Depression (DASS) 6 weeks: –0.7 (–2.5 to 1.2), p=0.47 3 months: –0.3 (–2.1 to 1.6), p=0.78 12 months: –0.6 (–2.6 to 1.3), p=0.51	Mild adverse events (muscle soreness, increased pain, tiredness, nausea, weight gain, itchy scalp, and numbness in the legs): 8.1% (21/259) A vs. B vs. C vs. D 15.9% (10/63) vs. 4.8% (3/63) vs. 9.2% (6/65) vs. 2.9% (2/68) EPC calculated RR any exercise (groups A and C) vs. any sham ex or advice (Groups b and D) RR 3.3 (95% CI 1.2 to 8.7) p = 0.0105	National Health and Medical Research Council of Australia and the Australasian Low Back Pain Trial Committee. The funding sources had no role in study design; collection, analysis, or interpretation of the data; or writing of the report.	Fair	Adjustment for the following baseline variables: currently taking pain medication, currently smoking, currently exercising, low back pain treatment in previous 6 weeks, and previous surgery for low back pain.

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Pengel, 2007 (cont.)	Exercise + Advice vs. No Exercise or Advice Pain (NRS) **6 weeks: –1.5 (–2.2 to –0.7) ,p<0.001** **3 months: –1.1 (–2.0 to –0.3), p=0.009** 12 months: –0.8 (–1.7 to 0.1),p=0.069 Function (PSFS) **6 weeks: 1.1 (0.3 to 1.9), p=0.006** **3 months: 1.3 (0.6 to 2.1), p=0.001** **12 months: 1.1 (0.3 to 1.8), p=0.005** Disability (RDQ): 6 weeks: –1.3 (–2.7 to 0.2), p=0.085 3 months: –1.0 (–2.6 to 0.6), p=0.20 12 months: –0.9 (–2.7 to 0.8), p=0.29 Global perceived effect **6 weeks: 1.3 (0.7 to 1.9), p<0.001** **3 months: 0.8 (0.2 to 1.5), p=0.017** 12 months: 0.8 (0.0 to 1.6), p=0.059 Depression (DASS) 6 weeks: 0.2 (–2.5 to 2.8), p=0.91 3 months: 0.2 (–2.4 to 2.7), p=0.91 12 months: –0.4 (–3.1 to 2.3), p=0.76				

Please see Appendix C. Included Studies for full study references.

Table E15. Data abstraction of systematic reviews of Pilates

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Wells, 2014	Pilates vs. standard care and physical activity Pilates vs. other exercise forms Pilates vs. other exercise	10 data bases; Cumulative Index to Nursing and AlliedHealth Literature; Cochrane Library; Medline; Physiotherapy Evidence Database; ProQuest: Health and Medical Complete, Nursing and Allied Health Source, Dissertation and Theses; Scopus; Sport Discus; Web of Science; hand searching. English only	14 RCTS; CLBP of >3 months duration; if studies included acute or subacute LPB with CLBP, were included, Pilates vs standard care and physical activity (9 studies) Pilates vs massage (1 study) Pilates vs. other exercise (4 studies)	A. Pilates (14 studies) B. Standard care and physical activity (9 trials); vs. other exercise (4 trials) vs. massage therapy (1 trial) Total N for studies of Pilates vs. standard care/physical activity (N=301); Pilates vs. other exercise (N=199); Pilates vs. massage (N=21)	Yes: Modified Guidelines for use of the McMasters Critical Appraisal Form for Quantitative Studies

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Wells, 2014	Qualitative synthesis due to heterogeneity	A vs. B Abstract outcomes in the following order (when reported): Pain Function Quality of life Work-related outcomes Global improvement Time between episodes Patient satisfaction	A vs. B	Fair

Please see Appendix C. Included Studies for full study references.

Table E16. Data abstraction of randomized controlled trials of tai chi

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Hall, 2011	Australia Community setting	Age 18-70 years, with persistent nonspecific LBP and moderate pain or moderate activity limitation Excluded: known or suspected serious spinal pathology, scheduled for spinal surgery, or contraindicated for exercise	160 randomized 151 completed 5.6% attrition	A. Tai chi, 18 sessions over 10 weeks (n=80) B. Waitlist (n=80)	A vs. B Mean age: 43 vs. 44 years Female sex: 79% vs. 70% Race: NR Pain duration >3 months: 100% vs. 100%	Chronic (100% with pain > 3 months)	10 weeks
Weifen, 2013	China Single center University medical center	Age 25-45 years, non-specific LBP with duration 1-5 years, mean VAS in previous week of 4, and not involved in physical therapy in previous 3 months	320 randomized Number completed NR Attrition NR	A. Tai chi chuan (n=141) B. Backward walking (n=47) C. Jogging (n=47) D. Swimming (n=38) E. No exercise (n=47)	A vs. B vs. C vs. D vs. E Mean age: 37.5 vs. 38.2 vs. 37.2 vs. 37.5 vs. 38.1 years Female sex: 39% vs. 45% vs. 40% vs. 45% vs. 40% Race: NR Mean VAS: 5.3 vs. 5.2 vs. 5.0 vs. 5.2 vs. 5.1 Mean duration of pain: 2.1 vs. 2.1 vs. 1.9 vs. 2.0 vs. 2.2 years	Chronic (mean duration 2.1 ± 0.8 years)	26 weeks

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Hall, 2011	A vs. B Bothersomeness, NRS: 5.0-3.7 vs. 4.5-4.9; mean between-group difference 1.7 (95% CI 0.9 to 2.5) Pain, NRS: 4.4-3.4 vs. 4.4-4.7; mean between-group difference 1.3 (95% CI 0.7 to 1.9) PDI: 22.7-17.0 vs. 23.9-23.8; mean between-group difference 5.7 (95% CI 1.8 to 9.6) RDQ: 10.2-7.0 vs. 9.1-8.1; mean between-group difference 2.6 (95% CI 1.1 to 3.7) QBPDS: 29.2-22.0 vs. 30.2-29.6; mean between-group difference 6.6 (95% CI 2.4 to 10.7) PSFS: 3.5-4.7 vs. 4.0-4.1; mean between-group difference -1.0 (95% CI -1.7 to -0.4) GPE: 0.4-1.6 vs. -0.1-0.4: mean between-group difference -0.8 (95% CI -1.5 to -0.0); p=0.05 <u>Proportion achieving ≥30% improvement</u> Bothersomeness, NRS: 50% vs. 17.5%; NNT 4 Pain, NRS: 46.3% vs. 15%; NNT 4 PDI, 45% vs. 17.5%; NNT 4 RDQ: 50% vs. 23.8%; NNT 4 QBPDS: 40% vs. 7.5%; NNT 4 PSFS: 43.8% vs. 16.3%; NNT 4	Three participants reported a small initial increase in back pain symptoms that were alleviated by the third or fourth week, participant reported an increase in upper back pain that was alleviated once they corrected upper extremity posture.	Arthritis Foundation of Australia, Arthritis Care of the UK	Fair	
Weifen, 2013	A vs. B vs. C vs. D vs. E VAS, 3 months: 2.7 vs. 3.3 vs. 3.4 vs. 2.8 vs. 3.6; p<0.05 for A vs. all other groups except D VAS, 6 months: 2.3 vs. 2.9 vs. 3.1 vs. 2.4 vs. 3.2; p<0.05 for A vs. all other groups except D	No adverse events were reported in any of the groups	NR	Fair	Poor reporting

Please see Appendix C. Included Studies for full study references.

Appendix 17. Data abstraction of systematic reviews of yoga

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies
Cramer, 2013	Yoga vs. usual care (2 RCTs) Yoga vs. education (7 RCTs) Yoga vs. exercise (3 studies);	January 2012: Medline, EMBASE, the Cochrane Library, PsycINFO, and CAMBASE; no language restrictions	10 RCTs in qualitative synthesis; Two citations with different outcomes from same trial, treated as single study8 included in quantitative synthesis; 9/10 studies included CLBP patients; 1 included acute, subacute or chronic	A. Yoga B. Usual care C. Education D. Exercise TOTAL n for each intervention unclear across all studies; Total N for all studies = 1067	2009 Updated Method Guidelines for Systematic Reviews in the Cochrane Back Review Group	Random effects model (RevMan) - SMD (95% CI) for continuous outcomes (negative value favors Yoga) with use of Cohen categories for overall effect size; RR (95% CI) for dichotomous outcomes; Order of priority for analysis of overall effect - no treatment, usual care, education, exercise

Author, Year	Results	Adverse Events	Quality
Cramer, 2013	A vs. any control SMD (95% CI); p-value test for effect Short term (measures closest to 12 weeks, overall): Pain (6 studies): SMD -0. 48 (95%CI -0.65 to -0.31); p<0.00001; I^2=0% Back-specific disability (8 studies): SMD -0.59 (-0.87 to -0.30);p<0.0001; I^2=59% HRQOL (4 studies): SMD 0.41 (-0.11 to 0.93) p=0.12; I^2=72% Global improvement (2 studies) RR 3.27 (95% CI 1.89 to 5.66); p<0.01; I^2=0% Long Term (measures closest to 12 months, overall): Pain (5 studies): SMD -0.33 (95%CI -0.59 to -0.07) p=0.01; I^2=48% Back-specific disability (5 studies): SMD -0.35 (-0.55 to -0.15); p=0.0007; I^2=20% HRQOL (2 studies): SMD 0.18 (-0.05 to 0.41);p=0.13; I^2=0% By control group: A vs. B: Short term back-specific disability (2 studies, n=106): SMD -0.65 (-1.62 to 0.33); p=0.20; I^2=62% A vs. C: Short-term: Pain (5 studies): SMD -0.45 (-0.63 to -0.26); p<0.01; I^2=0% Back-specific disability (5 studies): SMD 0.45 (-0.65 to -0.25); p<0.01; I^2=8% HRQOL (3 studies): SMD 0.25 (0.02 to 0.47) p=0.03; I^2= 0% Long term: Pain (4 studies): SMD -0.28 (-0.58 to -0.02); p=0.07; I^2=47% Back-specific disability (4 studies): SMD 0.39 (-0.66 to -0.11); p<0.01; I^2=40% HRQOL (2 studies): SMD 0.18 (-0.05 to 0.41); p=0.13; I^2=0% A vs. D: Short-term, back-specific disability (disability) SMD -0.59 (-1.87 to 0.67); p=0.36; I^2=95%	Safety: 3 studies, 10.5 % (26/248); No major adverse events (1 study) 13 "mild to moderate" adverse events, 1 herniated disc in Yoga (1 study) 11 adverse events (mainly pain), 1 serious adverse event in yoga (severe pain) (1 study) drop out due to respiratory infection (n=2 in 2 studies-unclear)' Denominators not provided	Good

Please see Appendix C. Included Studies for full study references.

Table E18. Data abstraction of randomized controlled trials of yoga

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants
Nambi, 2014	1 center: C.U. Shah Physiotherapy College, Gujarat, India	>18 years old with nonspecific LPB for 3 months; EXCLUDED: 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 Analyzed:54 Attrition: 10% (6/60)	A: 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 (n=30) B: 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 (n=30)	A vs. B Mean age: 44.26 vs. 43.66 Female: 63.34% vs. 43.34% 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

Author, Year	Duration of Pain (acute, subacute, chronic)	Duration of Followup	Results
Nambi, 2014	Chronic (>3 months), mean duration; nonspecific	6 months	A vs. B Pain intensity (10 cm VAS, mean): 4weeks 3.8 vs. 5.3; 6 months 1.8 vs. 3.8, % improvement 72.81% vs. 42.5%, p=0.001; SMD* 4 weeks (-1.66, 95% CI -2.24 to -1.07); 6 months (-2.17, 95% CI -2.81 to -1.53) Physically unhealthy days (mean): 4 weeks 7.7 vs. 12.0; 6 months 2.6 vs. 6.9, % improvement 85.61% vs. 61.0%, p=0.001; Mentally unhealthy days (mean): 4 weeks 8.4 vs. 10.5; 6 months 2.6 vs. 6.9, % improvement 87.53% vs. 71.37%, p=0.001; Activity limitation days (mean): 4 weeks 7.5 vs. 12.0; 6 months 2.0 vs. 5.0, % improvement 87.83% vs. 70.59%, p=0.001; *SMD calculated from means and SD based on sample before attrition

Author, Year	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Nambi, 2014	Not evaluated or reported	None	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants
Saper, 2013	Boston Medical Center and 5 affiliated federally qualified community health centers	18-64 years old, current non-specific LBP persisting ≥12 weeks with average intensity of ≥4 for previous week (0=no pain, 10 worst possible pain); sufficient English fluency to understand class instructions and complete questionnaires; EXCLUDED- known specific back pain pathology (spinal stenosis, spondylolisthesis, ankylosing spondylitis, severe scoliosis, malignancy, fracture); sciatic pain ≥ low back pain, spine surgery in previous 3 years, severe or progressive neurological deficit, new back pain treatment started within previous month or anticipated during study; pregnancy, Yoga practice in previous 6 months, active or planned workers compensation, disability or personal injury claims; perceived religious conflict.	Randomized: 95 Analyzed: at 6 weeks - 88; at 12 weeks 91 Attrition: 4.2 % (4/95)	A: 75 minute Hatha Yoga class once per week + recommended 30 minute home practice (n=49) B: 75 minute Hatha Yoga class twice per week + recommended 30 minute home practice (n=46) 12 weeks	Mean age: 46.4 vs. 48.7 years Female: 71% vs. 80% Race: White: 10% vs. 26% Black: 67% vs. 41% Other: 22% vs. 33% Hispanic: 6% vs. 13% Baseline pain (mean, low back pain intensity, 11 point numeric scale) 7.1 vs. 6.7 Back-specific function: (mean RDQ) 13.7 vs. 13.6 SF-26 Physical: 37.5 vs. 37.4; Mental 44.8 vs.44.1

Author, Year	Duration of Pain (acute, subacute, chronic)	Duration of Followup	Results
Saper, 2013	Chronic (nonspecific, ≥ months); reported duration varied from <1 year to ≥10 years; statistical difference between groups at baseline treated as confounder	12 weeks	A vs. B Change from baseline, *between group* difference in means: Pain: 6 weeks, −0.3 (−1.1 to 0.6), p=0.49; 12 weeks, 0.3 (−0.2 to 0.8), p=0.62 RDQ: 6 weeks −0.6 (−2.7 to 1.6), p-0.62; 12 weeks, −0.1 (−1.4 to 1.2), p= 0.83 Pain: proportion experiencing ≥30% improvement from baseline: 29% (23/47) vs. 59%(26/44), p=0.33, RR 0.83 (95% CI 0.57 to 1.12): proportion experiencing ≥50% improvement from baseline: 57% (27/47) vs. 66% (29/44), p=0.41, RR 1.14 (95% CI 0.64 to 2.02; RDQ proportion experiencing ≥30% improvement from baseline: 57% (27/47) vs. 66%(29/44), p=0.41, RR 0.87 (95% CI 0.63 to 1.21): proportion experiencing ≥50% improvement from baseline: 47% (22/47) vs. 50% (22/44), p=0.76, RR 0.94 (95% CI 0.61 to 1.43) Change from baseline, between group difference in means SF-36 Physical: 6 weeks 1.6 (95% CI -1.6 to 4.9) p=0.33; 12 weeks 0.2 (-3.4 to 3.7) p =0.93; SF-36 Mental 6 weeks 2.2 (-1.9 to 6.3) p=0.29; 12 weeks 1.5 (-2.6 to 5.6) p=0.47 A vs. B Other outcomes: Overall improvement scores: Same for A and B (mean 4.5, median 5) Satisfaction scores: mean 1.3 vs. 1.5, median 1 for both Medication use: Use of any pain medication decrease at 6 weeks (27% vs. 35%) and remained similar at 12 weeks, but NS difference in use of any pain medication or specific analgesic categories. Per protocol analyses did not reveal any statistical differences between groups for any outcome; Dose-response: Substantial variability in data; authors report potential for a "modest" dose-response" relationship with decrease in relationship slope for change in pain at approximately 12 class and approximately 9 classes for RDQ -figure provided, but not detailed data -Authors indicated the conclusions regarding the causality of the association are not possible. Adherence: Class attendance: 65% (32/47) vs. 44% (20/44), p=0.04; weekly amount of home practice 93 vs. 97 minutes; home practice for both groups a median of 4 days/week; Hours of class + home 37 vs. 29, p =0.037

Author, Year	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Saper, 2013	A vs. B Total: 27% (13/49) vs. 37% (17/46), p= 0.47; mostly musculoskeletal with LBP exacerbation most common; Related to intervention (total events): Definitely 1. vs. 2 ; Possibly 12 vs. 15; Serious 0 vs. 1 (persistent symptoms of cervical radiculopathy possibly from hyperextension in setting of preexisting cervical disc disease; Detailed list (number) of adverse events: Back pain 5 vs.8 Neck pain 1 vs. 3 (includes the participant with radiculopathy) Sciatica 1 vs. 2 Headache 1 vs. 2 Dizziness 1 vs. 1 Knee pain 1 vs. 0 Ankle pain 0 vs. 1 Shoulder pain 1 vs. 0 Abdominal pain 1 vs. 0 Wheezing 1 vs. 0	NCCAM, NIH RO1 grant	Fair

Please see Appendix C. Included Studies for full study references.

Table E19. Data abstraction of systematic reviews of psychological therapies

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral vs. waiting list control	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	3 RCTs (n=74) ROB: 0 low, 3 high Followup: post-treatment only Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Respondent therapy (progressive relaxation) (n=39) B. Waiting list control (n=35)	Risk of bias (Cochrane Back Review Group)
Henschke, 2010	Behavioral vs. waiting list control	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	4 RCTs (n=108) ROB: 3 low, 1 high Followup: post-treatment only Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Respondent therapy (EMG biofeedback) (n=56) B. Waiting list control (n=52)	Risk of bias (Cochrane Back Review Group)
Henschke, 2010	Behavioral therapy vs. waiting list control	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	4 RCTs (n=243) ROB: 3 low, 1 high Followup: post-treatment only Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Operant therapy (n=142) B. Waiting list control (n=101)	Risk of bias (Cochrane Back Review Group)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	Meta-analysis Note. Negative MD or SMD favors treatment A.	Pain intensity (VAS, 0-100): Post-treatment MD: -19.77 (95% CI -34 to -5.20), p=0.0078 (3 studies, N=74) (SOE: low) Functional status (generic) (various scales): Post-treatment SMD: -0.88 (95% CI -1.36 to -0.39), p=0.00041 (3 studies, N=74) (SOE: low) Depression (Beck Depression Inventory, 0-63): Post-treatment MD: -6.80 (95% CI -20 to 6.12), p=0.30 (2 studies, N=58) (SOE: very low)	NR	Good	Stuckey 1986; Turner 1982; Turner 1993
Henschke, 2010	Meta-analysis of 3 studies (not Bush) Note. Negative MD or SMD favors treatment A.	Pain intensity (various scales) Post-treatment SMD: -0.80 (95% CI -1.32 to -0.28) p=0.0025 (3 studies, N=64) (SOE: low) Functional status (generic) (various scales): Post-treatment SMD: -0.17 (95% CI -1.56 to 1.22), p=0.81 (2 studies, N=44) (SOE: very low) Results for Bush study (not poolable): no differences between groups in pain or functional status.	NR	Good	Bush 1985; Newton-John 1995 Nouwen 1983; Stuckey 1986;
Henschke, 2010	Meta-analysis of up to 3 studies (not Kole-Snijders 1996) Note. Negative MD or SMD favors treatment A.	Pain intensity (various scales): Post-treatment SMD: -0.43 (95% CI, -0.75 to -0.11) p=0.0091 (3 studies, N=153) (SOE: moderate) Functional status (generic) (Sickness Impact Profile, 0-136): Post-treatment MD: -1.18 (95% CI -3.53, 1.18), p=0.33 (2 studies, N=87) (SOE: low) Depression (various scales: Post-treatment SMD: -0.11 (95% CI -0.67 to 0.44), p=0.69 (2 studies, N=103) (SOE: low)	NR	Good	Kole-Snijders 1996; Linton 1989; Turner 1988; Turner 1990

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral therapy vs. waiting list control	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	2 RCTs (n=68) ROB: 0 low, 2 high Followup: post-treatment only Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Cognitive therapy (n=29) B. Waiting list control (n=39)	Risk of bias (Cochrane Back Review Group)
Henschke, 2010	Behavioral therapy vs. waiting list control	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	5 RCTs (n=239) ROB: 3 low, 2 high Followup: post-treatment only Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Cognitive-behavioral therapy (n=129) B. Waiting list control (n=110)	Risk of bias (Cochrane Back Review Group)
Henschke, 2010	Behavioral therapy vs. behavioral therapy	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	1 RCT (n=24) ROB: 0 low, 1 high Followup: post-treatment, 3 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Respondent therapy (EMG biofeedback) (n=12) B. Respondent therapy (progressive relaxation) (n=12)	Risk of bias (Cochrane Back Review Group)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	Meta-analysis Note. Negative MD or SMD favors treatment A.	Pain intensity (various scales): Post-treatment SMD: -0.27 (95% CI -0.75 to 0.22), p=0.29 (2 studies, N=68) (SOE: low) Functional status (generic) (various scales): Post-treatment SMD: -0.15 (95% CI -0.64 to 0.33), p=0.53 (2 studies, N=68) (SOE: low)	NR	Good	Linton 2008; Turner 1993
Henschke, 2010	Meta-analysis Note. Negative MD or SMD favors treatment A.	Pain intensity (various scales): Post-treatment SMD: -0.60 (95% CI -0.97 to -0.22), p=0.0017 (5 studies, N=239) (SOE: low) Functional status (generic) (various scales): Post-treatment SMD:-0.37 (95% CI -0.87, 0.13), p=0.15 (4 studies, N=134) (SOE: low) Depression (Beck Depression Inventory, 0-63): Post-treatment MD: -1.92 (95% CI -6.16, 2.32), p=0.38 (4 studies, N=194) (SOE: very low)	NR	Good	Newton-John 1995; Smeets 2006; Turner 1982; Turner 1988; Turner 1993
Henschke, 2010	No pooling (single study) Note. Negative difference favors treatment A	Pain intensity (McGill Pain Questionnaire): Post-treatment, difference between groups:-11.59, p>0.05; 3 months, difference between groups: -17.00, p>0.05 Pain intensity (0-10 VAS) Post-treatment, difference between groups:-0.64, p=N; 3 months, difference between groups: -1.06, p>0.05 SOE: NR	NR	Good	Donaldson 1994

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral therapy vs. behavioral therapy	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	2 RCTs (n=93) ROB: 1 low, 1 high Followup: post-treatment, 6 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Cognitive therapy (n=49) B. Operant therapy (n=44)	Risk of bias (Cochrane Back Review Group)
Henschke, 2010	Behavioral therapy vs. behavioral therapy	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	1 RCT (n=47) ROB: 0 low, 1 high Followup: post-treatment, 6 months, 12 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Cognitive therapy (n=49) B. Respondent therapy (progressive muscle relaxation) (n=44)	Risk of bias (Cochrane Back Review Group)
Henschke, 2010	Behavioral therapy vs. behavioral therapy	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	No studies	A. Operant therapy (n=0) B. Respondent therapy (n=0)	

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	Meta-analysis Note. Negative MD or SMD favors treatment A.	Pain intensity: Post-treatment SMD: 0.41 (95% CI -0.63 to 1.45), p=0.44 (2 studies, N=93) (moderate SOE) 6 months SMD: 0.35 (95% CI -0.64 to 1.35), p=0.48 (2 studies, N=82) (moderate SOE)	NR	Good	Leeuw 2008; Nicholas 1991
Henschke, 2010	No pooling (single study) Note. Negative difference favors treatment A	Pain intensity (VAS): Post-treatment difference between groups: 1.00, p>0.05; 6 months: data NR, p>0.05; 12 months: data NR, p>0.05 Functional status (generic) (Sickness Impact Profile): 6 months, data NR, p>0.05; 12 months, data NR, p>0.05 Global measure of improvement (measure NR): 6 months, data NR, p>0.05; 12 months, data NR, p>0.05 SOE: NR	NR	Good	Turner 1993
Henschke, 2010				Good	

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral therapy vs. behavioral therapy	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	2 RCTs (n=61) ROB: 0 low, 2 high Followup: post-treatment, 6 months, 12 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Combination of cognitive and behavioral therapies (n=37) B. Cognitive therapy (n=24)	Risk of bias (Cochrane Back Review Group)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	Meta-analysis Note. Negative MD or SMD favors treatment A.	Pain intensity (various scales): Post-treatment SMD: -0.24 (95% CI -1.36 to 0.87), p=0.67 (2 studies, N=61) (SOE: very low) 6 months SMD: -0.30 (95% CI -2.59 to 1.98), p=0.79 (2 studies, N=44) (SOE: very low) 12 months SMD: -0.89 (95% CI -3.64 to 1.87), p=0.53 (2 studies, N=48) (SOE: very low) Functional status (generic) (Sickness Impact Profile, 0-136): Post-treatment MD: -2.01 (95% CI -10 to 5.99), p=0.62 (2 studies, N=61) (SOE: low) 6 month MD: -3.20 (95% CI -16 to 10), p=0.64 (2 studies, N=47) (SOE: very low) 12 month MD: -2.23 (-13 to 8.13), p=0.67 (2 studies, N=51) Depression (Beck Depression Inventory, 0-63): Post-treatment MD: -3.10 (95% CI -11 to 5.23), p=0.47 (2 studies, N=61) (SOE: very low) 6 month MD: -4.66 (95% CI -11 to 1.61), p=0.15 (2 studies, N=47) (SOE: low) 12 month MD: -0.64 (95% CI -4.61 to 3.32), p=0.75 (2 studies, N=51) (SOE: low)	NR	Good	Nicholas 1991; Turner 1993

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral therapy vs. behavioral therapy	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	4 RCTs (n=278) ROB: 3 low, 1 high Followup: post-treatment, 6 months, 12 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Combination of cognitive and behavioral therapies (n=144) B. Operant therapy (n=134)	Risk of bias (Cochrane Back Review Group)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	Meta-analysis of 3 RCTs (except Kole-Snijders) Note. Negative MD or SMD favors treatment A.	Pain intensity (various scales) Post-treatment SMD:-0.15 (95% CI -0.46 to 0.16), p=0.35 (3 studies, N=161) (SOE: moderate) 6 months SMD: -0.23 (95% CI -0.57 to 0.11), p=0.19 (3 studies, N=139) (SOE: moderate) 12 months SMD:-0.31 (95% CI -0.65 to 0.03), p=0.073 (3 studies, N=140) (SOE: moderate) Functional status (generic) (various scales): Post-treatment SMD: 0.21 (95% CI -0.24 to 0.67), p=0.36 (2 studies, N=77) (SOE: low) 6 month SMD: -0.23 (95% CI -1.01 to 0.55), p=0.57 (2 studies, N=61) (SOE: low) 12 month SMD: -0.50 (95% CI -1.56 to 0.56), p=0.36 (2 studies, N=66) (SOE: low) Kole-Snijders 1996: Pain coping, pain control: results favored A (p<0.05), data NR.	NR	Good	Kole-Snijders 1996; Nicholas 1991; Turner 1988; van den Hout 2003

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral therapy vs. behavioral therapy	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	4 RCTs (n=157) ROB: 1 low, 3 high Followup: post-treatment, 6 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Combination of cognitive and behavioral therapies (n=50) B. Respondent therapy (n=47)	Risk of bias (Cochrane Back Review Group)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	Meta-analysis of 3 studies (not Rose 1997) Note. Negative MD or SMD favors treatment A.	Pain intensity (various scales): Post-treatment SMD: 0.09 (95% CI -0.31 to 0.50), p=0.64 (3 studies, N=97) (SOE: low) 6 months SMD: 0.47 (95% CI -0.42 to 1.35), p=0.30 (2 studies, N=62) (SOE: low) Functional status (generic) (various scales): Post-treatment SMD: 0.38 (95% CI -0.02 to 0.78), p=0.065 (3 studies, N=97) (SOE: low) 6 month SMD: 0.13 (95% CI -0.81 to 1.07), p=0.78 (2 studies, N=62) (SOE: low) Depression (Beck Depression Inventory, 0-63): Post-treatment SMD: 2.89 (95% CI 0.55 to 5.24), p=0.016 (3 studies, N=97) (SOE: low) 6 month SMD: 1.84 (95% CI -0.43 to 4.11), p=0.11 (2 studies, N=62) (SOE: low) Rose 1997 RCT not included in pooled analyses: Pain, post-treatment & 6 months: p>0.05 (NS, data NR) Functional status, post-treatment & 6 months: p>0.05 (NS, data NR) Psychological domain, post-treatment & 6 months: p>0.05 (NS, data NR)	NR	Good	Newton-John 1995; Rose 1997; Turner 1982; Turner 1993;

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral therapy vs. usual care	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	2 RCTs (N=330) ROB: 0 low, 2 high Followup: post-treatment, 6 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Behavioral therapy (n=167) B. Usual care (n=163)	Risk of bias (Cochrane Back Review Group)
Henschke, 2010	Behavioral therapy vs. group exercise	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	2 RCTs (N=146) ROB: 1 low, 1 high Followup: post-treatment, 6 months, 12 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Behavioral therapy (n=73) B. Group exercise (n=73)	Risk of bias (Cochrane Back Review Group)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	Meta-analysis Note. Negative MD or SMD favors treatment A.	Pain intensity (VAS, 0-100): Post-treatment MD: -5.18 (95% CI -9.79 to -0.57), p=0.028 (2 studies, N=330) (SOE: moderate) 6 months MD:-4.29 (95% CI -9.28 to 0.69), p=0.091 (2 studies, N=319) (SOE: moderate) Functional status (back-specific) (various scales): Post-treatment SMD: -0.20 (95% CI -0.41 to 0.02), p=0.077 (2 studies, N=330) (SOE: moderate) 6 month SMD: -0.12 (95% CI -0.34 to 0.10), p=0.28 (2 studies, N=319) (SOE: moderate)	NR	Good	Poole 2007; van Korff 2005
Henschke, 2010	Meta-analysis Note. Negative MD or SMD favors treatment A.	Pain intensity (Pain Rating Index, 0-45) Post-treatment MD: -2.31 (95% CI -6.33 to 1.70), p=0.26 (2 studies, N=146) (SOE: low) 6 months MD: 1.18 (95% CI -3.16 to 5.53), p=0.59 (2 studies, N=137) (SOE: moderate) 12 months MD: 0.14 (95% CI -4.40 to 4.67), p=0.95 (2 studies, N=136) (SOE: moderate) Depression (various scales): Post-treatment SMD: 0.25 (95% CI -0.07 to 0.58), p=0.13 (2 studies, N=146) (SOE: low) 6 months SMD: 0.02 (95% CI -0.32 to 0.35), p=0.92 (2 studies, N=137) (SOE: moderate) 12 months SMD: 0.07 (95% CI -0.27 to 0.41), p=0.68 (2 studies, N=136) (SOE: moderate)	NR	Good	Turner 1990; Smeets 2006

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral therapy vs. guideline-based care	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	1 RCT (N=114) ROB: 0 low, 1 high Followup: 6 months, 12 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Behavioral therapy (n=60) B. Guideline-based care (n=54)	Risk of bias (Cochrane Back Review Group)
Henschke, 2010	Behavioral therapy vs. guideline-based care	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	1 RCT (N=36) ROB: 0 low, 1 high Followup: posttreatment, 3 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Behavioral therapy (n=24) (2 different types of behavioral therapy, results presented as 2 groups but were combined for this outcome) B. Education (n=12)	Risk of bias (Cochrane Back Review Group)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	No analysis performed; data available in appendix only	Pain intensity (measure NR) 6 months: data NR, favors behavioral therapy, p<0.05 (NS); 12 months: data NR, p>0.05 (NS) Functional status (measure NR): 6 months: data NR, p>0.05 (NS); 12 months: data NR, p>0.05 (NS) SOE: NR	NR	Good	van der Roer 2008
Henschke, 2010	No analysis performed; data available in appendix only Note. Negative difference favors treatment A.	Pain (McGill Pain Questionnaire): Post-treatment, difference between groups: -6.7, p=NR (not calculable) 3 months, difference between groups: 3.55 p=NR (not calculable) Pain intensity (0-10 VAS) Post-treatment, difference between groups:-1.11, p=NR (not calculable) 3 months, difference between groups: 0.38, p=NR (not calculable) SOE: NR	NR	Good	Donaldson 1994

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral therapy vs. hypnosis	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	1 RCT (N=17) ROB: 0 low, 1 high Followup: posttreatment, 3 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Behavioral therapy (n=8) B. Hypnosis (n=7)	Risk of bias (Cochrane Back Review Group)
Henschke, 2010	Behavioral therapy plus physiotherapy vs. physiotherapy	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	2 RCTs (N=47) ROB: 0 low, 2 high Followup: post-treatment, 6 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Behavioral therapy plus physiotherapy (n=41) B. Physiotherapy (n=18)	Risk of bias (Cochrane Back Review Group)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	No analysis performed; data available in appendix only Note. Negative difference favors treatment A.	Pain (VAS, 0-100): Post-treatment, difference between groups: -4.5, p>0.05 (NS) (not calculable) 3 months, difference between groups: -6.3p>0.05 (NS) (not calculable) Depression (measure NR): Post-treatment: data NR, p>0.05 (NS); 3 months: data NR, p>0.05 (NS) SOE: NR	NR	Good	McCauley 1983
Henschke, 2010		Pain intensity (5-point scale) Post-treatment MD: -0.13 (95% CI -1.01 to 0.75), p=0.77 (2 studies, N=59) (SOE: low) 6 months MD: -0.11 (-0.67 to 0.44), p=0.69 (2 studies, N=45) (SOE: low) Functional status (generic) (Sickness Impact Profile, 0-136): Post-treatment MD: -6.26 (95% CI -13 to 0.19), p=0.057 (2 studies, N=59) (SOE: low) 6 months MD:-0.93 (95% CI -6.71 to 4.84), p=0.75 (2 studies, N=51) (SOE: low) Depression (Beck Depression Inventory, 0-63): Post-treatment MD: 1.56 (95% CI -1.71 to 4.83), p=0.35 (2 studies, N=59) (SOE: low) 6 months MD: 0.17 (95% CI -6.85 to 7.19), p=0.96 (2 studies, N=50) (SOE: low)	NR	Good	Nicholas 1991; Nicholas 1992

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral therapy plus inpatient rehabilitation vs. inpatient rehabilitation	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	3 RCTs (N=435) ROB: 1 low, 2 high Followup: post-treatment Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Behavioral therapy plus inpatient rehabilitation (n=206) B. Inpatient rehabilitation (n=229)	Risk of bias (Cochrane Back Review Group)
Henschke, 2010	Behavioral therapy plus educational booklet/audio cassette vs. educational booklet/audio cassette	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	1 RCT (N=234) ROB: 1 low, 0 high Followup: NR Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Behavioral therapy plus educational booklet/audio cassette (n=116) B. Educational booklet/audio cassette (n=118)	Risk of bias (Cochrane Back Review Group)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	Meta-analysis of 2 RCTs (not Strong 1998) Note. Negative MD or SMD favors treatment A.	Pain intensity (various scales): Post-treatment SMD: -0.14 (95% CI -0.34 to 0.05), p=0.15 (2 studies, N=405) (SOE: moderate)	NR	Good	Altmaier 1992; Schweikert 2006; Strong 1998
Henschke, 2010	No analysis performed; data available in appendix only Note. Negative difference favors treatment A.	Note. Length of followup NR. Pain intensity (VAS scale NR) difference between groups: -3.6 (95% CI -8.5 to 1.2), p>0.05 (NS) Function (back-specific) (Roland-Morris Disability Questionnaire) difference between groups: -0.6 (95% CI -1.6 to 0.4), p>0.05 (NS)	NR	Good	Johnson 2007

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Henschke, 2010	Behavioral therapy plus exercise therapy vs. exercise therapy	Cochrane Back Review Group Trials Register (2/2009); The Cochrane Library (2009, issue 2); MEDLINE (through 2/2009); EMBASE (1988 - 2/2009); PsycINFO (1974-2/2009) No language restrictions.	3 RCTs (N=262) ROB: 1 low, 2 high Followup: posttreatment, 4 months, 6 months, 12 months Diagnosis: Nonspecific chronic (12+ weeks) LBP (all) Age: 18-65	A. Behavioral therapy plus exercise (n=135) B. Exercise (n=127)	Risk of bias (Cochrane Back Review Group)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Studies Included
Henschke, 2010	No pooling performed (clinical heterogeneity across studies); data available in appendix only Note. Negative difference favors treatment A.	Friedrich 1998 (N=98) Pain intensity (VAS, 0-100), 4 month difference between groups: -7.1, p<0.05 (not calculable) Disability (low-back outcome score), 4 month difference between groups: -6.2, p<0.05 (not calculable) Modified Waddel Score, 4 months: data NR, p>0.05 (NS) Smeets 2006 (N=116): "No clinically relevant differences" for post-treatment outcomes: Roland-Morris Disability Questionnaire, functional limitations, pain intensity." (data NR) Turner 1990 (N=48) Pain (McGill Pain Questionnaire): Post-treatment, difference between groups: -5.11, p<0.05 (not calculable) 6 months: data NR, p>0.05 (NR) 12 months: data NR, p>0.05 (NR) Function (Sickness Impact Profile): Post-treatment, difference between groups: -0.90, p<0.05 (not calculable) 6 months: data NR, p>0.05 (NR) 12 months: data NR, p>0.05 (NR) Depression (measure, scale NR): Post-treatment, difference between groups: -0.07, p=NR (not calculable) 6 months: data NR, p>0.05 (NR) 12 months: data NR, p>0.05 (NR) SOE: NR	NR	Good	Friedrich 1998; Smeets 2006; Turner 1990

Please see Appendix C. Included Studies for full study references.

Table E20. Data abstraction of randomized controlled trials of psychological therapies

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Behavioral therapy versus waiting list control						
Siemonsma, 2013	Netherlands Single center Outpatient rehabilitation center	Age 18-70 years; nonspecific low back pain with or without radiation to legs ≥ 3 months; current episode of back pain < 5 years; limitations of activity (RMDA score > 3); no previous multidisciplinary treatment for chronic low back pain Exclude: involvement in litigation for pain; serious psychological or psychiatric problems; substance abuse interfering with treatment; pregnancy	Randomized: 156 Analyzed: 139 Attrition:89% (136/156) at 18 weeks	A: Cognitive treatment of illness perceptions (n=104): 10-14 one hour individual treatment sessions provided by physical or occupational therapist; treatment mapped existing illness perceptions, challenged maladaptive illness perceptions, formulated, tested, and strengthened alternative illness perceptions B: Waiting list control (no treatment, no co-interventions permitted) (n=52); note that patients expected to enter cognitive treatment therapy at end of 18 weeks	A vs. B Mean age: 45 vs. 47 years Female: 54% vs. 60% Race: Not reported Baseline pain (0-100 VAS): 56 vs. 56 (mean) Baseline function (0-24 RDQ): 12.2 vs. 12.7 (mean) Other characteristics: Anxiety (0-24 HADS): 5.5 vs. 5.0 (median) Depression (0-24 HADS): 5.0 vs. 4.0 Overall complaints (90-450 SCL-90): 132 vs. 126 (median) Fear of movement (17-68 TSK-R): 29.1 vs. 28.3 p>0.05 between groups for all baseline characteristics	Eligibility: chronic: ≥ 3 months; Median duration (A vs. B): 60 vs. 72 months

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Behavioral therapy versus waiting list control					
Siemonsma, 2013	Post-treatment	A vs. B **Activity-specific pain (mean, 0 to 100 PSC):** ~76 vs. ~70 at baseline, ~44 vs. ~64 post-treatment (values estimated from graph) **Activity-specific pain (mean improvement from baseline, 0 to 100 PSC):** -19.1 (95% CI -24.3 to -13.9) vs. -5.2 (95% CI -14.7 to 4.2) (p=0.018) post-treatment (similar results for adjusted analysis) **Activity-specific pain (% of patients with clinically relevant change: decrease of 18 to 24 mm)**: 49% (46/93) vs. 26% (12/46) post-treatment (OR 2.77 (95% CI 1.28 to 6.01)) **Function (0-100 QBPDS):** 40.4 vs. 40.3 at baseline; 36.9 vs. 38.7 post-treatment (p=0.27) **Illness perception, time line/duration (0-30 IPQ):** 23.6 vs. 23.3 at baseline; 23.9 vs. 23.5 post-treatment (p=0.741) **Illness perception, time line cyclical nature (4-20 IPQ)**: 13.6 vs. 13.0 at baseline, 14.1 vs. 12.4 post-treatment (p=0.004) **Illness perception, consequences (6-30 IPQ):** 19.0 vs. 18.2 at baseline, 17.7 vs. 18.2 post-treatment (p=0.063) **Illness perception, personal control (6-30 IPQ)**: 19.1 vs. 19.2 at baseline, 21.1 vs. 18.9 post-treatment (p=0.001) **Illness perception, treatment control (5-25 IPQ):** 17.1 vs. 17.1 at baseline, 15.9 vs. 16.8 post-treatment (p=0.113) **Illness perception, coherence (5-25 IPQ):** 14.3 vs. 13.7 at baseline, 11.7 vs. 12.7 post-treatment (p=0.024) **Illness perception, emotional response (6-30 IPQ):** 16.9 vs. 17.5 at baseline, 15.5 vs. 16.4 post-treatment (p=0.425)	Not reported	The Netherlands Organization for Health Research and Development grant	Fair

Author, Year	Country Number of Centers and Setting	Inclusion	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute,
Behavioral therapy versus other intervention						
(no trials)						

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Behavioral therapy versus other intervention					
(no trials)					

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Comparisons of different behavioral therapies						
(no trials)						

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Comparisons of different behavioral therapies					
(no trials)					

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Behavioral therapy plus other intervention versus other intervention alone						
Khan, 2014	Pakistan Multicenter Outpatient	Age 25-45 years; chronic non-specific low back pain for 3 to 24 months' duration; MRI of lumbar spine to rule out underlying pathology; no associated medical conditions. Exclusion: back pain less for less than 3 months in duration; history of back surgery; inflammatory arthritis; tumors; spinal or hip fractures; pregnancy; lumbar radiculopathy; severe cardiopulmonary disease affecting exercise tolerance.	Randomized: 54 Analyzed: 54 Attrition: 100% (54/54)	A: Behavioral therapy plus exercise (n=27). Physical-therapist guided sessions 3 times per week for 12 weeks; patients instructed to continue exercises at home twice a day at least 5 times a week. Cognitive behavioral therapy aimed to guide patients to achieve their daily life goals, consisting of operant behavioral graded activity and problem solving training. Graded activity same as described for group B but patients were given instruction by the physical therapist to modify dysfunctional beliefs. B: Exercise (n=27). Physical-therapist guided sessions 3 times per week for 12 weeks; patients instructed to continue exercises at home twice a day at least 5 times a week. Graded activity led by physical therapist who focused on gradual increase or pacing of activities important for individual patients with general exercises consisting of rolling, bridging, knee to chest, hamstring stretching (20 repetitions of each exercise) and cycling plus treadmill (10 minutes each) with resistance and speed adjusted to patient.	A vs. B Mean age: 40 years (NR for A vs. B) Female: 54% (NR for A vs. B) Caucasian: NR Baseline pain (0-10 VAS): 6.5 vs. 7.0 (mean) (p=0.1877) Baseline function (0-24 RDQ):13.8 vs. 12.9 (mean) (p=0.1842) Other characteristics: non reported	Eligibility: 3-24 months (chronic) Mean duration (A vs. B): NR

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Behavioral therapy plus other intervention versus other intervention alone					
Khan, 2014	Post-treatment	A vs. B **Pain** (mean 0-10 VAS): 6.5 vs. 7.0 at baseline; 2.7 vs. 5.3 post-treatment (p<0.0001) **Function** (mean 0-24 RDQ): 13.8 vs. 12.9 at baseline; 5.3 vs. 9.9 post-treatment (p<0.0001)	Not reported	Not reported	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Lamb, 2010 Lamb, 2012	England Multicenter General family practice	Age ≥18 years; low back pain of at least moderate intensity for ≥ 6 weeks Exclude: Physician's belief that the pain is caused by infection, fracture, malignancy or other potential serious cause; severe psychiatric or psychological disorder; previous participation n cognitive behavioral intervention for low back pain.	Randomized: 701 Analyzed: 598 at 12 months (end of original study period according to published protocol); 395 at extended followup (mean 34 (20-50) months) Attrition: 85.3% (598/701) at 12 months (end of original study period according to published protocol); 56.3% (395/701) at extended followup (mean 34 (20-50) months)	A: Group cognitive behavioral therapy plus active management advisory consult (n=468) (CBT: One individual assessment session (<90 minutes) plus six 90-minute group therapy sessions (duration of therapy not reported) that targeted behaviors and beliefs about physical activity and avoidance of activity; primary care physicians told to avoid referrals during intervention but otherwise no attempt was made to control consultations in the followup period) B: Active management advisory consult alone (n=233) (one 15 minute session of active management advice- info on remaining active, avoiding bed rest, use of pain medication, and symptom management- plus informational book) (patients free to seek further care on their own)	A vs. B Mean age: 53 vs. 54 years Female: 59% vs. 61% Caucasian: 88% vs. 88% Baseline pain (0-100% modified Van Korff pain): 59 vs. 59 (mean) Baseline function (0-24 RDQ): 9 vs. 9 (mean) Function (0-100% Von Korff disability): 49 vs. 46 Other characteristics: Severity of back pain "very or extremely troublesome": 54% vs. 56% Severity of back pain "moderately troublesome": 46% vs. 44% Unable to work because of back pain: 11% vs. 9% Back pain every day in last 6 weeks: 67% vs. 70% Stiff or restricted movement: 67% vs. 70% Quality of life (-0.50-1.0 EQ-5D): not reported Quality of life (0-100 SF-12 physical): 37 vs. 38 (mean) Quality of life (0-100 SF-12 mental): 45 vs. 46 (mean) Pain Self-efficacy (0-60 Pain Self Efficacy): 40 vs. 41 (mean) Fear avoidance beliefs (0-24 Fear avoidance beliefs questionnaire): 14 vs. 14 (mean)	Eligibility: subacute to chronic: ≥ 6 weeks; Mean duration (A vs. B): 13 vs. 13 years

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Lamb, 2010 Lamb, 2012	12 months (protocol; Lamb 2010A) >12 month extended followup (mean 34 (20-50) months) (Lamb 2012)	**A vs. B** **Pain** (mean change from baseline, 0-100% Von Korff pain): 12.2 vs. 5.4 at 3 months (p<0.0001), 13.7 vs. 5.7 at 6 months (p<0.0001),13.4 vs. 6.4 at 12 months (p<0.0001), 17.4 vs. 12.8 at mean 34 (20-50) months (p=0.107) **Function** (mean change from baseline, 0-24 RDQ): 2.0 vs. 1.1 at 3 months (p=0.0021), 2.5 vs. 1.0 at 6 months (p=0.0002), 2.4 vs. 1.1 at 12 months (p=0.0008), 2.9 vs. 1.6 at mean 34 (20-50) months (p=0.013) **Function** (mean change from baseline, 0-100% Von Korff disability): 13.2 vs. 8.9 at 3 months (p=0.0316), 13.9 vs. 5.7 at 6 months (p<0.0001),13.8 vs. 5.4 at 12 months (p<0.0001), 16.7 vs. 11.2 at mean 34 (20-50) months (p=0.039) **Quality of life** (mean change from baseline, -0.59 to 1 EQ-5D): -0.06 vs. 0.01 at 3 months (p=0.007), -0.05 vs. -0.03 at 6 months (p=0.382), -0.06 vs. -0.0003 at 12 months (p=0.027), -0.07 vs. -0.04 at mean 34 (20-50) months (p=0.387) **Quality of life** (mean change from baseline, 0-100 SF-12 physical): -3.7 vs. -1.5 at 3 months (p=0.0031), -3.6 vs. -1.8 at 6 months (p=0.0144), -4.9 vs. -0.8 at 12 months (p<0.0001) **Quality of life** (mean change from baseline 0-100 SF-12 mental): -1.3 vs. 0 at 3 months (p=0.1276), -2.5 vs. 0.09 at 6 months (p=0.0035), -0.9 vs. -0.7 at 12 months (p=0.8323) **Pain self-efficacy** (mean change from baseline 0-60 Pain Self Efficacy): -2.4 vs. 0.9 at 3 months (p<0.0001), -2.6 vs. 1.5 at 6 months (p<0.0001), -3.0 vs. 0.8 at 12 months (p<0.0001) **Fear avoidance beliefs** (mean change from baseline 0-24 Fear Avoidance Beliefs Questionnaire): 3.4 vs. 0.7 at 3 months (p=0.0004), 3.0 vs. -0.1 at 6 months (p<0.0001), 3.4 vs. 0.5 at 12 months (p<0.0001) **Treatment benefit** (% of patients who considered themselves recovered)**:** 59% (235/395) vs. 31% (62/197) at 12 months (p<0.0001) **Treatment satisfaction** (% of patients satisfied with treatment): 65% (212/328) vs. 28% (43/151) at 12 months (p=0.463)	"There were no serious events attributable to either treatment."	National Institute for Health Research Health Technology Assessment Program	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Vong, 2011	China Single center Physical therapy outpatient department	Age 18-65 years; chronic low back pain of at least 3 months' duration. Exclusion: pregnancy; cardiac pacemaker; pain from neurologic disorders or rheumatologic disease; consistent symptoms of sciatica; spondylolisthesis more than 1 cm; received physical therapy for low back pain in the past 3 months; psychiatric problems; received compensation for work-related disabilities	Randomized: 88 Analyzed: 76 Attrition: 86% (76/88)	A: Motivational enhancement treatment plus physical therapy (n=45) (physical therapy: see group B for details) (motivational enhancement: motivational enhancement given during the physical therapy sessions to enhance motivation and make appropriate behavioral changes) B: Physical therapy (n=43) (ten 30-minute sessions over 8 weeks, including 15 minutes of interferential (electrophysical) therapy and a tailor-made back exercise program; interferential therapy employed 4 interferential suction electrodes placed over the L2 to S1 paraspinal muscles on both sides of the back and a current of 80-100Hz was used; physical therapy began with thorough assessment followed by a prescription of a specific set of exercises to include stretching/strengthening exercises for trunk and lower limbs; patients also requested to exercise at home every day)	NOTE- Demographics reported for patients analyzed only A vs. B Mean age: 45 vs. 45 years Female: 58% vs. 68% Race: not reported Baseline pain (0-10 VAS) (mean): 5.3 vs. 5.3 Baseline function (0-24 RDQ) (mean): 10.0 vs. 10.0 Other characteristics: Previous physical therapy: 16% vs. 29% Recurrent low back pain: 21% vs. 34% Regular analgesia: 32% vs. 29% SF-36 (0-100) physical function: 67 vs. 63 SF-36 (0-100) role-physical: 22 vs. 30 SF-36 (0-100) bodily pain: 41 vs. 49 (p=0.047) SF-36 (0-100) general health: 41 vs. 49 p>0.05 between groups for all baseline characteristics unless noted	Eligibility: 3+ months (chronic) Mean duration (A vs. B): 41.6 vs. 51.0 months

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Vong, 2011	1 month post-treatment	A vs. B **Pain** (mean 0-10 VAS): 5.3 vs. 5.3 at baseline; 3.1 vs. 3.9 at 1 month (p>0.05) **Function** (mean 0-24 RDQ): 10.0 vs. 10.1 at baseline; 5.6 vs. 7.6 at 1 month (p>0.05) **Quality of life** (mean 0-100 SF-36): SF-36 (0-100) physical function: 67 vs. 63 (p>0.05) at baseline; p> 0.05 at 1 month (data not reported) SF-36 (0-100) role-physical: 22 vs. 30 (p>0.05) at baseline; p> 0.05 at 1 month (data not reported) SF-36 (0-100) bodily pain: 41 vs. 49 (p=0.047) at baseline; p> 0.05 at 1 month (data not reported) SF-36 (0-100) general health: 41 vs. 49 (p>0.05) at baseline; p> 0.05 at 1 month (data not reported) **Pain self-efficacy** (mean 0-60 PSEQ): 39.5 vs. 40.5 at baseline (p>0.05); 45.4 vs. 45.6 at 1 month (p>0.05)	Not reported	None stated (noted that there was no commercial party funding or conflict of interest)	Fair

Please see Appendix C. Included Studies for full study references.

Table E21. Data abstraction of systematic reviews of multidisciplinary rehabilitation

Author, Year	Comparison	Data Sources and Dates	Number and Type of Studies (sample sizes), Duration of followup, duration of low back pain	Interventions and Number of Patients	Techniques Evaluated, Duration and Number of Sessions
Kamper, 2014	MBR 1. MBR (A) vs. usual care (B) 2. MBR vs. physical treatment (C) 3. MBR vs. surgery (D) 4. MBR vs. wait list (E)	CENTRAL, MEDLINE, EMBASE, PsycINFO and CINAHL databases, hand searches of the reference lists of included and related studies, forward citation tracking of included studies and screening of studies excluded in the previous version of this review Dates: 1998 - January and March 2014, no language restriction	41 RCTs of adult chronic mechanical or non-specific low back pain (≥12 weeks of pain) Short-term outcomes=up to 3 months Med-term outcomes ≥3 mo to <12 mo Long-term outcomes ≥12 or more	Total participants=6858 A vs. B (n=16 trials) A vs. C (n=19 trials) A vs. D (n=2 trials) A vs. E (n=4 trials) See results section for number of trials and participants	MBR (defined as a physical treatment + at least one element from biopsychosocial model, delivered by different providers but in an integrated fashion involving communication among providers). Clinicians included physicians, psychologists, physiotherapists, social workers, occupational workers and exercise therapists) 15 studies = high intervention intensity (>100 hrs contact delivered on daily basis) 15 studies = low intervention intensity (<30 hrs on non-daily basis) 11 studies = neither high nor low intensity

Author, Year	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Kamper, 2014	GRADE and Cochrane Back Review Group (2009)	Meta-analysis using random effects models	A vs. B Pain Short-term outcome (n=9 studies; 879 pts): SMD -0.55 (95% CI -0.83 to -0.28) Medium Term Outcome (n=6 studies; 740 pts): SMD -0.60 (95% CI -0.85 to -0.34) Long term outcome (n=7; 821 pts): SMD -0.21 (95% CI -0.37 to -0.04) Back specific disability Short Term Outcome (n=9 studies, 939 pts) SMD -0.41 (95% CI -0.62 to -0.19) Medium Term Outcome (n=6 studies; 786 pts) SMD -0.43 (95% CI -0.66 to -0.19) Long Term Outcome (n= 6; 722 pts) SMD -0.23 (95% CI -0.40 to -0.06) Work status Short Term Outcome (n=2; 373 pts) OR 1.07 (95% CI 0.60 to 1.90) Medium Term Outcome (n=3; 457 pts) OR 1.60 (95% CI 0.52 to 4.91) Long Term Outcome (n=7, 1360 pts) OR 1.04 (95% CI 0.73 to 1.47) A vs. C Pain Short-term outcome (n=12 studies; 1661 pts): SMD -0.30 (95% CI -0.54 to -0.06) Medium Term Outcome (n=9 studies, 531 pts) SMD -0.28 (95% CI -0.54 to -0.02) Long-term outcome (n= 9 studies, 872 pts) SMD -0.51 (95% CI -1.04 to 0.01)	Only reported in one study with no adverse events, otherwise not reported	Good

Author, Year	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Kamper, 2014 (Continued)			Back specific disability Short-term outcome (n=13 studies, 1878 pts) SMD -0.39 (95% CI -0.68 to -0.10) Moderate-term outcome (n=9 studies, 511 pts) SMD -0.21 (95% CI -0.48 to 0.06) Long-term outcome (n=10 studies, 1169 pts) SMD -0.68 (95% CI -1.19 to -0.16) Work status Short-term outcome (n=3 studies, 379 pts) pooled OR 1.60 (95% CI 0.92 to 2.78) Moderate-term outcome (n=3 studies, 221 pts) OR 2.14 (95% CI 1.12 to 4.10) Long-term outcome (n=8 studies, 1006 pts) OR 1.87 (95% CI 1.39 to 2.53) ~~A vs. D - not included in the review~~ Pain Short-term outcome NR Moderate-term outcome NR Long-term outcome (n=2 studies; 385 pts): SMD -0.25 (95% CI -0.53 to 0.04) Back specific disability Short-term outcome NR Moderate-term outcome NR Long-term outcome (n=2 studies, 423 pts) SMD 0.25 (95% CI -0.08 to 0.57) Work status Short-term outcome NR Moderate-term outcome NR Long-term outcome(n=1 studies, 133 pts) OR 0.67 (95% CI 0.31 to 1.45)		

Author, Year	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Kamper, 2014 (Continued)			A vs. E Pain Short-term outcome (n=3 studies, 213 pts) SMD -0.73 (95% CI -1.22 to -0.24) Moderate-term outcome not estimable Long-term outcome not estimable Back specific disability Short-term outcome (n=3 studies, 213 pts) pooled SMD -0.49 (95% CI -0.76 to -0.22) Moderate-term outcome not estimable Long-term outcome not estimable Work status NR		

Please see Appendix C. Included Studies for full study references.

Table E22. Data abstraction of randomized controlled trials of multidisciplinary rehabilitation

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Eisenberg, 2012	Boston, USA	LBP 3-12 weeks 18-70 years old Excluded: LBP < 21 days or >84 days, pain <3, history of back surgery in last 3 years, history of vertebral fracture or dislocation, progressive or severe neurological symptoms, spondylolisthesis, scoliosis, ankylosing spondylitis, pacemaker or implantable cardioverter defibrillator, systemic or visceral disease cause back pain, osteoporosis, taking steroids, pregnancy, history of cancer within 5 yrs, unexplained fever or weight loss, bleeding disorder, disabling condition, transplant, immunosuppression, intravenous drug use, non-English speaking	20 randomized A: 14 allocated, 2 lost to followup, 14 analyzed B: 6 allocated, 2 lost to followup, 6 analyzed	Integrative care (acupuncture, chiropractic, internal med consult, massage, occupational therapy, physical therapy, mind-body techniques, neuro consult, nutrition counseling, ortho consult, psych and rheum consult as needed) + usual care (A) vs. Usual care (medical care) 12 weeks	Mean Age: 47 vs. 48 Female: 50% vs. 67% Average Pain (0-10): 4.8 vs. 5.7 Modified RDQ: 15.7 vs. 16	NR	2, 5, 12, and 26 weeks

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Eisenberg, 2012	RDQ mean differences, A vs. B Week 2: 12 vs. 11.3 (p=0.87) Week 5: 8.5 vs. 13 (p=0.26) Week 12: 3.9 vs. 11 (p=0.08) Week 26: 4.3 vs. 10.7 (p=0.10) Pain (0-10 scale) Week 2: 3.6 vs. 4.8 (p=0.62) Week 5: 1.9 vs. 5.5 (p=0.05) Week 12: 0.6 vs. 5.0 (p=0.005) Week 26: 1.0 vs. 4.7 (p=0.04) SF-12 physical Week 2: 35 vs. 41 (p=0.90) Week 5: 42 vs. 42 (p=0.38) Week 12: 49 vs. 43 (p=0.06) Week 26: 51 vs. 44 (p=0.03) SF-12 mental Week 2: 47 vs. 51 (p=0.26) Week 5: 51 vs. 50 (p=0.59) Week 12: 501 vs. 51 (p=0.48) Week 26: 54 vs. 51 (p=1.00) Days in bed, days at home and reduced activity days NS Regression showed positive differences significant for RDQ, pain, and bothersomness at 12 weeks, but not at 26 weeks	1 pain at acupuncture site	NIH NCAM and Bernard Osher Foundation	Good

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Gatchel, 2003	USA, Texas, single center	LBP >10 weeks since work injury Aged 18-65 No history of chronic LBP No need for surgery constant daily pain Work disability Excluded: cancer, fibromyalgia, DSM-IV axis 1 diagnosis, psychosis or suicidal ideation	Randomized 22 early intervention 48 nonintervention Analyzed: 70 Attrition: NR	(A) Intensive Multidisciplinary rehabilitation (physician evaluation, psychology, physical therapy, biofeedback, case management, occupational therapy) vs. (B) usual care	Mean Age 38 Female 35% Comparison of groups NR	Subacute (3.8 weeks since original injury)	3,6,9,12 months
Monticone, 2014	Italy, single center	LBP >3 months Age >18 Exclude: Central or peripheral neurological signs, cognitive impairment, severe cardiovascular and respiratory comorbidity, prior spine surgery, ambulation deficits due to neurologic or orthopedic impairment, pregnancy or previous participation in CBT	Randomized 10 A intervention 10 B intervention Analyzed: 20 Attrition: 0	(A) Multidisciplinary rehabilitation of 2 months duration (physiatry, psychology, occupational therapy, and physiotherapy) providing spinal stabilization and cognitive behavioral therapy to address fear avoidance vs. (B) Usual care=passive spinal mobilization, stretching, muscle strengthening, and posture control	Mean Age 59 vs. 57 Female 70% vs. 40% BMI 27 vs. 25	Pain Duration (A) 15 mo vs. (B) 14 mo	0, 8 weeks, 3 months

Author, Year	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Gatchel, 2003	A vs. B Return to work at 12 months: 91% vs. 69%, OR 4.55 (p=0.027) Average number of disability days due to back pain: 38 vs. 102, p=0.001 Average self-rated pain over last 3 months: 27 vs. 43, p=0.001 Taking opioid analgesics: 27% vs. 44%, OR 0.44, p=0.020 Cost: $12,721 vs. $21,843, p<0.05	NR	National Institute of Mental Health	Fair
Monticone, 2014	A vs. B Baseline ODI 26 vs. 24 (p=0.43) TSK 29 vs. 27 (p=0.55) NRS 5 vs. 4 (p=0.67) PCS 25 vs. 23 (0.43) SF-36 Physical Activity 41 vs. 43 (p=0.55) 6 minute walk test 1.17 m/s vs. 1.26 m/s (p=0.29) 8 weeks ODI 10 vs. 8 (p=0.03) TSK 29 vs. 27 (p=0.01) NRS 5 vs. 4 (p=1.0) PCS 25 vs. 23 (p=0.006) SF-36 Physical Activity 41 vs. 43 (p=0.001) 6 minute walk test 1.17 m/s vs. 1.26 m/s (p=0.478) 3 months ODI 8 vs. 15 TSK 15 vs. 27 NRS 2 vs. 3 PCS 9 vs. 18 SF-36 Physical Activity 84 vs. 67 6 minute walk test 1.53 vs. 1.42	3 had transitory worsening pain in group A, 2 in group B 1 mood alteration in group A, 2 in group B	EuroSpine Task Force on Research	Good

Please see Appendix C. Included Studies for full study references.

Table E23. Data abstraction of systematic reviews of acupuncture

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Lam, 2013	(A) Acupuncture versus no treatment, (B) Acupuncture versus medication, (C) acupuncture versus TENS, (D) Acupuncture versus sham acupuncture, (E) Acupuncture in addition to usual care versus self-care or usual care, and (F) Electroacupuncture versus usual care.	PubMed, EMBASE, AMED, CINAHL ScienceDirect, CENTRAL, and Cochrane Library	32 studies SR, 25 meta; Chronic LBP, 7 LROB, 0-48 months followup	A. Acupuncture versus no treatment (n=5) B. Acupuncture versus medication (n=3), C. Acupuncture versus TENS, (n=3 studies, 122 patients) D. Acupuncture versus sham (n=4) acupuncture, E. Acupuncture in addition to usual care versus self-care or usual care, (n=4) and F. electroacupuncture versus usual care.(n=6)	Cochrane, 2011

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Lam, 2013	n=32 qualitative; n=25 meta analysis; Statistical heterogeneity was measured using the I 2 statistic, Fixed effects model used below the 50% cut off for I^2 statistic, used clinical cutoffs for pain and function to determine clinical significance	A. Pain, mean between-group difference (95% CI): - Immediate post-intervention: (5 studies) −0.72 [−0.94 to −0.49] Function, mean between-group difference (95% CI): Immediate post-intervention: (5 studies) −0.94 [−1.41 to −0.47] B. Pain, mean between-group difference (95% CI): -Immediate post-intervention: (3 studies) −10.56 [−20.34 to −0.78] Function, mean between-group difference (95% CI): - Immediate post-intervention: (3 studies) −0.36 [−0.67 to −0.04] C. Pain immediate post-intervention: (3 studies) "no significant difference" Pain 10-12 week followup (2 studies): "no significant difference" Function not reported D. Pain, mean between-group difference (95% CI): -Immediate post-intervention: (4 studies) −16.76 [−33.33 to −0.19] -6-12 weeks: (3 studies) −9.55 [−16.52 to −2.58] Function (3 studies) "no differences" E. Pain, mean between-group difference (95% CI) -Immediate post-intervention: (4 studies) −13.99 [−20.48 to −7.50] -6-12 weeks: (4 studies) −12.91 [−21.97 to −3.85] Function: mean between-group difference (95% CI) -Immediate post-intervention: (4 studies) −0.87 [−1.61 to −0 -6-12 weeks: (4 studies) −0.51 [−0.91 to −0.12] F. Pain, mean between-group difference (95% CI): -Immediate post-intervention: (5 studies) −1.39 [−2.37 to −0.40] -6-12 weeks: (4 studies) − 0.66 [−1.17 to −0.15] function: not examined	NR	Fair

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Lee, 2013	Acupuncture (as a single treatment, needle only) vs. sham, usual care, nothing	The Cochrane Central Register of Controlled Trials(CENTRAL), Ovid Medline, Embase (1980 to July 2011),and Chinese databases of the China Academic Journal, 4 related Korean journals, trial registries	11 RCTs, Acute LBP (<12 weeks), 1139 patients (approximately 50 per arm), 5 LROB	A. Acupuncture vs. sham (n=3) B. Acupuncture vs. conventional treatment (i.e.,. meds) (n=7) C. Acupuncture + meds vs. meds alone (n=1)	Cochrane, 2009

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Lee, 2013	n=11 qualitative, n=7 meta analysis; Random effects model; heterogeneity assessed using I^2 statistic;	A. acupuncture vs. sham: 2 studies; VAS for acute pain, MD 9.38; 95% CI: 17.00, 1.76; p=0.02 - no effects for subacute pain or function B. Acupuncture vs. NSAIDs Global assessment: (5 studies; pooled RR, 1.11; 95% CI: 1.06, 1.16; p<0.00001)	Only 2 studies reported: 16 pts reported GI problems at 1 week, 12 at 2 weeks; 4 with changes in energy at 1 week, mild bleeding at site in 3 patients	p

Please see Appendix C. Included Studies for full study references.

Table E24. Data abstraction of randomized controlled trials of acupuncture

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Cho, 2013	Korea 3 hospital-based clinics	Age 18-65 years with nonspecific chronic LBP at least 3 months duration, VAS >5 (scale 0-10) and intact on neurological exam. Exclude: Sciatic pain, pain mainly below the knee, serious spinal disorders, vertebral fracture, spinal infection, inflammatory spondylitis, cauda equina compression, history of spinal surgery or scheduled surgery, other acupuncture treatment, severe psychiatric or psychological disorder, history of corticosteroid, narcotic, muscle relaxant or herbal medicine to treat LBP.	Randomized: 130 Analyzed: 116 Attrition: 11% (14/130)	A. Acupuncture 2x/week for 6 weeks (n=57) B. Sham acupuncture with blunt needles (n=59)	A vs. B Mean age 42 vs. 42 years 82% vs. 86% female Race not reported Pain intensity 6.52 vs. 6.37 Pain bothersomeness 6.44 vs. 6.32 ODI (Korean version) 28.23 vs. 24.17 (p=0.04) SF-36 (Korean version) 107.72 vs. 110.41 (unclear which subscales were used) BDI (Korean version)11.33 vs. 11.75	Chronic: Mean duration not reported; inclusion criteria required ≥3 months duration at study entry

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Cho, 2013	6 months	A vs. B 8-week outcomes (primary endpoint) Pain intensity: 3.00 (SD 2.41) vs. 4.10 (SD 1.85); p=0.007; mean change from baseline 0.53 (SD 0.39) vs. 0.35 (SD 0.29); p=0.007 Pain bothersomeness: 3.08 (SD 2.44) vs. 4.05 SD 1.84); p=0.02; mean change from baseline 0.53 (SD 0.34) vs. 0.35 (SD 0.30); p=0.003 ODI, mean change from baseline: 0.42 (SD 0.39) vs. 0.29 (SD 0.44); p=0.10 SF-36, mean change from baseline: 0.20 (SD 0.23) vs. 0.16 (SD 0.13); p=0.006 BDI, mean change from baseline: 0.39 (SD 0.56) vs. 0.26 (SD 0.83); p=0.34 6-month outcomes Pain intensity: 2.79 (SD 2.44) vs. 3.52 (SD 2.53); p=0.11; mean change from baseline 0.56 (SD 0.41) vs. 0.44 (SD 0.41); p=0.12 Pain bothersomeness: 2.85 (SD 2.44) vs. 3.63 SD 2.37); p=0.08; mean change from baseline 0.56 (SD 0.38) vs. 0.41 (SD 0.39); p=0.04 ODI, mean change from baseline: 0.44 (SD 0.38) vs. 0.24 (SD 1.10); p=0.20 SF-36, mean change from baseline: 0.20 (SD 0.23) vs. 0.14 (SD 0.15); p=0.09 BDI, mean change from baseline: 0.44 (SD 0.58) vs. 0.36 (SD 0.66); p=0.49	A vs. B Withdrawals: 11% (7/65) vs. 11% (7/65); RR 1.00 (95% CI 0.37 to 2.69) Withdrawals due to AEs: Not reported Serious AEs: None in either group Any AE: 15% (10/65) vs. 26% (17/65); RR 0.59 (95% CI 0.29 to 1.19) Pain at acupuncture site: 3% (2/65) vs. 3% (2/65); RR 1.00 (95% CI 0.15 to 6.89) Bruise at acupuncture site: 2% (1/65) vs. 0% (0/65); RR 3.00 (95% CI 0.12 to 72) Worsened LBP: 6% (4/65) vs. 12% (8/65); RR 0.50 (95% CI 0.16 to 1.58)	Not reported	Good

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Hasegawa, 2014	Brazil, 1 site	Inclusion criteria: 18–65 years seeking medical assistance for acute non-specific LBP, defined as pain and discomfort localized below the costal margin and above the inferior gluteal folds for a period of less than 30 days and unrelated to any specific anetiological factors with a score of 4–8 cm on the pain scale (0–10 cm) Exclusion criteria: secondary diagnosis such as spondyloarthropathy, infection, tumor or fracture, complete scatologia, previous surgery on the spinal column, litigation, who had changed physical activity or undergone acupuncture or physical therapy in the previous 3 months, had previously undergone scalp acupuncture or who were pregnant or had a contraindication to anti-inflammatory drugs	Randomized: 80 Analyzed: 80 Attrition: 0% (0/80)	A. Scalp acupuncture +diclofenac (n=40) B. Sham scalp acupuncture +diclofenac (n=40)	A vs. B Mean age 47 vs. 44 years 63% vs. 65% female 63% vs. 55% Caucasian Pain, VAS: 6.6 vs. 6.7 Disability, RDQ: 14.9 vs. 14.6	Acute: <30 days

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Hasegawa, 2014	Up to 28 days	A vs. B: Acute LBP Pain, VAS mean change from baseline: -4.6 vs. -3.3; p=0.005 A vs. B Disability, RDQ mean change from baseline: -10.8 vs. -8.6; p=0.002	No participants experienced AEs	Not reported	Good

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Vas, 2012	Spain, 4 centers	Inclusion criteria: new episode (defined as the first such episode in the last 6 months) of nonspecific LBP (defined as pain, muscle tension, or stiffness, localized below the costal margin and above the inferior gluteal folds, with or without referred or radicular leg pain) initiated less than 2 weeks previously, no prior experience of acupuncture treatment, patient's age ranging from 18 to 65 years exclusion: more than 1 absence from work as a result of LBP in the previous 6 months; LBP attributed to recognizable, known specific pathology; generalized dermatopathologies; treatment with dicoumarol anticoagulants; pregnancy	Randomized: 275 Analyzed: 210 Attrition: =23.6% (65/275)	A. True acupuncture (n=68) B. Sham acupuncture (n=68) C. Placebo acupuncture (n=69) D. Control group, conventional treatment (n-70)	A vs. B vs. C vs. D Mean age 42 vs. 44 vs. 44 vs. 41 63% vs. 57% vs. 49% vs. 64% female Race not reported (Spain)	Acute: <2 weeks
Weiss, 2013	Germany, 1 hospital	Inclusion criteria: CLBP of 6+ months and age 25–75 years. Exclusion criteria: contraindications to acupuncture, such as anticoagulation with phenprocoumon or warfarin; coagulation disorders or thrombocytopenia (platelet count < 150,000 cells/mm3); poor fluency in German language; insufficient adherence; recent surgical treatment; and herniated vertebral discs, either minor herniations of less than 6 months' duration or major herniations of any duration.	Randomized: 160 Analyzed: 143 Attrition: =10.6% (17/160)	A. Acupuncture plus intensive rehab (n=74) B. Intensive inpatient rehab only (n=69)	A vs. B Mean age 49.8 vs. 51.7 27% vs. 39.1% female Race not reported (Germany) Bodily Pain, SF-36 41.2 vs. 36.0 Physical function, SF-36 71.2 vs. 69.8	Chronic >6 months

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Vas, 2012	48 weeks	A vs. B vs. C vs. D Pain VAS not reported Continuing pain and recurrence of pain reported only A vs. B vs. C vs. D Disability (Proportion achieving 35% improvement in RDQ (0-24) at 3 weeks): 74% vs. 75% vs. 65% vs. 44% (p<0.05 for A vs. C and A vs. D)	No serious adverse reaction was recorded in any of the treatment groups. Twelve patients (4.4%) had possible adverse reactions to medication including epigastralgias and nausea, 1 in the true acupuncture group, 1 in the sham acupuncture group, 4 in the placebo acupuncture group, and 6 in the conventional treatment group. With respect to adverse effects provoked by all classes of acupuncture treatment, 8 patients (3.9%) reported increased pain after the treatment session, 3 in the TA group, 3 in the SA group, and 2 in the PA group.	Not reported	Good
Weiss, 2013	3 months	A vs. B Bodily pain, SF-36 mean change from baseline to 3 months post treatment 8.3 vs. 3.8 p=0.28 (p<0.05) Bodily pain, SF-36 mean change from baseline to end of treatment 24.5 vs. 22.6 p=0.56 A vs. B Physical function, SF-36 mean change from baseline to 3 months post treatment -3.6 vs. -11.8 p=0.0.02 Physical function, SF-36 mean change from baseline to end of treatment 9.8 vs. 6.4 p=0.20	No major adverse events occurred. Minor adverse effects were nausea in 2.7% of patients, dizziness in 13.5%, urgency in 20.3%, and pain at puncture site in 36.5%.	Funding not reported	Poor

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Yun, 2012	China, 1 hospital	Inclusion criteria: Participant plans to continue enrollment in health plan between 18 and 70 years of age At least one primary care visit for back pain within the past 3–12 months Non-specific, uncomplicated low back pain Exclusion criteria: Previous acupuncture for any reason Low back pain lasting less than 3 months Mild symptoms [less than 3 on 0–10 pain bothersomeness scale] Specific diseases that could be cause of back pain [metastatic cancer, discitis, herniated disc, vertebral fracture, spinal infection, osteitis condensans, severe or progressive scoliosis, spinal stenosis, spondylolisthesis, ankylosing spondylitis] Complicated back problems [sciatica, back surgery in prior 3 years]	Randomized: 236 Analyzed: 236 Attrition: =0% (0/236)	A. Back-pain-acupuncture (n=80) B. Standard acupuncture (n=82) C. Usual care (n=74)	A vs. B vs. C Mean age 33 vs. 34 vs. 31 33% vs. 27% vs. 31%female Race not reported (China) Pain, VAS 6.1 vs. 6.1 vs. 6.1 Disability, RDQ: 11.8 vs. 12 vs. 11.8	Chronic >3 months

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Yun, 2012	24 weeks	A vs. B vs. C Pain, bothersomeness (primary) mean change from baseline 24 weeks (0-10 VAS): 2.5 vs. 2.0 vs. 1.2 (p<0.0001) RDQ mean change from baseline: 6.2 vs. 5.3 vs. 4.1 (p<0.0001)	AEs not reported	Funding not reported	Fair

Please see Appendix C. Included Studies for full study references.

Table E25. Data abstraction of systematic reviews of massage

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Furlan, 2010	1) Massage vs. Sham/placebo massage 2) Massage vs. Other medical treatments 3) Massage vs. No treatment 4) compare the addition of massage to other treatments 5) assess the effectiveness of different techniques of massage	MEDLINE, EMBASE, CINAHL from their beginning to May 2008. We also searched the Cochrane Central Register of Controlled Trials (The Cochrane Library 2006, issue 3), HealthSTAR and Dissertation abstracts up to 2006	13 studies (1596 pts); 5 Lob	1. Massage vs. Sham/placebo massage (n=2 studies, 111 pts) 2. Massage vs. Other medical treatments 2a) A vs. SMT (n=1, 67 pts) 2b) A vs. exercise (n=1, 47 pts) 2c) A vs. relaxation (n=3, 297 pts) 2d) A vs. acupuncture (n=1, 172 pts) 2e) A vs. education (n=1, 168 pts) 2f) A vs. PT (n=2, 275 pts) 3) Massage vs. No treatment (n=0) 4) Compare the addition of massage to other treatments (n=5) 5) Assess the effectiveness of different techniques of massage (n=2)	Cochrane Back Group, 2003

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Furlan, 2010	Qualitative GRADE 2003, statistical pooling performed for only 2 studies due to heterogeneity (no other details provided)	1. Pain, mean between-group difference (95% CI): Short-term followup (1 month) -0.92 (-1.35 to -0.48) Function, mean between-group difference (95% CI): Short-term followup (1 month) -1.76 (-3.19 to -0.32) 2a) Pain, mean between-group difference (95% CI): Immediate: -0.94 (-1.76 to -0.12) 2b) Pain, mean between-group difference (95% CI): Immediate:0.6 (-10.3 to -0.17) 2b) Function, mean between-group difference (95% CI): Immediate:-3.38 (-5.96 to -0.8) 2c) Pain, mean between-group difference (95% CI): Immediate (2 studies only)-1.27 (-2.46; -0.08) 2d) no pooled data, 1 study 2e) no pooled data, 1 study 2f) Pain, mean between-group difference (95% CI): Immediate: -0.72 (-0.96 to -0.47) Pain, mean between-group difference (95% CI): long-term followup it was -0.95 (-1.39 to -0.51) 3) No data 4) No pooled data 5) Thai vs. Swedish (1 study): Pain, mean between-group difference (95% CI), immediate: 0.2, (-0.4 to 0.7) Pain, mean between-group difference,1 month (95% CI): 0.2 (-0.8 to 0.4)	No SAEs; patients reported soreness during or shortly after the treatment. Some patients also reported an allergic reaction (e.g. rash or pimples) to the massage oil.	Good

Please see Appendix C. Included Studies for full study references.

Table E26. Data abstraction of randomized controlled trials of massage

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Ajimsha, 2014	India, 1 site	Inclusion criteria: Nursing professional; 20-40 years old; chronic musculoskeletal low back pain for ≥3 months Exclusion criteria: 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)	A. Myofascial release+ specific back exercise (n=38) B. Sham myofascial release + specific back exercise (n=36) Treatment given 3 times weekly for 8 weeks	Mean age (years): 35.8 vs. 34.2 Female: 76% vs. 78% Duration of condition (months): 28.3±14.7 vs. 26.8±16.0	Subacute; ≥3 months

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Ajimsha, 2014	12 weeks	Mean differences, B vs. A: MPQ, week 8: 4.813, p=0.000 MPQ, week 12: 3.25, p=0.000 QBPDS, 8 weeks: 3.413, p=0.000 QBPDS, 12 weeks: 2.023, p=0.000	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: 10 vs. 1	Mahatma Gandhi University	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Borges, 2014	Brazil, 1 site	Inclusion criteria: Self-reported or medically diagnosed low back pain, pain score of 4-7 in the Pain Numerical Scale; Exclusion criteria: Pregnancy, vacation during study period, spondylolisthesis, herniated disc, lumbar sciatic pain, use of anti-inflammatory medication from 7 days before start of study through the 12 massage sessions, complementary practices, open wounds on back or buttocks, skin cancer, acute or chronic cutaneous conditions on back or buttocks, radiotherapy in back or buttocks three to six months before the study	Randomized: 45 Analyzed: 43 Attrition: 4.4%	A. Massage by acupressure (n=14) B. Laser applied but turned off (placebo) (n=15) C. No treatment (n=14)	Mean age (years): 39.6 overall Female: 92.9% vs. 73.3% vs. 64.3% No underlying disease: 71.4% vs. 80% vs. 92.9% Pain score of 7: 64.3% vs. 26.7% vs. 21.4%	NR
Cherkin, 2011	USA, 1 site (Group Health)	Inclusion criteria: LBP 3+ months without 2 or more pain-free weeks and pain bothersomeness rated at least 3 on a scale of 0 to 10 Exclusion criteria: 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)	A. Structural massage (n=132) B. Relaxation massage (n=136) C. Usual care (n=133)	A vs. B vs. C 46 vs. 47 vs. 48 Mean age 66% vs. 65% vs. 62% female 86% vs. 87% vs. 86% white LBP Bothersomeness, VAS: 5.6 vs. 5.6 vs. 5.8 Disability, RDQ: 10.1 vs. 11.6 vs 10.5	> 12 weeks

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Borges, 2014	6 weeks	Pain scores, baseline vs. 3 weeks vs. 6 weeks: A: 6.4 vs. 3.4 vs. 0.9, p<0.001 B: 5.7 vs. 4.8 vs. 4.7, p>0.05 C: 5.0 vs. 5.3 vs. 5.9, p>0.05	Withdrawals: 2 Withdrawals due to AE: 0 Serious AEs: 0 Nonserious AEs: 0	Not reported	Fair
Cherkin, 2011	52 weeks	A vs. B: LBP bothersomeness, VAS mean change from baseline (10 weeks): A vs. C: –1.4 (–1.9 to –0.8) B vs. C: –1.7 (–2.2 to –1.2)A vs. B: 0.3 (–0.2 to 0.8) p<0.05 but not reported separately Disability, RDQ mean change from baseline (10 weeks): A vs. C: –2.5 (–3.5 to –1.4) B vs. C: –2.9 (–4.0 to –1.8) A vs. B: 0.5 (–0.5 to 1.5) p<0.05 but not reported separately	Five of 134 (4%) relaxation massage recipients and 9 of 131 (7%) structural massage recipients reported adverse events possibly related to massage, mostly increased pain.	NCCAM	Good

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Kong, 2012	China, 1 site	Inclusion criteria: 15–35 years old; nonspecific low back pain without any relevant ongoing pathologies such as disc prolapse, fractures, spondylolisthesis, tumor, osteoporosis, or infection Exclusion criteria: other pain syndromes; spinal surgery in the past 6 months or having to undergo surgery or invasive examinations during the study; neurological disease; psychiatric disease; serious chronic disease that could interfere with the outcomes, pregnant or planning to become pregnant during the study	Randomized: 110 Analyzed: 101 Attrition: =8.1% (9/110)	A: Chinese massage with herbal ointment (n=55) B: Standard massage (n=55)	A vs. B Mean age 21 vs. 20 (male athletes) 26/55 vs. 27/55 female Race not reported (Shanghai) Pain, 5.4 vs. 5.4 Disability, not reported	Acute (duration not specified)

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Kong, 2012	1 month and 3 months	A vs. B Immediately after treatment: Pain mean change from baseline (0-10 VAS): (− 0.64 points [95% CI, − 1.04 to − 0.24]; p=0. 002 Disability not reported C-SFMPQ scores favored A vs. B Outcomes at 1 month post treatment: VAS scores (−0.66 points [95% CI, −1.13 to −0.19]; p=0.007).	No AEs occurred, no people withdrew	National Natural Science Foundation of China	Good

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Sritoomma, 2014	Thailand, 1 clinic	Inclusion criteria: aged 60 years and older; able to listen, speak, read and write Thai language; and diagnosed with CLBP by a medical practitioner (lasting for over 12 weeks). Exclusion criteria: skin disease, inflammation or infection on back, a history of back fracture or back surgery, body temperature of more than 38.5 ◦C on the examination day, hemi/paraparesis, infectious diseases (e.g. tuberculosis or AIDS), cancer, prior experience of receiving any type of massage in the three months before this study.	Randomized: 140 Analyzed: 140 Attrition: 0%	A. Swedish massage with ginger oil (n=70) B. Thai massage (n=70)	A vs. B Mean age not described (60 and older) 77% vs. 83% female Race not described (Thailand) Pain, VAS: 66.66 vs. 63.27 Disability, ODI: 26.9 vs. 29.5	Chronic
Romanowski, 2012	Poland, 1 site	Inclusion criteria: age between 60 and 75, the medication had to be stable for at least one month before the study and no intra-articular injections carried out during previous month. Exclusion criteria: skin diseases, abuse of alcohol, legal or illegal drugs, pregnancy, hemophilia, arteriosclerotic diseases, including ischemic heart disease or myocardial infarction, diseases that call for anticoagulating therapy, skin diseases.	Randomized: 26 Analyzed: 26 Attrition: 0%	A. Therapeutic massage (n=13) B. Deep tissue massage (n=13)	A vs. B Not described except to say there were no differences in age and gender	Chronic

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Sritoomma, 2014	6th and 15th week	A vs. B: 15 weeks: Pain, VAS mean change from baseline: −6.37 (−12.58,−0.17) 0.044 ODI mean difference in change from baseline: −3.66 (−7.17, −0.14) 0.042	AES not reported, no withdrawals reported	Centre for Health Practice Innovation	Fair
Romanowski, 2012	10 days "after treatment"	A vs. B Mean change in VAS: 13.54 ± 7.75 vs. 24.92 ± 13.55 p<0.001 Mean change in ODI: 9.46 ± 11.22 vs. 16.38 ± 11.68 p<0.001	AES not reported, no withdrawals reported	Funding source not described	Poor

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Zhang, 2015	China, 1 site	Inclusion criteria: <55 years old, nonspecific low back pain; Exclusion criteria: Ongoing pathologies such as disc prolapse, fractures, spondylolisthesis, tumor, osteoporosis, infection, other pain syndromes, spinal surgery in past 6 months, neurological disease, psychiatric disease, chronic disease that could interfere with the outcomes	Randomized: 92 Analyzed: 92 Attrition: 0	A. Chinese massage + core stabilization exercises B. Chinese massage only	Mean age: 48.71 vs. 51.62 Female: 37% vs. 33% Duration of pain: ≥12 weeks: 43% vs. 37%	Unclear
Zheng, 2012	China	Inclusion criteria: nonspecific low back pain lasting more than 3 months and an age of 21 to 75 years. Exclusion criteria: language barriers and those with low back pain caused by neoplasm, osteoporosis, vertebral fracture, rheumatoid arthritis, acute herniated disc accompanied by nerve root entrapment, and unstable spondylolisthesis.	Randomized: 64 Analyzed: 62 Attrition: =3.1% (2/64)	A. Massage + traction (n=32) B. Traction alone (n=32)	A vs. B 14/32 vs. 15/30 females 43 vs. 42 mean age Pain, function not reported Race not reported (China)	CLBP > 12 weeks

Author, Year	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality
Zhang, 2015	1 year	A vs. B: VAS, 2 weeks: 3.88±1.31 vs. 4.12±1.33, p>0.05 VAS, 8 weeks: 1.46±0.76 vs. 2.85±1.58, p<0.05 ODI, 2 weeks: 21.58±6.34 vs. 23.41±7.43, p>0.05 ODI, 8 weeks: 13.20±2.42 vs. 18.39±3.67, p<0.05	Withdrawals: 5 Withdrawals due to AEs: 0 Serious AEs: NR Nonserious AEs: NR	None	Fair
Zheng, 2012	Immediately after treatment at 3 weeks	A vs. B Immediately at end of treatment at 3 weeks?: Mean difference in pain VAS 1.9±0.9 vs. 1.4±0.8 p <0.05	AEs not reported; 2 discontinued due to worsening symptoms, but unclear from which group; 2 withdrew from study, but no reason given and treatment group not described	National Natural Science Foundation of China	Fair

Please see Appendix C. Included Studies for full study references.

Table E27. Data abstraction of systematic reviews of spinal manipulation

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Rubinstein, 2012	1) SMT versus inert interventions; 2) SMT versus sham SMT; 3) SMT versus all other therapies; 4) SMT plus any intervention versus that same intervention alone (i.e. SMT as an adjunct therapy); 5) SMT versus another SMT technique	2000-3/2011: Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE CINAHL, PEDro, Index to Chiropractic Literature	20 RCTs (n=2674); 6 with LRoB, , acute LBP < 6 weeks, 18+ yrs old; outcomes short, intermediate and long term (>12 months)	1) A: SMT versus B: inert interventions (n=7) 2) A: SMT versus B: sham SMT (n=1) 3) A: SMT versus B: all other therapies (n=8) 4) A: SMT plus any intervention versus B: that same intervention alone (n=4) 5) A: SMT versus B: another SMT technique (n=3)	Cochrane Back Group - 2011

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Rubinstein, 2012		All outcomes- pain, function, QOL, work, global improvement: low to very low quality evidence of no difference in effect of SMT compared to inert interventions, shamSMT, or when added to another intervention, low to mod no difference vs. other interventions, exception: moderate short-term effect of SMT on functional status when added to another intervention (two RCTs, SMD -0.41, 95% CI -0.73 to -0.10	6 studies reported AEs; 1 study 25% had minor AEs, but no difference between groups; 1 study 4 SAEs, but not related	Good

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Rubinstein, 2012	Spinal manipulation therapy (SMT) vs. no SMT or one SMT technique vs. another for acute LBP	Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE CINAHL, PEDro, Index to Chiropractic Literature through March 2011	20 RCTs: 9 acute LBP; 4 mixed acute and subacute LBP; 6 any LBP Duration of followup 2 days to 1 to 2 years	A. Any SMT (n=20) A1. Thrust SMT (n=13) A2. Non-thrust or unclear SMT (n=7) B. Other active interventions (exercise; physical therapy; massage; standard care; back school; n=8) C. Sham SMT (n=1) D. Intert interventions (education; ultrasound alone; ultrasound + cold; ultrasound; short-wave diathermy; anti- edema gel; bed rest; n=7)	Cochrane Back Group Criteria (2011)

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Rubinstein, 2012	n=20 qualitative, GRADE, 2008; meta analysis n=16, Random effects model; heterogeneity assessed using I^2 statistic; funnel plots constructed to test for publication bias; pooled effects assessed for clinical relevance according to predefined cut-offs	A vs. A+B, B, C or D Pain, mean between-group difference (95% CI) - -1 week (8 studies): -0.13 (-0.82 to 0.56) -1 month (5 studies): -0.56 (-1.07 to -0.06) -3 to 6 months (3 studies): -0.42 (-1.00 to 0.17) -12 months (1 study): 0.40 (-0.08 to 0.88) Functional status, standardized mean difference (95% CI) - -1 week (6 studies): -0.31 (-0.59 to -0.03) -1 month (9 studies): -0.23 (-0.42 to -0.03) -3 to 6 months (5 studies): -0.26 (-0.49 to -0.02) -12 months (2 studies): 0.06 (-0.14 to 0.25) A vs. B Pain, mean between-group difference (95% CI) - -1 week (3 studies): 0.06 (-0.53 to 0.65) -1 month (3 studies): -0.15 (-0.49 to 0.18) -3 to 6 months (2 studies): -0.20 (-1.13 to 0.73) -12 months (1 study): 0.40 (-0.08 to 0.88) Functional status, standardized mean difference (95% CI) - -1 week (1 study): 0.07 (-0.18 to 0.33) -1 month (3 studies): -0.11 (-0.26 to 0.05) -3 to 6 months (2 studies): -0.09 (-0.33 to 0.15) -12 months (2 studies): 0.06 (-0.14 to 0.25) Recovery, RR (95% CI) - -1 month (2 studies): 1.06 (0.94 to 1.12) -3 months (1 study): 1.29 (0.96 to 1.74) Return to work, RR (95% CI) - -1 month (1 study): 1.01 (0.91 to 1.12) -6 months (1 study): 1.07 (0.98 to 1.16) A vs. C Pain, mean difference (95% CI) - -1 month (1 study): -0.5 (-1.39 to 0.39) Functional status, standardized mean difference (95% CI) - -1 month (1 study): -0.35 (-0.76 to 0.06)		

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Rubinstein, 2012 (continued)		A vs. D Pain, mean between-group difference (95% CI) - -1 week (3 studies): 0.14 (-0.69 to 0.96) -1 month (1 study): -1.20 (-2.01 to -0.39) -3 months (1 study): -1.20 (-2.11 to -0.29) Functional status, standardized mean difference (95% CI) - -1 week (2 studies): -0.08 (-0.37 to 0.21) -1 month (1 study): -0.27 (-0.58 to 0.04) -3 months (1 study): -0.28 (-0.59 to 0.02) Recovery, RR (95% CI) - -1 week (2 studies): 0.96 (0.50 to 1.85) -1 month (1 study): 0.97 (0.85 to 1.10) -3 months (1 study): 1.00 (0.98 to 1.02) A +B vs. B Pain, mean between-group difference (95% CI) - -1 week (1 study): 0.84 (-0.04 to 1.72) -3 to 6 months (1 study): 0.65 (-0.32 to 1.62) Functional status, standardized mean difference (95% CI) - -1 week (2 studies): -0.41 (-0.73 to -0.10) -1 month (3 studies): -0.09 (-0.39 to 0.21) -3 to 6 months (2 studies): -0.22 (-0.61 to 0.16) Recovery, RR (95% CI) - -1 week (2 studies): 0.88 (0.36 to 2.19) -1 month (2 studies): 1.15 (0.60 to 2.19) -3 to 6 months (2 studies): 0.96 (0.71 to 1.31) Return to work, RR (95% CI) - -6 months (1 study): 1.21 (0.99 to 1.47) A1 vs. A2 No pooled estimates for any outcome		

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Rubinstein, 2011	1) SMT versus inert interventions 2) SMT versus sham SMT 3) SMT versus all other interventions4) SMT in addition to any intervention versus that intervention	CENTRAL MEDLINE EMBASE, CINAHL, PEDro, Index to Chiropractic Literature through June 2009	26 total studies with wide variety of comparisons, 9 with LRoB, LBP >12 weeks, 18+ years old, outcomes short, intermediate and long term (>12 months)	1) A: SMT versus B: inert interventions (n=4) 2) A: SMT versus B: sham SMT (n=3)3) A: SMT versus B: all other therapies (n=21)4) A: SMT plus any intervention versus B: that same intervention alone (n=5)	Cochrane Back Group 2009

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Rubinstein, 2011	Random effects model; heterogeneity assessed using eyeball and I^2 statistic; funnel plots constructed to test for publication bias; pooled effects assessed for clinical relevance according to predefined cut-offs	High quality: SMT has statistically sig short-term effect on pain and function compared to other interventions; varying quality that SMT has a statistically significant short-term effect on pain and function when SMT is added to another intervention. Effect sizes were small - not clinically relevant. Very low quality evidence that SMT is no more effective than inert interventions or sham SMT for short-term pain relief or functional status.	Not reported	Good

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
Rubinstein, 2011 (continued)				A. Any SMT (n=26) B. Inert interventions ((i.e. detuned short-wave diathermy and detuned ultrasound; n=4) C. Other active interventions (exercise; physical therapy; massage; standard care; back school; n=15) D. Sham SMT (n=3)	

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Rubinstein, 2011 (continued)		A vs. B Pain, mean between-group difference (95% CI) - -1 month (1 study, HRoB): - 6.00 (-15.82 to 3.82) -3 months (1 study, HRoB): 7.00 (-3.58 to 17.58) Functional status, standardized mean difference (95% CI) - No data available Recovery, RR (95% CI) - -1 month (1 study, HRoB): 1.03 (0.49 to 2.19) -3 months (1 study, HRoB): 0.96 (0.56 to 1.65) Return to work, RR (95% CI) - -1 month (1 study, HRoB): 1.29 (1.00 to 1.65) -6 months (1 study, HRoB): 1.17 (0.97 to 1.40) A vs. C Pain, mean difference (95% CI) - -1 month (10 studies, LRoB): -2.76 (-5.19 to 0.32) -3 months (6 studies, LRoB): -4.55 (-8.68 to -0.43) - 6 months (7 studies, LRoB): -3.07 (-5.42 to -0.71) - 12 months (4 studies, LRoB): -0.76 (-3.19 to 1.66) Functional status, standardized mean difference (95% CI) - -1 month (10 studies, LRoB): -0.17 (-0.29 to -0.06) -3 months (8 studies, LRoB): -0.18 (-0.37 to 0.01) -6 months (9 studies, LRoB): -0.12 (-0.23 to 0.00) -12 months (6 studies, LRoB):-0.06 (-0.16 to 0.05) Recovery RR (95% CI): -1 month (3 studies, HRoB): 1.20 (1.04 to 1.37) -3 months (2 studies, HRoB): 1.70 (1.20 to 2.40) - 6 months (1 study): 1.05 (0.81 to 1.38) - 12 months (1 study): 0.87 to 1.55) HRQoL, RR (95% CI) -1 month (3 studies, HRoB): -0.8 (-0.29 to 0.13) - 3 months 3 studies, HRoB): 0.21 (-0.27 to 0.70)		

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Rubinstein, 2011 (continued)		A vs. D Pain, mean between-group difference (95% CI) - -3 months (1 study, HRoB): 2.50(-9.64 to 14.64) -6 months (1 study, HRoB): 7.10 (-5.16 to 19.36) Functional status, standardized mean difference (95% CI) - -1 month (1 study, HRoB): -0.45,(-0.97 to 0.06) -3 months (1 study, HRoB):0.00, (-0.56 to 0.56) -6 months (1 study, HRoB):0.04, (-0.52 to 0.61) Recovery, RR (95% CI) - -1 week (2 studies): 0.96 (0.50 to 1.85) -1 month (1 study): 0.97 (0.85 to 1.10) -3 months (1 study): 1.00 (0.98 to 1.02) A +B vs. B Pain, mean between-group difference (95% CI) - -1 week (1 study): 0.84 (-0.04 to 1.72) -3 to 6 months (1 study): 0.65 (-0.32 to 1.62) Functional status, standardized mean difference (95% CI) - -1 week (2 studies): -0.41 (-0.73 to -0.10) -1 month (3 studies): -0.09 (-0.39 to 0.21) -3 to 6 months (2 studies): -0.22 (-0.61 to 0.16) Recovery, RR (95% CI) - -1 week (2 studies): 0.88 (0.36 to 2.19) -1 month (2 studies): 1.15 (0.60 to 2.19) -3 to 6 months (2 studies): 0.96 (0.71 to 1.31) Return to work, RR (95% CI) - -6 months (1 study): 1.21 (0.99 to 1.47)		

Please see Appendix C. Included Studies for full study references.

Table E28. Data abstraction of randomized controlled trials of spinal manipulation

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Balthazard, 2012	Switzerland	Inclusion criteria: 1) aged from 20 to 65 year old, male or female, suffering from nonspecific low back pain with or without symptoms in the lower extremity for a period between 12 and 26 weeks; 2) the usual medication can be continued; exclusion criteria: 1) spinal fracture or surgery within the previous 6 months; 2) pregnancy; 3) neoplasia; 4) spinal infection; 5) spinal inflammatory arthritis; 6) low back pain of visceral origin; 7) severe sensitive and/or motor radicular deficit from nerve root origin of less than 6 months; 8) score of 3/5 or more on the Waddell Score [36]; 9) on sick leaves from work for 6 months or more; 10) psychiatric disorders; 11) opioid medication	Randomized: 42 Analyzed: 37 Attrition: 5/42	A. HVLA + 5-10 min active exercises (n=22) B. Detuned ultrasound (sham) + 5-10 min active exercises (n=20)	A vs. B Mean age 44 vs. 42 years 36% vs. 30% female Race not reported Pain VAS 53 vs. 65 ODI: 30 vs. 32	Chronic: 12-26 weeks
Bicalho, 2010	Brazil, sites not stated	Inclusion criteria: age 18 to 55, LBP 3+ months, no treatment or SMT within the last 6 months. Exclusion criteria: pain radiating below the knee, skeletal or neuromuscular disorders identified by imaging or any Accident Compensation Corporation red flags	Randomized: 40 Analyzed:40 Attrition: 0%	A. HVLA (n=20) B. Control (side lying) (n=20)	A vs. B Mean age 30 vs. 27 ODI: 14.6 vs. 16.6 Race not reported (Brazil)	Chronic >3 months

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Balthazard, 2012	Pain intensity (VAS scale 0-10; higher score=more pain) ODI (scale 0-100; higher score=more disability)	Up to 6 months	A vs. B Pain, VAS-pain mean group difference: -1.24; 95% CI: -2.37 to − 0.30; P = 0.032, statistically not significant at the 0.025 level. A vs. B ODI mean group difference: -7.14; 95% CI: -12.8 to − 1.52; p=0.013	AEs not reported	Swiss National Science Foundation	Fair	
Bicalho, 2010	Pain intensity (VAS scale 0-10; higher score=more pain) ODI (scale 0-100; higher score=more disability)	immediate	A vs. B Pain VAS mean group difference (0-100): -11 vs. -2.2, no CI provided, p=0.04) A vs. B Finger to floor, EMG flex-ext reported (favored SMT), ODI measured but not reported	AEs not reported	Not reported	Fair	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Bronfort, 2004	USA, 1 center	18-65 sciatica >=4 weeks Quebec Classification Category 2,3,4 or 6 Excluded: spinal fracture, spinal stenosis, or other diagnoses, including visceral diseases, compression fractures, and metastases, progressive neurological deficits, cauda equina syndrome, surgical lumbar spine fusion, contraindications to study treatments, a leg pain score of less than 3, current or pending litigation, or ongoing treatment for low back and leg pain from other health care providers. Pregnant or nursing	Randomized=32 Analyzed=NR Attrition=NR	A=chiropractic (n=11) B=epidural steroid injection (n=11) C=self-care education (n=10)	A vs. B vs. C Mean Age: 44 vs. 52 vs. 52 Female=45% v 36% v 50% RMD=43 vs. 56 vs. 41 Smoker=1 vs. 4 vs. 3 QTF Classification 2=5 vs. 4 vs. 4 QTF Classification 3=5 vs. 6 vs. 5 QTF classification 4=1 vs. 1 vs. 1 Low back pain score: 4 vs. 6 vs. 5 Leg pain score: 6 vs. 5 vs. 5	A vs. B vs. C 1-3 mo=2 vs. 2 vs. 2 4-6 mo=1 vs. 1 vs. 0 7-12 mo=2 vs. 0 vs. 1 >12 mo=7 vs. 7 vs. 7

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Bronfort, 2004	Self-report questionnaires straight leg raise lumbar spinal motion Roland Morris Disability Oswestry Disability National Health Interview Survey	52 weeks	All results were compiled together, no group comparisons 3 week outcomes Leg Pain=1.8 (Effect Size 1.1) Low back pain=0.9 (0.4) Roland Morris=13.7 (0.6) Oswestry 11 (0.9) Bothersome symptoms=14.6 (0.91) Frequency of symptoms=12.4 (0.74) Cut back on activities=3.3 (0.38) Stayed in bed (# days)=0.2 (0.08) Missed work or school=0.8 (0.15) 12 week outcomes Leg Pain=2.9 (Effect Size 1.71) Low back pain=1.7 (0.8) Roland Morris=22.7 (1.1) Oswestry 22.9 (1.8) Bothersome symptoms=25.2 (1.58) Frequency of symptoms=23.0 (1.37) Cut back on activities=5.3 (0.61) Stayed in bed (# days)=1.2 (0.47) Missed work or school=1.9 (0.35) 52 week outcomes Leg Pain=2.3 (Effect Size 1.35) Low back pain=1.9 (0.9) Roland Morris=19.6 (0.9) Oswestry 15.6 (1.2) Bothersome symptoms=18.1 (1.13) Frequency of symptoms=17.5 (1.04) Cut back on activities=5.3 (0.61) Stayed in bed (# days)=0.5 (0.20) Missed work or school=2.3 (0.43)	NR	Foundation for Chiropractic Education and Research.	Poor	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Bronfort, 2011	United States Single center University research clinic	Age 18-65 years, primary complaint of mechanical LBP ≥6 weeks w/w/o radiating pain to the lower extremity Excluded: previous lumbar surgery, vascular disease, pain score <3	301 randomized 245 completed 19% attrition	A. Supervised exercise therapy for 12 weeks (n=100) B. Chiropractic spinal manipulation for 12 weeks (n=100) C. Home exercise and advice for 12 weeks (n=101)	A vs. B vs. C Mean age: 44.5 vs. 45.2 vs. 45.6 years Female sex: 57% vs. 66% vs. 58% Race: NR Duration of back pain: 4.8 vs. 5.0 vs. 5.0 years Mean pain severity score (0-10): 5.1 vs. 5.4 vs. 5.2 Roland-Morris disability score (0-23): 8.4 vs. 8.7 vs. 8.7	Chronic; median duration 4.8 to 5 (0-51) years
Bronfort, 2014	US, 2	Inclusion: 21+ years or older, back related leg pain (BRLP) >3 on 0-10 scale, current episode 4+ weeks, stable medications x 1 month Exclusion: LBP without radiation, prior fusion, spinal stenosis, neurologic signs, receiving ongoing treatment for LBP,	Randomized (minimization): 192 Analyzed: 192 Attrition: 13	A=SMT plus HEA (home exercise with advice) B HEA	Mean age 57 vs. 58 Women % 59% vs. 68% mean NRS leg pain 5.4 vs. 5.4 mean RDQ 10.2 vs. 10.2	Subacute to chronic > 4 weeks

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Bronfort, 2011	Self-reported questionnaire assessing pain, disability, and quality of life; lumbar range of motion; strength; and endurance	52 weeks	Only significant between-group differences in patient-reported outcomes were for satisfaction (favoring A, p<0.01 at 12 weeks and p<0.001 at 52 weeks) Overall treatment effect was significant for endurance (p<0.05) and strength (p<0.05) but not range of motion (also favoring A).	A vs. B vs. C Nonserious adverse events: 1% (1/100) vs. 1% (1/100) vs. 4% (4/101) All adverse events were transient, required little to no change in activity level, and were considered non-serious	NR	Good	Large tables of data at each time point available
Bronfort, 2014	Leg Pain NRS, LBP NRS, RDQ, global improvement, medications	52 weeks	A vs. B Leg Pain 12 weeks -1.0 (-1.9 to -0.2), p=0.008 Leg Pain 52 weeks -0.7 (-1.5 to 0.2), p=0.15 LBP at 12 weeks -0.9 (-1.6 to -0.3), p=0.005, 52 weeks -0.3 (-1.0 to 0.4) p=0.4	5 SAEs (1 bowel obstruction in HEA, 4 anal phylaxis, sports-trauma, heart condition, menorrhagia in SMT group. Expected AEs were reported in 30% of SMT group vs. 42% in HEA group.	US Department of Health and Human Services	Fair	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Burton,2000	England, one	18-60 years unilateral sciatica from lumbar disc herniation based on CT or MRI No surgical intervention needed Exclusion: Sequestrated herniation multiple level DJD previous lumbar surgery previous chemonucleolysis previous manipulation for present complaint litigation	Randomized=40 Analyzed=40 at 2 weeks, 37 at 6 weeks, 30 at 12 months Attrition=10	A=osteopathic manipulation (15 min treatment sessions over 12 weeks) B=chemonucleolysis (control)	Mean Age 42 53% female a= mean 30 weeks symptoms b=mean 32 weeks	Chronic pain

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Burton,2000	Leg pain (0-10 scale) Back pain (0-10 scale) Roland Disability scale	12 months	A vs. B (*=statistically sig, p value not provided) Baseline leg pain 4 vs. 3.7 Back pain 3.8 vs. 4.1* RDQ 11.9 vs. 12 2 weeks leg pain 3.2 vs. 3.3 back pain 3.2 vs. 4 RDQ 10.2 vs. 13.9* 6 weeks leg pain 2.7 vs. 2.7 back pain 2.7 vs. 3.6* RDQ 7.8 vs. 11 12 months leg pain 2.1 vs. 2.3 back pain 2.3 vs. 2.9 RDQ 5.9 vs. 7.3	NR	NHS Executive	Poor	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Cecchi, 2010	Italy, 1 site	Inclusion criteria: Home dwelling, seeking care from rehab department, nonspecific low back pain, reported 'often' to 'always' at least for the past 6 months Exclusion criteria: neurological signs or symptoms, spondylolisthesis 4 second degree, spinal stenosis, lumbar scoliosis 420 degrees, rheumatoid arthritis or spondylitis, previous vertebral fractures, psychiatric disease, cognitive impairment or pain-related litigation	Randomized: 210 Analyzed: 205 Attrition: 2.5% 5/210	A. Back school (n=70) B. PT (n=70) C. SMT (n=70)	A vs. B vs. C Mean age 58 vs. 61 vs. 58 49% vs. 43% vs. 48% female Race not reported (Italy) Pain, NRS (mean): 2 vs. 2 vs. 2.2 RDQ (0-24) (mean): 9.5 vs. 9.7 vs. 8.5 (sick leave due to LBP higher in A vs. B and C – p =0.001)	Chronic > 6 months

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Cecchi, 2010	Pain intensity (VAS scale 0-10; higher score=more pain) RDQ (scale 0-23; higher score=more disability)	3, 6 and 12 months	A vs. B vs. C Mean differences not reported – will need to calculate Back Pain NRS 12 month mean change from baseline (0.7 vs. 0.4 vs. 1.5) C improved to greater degree than B or A at 12 months in terms of pain (but small, clinically insignificant) A vs. B vs. C RDQ mean (SD) reduction from baseline to 12 months: 4.2+/- 4.8 vs. 4.0+/-5.1 vs. 5.9+/-4.6 C improved to greater degree than B or A at 12 months in terms of disability (but small, clinically insignificant)	No AEs reported by patients, no drop-outs due to AEs	Fondazione Don Gnocchi Foundation, Scientific Institute	Fair	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
de Olivera, 2013	Brazil, 1 outpatient PT clinic	Inclusion criteria: chronic nonspecific low back pain (12+ weeks) aged 18 to 80 years, minimum pain intensity score of 3 on an 11-point numeric pain rating scale (ranging from 0 to 10 points) Exclusion criteria: contraindications to the treatment (e.g., spinal canal stenosis, spinal fracture, acute rheumatic diseases, hemorrhagic diseases, active tuberculosis, recent deep vein thrombosis), pregnancy, nerve root compromise, and previous spinal surgery	Randomized: 148 Analyzed:148 Attrition:0%	A: HVLA – region specific (n=74) B: HVLA non-specific (n=74)	A vs. B Mean age 46 vs. 46 80% vs. 68% female Race not reported Pain, NPRS 6.1 vs. 6.0 Disability, RDQ: 11.3 vs. 9.3	Chronic > 12 weeks
Goertz, 2013	William Beaumont Army Medical Center (WBAMC), Fort Bliss, El Paso, TX	Eligibility criteria: male and female US active-duty military personnel between 18 and 35 years of age with acute LBP, less than 4 weeks duration. Soldiers were excluded if they were relocating or leaving the post within 6 weeks from the day of the screening, had LBP for more than 4 weeks, were pregnant, or had a condition in which CMT was contraindicated	Randomized: 91 Analyzed:73 Attrition: 24% (22/91)	A: HVLA + standard medical care (n=45) B: Standard medical care (n=46)	A vs. B Mean age 25 vs. 26 15% vs. 14% female 73% vs. 52% White, more missing in SMC Pain, NPRS 5.8 vs. 5.8 Disability, RDQ: 11 vs. 12.7	Acute

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
de Olivera, 2013	Pain intensity (VAS scale 0-10; higher score=more pain) RDQ (scale 0-23; higher score=more disability)	immediate	A vs. B Pain, intensity (NRS) mean group difference: 0.50 (-0.10 to 1.10), p=.10 A vs. B Pressure pain thresholds measured, no difference between groups, RDQ not reported	AEs not reported	Not reported	Good	
Goertz, 2013	Pain intensity (VAS scale 0-10; higher score=more pain) RDQ (scale 0-23; higher score=more disability)	4 weeks	4 week outcomes: A vs. B Pain, intensity (NRS) mean group difference: 1.2 (0.2, 2.3) p=0.02 A vs. B Disability (RDQ): 4.0 (1.3, 6.7), p=0.004	No SAEs reported. Two mild AEs (increased sharp pain at site)	Samueli Institute, NIH	Fair	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Haas, 2014	University of Western States, Portland, OR, 1 site	Inclusion criteria: 18+ years old, current episode of cLBP of mechanical origin of 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. Exclusion criteria: received manual therapy within the previous 90 days or for contraindications to study interventions and complicating conditions such as 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 Analyzed: 391 Attrition: =2.3% (9/400)	A: Massage (n=100) B. Massage + 6 SMT (n=100) C. Massage + 12 SMT (n=100) D. Massage + 18 SMT (n=100)	A vs. B vs. C vs. D Mean age 41 vs. 41 vs. 42 vs. 41 49% vs. 49% vs. 49% vs. 52% female Nonwhite: 14% vs. 18% vs. 11% vs. 16% Pain, VAS 52.2 vs. 51.0 vs. 51.6 vs. 51.5	Chronic >3 months

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Haas, 2014	Primary outcomes: pain score is the average of three 11-point numeric rating scales converted to a 100-point scale: back pain today, worst back pain in the last 4 weeks, and average back pain in the last 4 weeks. The disability score is also the average of three scales: interference with daily activities, social and recreational activities, and the ability to work (outside or around the house). Secondary outcomes included pain unpleasantness, Physical and Mental Component Summary Scales of the short-form 12, Health State Visual Analog Scale from EuroQol, perceived pain and disability improvement, and the number of the following in the previous 4 weeks: days with pain and disability and medication use	up to 52 weeks	A vs. D Pain intensity, percentage responders (>50%) at 52 weeks 10.6 (-3.2, 24.4), NS NS differences in A vs. B, A vs. C Only sig difference in 12 week A vs. C 21.1 (7.7, 34.6)* p <0.025 Disability score calculated, but unclear what measure	No SAEs; 4 participants had increased back pain. One withdrew due to exacerbation from lifting a child.	NCCAM	Good	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Paatelma, 2008	Finland, 4 clinics	Inclusion criteria: 18–65-year-old employed people with current non-specific LBP with or without radiating pain to one or both lower legs. The back pain episode could be acute to chronic, the first or recurrent. Exclusion criteria were: pregnancy, low back surgery less than 2 months previously, and "red flags" that indicate serious spinal pathology	Randomized: 134 Analyzed:106 Attrition: =21% (28/134)14% in the McKenzie method group, to 22% in the OMT group, to 30% in the advice-only group	A. SMT (n=45) B. McKenzie (n=52), C. "advice only to be active" (n=37)	A vs. B vs. C Mean age 44 vs. 44 vs. 44 42% vs. 29% vs. 35% female Race not reported (Finland) Pain, VAS (median): 20 vs. 16 vs. 16 RDQ (0-24) (median): 9 vs. 9 vs. 8	duration not specified

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Paatelma, 2008	Pain intensity (VAS scale 0-10; higher score=more pain) Pain bothersomeness (VAS scale 0-10; higher score=more bothersomeness) RDQ (scale 0-23; higher score=more disability)	1 year	A vs. C (12 months) Pain, intensity (VAS) mean group difference: –4 (–17 to 9) p= 0.714 B vs. C Pain, intensity (VAS) mean group difference: –10 (–23 to 2) p=0.144 A vs. C (12 months) Disability (RDQ): –3 (–6 to 0) p= 0.068 B vs. C Disability (RDQ): –3 (–6 to 0) 0.028	AEs not reported	Not reported	Fair	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Petersen, 2011	Denmark, 1 primary care clinic	Eligible patients were between 18 and 60 years of age, suffering from LBP with or without leg pain for a period of more than 6 weeks, able to speak and understand the Danish language, and with a presentation of clinical signs of disc-related symptoms Exclusion criteria: were free of symptoms at the day of inclusion, demonstrated positive nonorganic signs, 19 or if serious pathology was suspected based on physical examination and/or magnetic resonance imaging, application for disability pension, pending litigation, pregnancy, comorbidity, recent back surgery, language problems, or problems with communication including abuse of drugs or alcohol	Randomized: 350 Analyzed: 324 Attrition: 10% (26/350) 91 patients "withdrew" from treatment, but a total of 324/350 were followed to the end of the study	A. McKensie exercise (n=175) B. SMT (n=175)	A vs. B Mean age 38 vs. 37 59% vs. 53% female Race not reported (Denmark) Pain (3 0-10 scales), 30/60 vs. 29/30 Disability, RDQ: 13 vs. 13	Chronic >6 weeks

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Petersen, 2011	Primary outcome: RDQ (scale 0-23; higher score=more disability) Secondary outcomes: Pain intensity (VAS scale 0-10; higher score=more pain), global perceived effect, 29 quality of life, 30 days with reduced activity, 31 return-to-work, satisfaction with treatment, and use of health care after the completion of treatment	2 months	A vs. B Pain, intensity (NRS) mean group difference: 2.8 (− 0.2 to 5.8) p=0.063 (12 months) A vs. B Disability (RDQ): 1.5 (0.2 to 2.9) p=0.030 (12 months, favoring A)	AEs not reported; 28 from Mckensie group "withdrew" from treatment due to lack of effect, but were followed to end of study; 48 from SMT group withdrew due to lack of effect.	Grants, Foundation funds, but not specified	Good	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Santilli, 2006	Italy, two	18-65 acute pain <10 days Moderate to severe pain (>5 on VAS) Pain radiating to one leg MRI evidence of disc protrusion	Randomized=102 (53 vs. 49) Analyzed=102 Attrition=6	A=active manipulation 5 days/week B=control (simulated manipulation)	Mean age <40 Female 30% vs. 45% Pain 6.4 vs. 6.4 Radiating Pain 5.3 vs. 5.1	Acute
Schneider, 2015	US, one	18+ years new LBP episode within last 3 months, pain 3+/10, disability 20+/100 Exclusion: chronic LBP >3 months, prior treatment for the current LBP episode, radicular pain, current use of pain meds	Randomized=112, analyzed=107 attrition=8	A=manual thrust SMT B=mechanical assisted SMT C=usual care	Mean age 41 vs. 41 vs. 40 Pain=5.7 vs. 5.5 vs. 6.0 ODI 33.9 vs. 33.1 vs. 34.6	Acute to subacute LBP (<3 months)

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Santilli, 2006	Pain days VAS pain score NSAID use SF-36	180 days	A vs. B 180 days No. of patients with reduction of local pain 98% vs. 94% (NS) No. of patients with reduction of radiating pain 100% vs. 83% (p<0.01) No. of Patients pain free (local pain) 28% vs. 6% (p<0.005) No. of Patients who are pain free (radiating pain) 55% vs. 20% (p<0.001) NS difference between SF-36 results	None reported	No profit Institute of Rome	Good	
Schneider, 2015	ODI (0-100) Pain (0-10)	6 months	A vs. B vs. C Adjusted group differences, mean (95% CI) ODI 0.4 (-10.2 to 11.0) vs. 1.4 (-9.1 to 12.0) vs. 1.0 (-9.6 to 11.6) Pain -1.2 (-3.2 to 0.7) vs. -0.9 (-2.9 to 1.1) vs. 0.3 (-1.6 to 2.3)	NR	NIH/NCCAM	Good	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Senna, 2011	Egypt, 1 hospital	Inclusion criteria: 20 to 60years old with chronic nonspecific LBP (that lasted for at least 6 months) Exclusion criteria: "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 Analyzed:60 Attrition: =35% (33/93)	A. sham SMT (12 sessions over 1 month) (n=40) B. SMT (12 sessions over 1 month) (n=27) C. SMT (12 sessions over 1 month + every 2 weeks x 9 months) (n=27)	A vs. B vs. C Mean age 42 vs. 40 vs. 42 24% vs. 27% vs. 24% female Race not reported (Egypt) Pain, VAS 41 vs. 42 vs. 43 ODI: 38 vs. 39 vs. 40	Chronic > 6 months
von Heymann, 2013	Germany, 5 orthopedic or general practices in 4 different cities	Inclusion criteria: 18 to 55 years of age, acute (< 48 hr) LBP. Exclusion criteria: known intolerance to NSAID or paracetamol, occurrence of LBP or spinal manipulation for any cause within the last 3 months, known or suspected abuse of alcohol or drugs, metabolic or malignant or any serious organic or neurological disease, atopic diathesis, any structural disturbances of the spine	Randomized: 101 Analyzed:93* Attrition: ?8% (8/101) Very unclear description and text does not match the consort diagram	A. SMT and placebo-diclofenac (n=37) B. Sham SMT and diclofenac (n=38) C. Sham SMT and placebo diclofenac. (n=25)	A vs. B vs. C Mean age 34 vs. 38 vs. 39 36% vs. 38% vs. 46% female Race not reported (Germany) Pain, VAS 41 vs. 42 vs. 43 ODI: 38 vs. 39 vs. 40	Acute <48 hours

Author, Year	Outcome Measures	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Senna, 2011	Pain intensity (VAS scale 0-10; higher score=more pain) SF-36 (scale 0-100 for each subscale; higher score=less disability) Global perception of improvement	1, 4, 7, 10 months	A vs. B vs. C Pain, intensity (NRS) mean group difference: A vs. B Unadjusted mean difference in VAS at 1 month 4; at 10 months 0 A vs. C Unadjusted mean difference at 1 month 6, at 10 months 17 Results not reported as group mean differences – will need to calculate these; overall B and C improved to similar degree compared to A at 1 month, group C maintained the improvement through 10 months whereas B returned to baseline for both pain and function	Most common: local tenderness and tiredness (frequency not reported), no SAEs	No funds	Fair	
von Heymann, 2013	Pain intensity (VAS scale 0-10; higher score=more pain) RDQ (scale 0-23; higher score=more disability) SF-12	12 weeks	A vs. B vs. C (only reported to 9 days) Pain VAS – unable to calculate group mean differences based on the way presented (graphs) And only A vs. B was presented, not A vs. B vs. CA vs. B. vs. C. A vs. B: Unadjusted mean difference in RDQ at 12 weeks: 3.0 (P value not reported) RDQ - unable to calculate group mean differences based on the way presented (graphs)	No AEs reported by patients; Early termination due to treatment failure occurred in 10 of 22 subjects in the placebo group. In the spinal manipulation group, 1 of the 35 subjects opted out early because of treatment failure. In the diclofenac group 3 of the 35 subjects opted out early because of treatment failure	Deutsche Gesellschaft für Manuelle Medizin (DGMM) - Aerzteseminar für Manuelle Wirbelsaeulenu nd Extremitaetenth erapie (MWE)	Fair	

Please see Appendix C. Included Studies for full study references.

Table E29. Data abstraction of systematic reviews of ultrasound

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
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	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=222)	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	Chronic: All chronic, mean duration 5.8 vs. 8.1 years

Author, Year	Duration of Followup	Results (list results for acute, subacute, and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality (Cochrane Back Group)
Ebadi, 2012	8 weeks (4 weeks after completion of therapy)	A vs. B Pain (mean, 0-100 VAS): 27 vs. 31 at 4 w, 28 vs. 26 at 8 w (p=0.48 for overall effect) Functional Rating Index (mean, 0-100 VAS): 23 vs. 31 at 4 w, 23 vs. 30 at 8 w (p=0.04 for overall effect)	Not reported	Tehran University of Medical Sciences	Good

Please see Appendix C. Included Studies for full study references.

Table E30. Data abstraction of randomized controlled trials of ultrasound

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Bronfort, 2011	United States Single center University research clinic	Age 18-65 years, primary complaint of mechanical LBP ≥6 weeks w/w/o radiating pain to the lower extremity Excluded: previous lumbar surgery, vascular disease, pain score <3	301 randomized 245 completed 19% attrition	A. Supervised exercise therapy for 12 weeks (n=100) B. Chiropractic spinal manipulation for 12 weeks (n=100) C. Home exercise and advice for 12 weeks (n=101)
Fiore, 2011	Italy Single center	Low back pain for ≥3 weeks Exclude: Anesthetic or corticosteroid injection within 4 weeks, radicular pain, osteoporosis, surgery or previous spine fracture, spinal stenosis, history of acute trauma, osteoarthritis, myofascial pain syndrome, inflammatory rheumatic disease, systemic lupus erythematosus, diabetes mellitus type I or II, thyroid dysfunction, obesity, pacemaker, neurological pathologies, anxious-depressive syndromes	Randomized: 30 Analyzed: 30 Attrition: 0% at 3 weeks	A: Ultrasound 2 W/cm^2 at 1 MHz; fifteen 10 minutes sessions over 3 weeks (n=15) B: Low level laser therapy with Nd:YAG laser pulsated waveform, 1 KW, wavelength 1064 nm, maximum energy for single impulse 150 mJ, average power 6 W, fluency 760 mJ/cm^2, duration of single impulse <150 ms applied in 3 phases, total 10 minutes and 2,600 J, fifteen sessions over 3 weeks (n=15)
Goren, 2010	Turkey Single center	>18 years of age, clinical symptoms and signs consistent with lumbar spinal stenosis for >3 months, MRI findings of spinal stenosis, neurogenic claudication on treadmill walk test Exclude: Movement disorder or orthopedic problem affecting ability to ambulate, moderate to severe knee or hip arthritis, peripheral vascular disease or vascular claudication, previous lumbar spinal stenosis surgery, serious medical comorbidity, another specific spinal disorder, major or progressive neurological deficit, contraindication to ultrasound treatment, malignancy	Randomized: 50 Analyzed: 45 Attrition: 10% (5/50) at 3 weeks	A: Ultrasound 1.5 W/cm2 at 1 MHz; fifteen 10 minutes sessions over 3 weeks + exercise therapy with stretching and strengthening for 20 minutes, and low-intensity cycling for 15 minutes (n=15) B: Sham ultrasound + exercise therapy (n=15) C: No ultrasound or exercise (n=15)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Bronfort, 2011	A vs. B vs. C Mean age: 44.5 vs. 45.2 vs. 45.6 years Female sex: 57% vs. 66% vs. 58% Race: NR Duration of back pain: 4.8 vs. 5.0 vs. 5.0 years Mean pain severity score (0-10): 5.1 vs. 5.4 vs. 5.2 Roland-Morris disability score (0-23): 8.4 vs. 8.7 vs. 8.7	Chronic; median duration 4.8 to 5 (0-51) years	52 weeks
Fiore, 2011	Mean age: 51 years (entire sample) Female: 63% (entire sample) Race: Not reported Pain intensity (median, 0-10 VAS): 7 vs. 7 ODI (median, 0-100): 28 vs. 28	All ≥3 weeks, mean duration not reported	3 weeks (at completion of therapy)
Goren, 2010	Mean age: 57 vs. 49 vs. 53 years Female: 53% vs. 87% vs. 73% Race: Not reported Back pain (mean, 0-10 VAS): 5.5 vs. 6.2 vs. 5.3 Leg pain (mean, 0-10 VAS): 5.8 vs. 6.3 vs. 6.6 ODI (mean, 0-100): 25 vs. 27 vs. 32 Central stenosis: 100% vs. 93% vs. 93% Lateral stenosis: 13% vs. 13% vs. 13%	All > 3 months, 67% vs. 73% vs. 67% >12 months	3 weeks (at completion of therapy)

Author, Year	Results (list results for acute, subacute, and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality (Cochrane Back Group)	Comments
Bronfort, 2011	Only significant between-group differences in patient-reported outcomes were for satisfaction (favoring A, p<0.01 at 12 weeks and p<0.001 at 52 weeks) Overall treatment effect was significant for endurance (p<0.05) and strength (p<0.05) but not range of motion (also favoring A).	A vs. B vs. C Nonserious adverse events: 1% (1/100) vs. 1% (1/100) vs. 4% (4/101) All adverse events were transient, required little to no change in activity level, and were considered non-serious	NR	Good	Large tables of data at each time point available
Fiore, 2011	A vs. B Pain (median, 0-10 VAS): 4 vs. 3 at 3 w (p=0.009) ODI (median, 0-100): 16 vs. 12 at 3 w (p=0.006)	Not reported	Not reported	Fair	
Goren, 2010	A vs. B Back pain (mean, 0-10 VAS): 3.33 vs. 4.26 vs. 5.66 at 3 w (p=0.10) Leg pain (mean, 0-10 VAS): 4.33 vs. 3.86 vs. 7.13 at 3 w (p=0.007 for A vs. C, p=0.006 for B vs. C) ODI (mean, 0-100): 22 vs. 19 vs. 29 at 3 w (p=0.01 for A vs. C, p=0.01 for B vs. C) Paracetamol tablet use (mean): 8.33 vs. 16.0 vs. 31 at 3 w (p=0.02 for A vs. C)	"No complications or side effects were recorded"	Not reported	Fair	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
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	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
Unlu, 2008	Turkey Single center	20 to 60 years of age, acute leg pain and leg pain of <3 months' duration due to lumbar disc herniation, with MRI verification and concordant symptoms, imaging findings, and physical examination Exclude: Abnormal laboratory findings, systemic and psychiatric illness, pregnant, previous spinal surgery, spinal stenosis, spondylolisthesis	Randomized: 60 Analyzed: 60 Attrition: Not reported	A: Ultrasound 1.5 W/cm^2 at 1 MHz; 15 sessions over 3 weeks (n=20) B: Lumbar traction: Motorized traction system (Tru-trac 401), 15 minutes per session (hold for 30 seconds and rest for 10 seconds), traction forced increased as tolerated from minimum traction force 35% to maximum 50% of body weight; 90 degree hip and knee flexion C: Low-level laser: Gal-Al-As diode laser at 50 mV and wavelength 830 nm, diameter 1 mm, 4 minute application over both sides of disc spaces where herniation detected, dose 1 J at each point

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Licciardone, 2013	A vs. B Median age: 38 vs. 43 years 58% vs. 68% female Race: Not reported Pain intensity (median, 0-100 VAS): 44 vs. 44 RDQ (median, 0-24): 5 vs. 5 SF-36 general health (median, 0-100): 72 vs. 67	Chronic: All >3 months, 51% vs. 49% >1 year	12 weeks (4 weeks after completion of therapy)
Unlu, 2008	A vs. B vs. C Mean age: 48 vs. 42 vs. 43 years 65% vs. 80% vs. 65% female Race: Not reported Pain intensity, low back (mean, 0-100 VAS): 52 vs. 58 vs. 54 Pain intensity, leg (mean, 0-100 VAS): 56 vs. 60 vs. 53 RDQ (mean, 0-24): 13 vs. 14 vs. 12 Modified ODI (mean, 0-50): 20 vs. 15 vs. 18	Acute: All <3 months	3 months after completion of therapy

Author, Year	Results (list results for acute, subacute, and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality (Cochrane Back Group)	Comments
Licciardone, 2013	A vs. B ≥30% improvement in pain: RR 1.02 (95% CI 0.86 to 1.20) at w 12 ≥50% improvement in pain: RR 1.09 (95% CI 0.88 to 1.35) at w 12 RDQ (median, 0-24): 4 vs. 4 at w 4 (p=0.99), 3 vs. 4 at week 8 (p=0.76), 3 vs. 3 at w 12 (p=0.93) SF-36 general health (median, 0-100): 72 vs. 72 at w 4 (p=0.73), 72 vs. 72 at w 8 (p=0.53), 72 vs. 74 at w 12 (p=0.66) Lost 1 or more days work in past 4 weeks because of low back pain: 16% vs. 7% (p=0.04) at w 4, 17% vs. 8% at w 8 (p=0.54), 13% vs. 6% at w 12 (p=0.11) Very satisfied with back care: 41% vs. 45% at w 4 (p=0.44), 49% vs. 51% at w 8 (p=0.77), 55% vs. 55% at w 12 (p=0.99)	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)	National Institutes of Health-National Center for Complementary and Alternative Medicine and the Osteopathic Heritage Foundation	Good	
Unlu, 2008	A vs. B vs. C Pain intensity, low back (0-100 VAS): 30 vs. 30 vs. 34 at end of treatment, 27 vs. 26 vs. 31 1 month after end of treatment, 27 vs. 31 vs. 30 3 months after end of treatment Pain intensity, leg (0-100 VAS): 29 vs. 28 vs. 33 at end of treatment, 27 vs. 22 vs. 26 1 month after end of treatment, 25 vs. 30 vs. 24 3 months after end of treatment RDQ (0-24): 9.3 vs. 9.8 vs. 9.9 at end of treatment, 8.2 vs. 8.5 vs. 7.3 1 month after end of treatment, 8.6 vs. 8.9 vs. 6.7 3 months after end of treatment Modified ODI (0-50): 14 vs. 15 vs. 15 at end of treatment, 14 vs. 14 vs. 14 1 month after end of treatment, 14 vs. 15 vs. 14 3 months after end of treatment	Not reported	Not reported	Poor	

Please see Appendix C. Included Studies for full study references.

Table E31. Data abstraction of systematic reviews of TENS

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies
van Middelkoop, 2011	TENS vs. sham TENS vs. active treatments	MEDLINE, EMBASE, CINAHL, CCRCT, PEDro through December 2008; reference lists of relevant Cochrane reviews	6 RCTs; n=699 Duration of followup 2-16 weeks All chronic pain	A. TENS B. Other active intervention C. Sham TENS	Cochrane Back Group criteria - 2011

Author, Year	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality	Comments
van Middelkoop, 2011	Continuous outcomes: scales converted to 100 point scales, weighted mean difference calculated Dichotomous outcomes: RR and CI calculated; heterogeneity assessed using I^2 Funnel plot constructed to assess risk of publication bias	A vs. C Pain score: 4 trials; WMD -4.47 (95% CI -12.84 to 3.89) Disability: 2 trials; WMD -1.36 (95% CI -4.38 to 1.66) A vs. B No meta-analysis; narrative report of 2 trials of exercise or exercise + PENS found no significant difference between TENS and other treatments	Not reported	Good	

Please see Appendix C. Included Studies for full study references.

Table E32. Data abstraction of randomized controlled trials of TENS

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants
Buchmuller, 2012	Multi-center France	Age >18 years with chronic low back pain ≥40 VAS with or without radicular pain Excluded: pain duration <3 months, previous TENS treatment, prior surgery for radiculopathy or planned surgery within 6 months, planned use of other treatment for LBP	Randomized: 236 Analyzed: unclear (varied by outcome) Attrition: unclear	A. Active TENS 4 1-hour sessions per day (n=117) B. Sham TENS 4 1-hour sessions per day (n=119)	A vs. B Mean age 53 vs. 53 years 62% vs. 64% female Race not reported LBP alone 39% vs. 43%; LBP + radicular pain: 61% vs. 57% VAS 63 vs. 66 Roland-Morris disability score 15 vs. 15
Facci, 2011	Single-center Brazil	Age >18 years with nonspecific, chronic low back pain Excluded: low back pain duration <3 months, receiving other nonpharmacologic treatment, prior back surgery, contraindication to electrotherapy	Randomized: 150 Analyzed: 150 Attrition: 0%	A. TENS 10 30-minutes sessions over 2 weeks (n=50) B. Interferential therapy 10 30-minutes sessions over 2 weeks (n=50) C. No treatment (n=50)	A vs. B vs. C Mean age 50 vs. 45 vs. 47 years 70% vs. 74% vs. 74% female Race not reported LBP alone 78% vs. 78% vs. 70%; LBP + sciatica 22% vs. 22% vs. 30% Use of pharmacologic treatments 65% vs. 69% vs. 67%

Author, Year	Duration of Pain (acute, subacute, chronic)	Duration of Followup	Results (list results for acute, subacute and chronic separately)
Buchmuller, 2012	Chronic: 40 vs. 35 months	3 months	A vs. B Improvement of ≥50% in lumbar pain VAS from baseline: 25% (26/104) vs. 7% (7/104); RR 3.71 (95% CI 1.69 to 8.18) Improvement of ≥50% in radicular pain VAS from baseline: 34% (22/65) vs. 15% (9/60); RR 2.26 (95% CI 1.13 to 4.51) Improvement on Roland-Morris disability questionnaire at 6 weeks: 30% (32/107) vs. 24% (28/115); RR 1.23 (95% CI 0.80 to 1.89) Improvement on Roland-Morris disability questionnaire at 3 months: 26% (29/110) vs. 25% (28/112); RR 1.05 (95% CI 0.67 to 1.65) Dallas functional repercussion of pain score, everyday activities: 69 vs. 69; p=0.84 Dallas functional repercussion of pain score, professional and leisure activities: 70 vs. 70; p=0.98 Dallas functional repercussion of pain score, anxiety and depression: 43 vs. 43; p=0.95 Dallas functional repercussion of pain score, sociability: 30 vs. 35; p=0.80 SF-36 physical dimensions score: 35.3 vs. 34.4; p=0.22 SF-36 psychological dimensions score: 39.3 vs. 39.1; p=0.96 Patient satisfaction scale >50% at 6 weeks: 53% (51/96) vs. 57% (55/96); RR 0.93 (95% CI 0.72 to 1.20) Patient satisfaction scale >50% at 3 months: 62% (53/86) vs. 57% (43/75); RR 1.07 (95% CI 0.83 to 1.39)
Facci, 2011	Chronic: 3 to 6 months 16% vs. 14% vs. 20%; 6 to 12 months 18% vs. 16% vs. 14%; >12 months 66% vs. 70% vs. 66%	2 weeks	A vs. B vs. C VAS, mean change from baseline: -3.91 vs. -4.48 vs. -0.85; A vs. B, p=NS; A vs. C and B vs. C p>0.05 McGill pain intensity index, mean change from baseline: -1.45 vs. -1.41 vs. -0.66; A vs. B, p=NS; A vs. C and B vs. C p>0.05 McGill pain rating index, mean change from baseline: -17.66 vs. -25.34 vs. -3.53; A vs. B p>0.05; A vs. C and B vs. C p>0.05 McGill number of words describing pain, mean change from baseline: -6.80 vs. -8.30 vs. -0.12; A vs. B, p=NS; A vs. C and B vs. C p>0.05 RDQ, mean change from baseline (scores approximated based on graphic description): -6.26 vs. -7.42 vs. -0.91; A vs. B, p=NS; A vs. C and B vs. C p>0.05

Author, Year	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Buchmuller, 2012	A vs. B Withdrawals: 22% (26/117) vs. 30% (36/119); RR 0.73 (95% CI 0.48 to 1.14) Withdrawals due to adverse events: 3% (3/117) vs. 0.8% (1/119); RR 3.05 (95% CI 0.32 to 29) Serious adverse events: 4% (5/117) vs. 6% (7/119); RR 0.73 (95% CI 0.24 to 2.22) TENS application site skin reaction: 9% (11/117) vs. 3% (3/119); RR 3.73 (95% CI 1.07 to 13)	French Ministere de la Sante et Sports; Fondation CNP Assurances; Institut UPSA Douleurs; CEFAR France	Fair	
Facci, 2011	None reported	None reported	Good	p values not reported but narratively described as significant or not significant

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants
Shimoji, 2007	Single-center Japan	Chronic back pain outpatients with or without osteoarthritis Excluded: inability to attend sessions, use of analgesics	Randomized: 21 Analyzed: 21 Attrition: 0% (0/21)	A. Active TENS + massage twice a week for 5 weeks (n=11) B. Sham TENS + massage twice a week for 5 weeks (n=10)	A vs. B Mean age 62 vs. 64 years 18% vs. 20% female Race not reported Spondylosis deformans 82% vs. 80% Mean NRS 4.5 vs. 5.0
Tsukayama, 2002	Single-center Japan	Low back pain without sciatica, >2 week history of low back pain, >20 years old Excluded: radiculopathy or neuropathy in lower extremity, tumor, fracture, infection or internal disease	Randomized: 20 Analyzed: 19 Attrition: 5% (1/20)	A: TENS twice a week for 2 weeks (n=10) B: Electroacupuncture twice a week for 2 weeks (n=10)	A vs. B Mean age 43 vs. 47 Female: 80% vs. 89% Race not reported Japanese Orthopedic Pain score: 15.6 vs. 16.3

Author, Year	Duration of Pain (acute, subacute, chronic)	Duration of Followup	Results (list results for acute, subacute and chronic separately)
Shimoji, 2007	Chronic: 2.5 vs. 2.8 months	6 weeks	A vs. B Pain, mean change from baseline: -1.4 vs. -1.1; p=0.4
Tsukayama, 2002	Chronic; Duration of pain (days): 3120 vs. 2900	2 weeks	A vs. B VAS, mean during intervention period: 86mm vs. 65mm VAS, difference between groups: 21mm, 95% CI 4.126 to 37.953, p=0.02 JOA, mean change from baseline: -0.802 vs. -2.222, p=0.24

Author, Year	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Shimoji, 2007	None reported	Omron Healthcare	Fair	
Tsukayama, 2002	1 withdrawal due to influenza Transient aggravation of LBP: 1 vs. 1 Discomfort due to press tack needles: 0 vs. 1 Pain on needle insertion: 0 vs. 1 Small subcutaneous bleeding: 0 vs. 1 Transient fatigue: 1 vs. 0 Itching with electrode: 1 vs. 0	Foundation for Training and Licensure Examination in Anma-Massage-Accupressure, Acupuncture and Moxibustion	Fair	

Please see Appendix C. Included Studies for full study references.

Table E33. Data abstraction of randomized controlled trials of electrical stimulation

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Durmus, 2009	Turkey Single center	Low back pain for >3 months, female Exclude: Acute radicular signs or symptoms, radiographic evidence of inflammatory spinal disease, tumor, spondylolysis, spondylolisthesis, sacroiliitis, serious medical conditions, neuromuscular or dermatological disease of the lumbar and abdominal areas, recent exercise program, pacemaker or defibrillator, contracture, previous trauma	Randomized: 41 Analyzed: Unclear Attrition: Not reported	A: Electrical muscle stimulation + exercise: Applied at L2-L4 levels over erector spinae muscles bulks motor points when prone (15 minutes) and obliquus externus abdominus muscles motor points when supine (15 minutes), symmetric biphasic wave at 50 Hz and 50 ms phase time, intensity increased until apparent muscle contraction established (70-120 mA), applied for 10 s of contraction and 10 s of relaxation; 30 minutes 3 times weekly for 8 weeks plus exercise (see below) (n=21) B: Exercise: Group exercise 20 minute back and abdominal exercises and 5 minute stretching 3 times a week for 8 weeks; also given an exercise program consisting of six exercises (n=20)
Durmus, 2010	Turkey Single center	Low back pain for >3 months, female Exclude: Acute radicular signs or symptoms, radiographic evidence of inflammatory spinal disease, tumor, spondylolysis, spondylolisthesis, sacroiliitis, serious medical conditions, neuromuscular or dermatological disease of the lumbar and abdominal areas, recent exercise program, pacemaker or defibrillator, contracture, previous trauma, severe structural deformity, previous spinal surgery, pregnant	Randomized: 68 Analyzed: 59 Attrition: 13% (9/68) at 6 weeks	A: Electrical muscle stimulation + exercise: Applied at L2-L4 levels over erector spinae muscles bulks motor points when prone (15 minutes), symmetric biphasic wave at 50 Hz and 50 ms phase time, intensity increased until apparent muscle contraction established (60-130 mA), applied for 10 s of contraction and 10 s of relaxation; 15 minutes 3 times weekly for 6 weeks + exercise (see below) (n=20) B: Ultrasound + exercise: 1 MHz at 1 W/cm^2, applied for 10 minutes 3 times a week for 6 week + exercise (see below) (n=19) C: Exercise: 45 minute back and abdominal exercises and 5 minute stretching 3 times a week for 6 weeks; also given an exercise program consisting of four exercises (n=20)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Durmus, 2009	A vs. B Mean age: 47 vs. 43 years Female: 100% vs. 100% Race: Not reported Pain intensity (mean, 0-10 VAS): 7.9 vs. 7.5 ODI (mean, 0-100): 37 vs. 37	All chronic, mean duration 6.5 vs. 8.8 years	8 weeks (at end of therapy)
Durmus, 2010	A vs. B Mean age: 49 vs. 48 vs. 47 years Female: 100% vs. 100% vs. 100% Race: Not reported Pain intensity (median, 0-10 VAS): 4.9 vs. 3.9 vs. 2.4 ODI (mean, 0-100): 28 vs. 26 vs. 26	All chronic, mean duration 11 vs. 11 vs. 11 years	6 weeks (at end of therapy)

Author, Year	Results (list results for acute, subacute, and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality (Cochrane Back Group)	Comments
Durmus, 2009	A vs. B Pain (mean, 0-10 VAS, estimated from graph): 4.9 vs. 5.8 at 2 w, 2.9 vs. 4.8 at 4 w, 0.9 vs. 3.8 at 8 w (p not reported and not estimable) ODI (mean, 0-100): 6.6 vs. 19.2 at 8 w (p=0.001) Pain Disability Index (median, 0-50): 4 vs. 9.5 at 8 w (p=0.01) Beck Depression Inventory (mean, 0-63): 2.8 vs. 3.3 at 8 w (p>0.05) SF-36 Physical Function (mean, 0-100): 92 vs. 73 at 8 w (p=0.001) SF-36 Mental Health (mean): 82 vs. 70 at 8 w (p=0.006) SF-36 Pain (mean): 87 vs. 64 at 8 w (p=0.001) SF-36 General health (mean): 76 vs. 64 at 8 w (p=0.01) SF-36 Social function (median): 55 vs. 44 at 8 w (p>0.05) SF-36 Physical role limitations (median): 100 vs. 65 at 8 w (p=0.001) SF-36 Emotional role limitations (median): 100 vs. 82 at 8 w (p=0.01) SF-36 Energy (median): 85 vs. 70 at 8 w (p=0.001)	Not reported	Not reported	Poor	
Durmus, 2010	A vs. B Pain (mean, 0-10 VAS, estimated from graph): 2.9 vs. 2.9 vs. 3.9 at 3 w, 0.4 vs. 0.9 vs. 2.4 at 6 w (p<0.05 for A or B vs. C) ODI (mean, 0-100): 6.80 vs. 8.69 vs. 8.40 at 6 w (p=0.07) Pain Disability Index (median, 0-50): 5.15 vs. 6.21 vs. 6.50 at 6 w (p=0.62) Beck Depression Inventory (mean, 0-63): 3.35 vs. 3.94 vs. 4.85 at 6 w (p=0.37) SF-36 Physical Function (mean, 0-100): 97.5 vs. 90.0 vs. 90.0 at 6 w (p=0.009) SF-36 Mental Health (mean): 78.7 vs. 73.0 vs. 71.8 at 6 w (p=0.17) SF-36 Pain (median): 88.0 vs. 88.0 vs. 77.0 at 6 w (p=0.28) SF-36 General health (mean): 70.4 vs. 65.5 vs. 64.2 at 6 w (p=0.23) SF-36 Social function (median): 88.0 vs. 77.0 vs. 77.0 at 6 w (p=0.02) SF-36 Physical role limitations (median): 100 vs. 100 vs. 100 at 6 w (p=0.30) SF-36 Emotional role limitations (median): 100 vs. 100 vs. 100 at 6 w (p=0.58) SF-36 Energy (median): 83.8 vs. 68.7 vs. 67.8 at 6 w (p=0.001)	Not reported	Not reported	Poor	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Glaser, 2001	United States Single center	18 to 60 years of age, LBP ≥6 months, LBP greater than radicular pain Exclude: Prior electrical stimulation treatment (including TENS), pregnant, morbid obesity, nonspinal cause of low back pain, end-stage or terminal medical problem	Randomized: 80 Analyzed: 55 at 2 m, 38 at 6 m Attrition: 31% (25/80) at 2 m, 52% (42/80) at 6 m	A: Electrical muscle stimulation + exercise: Placed on lower back, parameters not reported + exercise (see below), 30 minutes 2 times daily for 2 months (n=32) B: Sham stimulation + exercise: Group instruction on strength and flexibility exercises, 3 sessions once weekly for 3 weeks and instructed to perform home exercises for 6 months (n=23)
Moore, 1997	United States Single center	Back pain for ≥6 months largely unresponsive to previous treatments Exclude: Pregnancy, cardiac pacemaker, serious psychological disorder, previous treatment with TENS or electrical muscle stimulation	Randomized: 28 Analyzed: 24 Attrition: 14% (4/28) prior to completion of trial (4 crossover periods of 2 days each with 2 day hiatus)	A: Electrical muscle stimulation: Location not specified, symmetric biphasic wave at 70 Hz and 200 ms pulse width, amplitude adjustable from 0 to 100 mA to produce muscle contractions, cycle on-time 5 seconds and off-time 15 seconds; three 10 minute periods of stimulation alternating with 130 minute periods of no treatment B: TENS: Asymmetrical biphasic square pulse, 100 Hz and 100 ms pulse width, amplitude 0 to 60 mA C: Electrical muscle stimulation + TENS: Alternating one 10 minute and one 20 minute period of electrical muscle stimulation with 3 periods of TENS stimulation D: Sham TENS Crossover design (n=24), each intervention 5 hours/day for 2 days, with 2 day hiatus between interventions

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Glaser, 2001	Mean age: 51 vs. 53 years Female: 62% vs. 52% Non-white race: 30% vs. 32% Pain: Not reported Back-specific function: Not reported	All chronic, mean duration not reported	6 months (4 months after completion of stimulation intervention)
Moore, 1997	Mean age: 52 years Female: 67% Race: Not reported Pain intensity: 49 vs. 46 vs. 48 vs. 51 Back-specific function: Not reported Conditions: 9 bulging disc, 7 postlaminectomy, 5 spinal stenosis, 1 spondylolisthesis; 15 low back pain, 3 middle back pain 4 upper back pain, 2 diffuse back pain	All chronic; mean 3.8 years	Assessed after 2 days of each intervention

Author, Year	Results (list results for acute, subacute, and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality (Cochrane Back Group)	Comments
Glaser, 2001	A vs. B Low Back Pain Outcome Instrument Job Exertion (mean, 1-6): 2.69 vs. 2.83 at 2 m, 2.74 vs. 2.89 at 6 m LBPOI Job Stress/Satisfaction (mean, 1-6): 3.20 vs. 2.25 at 2 m, 3.02 vs. 2.44 at 6 m LBPOI Back Pain/Disability (mean, 1-6): 2.36 vs. 2.13 at 2 m, 2.45 vs. 2.30 at 6 m LBPOI Neurogenic Symptoms (mean, 1-6): 1.92 vs. 1.87 at 2 m, 2.17 vs. 1.89 at 6 m LBPOI Expectations Met (mean, 1-6): 4.21 vs. 3.79 at 2 m, 4.02 vs. 3.72 at 6 m SF-36 Mental health (mean, 0-100): 70 .2 vs. 80.0 at 2 m, 67.9 vs. 76.2 at 6 m	Not reported	Not reported	Poor	Some differences on LBPOI subscales reported as statistically significant, but does not appear to be possible based on reported point estimates and standard deviations
Moore, 1997	A vs. B vs. C vs. D Pain (mean, 0-100 VAS): 39.7 vs. 40.6 vs. 36.3 vs. 44.8 ($p>0.05$ for overall effect, but $p=0.02$ for C vs. D) Present Pain Intensity (mean, 0-4): 2.21 vs. 2.27 vs. 1.94 vs. 2.42 ($p=0.03$ for overall effect, $p<0.02$ for C vs. A, B, or D)	"No adverse treatment effects were reported"	Not reported	Poor	

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Pope, 1994	United States Single center	18 to 55 years of age, low back pain for 3 weeks to 6 months Exclude: Pregnant, sciatica, neurologic deficits, prior vertebral fracture, tumor, infection, or spondyloarthropathy, prior back surgery, BMI >33, prior manipulation for current episode, pacemaker, workmen's compensation or disability insurance issues	Randomized: 164 Analyzed: Unclear Attrition: 12% did not complete baseline and week 3 evaluations	A: Electrical muscle stimulation: Applied to painful back on back, symmetric biphasic wave at 37 Hz and 225 ms pulse width, amplitude adjustable from 0 to 91 mA to produce muscle contractions, pulse ramped up for 2 seconds, held for 6 seconds, ramped off for 2 seconds, 6 second pause; used for at least 8 hours per day for 3 weeks (n=28) B: Manipulation: Dynamic short lever, high velocity, low amplitude thrust exerting force on the lumbar spine and/or sacroiliac joint, unilaterally or bilaterally as determined by treating physicians, 3 sessions per week for 3 weeks (n=70) C: Massage: Effleurage massage for up to 15 minutes, 3 sessions per week for 3 weeks (n=37) D: Lumbar support: Freeman Lumbosacral Corset to be worn during waking hours except while bathing, could be removed up to 10 minutes up to 3 times daily (n=29)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Pope, 1994	Age: Not reported Sex: Not reported Race: Not reported Pain intensity: States no statistically significant differences, data not reported Back-specific function: Not reported	3 weeks to 6 months; mean duration not reported	3 weeks (at end of treatment)

Author, Year	Results (list results for acute, subacute, and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality (Cochrane Back Group)	Comments
Pope, 1994	A vs. B vs. C vs. D Pain (mean change from baseline, 0-100 VAS): -9.6 vs. -24 vs. -17 vs. -16 (p>0.05 for all between-group comparisons)	Not reported	Foundation for Chiropractic Research and Education	Fair	

Please see Appendix C. Included Studies for full study references.

Table E34. Data abstraction of randomized controlled trials of PENS

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Hamza, 1999	USA Single center	>18 years of age, low back pain with radiologically confirmed degenerative lumbar disc disease, pain level stable for ≥3 months Exclude: Radicular component, history of drug or alcohol abuse, previous acupuncture, recent change in analgesic medications or use of opioids	Number randomized: 75 Analyzed: Unclear Attrition: Not reported	A: PENS: 10 32-gauge needles placed into low back pain to depth of 2-4 cm in a dermatomal (or sclerotomal) distribution of pain for 60 minutes; connected to bipolar leads at alternating frequency of 15 and 30 Hz for 45 minutes (maximum amplitude 25 mA using unipolar square-wave pattern and pulse width of 0.5 ms) B: PENS: Stimulation for 30 minutes C: PENS: Stimulation for 15 minutes D: PENS: Stimulation for 0 minutes Crossover design, each intervention administered 3 times a week for 2 weeks, with 1 week between treatments (total 11 weeks)
Pérez-Palomares, 2010	Spain Single center	>18 years of age, non-radicular low back pain ≥4 months or shorter duration if unresponsive to therapy Exclude: Fibromyalgia syndrome, structural lesions in the lumbar column, concomitant non-pharmacological treatments, co-morbid medical conditions or circumstances that might have impacted results	Number randomized: 122 Analyzed: 112 Attrition: 8.9% (10/122)	A: PENS: Eight 0.3 x 25 mm needles placed into low back pain to depth of 2-2.5 cm 8 in a dermatomal distribution, 0.3 ms impulse duration, for 30 minutes (n not reported) B: Dry needling: 0.30 x 40 mm needles inserted into trigger points using fast-in and fast-out Hong's technique, followed by spray and stretch technique (n not reported) 3 sessions weekly for total of 9 sessions over 3 weeks

Weiner, 2008	USA Single center	≥65 years of age, ≥moderate intensity low back pain for ≥3 months Exclude: Red flags, prominent radicular pain, prior back surgery, known spinal pathology other than degenerative disease, pain outside back greater than back pain, conditions that make PENS unsafe, absolute contraindications to exercise, medical instability, medical instability, neurological or psychiatric disorder that could interfere with pain reporting	Number randomized: 200 Analyzed: 184 Attrition: 8.0% (16/200)	A: PENS: Ten 32 gauge 40 mm needles placed at 15 mm depth placed bilaterally at levels corresponding to T12, L3, L5, and S2, and the motor point for the piriformis muscle, for 30 minutes, frequency based on algorithm; also two needles placed at T12 level with transient high frequency stimulation (control PENS procedure) (n=47) B: PENS + exercise: Supervised strength, flexibility, and aerobic exercise, sessions 60 minutes, plus home exercise (flexibility anc graded walking) three times a week for 6 weeks (n=45) C: Control PENS + exercise (n=44) D: Control PENS: Needles placed as for PENS, but stimulation (transient high frequency stimulation) only applied to needles at

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Hamza, 1999	Mean age: 47 years (overall) Female: Not reported Race: Not reported Baseline pain (mean, 0-10 VAS): 6.3 vs. 6.4 vs. 6.8 vs. 6.2 Baseline function: Not reported Prior surgery: 42% (overall)	All chronic (≥3 months), mean duration 38 months	2 weeks (at end of each treatment period)
Pérez-Palomares, 2010	Mean age: Not reported, 34% vs. 50% <40 years of age Female: 81% vs. 67% Race: Not reported Baseline pain (mean, 0-10 VAS): 6.27 vs. 6.04 Baseline function: Not reported	Acute to chronic; 84% vs. 74% <3 months	3 weeks (at end of therapy)
Weiner, 2008	Mean age (years): 74 vs. 74 vs. 73 vs. 74 Female: 58% vs. 56% vs. 60% Vs. 54% White race: 86% vs. 90% vs. 88% Vs. 94% Baseline pain (0-10): 2.5 vs. 2.4 vs. 2.4 vs. 2.3 Baseline RDQ: 10.5 vs. 10.2 vs. 11.0 vs. 10.5	Chronic; mean duration 10.0 vs. 9.0 vs. 5.0 vs. 7.0 years	6 months (18 weeks after end of therapy)

Author, Year	Results (list results for acute, subacute, and chronic separately)	Adverse Events Including Withdrawal	Funding Source	Quality Rating
Hamza, 1999	A vs. B vs. C vs. D Pain (mean, 0-10 VAS): 1.5 vs. 1.6 vs. 2.0 vs. 5.4 at 2 weeks Pain (percent improvement from baseline, 0-10 VAS): 40% vs. 46% vs. 22% vs. 10% (p<0.01 for A or B vs. D and p<0.05 for C vs. D) SF-36 Physical component summary (mean improvement, 0-100): +7.1 vs. +7.4 vs. +5.4 vs. not reported (p<0.001 for A or B vs. D and p<0.01 for C vs. D) SF-36 Mental component summary (mean improvement, 0-100): +2.9 vs. +3.1 vs. +2.1 vs. not reported (p<0.001 for A or B vs. D and p<0.01 for C vs. D) Physical activity (percent improvement from baseline, 0-10 VAS): 50% vs. 53% vs. 28% vs. 8% (p<0.01 for A or B vs. D, p<0.05 for C vs. D) Sleep quality (percent improvement from baseline, 0-10 VAS): 40% vs. 44% vs. 25% vs. 5% (p<0.01 for A or B vs. D, p<0.05 for C vs. D) Use of nonopioid analgesics (percent decreased in pills per day): 35% vs. 38% vs. 21% vs. 8% (p<0.01 for A or B vs. D, p<0.05 for C vs. D)	Not reported	Forest Park Institute and Egyptian Cultural and Educational Bureau	Poor
Pérez-Palomares, 2010	A vs. B Pain (mean difference from baseline, 0-10 VAS): 2.38 vs. 2.35 (p=0.94) >40% improvement in pain: 54% (28/52) vs. 46% (24/52), RR 1.17 (95% CI 0.79 to 1.72) Sleep quality (mean difference from baseline, 0-10 VAS): 1.72 vs. 1.85 (p=0.68) ODI Personal care (median difference from baseline, 0-1): 0.38 vs. 0.34 (p=0.94) ODI Lifting weight: 0.59 vs. 0.06 (p=0.03) ODI Walking: 0.17 vs. 0.15 (p=0.86) ODI Sitting: 0.21 vs. 0.33 (p=0.51) ODI Standing: 0.25 vs. 0.41 (p=0.26) ODI Social life: 0.72 vs. 0.72 (p=0.18)	Not reported	Not reported	Poor
Weiner, 2008	A vs. B vs. C vs. D (mean change from baseline) McGill Pain Questionnaire (0 to 78 scale): -2.9 vs. -4.1 vs. -3.1 vs. -2.3 at 6 w, -3.4 vs. -3.8 vs. -3.1 vs. -3.3 at 6 months RDQ (0 to 24): -2.6 vs. -2.6 vs. -3.0 vs. -2.7 at 6 w, -2.1 vs. -2.1 vs. -2.8 vs. -3.0 at 6 m Average pain last week (0 to 10): -0.7 vs. -0.7 vs. -0.6 vs. -0.6 at 6 w, -0.5 vs. -0.6 vs. -0.5 vs. -0.6 at 6 m Geriatric Depression Scale: 0.3 vs. -0.4 vs. -0.3 vs. -0.2 at 6 w, 0.5 vs. -0.1 vs. -0.1 vs. -0.4 at 6 m SF-36 composite mental health (0 to 100): 1.5 vs. -0.3 vs. 2.8 vs. -0.1 at 6 w, -1.8 vs. -0.2 vs. 1.5 vs. 1.2 at 6 m SF-36 composite physical health: -1.1 vs. 3.9 vs. 6.9 vs. 5.9 at 6 w, -0.4 vs. 0.1 vs. -0.6 vs. -0.4 at 6 m Pittsburgh sleep score: -0.2 vs. 0.002 vs. -0.7 vs. 0.0 at 6 w, -0.4 vs. 0.1 vs. -0.6 vs. -0.4 at 6 m Moderate or major global improvement: 58% vs. 58% vs. 66% vs. 56% at 6 w, 40% vs. 55% vs. 50% vs. 44% at 6 m	"No significant intervention-associated adverse events," one participant dropped out because of increased back pain	National Institutes of Health (NCCAM and NIA)	Fair

Please see Appendix C. Included Studies for full study references.

Table E35. Data abstraction of randomized controlled trials of interferential therapy

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Lara-Palomo, 2013	Spain Single center	Non-specific low back pain ≥3 months, 18 to 65 years of age, RDQ ≥4, unable to achieve lumbar muscle flexion-relaxation in trunk flexion Exclude: Undergoing other physical therapy treatment; presence of lumbar stenosis, fibromyalgia, or spondylolisthesis; history of spinal surgery or neuromuscular kinesiotape therapy; received corticosteroids in past 2 weeks; disease of central or peripheral nervous system	Number randomized: 62 Number analyzed: 61 Attrition: 1.6% (1/62) at 10 weeks	A: Interferential therapy: Bipolar current, carrier frequency 4000 Hz at constant voltage and amplitude modulation 80 Hz, applied to lumbar area for 30 minutes at 30-50 mA, 20 sessions over 10 weeks (n=31) B: Superficial massage: Effleurage, superficial pressure, and skin rolling on the lower back for 20 minutes, 20 sessions over 10 weeks (n=31)

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup
Lara-Palomo, 2013	Mean age: 50 vs. 47 years Female: 70% vs. 65% Race: Not reported Baseline pain (mean, 0-10 VAS): 6.67 vs. 6.52 Baseline ODI (mean, 0-100): 36.07 vs. 37.94	All chronic (≥ 3 months), mean duration not reported	10 weeks (at end of therapy)

Author, Year	Results (list results for acute, subacute, and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality Rating	Comments
Lara-Palomo, 2013	A vs. B, mean difference in change from baseline at 10 weeks Pain (0-10 VAS): -1.06 (95% CI -1.91 to -0.22) ODI (0-100): -5.20 (95% CI -10.82 to 0.42) RDQ (0-24): -3.01 (95% CI -4.53 to -1.47) SF-36 Physical function (0-100): 5.57 (95% CI -2.27 to 13.41) SF-36 Physical role (0-100): 7.02 (95% CI 1.05 to 12.98) SF-36 Body pain (0-100): 4.72 (95% CI -0.28 to 9.71) SF-36 General health (0-100): 1.09 (95% CI -3.22 to 5.41) SF-36 Vitality (0-100): 2.04 (95% CI -3.36 to 7.43) SF-36 Social functioning (0-100): 1.14 (95% CI -3.88 to 6.15) SF-36 Mental health (0-100): 2.37 (95% CI -3.39 to 8.14) SF-36 Emotional role (0-100): 3.27 (95% CI -1.58 to 8.12) RDQ worsened by >2.5 points: 10% (3/30) vs. 13% (4/31), RR 0.78 (95% CI 0.19 to 3.18)	Not reported	Reports no funding	Fair	

Please see Appendix C. Included Studies for full study references.

Table E36. Data abstraction of systematic reviews of heat-cold

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies
French, 2006 updated in French, 2011	Heat vs. no heat Cold vs. no cold Heat vs. cold Heat vs. other active treatments Cold vs. other active treatments Heat + another treatment vs. other treatment alone	MEDLINE, EMBASE, CCCRCT through October 2005	9 studies: 5 RCTs, 1 CCT, 3 crossover studies Acute pain (1 trial), mixed acute and subacute pain (4 trials), chronic pain (3 trials), mixed acute, subacute and chronic pain (1 trial) Heat vs. placebo (4 trials), heat vs. cold (2 trials), heat vs. other interventions (4 trials), cold vs. other interventions (1 trial) (some trials evaluated multiple comparisons)	A. Heat (hot pack or heated wrap; n=446) B. Cold (cold pack or ice massage; n=94) C. Other active interventions (NSAID, n=238; exercise, n=25; lumbar support, n=38; heat + other intervention, n=24) D. No heat/cold (n=216)	Cochrane Back Group criteria (2003)	Qualitative analysis judging level of evidence (strong, moderate, limited conflicting or no evidence) due to limited poolable data

Author, Year	Results	Adverse Events	Quality
French, 2006 updated in French, 2011	A vs. B No qualitative analysis; evidence from one CCT and one crossover study (both low quality). The CCT found no difference between hot packs and ice massage in a mixed population (treatment duration and followup not reported) and the crossover study found ice massage superior to hot packs in a chronic pain population after 2 20-minute treatments with each. A vs. C (specified below) Acute or subacute population Pain, VAS mean difference day 1 or 2, heat vs. (1 trial each): acetaminophen 0.90 (95% CI 0.50 to 1.30); ibuprofen 0.65 (95% CI 0.25 to 1.05); exercise 0.40 (95% CI -0.15 to 0.95) *higher score favors heat Pain, VAS mean difference day 4, heat vs. (1 trial each): acetaminophen 0.74 (95% CI 0.31 to 1.17); ibuprofen 1.05 (95% CI 0.62 to 1.48); exercise 0.30 (95% CI -0.41 to 1.01) *higher score favors heat Pain, VAS mean difference day 7, heat vs. (1 trial): exercise 0.30 (95% CI -0.68 to 1.28) *higher score favors heat Function, RDQ mean difference, day 4, heat vs. (1 trial each): acetaminophen 2.00 (95% CI 0.86 to 3.14); ibuprofen 2.20 (95% CI 1.11 to 3.29) *higher score favors heat Function, RDQ mean difference, day 2, heat vs. (1 trial): exercise -0.70 (95% CI -2.09 to 0.69)*lower score favors heat Function, RDQ mean difference, day 4, heat vs. (1 trial): exercise -0.90 (95% CI -2.84 to 1.04)*lower score favors heat Function, RDQ mean difference, day 7, heat vs. (1 trial): exercise -0.50 (95% CI -2.72 to 1.72)*lower score favors heat	None reported	Good

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies
French, 2006 updated in French, 2011						

Author, Year	Results	Adverse Events	Quality
French, 2006 updated in French, 2011	(A + C) vs. C alone Acute or subacute population Pain, VAS mean difference, heat + exercise vs. exercise, day 2 (1 trial): 0.50 (95% CI -0.21 to 1.21) *higher score favors heat + exercise Pain, VAS mean difference, heat + exercise vs. exercise, day 4 (1 trial): 0.80 (95% CI -0.03 to 1.63) *higher score favors heat + exercise Pain, VAS mean difference, heat + exercise vs. exercise, day 7 (1 trial): 1.40 (95% CI 0.69 to 2.11) *higher score favors heat + exercise Function, RDQ mean difference, heat + exercise vs. exercise, day 2 (1 trial): 0.60 (95% CI -0.79 to 1.99) *lower score favors heat + exercise Function, RDQ mean difference, heat + exercise vs. exercise, day 4 (1 trial): -1.20 (95% CI -3.14 to 0.74) *lower score favors heat + exercise Function, RDQ mean difference, heat + exercise vs. exercise, day 7 (1 trial): -3.20 (95% CI -5.42 to -0.98) *lower score favors heat + exercise (A + C) vs. A alone Pain, VAS mean difference, heat + exercise vs. heat, day 2 (1 trial): 0.10 (95% CI -0.61 to 0.81) *higher score favors heat + exercise Pain, VAS mean difference, heat + exercise vs. heat, day 4 (1 trial): 0.50 (95% CI -0.21 to 1.21) *higher score favors heat + exercise Pain, VAS mean difference, heat + exercise vs. heat, day 7 (1 trial): 1.10 (95% CI 0.22 to 1.98) *higher score favors heat + exercise Function, RDQ mean difference, heat + exercise vs. heat, day 2 (1 trial): 1.30 (95% CI -0.07 to 2.67) *lower score favors heat + exercise Function, RDQ mean difference, heat + exercise vs. heat, day 4 (1 trial): -0.30 (95% CI -2.24 to 1.64) *lower score favors heat + exercise Function, RDQ mean difference, heat + exercise vs. heat,, day 7 (1 trial): -2.70 (95% CI -4.92 to -0.48) *lower score favors heat + exercise		

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies
French, 2006 updated in French, 2011						

Author, Year	Results	Adverse Events	Quality
French, 2006 updated in French, 2011	A vs. D Acute or subacute population Pain, VAS mean difference up to day 5 (2 trials): 1.06 (95% CI 0.68 to 1.45) *higher score favors heat Function, RDQ mean difference day 4 (2 trials): -2.12 (95% CI -3.07 to -1.18) *lower score favors heat B vs. C One trial of ice massage vs. TENS; included in TENS section of the report (found no difference between ice massage and TENS) B vs. D No evidence	A vs. D Skin flushing at application site (2 trials): 5% (6/128) vs. 0.8% (1/130); RR 6.09 (95% CI 0.74 to 50) All other comparisons: not reported	

Please see Appendix C. Included Studies for full study references.

Table E37. Data abstraction of randomized controlled trials of heat-cold

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Dehgan, 2014	Iran Single-center	Low back pain for <1 month, 20 to 50 years of age Excluded: Medical comorbidities, trauma, taking analgesics apart from naproxen, undergoing physiotherapy	Randomized: 90 (30 vs. 30 vs. 30) Analyzed: 87 (29 vs. 29 vs. 29) Attrition: 3.3% (3/90)	A: Hot water bottle 20 minutes twice a day for 1 week + naproxen 500 mg po bid B: Ice 20 minutes twice daily for 1 week + naproxen 500 mg po bid C: Naproxen 500 mg po bid	A vs. B Mean age: 34 vs. 33 vs. 36 years Sex: Not reported Race: Not reported Mean McGill Pain Questionnaire (overall, 0 to 78): 12.1 vs. 12.1 vs. 13.0	Acute, mean 16 vs. 18 vs. 13 days
Kettenmann, 2007	Germany Single-center	Ambulatory orthopedic surgery patients age 18 to 80 years with acute low back pain VAS score >0 to <5 (scale 0-10) Excluded: chronic pain, RA, postsurgical pain, cardiovascular disorder, chronic skin condition, diabetes, pregnancy	Randomized: 38 Analyzed: 30 Attrition: 21% (8/38)	A. Continuous low-level heat wrap (ThermaCare®) 4 hours/day for 4 days (n=15) B. No heat wrap (oral NSAIDs allowed as needed but there was no formal protocol for their use) (n=15)	A vs. B Mean age 56 vs. 58 years 53% vs. 80% female Race not reported Mean pain (VAS) 4.1 vs. 3.9	Acute Mean not reported; duration >3 months excluded

Author, Year	Duration of Followup	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality
Dehgan, 2014	15 days (1 week after end of treatment)	A vs. B vs. C McGill Pain Questionnaire, overall pain (method for scoring unclear): 12.1 vs. 12.1 vs. 13.0 at baseline, 7.3 vs. 9.3 vs. 9.9 on d 3, 3.7 vs. 5.1 vs. 7.7 on d 8, 0.76 vs. 2.2 vs. 5.6 on d 15 (p<0.005 for between group differences on days 3, 8, and 15) McGill Pain Questionnaire, "affective dimension" (method for scoring unclear): 7.5 vs. 7.4 vs. 8.2 at baseline, 4.8 vs. 4.9 vs. 6.6 on d 3, 2.0 vs. 2.3 vs. 4.9 on d 8, 0.68 vs. 1.2 vs. 3.8 on d 15 (p<0.005 for between group differences on days 3, 8, and 15)	Not reported	Reports none	Fair
Kettenmann, 2007	5 days (4 treatment days + 1 day post-treatment)	A vs. B Pain, patient assessed severity (no pain to very severe pain, VAS scale 0-100) day 1: 40 vs. 52; p=NS; day 2: 30 vs. 44; p=NS; day 3: 31 vs. 57; p=0.02; day 4: 27 vs. 47; p=0.04 (pain values presented graphically) Function, proportion of patients woken from sleep due to pain: significantly lower proportion with heat wrap use at days 2 (p=0.16), 3 (p=0.002) and 4 (p=0.001)	Not reported	Proctor & Gamble	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Stark, 2014	USA Single-center	Acute low back pain, baseline pain >=2 on 0 to 5 categorical scale Excluded: Trauma, suspected pathological cause of low back pain, pregnant, radiculopathy, neurological deficits, history of back surgery, medical comorbidities, skin lesions in lumbar region, beta-blockers, antidepressant medications, supplements with central nervous system effects, analgesics within 24 or 48 hours, substance abuse, litigation or worker's compensation claim	Randomized: 51 (26 vs. 25) Analyzed: 51 Attrition: Not reported	A: Heat wrap (ThermaCare Lower Back/Hip HeatWrap), applied for 8 hours B: Oral placebo Acetaminophen 500 mg x 2 permitted for rescue analgesia 10 subjects randomized to sham wrap or oral ibuprofen but not included in analyses	A vs. B Mean age: 30 vs. 29 years 42% vs. 60% female 58% vs. 60% non-white Pain moderate (2 on 0 to 5 scale): 73% Vs. 80% Pain moderately severe or severe (3 or 4 on 0 to 5 scale): 27% vs. 20%	Acute (not defined) Mean duration not reported
Tao, 2005	USA Single-center	Full-time employees of a medical facility with acute LBP, 18 to 64 tears of age, pain intensity at least 5 on a 0 to 10 scale Excluded: history of chronic LBP, radiculopathy or neurologic deficits, other chronic pain problems, prior back surgery, taking antidepressants, traumatic injury	Randomized: Unclear Analyzed: 43 Attrition: Unclear	A: Heat-wrap during daytime hours for 3 days plus education (written material) (n=25) B: Education only (n=18)	A vs. B Mean age: 35 vs. 36 years 84% vs. 83% female Race: Not reported Baseline pain intensity: Not reported	Acute (mean duration not reported)

Author, Year	Duration of Followup	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality
Stark, 2014	8 hours (at end of treatment)	A vs. B Pain relief (mean, 0=no relief to 5=complete relief): 2.1 vs. 1.2 at 2 h (p<0.05), 3.0 vs. 1.5 at 8 h (p<0.001) Global evaluation of treatment 4 or 5 on 0 to 5 scale (0= very poor, 5=excellent): 84% (22/26) vs. 16% (4/25), RR 5.29 (95% CI 2.12 to 13.18)	A vs. B Headache: 2/26 vs. 0/25 Withdrawals or serious adverse events: None	Pfizer Consumer Healthcare	Fair
Tao, 2005	4 and 14 days from treatment initiation	A vs. B Pain intensity (mean difference in change from baseline, 0 to 10 scale): -1.01 (95% -2.08 to 0.06) at day 1, -2.05 (95% CI -3.34 to -0.76) at day 3, -1.66 (95% CI -2.97 to -0.37) at day 7, -1.63 (95% CI -2.92 to -0.34) at day 14 Pain relief (mean difference in change from baseline, 0 to 5 scale): 1.33 (95% CI 0.52 to 2.12) at day 1, 1.53 (95% CI 0.76 to 2.30) at day 3, 0.98 (95% CI 0.08 to 1.87) at day 7, 1.21 (0.26 to 2.14) at day 14 RDQ (mean difference in change from baseline, 0 to 24): -2.38 (95% CI -5.62 to 0.85) at day 4, -4.60 (95% CI -8.27 to -0.94) at day 7, -4.02 (95% CI -7.82 to -0.24) at day 14	No adverse events reported	Proctor & Gamble	Poor

Please see Appendix C. Included Studies for full study references.

Table E38. Data abstraction of randomized controlled trials of LLLT

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Ay, 2010	Turkey Single-center	Acute of chronic low back pain Excluded: neurological deficit, spondylosis, spinal stenosis, infection, malignant spinal disease, previous spinal surgery, pregnancy	Randomized: 80 Analyzed: 80 Attrition: 0% (0/80)	Acute LBP A. GaAlAs laser, 850 nm + heat 5 times/week for 3 weeks (n=20) B. Sham laser + heat 5 times/week for 3 weeks (n=20) Chronic LBP A. GaAlAs laser 850 nm + heat 5 times/week for 3 weeks (n=20) B. Sham laser + heat 5 times/week for 3 weeks (n=20)	A vs. B: Acute LBP Mean age 48 vs. 45 years 30% vs. 40% female Pain, VAS: 6.7 vs. 6.15 Pain, patient global assessment: 6.45 vs. 5.0 Pain, physician global assessment: 6.6 vs. 6.15 Disability, RDQ: 13.2 vs. 12.6 Disability, Modified ODI: 19.8 vs. 20.8 A vs. B: Chronic LBP Mean age 52 vs. 55 years 55% vs. 45% female Pain, VAS: 6.0 vs. 6.6 Pain, patient global assessment: 5.65 vs. 6.05 Pain, physician global assessment: 5.8 vs. 6.3 Disability, RDQ: 15.1 vs. 15.6 Disability, Modified ODI: 23.9 vs. 24.65	Acute: 2 vs. 2 months Chronic: 50 vs. 48 months
Djavid, 2007	Iran Single-center	Age 20-60 years with low back pain for at least 12 weeks Excluded: degenerative disc disease, herniation, fracture, spondylosis, spinal stenosis, neurologic deficits, systemic or psychiatric illness, pregnancy	Randomized: 61 Analyzed: 43 Attrition: 30% (18/61)	A. GaAlAs, 810 nm laser 2 times/week for 6 weeks (n=16) B. GaAlAs laser, 810 nm 2 times/week for 6 weeks + exercise (n=19) C. Sham laser 2 times/week for 6 weeks + exercise (n=18)	A vs. B vs. C Mean age 40 vs. 38 vs. 36 years 56% vs. 37% vs. 17% female Race not reported Pain, VAS 7.3 vs. 6.2 vs. 6.3 Disability, ODI 33.0 vs. 34.0 vs. 31.8	Chronic: mean 29 vs. 29 vs. 25 months

Author, Year	Duration of Followup	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Ay, 2010	3 weeks	A vs. B: Acute LBP Pain, VAS mean change from baseline: -4.0 vs. -4.15; p=0.07 Pain, patient global assessment mean change from baseline: -3.9 vs. -4.7; p=0.006 Pain, physician global assessment mean change from baseline: -4.1 vs. -4.2; p=-0.71 Disability, RDQ mean change from baseline: -6.0 vs. -5.65; p=0.39 Disability, Modified ODI mean change from baseline: -8.2 vs. -8.7; p=0.15 A vs. B: Chronic LBP Pain, VAS mean change from baseline: -3.35 vs. -3.95; p=0.03 Pain, patient global assessment mean change from baseline: -3.3 vs. -3.9; p=0.11 Pain, physician global assessment mean change from baseline: -3.15 vs. -4.05; p=0.01 Disability, RDQ mean change from baseline: -6.7 vs. -4.65; p=<0.0001 Disability, Modified ODI mean change from baseline: -9.6 vs. -6.2; p; p<0.0001	Not reported	Not reported	Good
Djavid, 2007	12 weeks	A vs. B vs. C Pain, VAS: 4.4 vs. 2.4 vs. 4.3; A vs. B, p=0.002; A vs. C, p=0.87; B vs. C, p=0.0005; mean change from baseline -2.9 vs. -3.8 vs. -2.0 Disability, ODI: 20.8 vs. 16.8 vs. 24.1; A vs. B, p=0.006; A vs. C, p=0.06; B vs. C, p=0.0001	No adverse events in any group (data not shown)	Not reported	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Hsieh, 2014	Taiwan Single center	18 to 85 years of age, nonspecific low back pain for >12 weeks Exclude: Specific conditions (infection, inflammation, fracture, tumor); history of cancer, vertigo, stroke, or other condition that may impair postural stability, low back surgery with implant; pregnant or plans to become pregnant	Randomized: 70 (35 vs. 35) Analyzed: 60 (33 vs. 27) Attrition: 14% (10/70)	A: GaAlAs, 890 nm laser with 780 mW power (total 83.2 J/cm^2), 40 minutes three times a week for 2 weeks (n=33) B: Sham laser, 40 minutes three times a week for 2 weeks (n=27)	A vs. B Mean age 60 vs. 58 years 58% vs. 70% female Race not reported Pain, VAS 7.9 vs. 7.9 Disability, ODI 2.3 vs. 2.6 Radiation in lower limb: 70% vs. 78%	Chronic: mean duration not reported, >12 weeks by inclusion criteria

Author, Year	Duration of Followup	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Hsieh, 2014	2 weeks	A vs. B Pain (mean, 0-10 VAS): 7.8 vs. 7.9 at baseline, mean change 0.73 vs. 0.4 at 2 weeks, difference -0.3 (95% CI -1.0 to 0.3) ODI (mean, scale unclear): 2.3 vs. 2.6 at baseline, mean change -0.4 vs. -0.1 at 2 weeks, difference -0.3 (95% CI -0.6 to -0.1) Frenchay Activities Index (mean, 0 to 45): 32.2 vs. 33.5 at baseline, mean change 1.9 vs. 1.5 at 2 weeks, difference -0.4 (95% CI -3.4 to 2.6) Osteoarthritis Quality of Life Questionnaire (mean, scale not reported): 3.8 vs. 5.9 at baseline, mean change -0.5 vs. -0.6 at 2 weeks, difference -0.1 (95% CI -1.4 to 1.1) Multidimensional Fatigue Inventory: No differences on any subscale	No systemic or local side effects noted during or after treatment	Shin Kong Wu Ho-Su Memorial Hospital and National Science Council, Taiwan	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Jovicic, 2012	Serbia Single-center	Acute, clinically diagnosed LBP (duration <4 weeks) Excluded: chronic low back pain or previous surgery	Randomized: 66 Analyzed: 66 Attrition: 0% (0.66)	A. 904 nm laser, 0.1 joule per point (0.4 points/day; n=22) B. 904 nm laser, 1.0 joule per point (4.0 points/day; n=22) C. 904 nm laser, 4.0 joules per point (16.0 points/day; n=22)	A vs. B vs. C Mean age 47 vs. 44 vs. 45 years Gender, race not reported Lumbar pain, VAS: 7 vs. 7 vs. 6.5	Acute: mean duration not reported; inclusion criteria required <4 weeks duration of symptoms

Author, Year	Duration of Followup	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Jovicic, 2012	2 weeks	A vs. B vs. C Lumbar pain, VAS mean change (results depicted graphically): -3 vs. -3 vs. -3.5; p>0.05 Function, Activities of Daily Life: walking, mean change from baseline in proportion able to complete activity - all outcomes A or B vs. C p=0.007 Able to walk: Not able to walk >1 hour: 4.5% vs. 4.6% vs. 13.6% Not able to walk >30 mins: 18.2% vs. 13.6% vs. 41% Not able to walk >10 mins: -4.6% vs. -13.7% vs. -18.2% Only able to walk a few steps: -27.3% vs. -22.8% vs. -31.8% Not able to walk at all: -4.5% vs. -4.5% vs. -9.1% Function, Activities of Daily Living: sitting, mean change from baseline in proportion able to complete activity - all outcomes A or B vs. C p=0.005 Able to sit: 4.6% vs. 4.5% vs. 4.5% Not able to sit >1 hour: 27.3% vs. 0% vs. 31.9% Not able to sit >30 mins: 13.7% vs. 50% vs. 0% Not able to sit > a few mins: -40.9% vs. -31.9% vs. -36.4% Not able to sit at all: -4.5% vs. -22.8% vs. -13.6% Function, Activities of Daily Living: standing, mean change from baseline in proportion able to complete activity - all outcomes A or B vs. C p=0.013 Able to stand: 9.1% vs. 0% vs. 13.6% Able to stand with pain: 4.6% vs. 22.7% vs. 22.8% Not able to stand >1 hour: 13.6% vs. 13.6% vs. 36.4% Not able to stand >30 mins: 27.3 vs. 18.2% vs. 9.1% Not able to stand >10 mins: -31.8% vs. -18.2% vs. -31.8% Not able to stand at all: -22.8% vs. -36.4% vs. -31.8%	No systemic or local side effects reported (data not shown)	Not reported	Fair

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Konstantinovic, 2010	Serbia Single-center	Acute LBP (symptomatic <4 weeks) and unilateral radiculopathy Excluded: Use of oral or injected corticosteroids within month preceding study entry or previous surgery	Randomized: 546 Analyzed: 546 Attrition: 0% (0/546)	A. 904 nm laser 5 times/week for 3 weeks + nimesulide 200 mg/day (n=182) B. Sham laser 5 times/week for 3 weeks + nimesulide 200 mg/day (n=182) C. Nimesulide 200 mg/day (n=182)	A vs. B vs. C Mean age 44 vs. 42 vs. 45 years 59% vs. 58% vs. 57% female Race not reported Lumbar pain, VAS: 66 vs. 65 vs. 67 Disability, ODI: 32 vs. 32 vs. 31 Quality of life, SF-36 PCS: 10 vs. 10 vs. 10 Quality of life, SF-36 MCS: 12 vs. 12 vs. 12	Acute: mean 15 vs. 18 vs. 16 days
Vallone, 2014	Italy Single center	Nonspecific low back pain >6 months duration, age >18 years Excluded: Nerve root systems, systemic disease and specific conditions, medication for psychological problems, pregnant	Randomized: 100 (50 vs. 50) Analyzed: Unclear Attrition: Unclear	A: GaAlAs, 980 nm laser, 1 minute per spot, total 1200 J per spot for 1 month at each spot 3 times a week for 3 weeks, applied to 6 spots + exercise (stretching, strengthening) (n=50) B: Sham laser as above + exercise (n=50)	A vs. B Mean age 68 years overall 57% female overall Race not reported Pain (0-10 VAS): 6.64 vs. 6.36 Function: Not reported	Chronic: mean not reported, all >6 months by inclusion criteria

Author, Year	Duration of Followup	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Konstantinovic, 2010	3 weeks	A vs. B vs. C Lumbar pain, VAS mean change: -30 vs. -15.7 vs. -20.8; p<0.01 for all comparisons Disability, ODI mean change: -12 vs. -6.5 vs. -10; p<0.01 for all comparisons Disability, ODI proportion improved (defined as change from moderate to minimal disability category): 72% (151/182) vs. 54% (98/182) vs. 18% (33/182); A vs. B, RR 1.54 (95% CI 1.33 to 1.79); A vs. C, RR 4.58 (95% CI 3.34 to 6.27); B vs. C, RR 2.97 (95% CI 2.12 to 4.16) Quality of life, SF-36 PCS: -4 vs. -2 vs. -3; A vs. B, A vs. C p<0.01; B vs. C p=0.06 Quality of life, SF-36 MCS: -6 vs. -3 vs. -4; p<0.01 for all comparisons	Two withdrawals due to worsening pain; intervention group(s) not reported	Not reported	Good
Vallone, 2014	3 weeks	A vs. B Pain (mean, 0-10 VAS): 6.64 vs. 6.36 at baseline, 2.68 vs. 4.08 at 3 w, change from baseline 3.96 vs. 2.32 (p<0.01) Complete pain relief: 10% (5/50) vs. 2.0% (1/50), RR 5.0 (95% CI 0.61 to 41.3)	Not reported	None reported	Fair

Please see Appendix C. Included Studies for full study references.

Table E39. Data abstraction of randomized controlled trials of diathermy

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Ahmed, 2009	Bangladesh Single center	20 to 80 years of age, low back pain ≥3 months Exclude: Traumatic low back pain, inflammatory back pain, back pain with complications	Randomized: Unclear Analyzed: 97 Attrition: Not reported	A: Short wave diathermy (n=47) B: Detuned (sham) diathermy (n=50) 15 minute sessions, 3 times a week for six weeks	Mean age: 40 years (overall) Female: Not reported Race: Not reported Baseline pain (mean, 0-34 [Lattinen's score plus tenderness score plus 0-10 VAS]): 20.4 vs. 20.1 Back-specific function: Not reported	Chronic (>3 months), mean duration not reported
Shakoor, 2008	Bangladesh Single center	30 to 70 years of age, low back pain >3 months Exclude: Traumatic low back pain, back pain with complications, infection on the skin over the back area	Randomized: "About" 127 Analyzed: 102 Attrition: Unclear	A: Short wave diathermy: 27.33 MHz, wavelength 11 meters (n=50) B: Detuned (sham) diathermy (n=52) 15 minute sessions, 3 times a week for six weeks Both groups also underwent extension and strengthening exercises (10 repetitions twice daily for 6 weeks) and received Naprosyn 250 mg po bid	Mean age: 44.5 vs. 40.0 years Female: 59% (overall) Race: Not reported Baseline pain (mean, 0-34 [Lattinen's score plus tenderness score plus 0-10 VAS]): 15.2 vs. 15.6 Back-specific function: Not reported	Chronic (>3 months), mean 40 vs. 35 months

Author, Year	Duration of Followup	Results (list results for acute, subacute, and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality
Ahmed, 2009	6 weeks (at end of therapy)	A vs. B Pain (mean, 0-34 [Lattinen's score (0-20) plus tenderness score (0-4) plus 0-10 VAS]): 17.8 vs. 18.8 at w 1 (p=0.14), 15.3 vs. 17.6 at w 2 (p=0.01), 11.1 vs. 15.0 at w 4 (p<0.05), 6.4 vs. 13.4 at w 6 (p<0.05)	Not reported	Not reported	Poor
Shakoor, 2008	6 weeks (at end of therapy)	A vs. B Pain (mean, 0-34 [Lattinen's score (0-20) plus tenderness score (0-4) plus 0-10 VAS]): 13.9 vs. 14.5 at w 1 (p=0.31), 11.9 vs. 12.4 at w 2 (p=0.33), 10.3 vs. 11.8 at w 4 (p=0.02), 9.66 vs. 11.6 at w 6 (p<0.05)	Not reported	Not reported	Poor

Please see Appendix C. Included Studies for full study references.

Table E40. Data abstraction of systematic reviews of lumbar supports

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies
van Duijvenbode, 2011	Lumbar supports vs. no intervention Lumbar supports vs. other active treatment One type of lumbar support vs. another	PubMed, CCRCT, EMBASE, CINAHL (through December 2006), Current Contents (through September 1999), reference lists, expert recommendation; no language restrictions reported	8 RCTs; 7 English-language, 1 German language Chronic pain (3 trials), mixed acute, subacute and chronic pain (4 trials); duration of pain not reported in 1 trial	A. Lumbar supports (n=418) B. Other active interventions (spinal manipulation therapy, n=186; other physiotherapy, n=114; massage, n=37; TENS, n=28; exercise [strength training], n=21; analgesics, n=113; nonsupportive corset, n=10) C. No support (n=309) *One trial that randomized 79 participants to support or no support did not report number in each treatment group*	Cochrane Back Review Group criteria (2003)	Qualitative analysis judging level of evidence (strong, moderate, limited conflicting or no evidence) due to no poolable data

Author, Year	Results	Adverse Events	Quality
van Duijvenbode, 2011	A vs. B (specified below; no data reported for any outcome) Mixed population (acute, subacute and/or chronic) Pain: 3 trials (1 higher quality, 2 lower quality) found no difference between lumbar support and traction, spinal manipulation, exercise, physiotherapy or TENS in short-term pain Function: 1 higher quality trial found no difference between lumbar support and massage using ODI; difference was significant (favoring lumbar support) using RDQ Return to work: No difference between lumbar support and traction, spinal manipulation, or exercise Global improvement: 2 lower-quality trials found no difference between lumbar support and other active treatments in global improvement A vs. C (no data reported for any outcome) Chronic population 1 lower-quality trial found no difference for pain and function outcomes after 2 months treatment Acute and subacute population Pain: 3/4 trials (1 higher quality, 2 lower quality) found no difference in short-term pain reduction; 1 lower quality trial found significant difference in short-term pain with use of lumbar support Function: 3 trials (1 higher quality, 2 lower quality) found significant effect in favor of lumbar support for short-term functional status Return to work: Mixed evidence from 2 lower-quality trials; one found no difference, one found an effect favoring lumbar support Global improvement: 2 lower-quality trials reported no difference in short-term global improvement (A+B) vs. A (no data reported for any outcome) Chronic population 1 lower quality trial comparing lumbar support + exercise (muscle strengthening) with lumbar support alone found no difference in short- or long-term pain or function 1 lower quality trial comparing lumbar support + nonsupportive corset to nonsupportive corset alone found significant effects in favor of lumbar support + nonsupportive corset in short-term pain and back-specific function A vs. A Chronic population 1 lower-quality trial found no difference between lumbar support, flexible corset and semi-rigid corset in short-term pain or function	Not reported	Good

Please see Appendix C. Included Studies for full study references.

Table E41. Data abstraction of randomized controlled trials of lumbar support

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention
Calmels 2009	France Single center	Age 20 to 60 years, duration of LBP 1 to 3 months Excluded: presence of radicular pain, prior surgery or lumbar belt use (within 6 months), traumatic LBP, chronic cardiovascular or respiratory disease, contraindication to NSAID	Randomized: 217 Analyzed: 197 Attrition: 9% (20/217)	A. Lumbar support (n=102) 5-8 hours/day, 3-5 days/week (varied according to study timepoint; hours of use/week decreased over time) B. No lumbar support (n=95)
Morrisette, 2014	United States Single center	≥18 years of age, low back pain of any duration Excluded: Prior spinal surgery, litigation related to low back pain, neurological disease or injury, systemic inflammatory disease, pregnant, acute fracture, tumor, systemic or spinal infection; 2 or more of the following: motor deficit in myotomal distribution, diminished sensation, and/or absent deep tendon reflexes	Randomized: 98 Analyzed: 98 Attrition: 0% (0/98)	A: Inextensible lumbar support, number of hours per day not specified (mean 5.0 hours/day) (n=37) + standard care B: Extensible lumbar support, mean 4.8 hours/day (n=32) + standard care C: Standard care (n=29) All interventions administered for 2 weeks, standard care consisted of physician advice and medication and physical therapy including exercise, manual therapy, electrical stimulation, traction, cold/heat, and ultrasound
Oleske, 2007	United States Multicenter	Workers identified through a corporate Health Information System having nontraumatic, work-related low back disorder within 8 weeks of study entry Excluded: Concomitant work-related injury or illness	Randomized: 433 Analyzed: 433 Attrition: 0% (0/433)	A. Lumbar support + education (n=222), timing of support use not reported B. Education only (n=211)
Sato, 2012	Japan	Chronic low back pain patients attending a university hospital clinic in Japan Excluded: LBP due to infection, osteoporosis, or malignancy	Randomized: 50 Analyzed: 40 Attrition: 20% (10/50)	A. Lumbar support (corset; n=not reported) worn during all waking hours for 6 months except during bathing B. No lumbar support (n=not reported)

Author, Year	Study Participants	Duration of Pain (acute, subacute,	Duration of Followup	Results (list results for acute, subacute and chronic separately)
Calmels 2009	Population characteristics not reported by treatment group Mean age 43 years 45% female Race not reported A vs. B Population characteristics reported by treatment group Mean pain (VAS, scale 0-100) 60.9 vs. 59.7 Mean function (EIFEL score, scale 0-24; higher score=more disability) 10.3 vs. 10.1	Subacute; mean duration not reported but inclusion criteria required pain duration 1-3 months at baseline	3 months (90 days)	A vs. B Pain, mean change in VAS, day 30: -26.8 (SD 18.2) vs. -21.3 (SD 18.7); p=0.04 Pain, mean change in VAS, day 90: -41.5 (SD 21.5) vs. -32.0 (SD 20.0); p=0.002 Function, mean change in EIFEL score, day 30: -5.4 (SD 4.1) vs. -4.0 (SD 4.3); p=0.02 Function, mean change in EIFEL score, day 90: -7.6 (SD 4.4) vs. -6.1 (SD 4.7); p=0.02
Morrisette, 2014	A vs. B vs. C Mean age: 50 vs. 49 vs. 45 years Female: 54% Vs. 69% vs. 62% African-American: 78% vs. 69% vs. 72% Mean pain (0-10): 7.6 vs. 7.6 vs. 7.6 Mean ODI (0-100): 40 vs. 36 vs. 34	Mixed duration, mean 14 vs. 18 vs. 10 weeks	2 weeks	A vs. B vs. C (mean difference from baseline) Pain (0-10 NRS): 3.3 (95% CI 2.3-4.3) vs. 3.3 (95% CI 2.2-4.4) vs. 2.4 (95% CI 1.4-3.5) at 2 w; p>0.05 for all comparisons ODI (0-100): 14.0 (95% CI 8.2-19.8) vs. 8.1 (95% CI 2.8-13.4) vs. 2.4 (95% CI -2.2-7.1) at 2 w; p=0.01 for A vs. C Patient Specific Activity Scale (0-10): -1.8 (95% CI -2.5 to -1.0) vs. -1.2 (95% CI -1.9 to -0.5) vs. -0.4 (95 %CI -1.3 to -0.4) at 2 w; p=0.01 for A vs. C ODI improved >50%: 35% (13/37) vs. 16% (5/32) vs. 10% (3/29); RR 2.25 (95% CI 0.90 to 5.62) for A vs. B, RR 3.40 (95% CI 1.07 to 10.8) for A vs. C, RR 1.51 (95% CI 0.40 to 5.77) for B vs. C ODI improved >6 points: 65% (24/37) vs. 59% (19/32) vs. 38% (11/29); RR 1.09 (95% CI 0.75 to 1.58) for A vs. B, RR 1.71 (95% CI 1.01 to 2.88) for A vs. C, RR 1.57 (95% CI 0.91 to 2.70) for B vs. C Patient Specific Activity Scale improved >2 points: 35% (13/37) vs. 31% (10/32) vs. 21% (6/29); RR 1.12 (95% CI 0.57 to 2.21) for A vs. B, RR 1.70 (95% CI 0.74 to 3.92) for A vs. C, RR 1.51 (95% CI 0.63 to 3.64) for B vs. C Pain improved >2.4 points: 70% (26/37) vs. 75% (24/32) vs. 55% (16/29); RR 0.94 (95% CI 0.70 to 1.25) for A vs. B, RR 1.27 (95% CI 0.86 to 1.88) for A vs. C, RR 1.36 (95% CI 0.93 to 2.00) for B vs. C

Author, Year	Study Participants	Duration of Pain (acute, subacute, chronic)	Duration of Followup	Results (list results for acute, subacute and chronic separately)
Oleske, 2007	A vs. B Mean age 46 vs. 46 years 17% vs. 24% female Race: 66% vs. 67% white; 34% vs. 33% non-white 67% vs. 69% onset of LBP <2 weeks prior to study entry Mean pain (VAS, scale 0-10) 4.09 vs. 4.18 Mean function (Oswestry, scale 0-100; higher score=more disability) 24.4 vs. 24.5	Acute or subacute; mean duration not reported but inclusion criteria required pain duration <8 weeks at baseline	1 year	A vs. B Pain, coefficient of change (group A=reference group): -0.248 days; p=0.3 Function, coefficient of change (group A=reference group): -0.298 days; p=0.8 Overall conclusion: no difference between treatment groups for pain or function outcomes
Sato, 2012	*Population characteristics not reported by treatment group* Mean age not reported; range 30 to 78 years 50% female Race not reported Mean pain and function score not reported	Chronic; mean duration not reported but inclusion criteria required pain duration >3 months at baseline	6 months	A vs. B Function, Japanese Orthopedic Association (JOA) criteria (includes patient-assessment of pain and function), 1 month: significant difference in JOA score, favoring lumbar support: p<0.01 (no data shown); no significant difference between groups at 3 and 6 months

Author, Year	Adverse Events Including Withdrawals	Funding Source	Quality	Comments
Calmels 2009	Not reported	No external funding	Fair	
Morrisette, 2014	Not reported	Aspen Medical Products, Inc; National Institutes of Health	Fair	
Oleske, 2007	Not reported	UAW-GM National Joint Committee on Health and Safety	Fair	
Sato, 2012	Not reported	Not reported	Fair	

Please see Appendix C. Included Studies for full study references.

Table E42. Data abstraction of systematic reviews of traction

Author, Year	Comparison	Data Sources	Number and Type of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies
Wegner, 2013	Traction vs. sham, placebo or no treatment Traction vs. other active treatments One type of traction vs. another type of traction	MEDLINE, CCRCT, EMBASE, CINAHL, Cochrane Back Group Specialized Register (all through August 2012)	32 RCTs (n=2,762) Traction vs. sham, placebo or no treatment: 13 trials Traction vs. other treatments: 15 trials Traction vs. traction: 5 trials Chronic LBP: 10 trials Subacute LBP: 1 trial Mixed acute, subacute and chronic: 17 trials Unspecified duration of LBP: 5 trials	A. Traction A1. Traction + physiotherapy B. Sham, placebo or no treatment B1. Physiotherapy alone C. Other interventions (exercise, interferential therapy, massage, balneotherapy)	Cochrane Back Review Group criteria (2009)	Qualitative synthesis (due to heterogeneity of outcomes reported) including study risk of bias; results pooled (qualitative analysis) when possible

Author, Year	Results	Adverse Events	Quality Rating	Comments
Wegner, 2013	A vs. B Difference in LBP population with or without radiation Pain, 3-5 weeks (2 trials): -18.49 (95% CI -24.12 to -12.87) Pain, 6-12 weeks (1 trial): 0.30 (95% CI -9.91 to 10.51) Pain, 6 months (1 trial): -0.5 (95% CI -11.55 to 10.55) Pain, 1 year (1 trial): -9.10 (95% CI -19.32 to 1.12) Functional status, 3-5 weeks (1 trial): -1.30 (95% CI -2.90 to 0.30) Functional status, 6-12 weeks (1 trial): 0.10 (95% CI -1.76 to 1.96) Functional status, 6 months (1 trial): 0.70 (95% CI -1.16 to 2.56) Global improvement, 3-5 weeks (2 trials): -0.03 (95% CI -0.17 to 0.12) Global improvement, 6-12 weeks (2 trials): 0.03 (95% CI -0.12 to 0.18) Global improvement, 6 months (1 trial): 0.02 (95% CI -0.14 to 0.18) Return to work, 3-5 weeks (1 trial): -1.80 (95% CI -5.51 to 1.91) Return to work, 6-12 weeks (1 trial): -4.30 (95% CI -14.71 to 6.11) Return to work, 6 months (1 trial): -8.00 (95% CI -26.99 to 10.99) Difference in LBP population with radiation Pain, 1-2 weeks (2 trials): 2.93 (95% CI -14.73 to 20.59) Global improvement, 1-2 weeks (4 trials): 0.13 (95% CI 0.04 to 0.22) Global improvement, 3-5 weeks (2 trials): 0.27 (95% CI 0.12 to 0.43) Global improvement, 12-16 weeks (1 trial): 0.06 (95% CI -0.16 to 0.28) Return to work, 2 years (1 trial): 0.15 (95% CI -0.15 to 0.45) Difference in LBP population without radiation Pain intensity, 12-16 weeks: -4.00 (95% CI -17.65 to 9.65) A vs. A (one traction type versus another) Difference in LBP population with or without radiation Global improvement, 1-2 weeks: -0.08 (95% CI -0.46 to 0.30; static traction vs. intermittent traction); 0.53 (95% CI 0.32 to 0.73; auto traction vs. mechanical traction) Difference in LBP population with radiation Pain, 1-2 weeks (3 trials): 6.58 (-2.77 to 15.93) Global improvement, 1-2 weeks (1 trial): -0.16 (-0.40 to 0.09)	Adverse events were reported in 11/32 studies; 4 reported no adverse events. A vs. B Aggravation of symptoms (2 trials): 24% (9/38) vs. 20% (4/20); RR 1.18 (95% CI 0.42 to 3.37); 12% (5/43) vs. 2% (1/43); RR 5.00 (95% CI 0.61 to 41) Subsequent surgery (1 trial): 9% (7/82) vs. 0% (0/60); RR 11 (95% CI 0.64 to 189) A vs. A Increased pain (2 trials): Inversion vs. conventional traction - 79% (11/14) vs. 15% (2/13); RR 5.11 (95% CI 1.39 to 19); Static vs. intermittent traction - 31% (4/13) vs. 15% (2/13); RR 2.00 (95% CI 0.44 to 9.08) A1 vs. B1 Worsening of symptoms (1 trial): 25% (5/21) vs. 37% (8/21); RR 0.63 (95% CI 0.24 to 1.60) A vs. C Temporary deterioration (1 trial): Traction vs. exercise - 17% (4/24) vs. 15% (4/26); RR 1.08 (95% CI 0.30 to 3.86)	Good	Results not stratified according to duration of LBP

Author, Year	Results	Adverse Events	Quality Rating	Comments
Wegner, 2013 (cont.)	A1 vs. B1 Difference in LBP population with or without radiation Pain, 1-2 weeks (1 trial): 0.00 (95% CI -7.61 to 7.61) Pain, 12-16 weeks (1 trial): 5.00 (95% CI -5.67 to 15.67) Functional status, 1-2 weeks (1 trial): 3.90 (-1.91 to 9.71) Functional status, 12-16 weeks (1 trial): 4.00 (95% CI -2.78 to 10.78) Global improvement, 1-2 weeks (1 trial): 0.05 (95% CI -0.25 to 0.35) Global improvement, 12-16 weeks (1 trial): 0.53 (95% CI 0.28 to 0.79) Difference in LBP population with radiation Pain, 1-2 weeks (2 trials): -7.96 (95% CI -16.53 to 0.61) Pain, 6 weeks (1 trial): 2.00 (95% CI -10.02 to 14.02) Functional status, 1-2 weeks (2 trials): -0.08 (95% CI -0.49 to 0.32) Functional status, 6-12 weeks (1 trial): 0.14 (95% CI -0.35 to 0.63) Functional status, 12-16 weeks (1 trial): 0.43 (95% CI -0.30 to 1.16) Functional status, 6 months (1 trial): 0.18 (95% CI -0.54 to 0.90) Global improvement: No pooled estimates for any timepoint. Results from three individual trials showed no significant difference between groups from timepoints ranging from 1-2 to 12-16 weeks. Return to work, 3-5 weeks (1 trial): OR 1.41 (95% CI 0.61 to 3.28) A vs. C Difference in LBP population with or without radiation Pain: No pooled estimates for any timepoint. Results from four individual trials were mixed for all timepoints ranging from 1-2 weeks to 1 year Functional status, 1-2 weeks (1 trial): -0.06 (95% CI -0.40 to 0.27) Functional status, 3-5 weeks (1 trial): 0.20 (95% CI -0.05 to 0.46) Functional status, 12-16 weeks (2 trials): -0.03 (95% CI -0.26 to 0.21) Functional status, 6 months (1 trial): 0.15 (95% CI -0.16 to 0.45) Functional status, 1 year (1 trial): 0.04 (95% CI -0.25 to 0.34) Global improvement: No pooled estimates for any timepoint. Results from three individual trials were mixed for timepoints ranging from 1-2 to 12-16 weeks. Difference in LBP population with radiation Pain: No pooled estimates for any timepoint. Results from two individual trials showed no significant difference between groups from timepoints ranging from 1-2 to 12-16 weeks. Functional status: No pooled estimates for any timepoint. Results from two individual trials showed no significant difference between groups from timepoints ranging from 1-2 to 12-16 weeks. Global improvement: No pooled estimates for any timepoint. Results from two individual trials showed no significant difference between groups from timepoints ranging from 1-2 and 3-5 weeks.			

Please see Appendix C. Included Studies for full study references.

Table E43. Data abstraction of randomized controlled trials of traction

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants	Duration of Pain (acute, subacute, chronic)
Diab, 2012 and Diab, 2013	Egypt Single center	Chronic low back pain (duration ≥3 months) with Cobb angle <40° Excluded: RA, OA, spinal stenosis, inability to tolerate lumbar extension, scoliotic or other lower extremity deformity	Randomized: 80 Analyzed: unclear Attrition: unclear (16% [13/80] withdrawn from study at 6 month followup)	A. Traction, radiation and stretching 3 times/week for 10 weeks (n=40) B. Radiation and stretching 3 times/week for 10 weeks (n=40)	A vs. B Mean age 46 vs. 46 years 45% vs. 43% female Race not reported Prior LBP treatment 100% vs. 100% Pain, VAS: 6.0 vs. 5.5 Disability, ODI: 32.4 vs. 31.1	Subacute/chronic: Mean duration not reported; entry criteria required duration ≥3 months
Moustafa, 2013	Egypt Single center	Chronic low back pain (duration ≥3 months) with Harrison angle <39°, unilateral leg pain, mild to moderate disability per ODI Excluded: history of back surgery, systemic illness including cancer, RA, OA, spinal stenosis, inability to tolerate lumbar extension, scoliotic or other lower extremity deformity	Randomized: 64 Analyzed: 58 Attrition: 9% (6/64)	A. Traction, hot packs and interferential therapy 3 times/week for 10 weeks (n=32) B. Hot packs and interferential therapy 3 times/week for 10 weeks (n=32)	A vs. B Mean age 44 vs. 43 years 41% vs. 47% female Race not reported Using medication for LBP treatment 38% vs. 44% Pain, VAS: 6.2 vs. 5.9 Disability, ODI: 32.4 vs. 31.7	Subacute/chronic: Mean duration not reported; entry criteria required duration ≥3 months
Prasad, 2012	UK Single center	Age 18 to 45 years with onset of LBP symptoms within 6 months of study entry Excluded: Neurological deficits, cardio-respiratory disorder, pregnancy, weight >20% of ideal, MRI evidence of large sequestrated disc fragment	Randomized: 24 Analyzed: Varied by outcome) Attrition: 8% (2/24)	A. Inversion traction 3 times/week for 4 weeks + physiotherapy (n=13) B. Physiotherapy alone (n=11)	A vs. B Mean age 34 vs. 37 years 46% vs. 64% female Race not reported Pain, VAS: 3.2 vs. 2.8 Disability, ODI: 50 vs. 48 Disability, RDQ: 12.5 vs. 10 Quality of life, SF36 physical function: 43.5 vs. 35.7	Acute/subacute: Mean duration not reported; entry criteria required <6 months duration of symptoms

Author, Year	Duration of Followup	Results (list results for acute, subacute and chronic separately)	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Diab, 2012 and Diab, 2013	6 months	A vs. B Pain, VAS at 10 weeks: 3.2 (SD 1.4) vs. 3.5 (SD 1.2); mean difference -0.30 (95% CI -0.88 to 0.28) Pain, VAS at 6 months: 2.6 (SD 1.1) vs. 3.5 (SD 1.2); mean difference -0.90 (95% CI -1.41 to -0.39) Disability, ODI at 10 weeks: 21.8 (SD 3.1) vs. 23.4 (SD 3.4); mean difference -1.60 (95% CI -3.05 to -0.15) Disability, ODI at 6 months: 23.8 (SD 2.7) vs. 27.1 (SD 3.0); mean difference -3.30 (95% CI -4.57 to -2.03)	Not reported	No external funding	Fair
Moustafa, 2013	6 months	A vs. B Pain, VAS at 10 weeks: 2.3 (SD 1.6) vs. 3.5 (SD 1.04); mean difference -1.20 (95% CI -1.87 to -0.53) Pain, VAS at 6 months: 2.4 (SD 0.9) vs. 4.6 (SD 1.3); mean difference -2.20 (95% CI -2.79 to -1.62) Disability, ODI at 10 weeks: 19.8 (SD 3.7) vs. 23.7 (SD 3.8); mean difference -3.90 (95% CI -5.77 to -2.03) Disability, ODI at 6 months: 23.1 (SD 2.8) vs. 31.2 (SD 2.9); mean difference -8.10 (95% CI -9.60 to -6.60)	Not reported	No external funding	Fair
Prasad, 2012	6 weeks	A vs. B Number analyzed for each outcome varied Pain, VAS: 0.9 (n=12) vs. 3.0 (n=7); p not reported (inadequate data provided to calculate) Disability, ODI: 31 (n=8) vs. 54 (n=3); p=0.3 Disability, RDQ: 7.5 (n=12) vs. 11 (n=7); p=0.55 Quality of life, SF-36 physical function mean change from baseline: 9.2 vs. 8.2; p=0.9; no significant difference between groups for other SF-36 measures including physical role, body pain, general health, vitality, social function, emotional role, mental health or change in health Need for surgery: 23% (3/13) vs. 82% (9/11); RR 0.28 (95% CI 0.10 to 0.79)	No serious adverse events in either group	Jacobson Charitable Trust	Poor

Please see Appendix C. Included Studies for full study references.

Table E44. Data abstraction of randomized controlled trials of taping

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants
Bae, 2013	South Korea Single center	Low back pain >12 weeks who had participated in a low back pain class, VAS >=6 and ODI >=60 Exclude: Prior lumbar surgery, structural malformation or other musculoskeletal disease, skin allergy to tape, no exercise in past 3 months, prior taping treatment, taking adrenocortical hormones or analgesics	Randomized: 20 (10 vs. 10) Analyzed: Unclear Attrition: Unclear	A: Kinesio Taping of lower back with tension, four "I" strips over area of maximum pain in star shape, 3 times per week for 12 weeks (n=10) B: Sham taping with one inelastic "I" strip transversely over lumbar area with maximum pain, 3 times per week for 12 weeks (n=10) All patients received hot pack (20 minutes), ultrasound (1.5 W/cm^2 for 5 minutes), and TENS (4 pps, 15 minutes) to L1-2 and L4-5 areas (40 minutes); 3 times per week for 12 weeks	A vs. B Mean age: 54 vs. 51 years Female: 50% vs. 60% Race: Not reported Pain intensity: 7.83 vs. 7.71 ODI: 16.3 vs. 15.4
Castro-Sanchez, 2012	Spain Single center	18 to 65 years of age, low back pain ≥3 months, RDQ ≥4, no flexion-relaxation in the lumbar muscles during trunk flexion Exclude: Clinical signs of radiculopathy, spinal stenosis, fibromyalgia, spondylolisthesis, previous surgery or Kinesio Tape therapy, corticosteroid treatment in past 2 weeks, central or peripheral nervous system disease	Randomized: 60 Analyzed: 60 Attrition: 0%	A: Kinesio Taping of lower back with 25% tension in star shape overlying point of maximum pain, applied for 7 days (n=30) B: Sham taping with single transverse strip above point of maximal pain, applied for 7 days (n=30)	A vs. B Mean age: 50 vs. 47 years Female: 70% vs. 66% Race: Not reported Pain intensity (0-10 VAS): 5.6 vs. 5.4 ODI (mean, 0-100): 28 vs. 29

Author, Year	Duration of Pain (acute, subacute, chronic)	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Bae, 2013	All chronic, mean duration 13 vs. 12 m	12 weeks (at completion of therapy)	A vs. B Pain (mean, 0-10 VAS): 7.83 vs. 7.71 at baseline, 5.07 vs. 5.14 at 12 w (p>0.05) ODI (mean, 0-100): mean 16.32 vs. 15.43 at baseline, 10.75 vs. 11.34 at 12 w (p>0.05)	Not reported	Not reported	Fair
Castro-Sanchez, 2012	All chronic, mean duration not reported	5 weeks (4 weeks after completion of therapy)	A vs. B Pain (mean difference in change from baseline, 0-10): -1.1 (95% CI -1.9 to -0.3) at 1 w, -1.0 (95% CI -1.7 to -0.2) at 5 w ODI (mean difference in change from baseline, 0-100): -4 (95% CI -6 to -2) at 1 w, 1 (95% CI -1 to 3) at 5 w RDQ (mean difference in change from baseline, 0-24): -1.2 (95% CI -2.0 to -0.4) at 1 w, 0.1 (95% CI -1.0 to 1.3) at 5 w	Not reported	Reports no funding support	Good

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants
Chen, 2012	Country unclear (author affiliations Taiwan and Australia) Single center	18 to 65 years of age, nonspecific low back pain >6 weeks Exclude: Spinal pathology, major trauma, systemic disease, cancer, osteoporosis, inflammatory disease, neurological deficit, pregnant, previous back surgery or waiting for surgery, active or pending legal proceedings due to low back pain, sensitivity to tape	Randomized: 43 Analyzed: 43 Attrition: 14% (19% vs. 9.1%)	A: Functional Fascial Taping with tension applied in direction that resulted in maximal pain reduction on trunk flexion, applied in 3 directions, reapplied daily for 2 weeks (n=21) B: Sham taping without tension (n=22) All patients given instruction for home trunk flexion exercises	A vs. B Mean age: 46 vs. 40 years Female: 48% vs. 45% Average pain (mean, 0-100 VAS): 43 vs. 42 ODI (mean, 0-100): 31 vs. 24
Kachanathu, 2014	Saudi Arabia Single center	Nonspecific low back pain for >3 months	Randomized: 40 Analyzed: Unclear Attrition: Not reported	A: Kinesio Taping with two strips from origin of lumbar erector spinae to insertion with slight traction with patient flexing + exercise therapy (stretching and strengthening three sessions/week for 4 weeks) (n=20) B: Exercise therapy without Kinesio Taping (n=20)	Patient characteristics reported for whole sample Mean age: 35 years 25% female Race: Not reported Pain intensity (mean , 0-10): 6.2 vs. 6.1 RDQ (mean 0-24): 10.3 vs. 1.8

Author, Year	Duration of Pain (acute, subacute, chronic)	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Chen, 2012	All >6 weeks, median 39 vs. 32 weeks	12 weeks (10 weeks after completion of therapy)	A vs. B Average pain (mean difference in change from baseline, 0-100): -7.6 +/- 6.2 (p=0.23) at 2 w, -0.73 +/- 5.9 (p=0.90) at 6 w, -3.6 +/-6.9 (p=0.60) at 12 w Worst pain (mean difference in change from baseline, 0-100): -17.3 +/- 7.2 (p=0.02) at 2 w, -11.3 +/- 8.1 (p=0.17) at 6 w, -5.8 +/- 7.6 (p=0.45) at 12 w ODI (mean difference in change from baseline, 0-100): -5.5 +/- 2.8 (p=0.05) at 2 w, -3.4 +/- 3.1 (p=0.28) at 6 w, -3.1 +/- 3.1 (p=0.33) at 12 w Average pain improved >20 points: 57% (12/21) vs. 36% (8/14) at 2 w, 57% (12/21) vs. 59% (13/22) at 6 w, 71% (15/21) vs. 59% (13/22) at 12 w Worst pain improved >20 points: 81% (17/21) vs. 41% (9/22) at 2 w, 67% (14/21) vs. 68% (15/22) at 6 w, 76% (16/21) vs. 77% (17/22) at 12 w ODI improved >10 points: 81% (17/21) vs. 41% (9/22) at 2 w, 71% (15/21) vs. 55% (12/22) at 6 w, 62% (13/21) vs. 50% (11/22) at 12 w	Not reported	Australian Centre for Research into Sports Injury and its Prevention	Fair
Kachanathu, 2014	All chronic, mean duration not reported	4 weeks (at end of therapy)	A vs. B Pain (mean, 0-10): 2.9 vs. 3.7 at 4 w (p=0.57) RDQ (mean, 0-24): 4.7 vs. 7.0 at 4 w (p=0.67)	Not reported	Not reported	Poor

Author, Year	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention	Study Participants
Paolini, 2011	Italy Single center	30 to 80 years of age, chronic (>12 weeks) low back pain, failed flexion relaxation during turn flexion Exclude: Clinical signs of radiculopathy, lumbar stenosis, spondylolisthesis, previous spinal surgery, corticosteroid treatment in past 2 weeks, central or peripheral nervous system diseases	Randomized: 39 Analyzed: 39 Attrition: Not reported	A: Kinesio Taping of lower back with 3 vertical strips placed with patient bending forward to create tension, applied for 3 days at time over 4 weeks (n=13) B: Exercise therapy, 30 minutes three times/week with stretching, relaxation, and active exercises (n=13) C: Kinesio Taping + exercise (n=13)	A vs. B vs. C Mean age: 63 vs. 63 vs. 62 years Female: 62% vs. 69% vs. 62% Race: Not reported Pain intensity (mean, 0-10 VAS): 7.1 vs. 7.6 vs. 7.6 RDQ (mean, 0-24): 10.3 vs. 9.9 vs. 9.5
Silva Parreira, 2014	Brazil Single center	18 to 60 years of age with nonspecific chronic (≥ 3 months) low back pain Exclude: Contraindication to physical exercise (serious spinal pathology, nerve root compromise, serious cardiopulmonary conditions, pregnancy, contraindication to taping)	Randomized: 148 Analyzed: 148 Attrition: 0% at 12 weeks	A: Kinesio Taping over erector spinae muscles parallel to the spinous processes starting near the posterior superior iliac crest with 10% to 15% tension to create convolutions in the skin, applied for 48 hours, twice weekly for 4 weeks (n=74) B: Sham taping without tension (0% tension), applied for 48 hours, twice weekly for 4 weeks (n=74)	A vs. B Mean age: 51 vs. 50 years 76% vs. 80% female Race: Not reported Pain intensity (mean, 0-10 NRS): 7.0 vs. 6.8 RDQ (mean, 0-24): 11.5 vs. 10.4

Author, Year	Duration of Pain (acute, subacute, chronic)	Duration of Followup	Results	Adverse Events Including Withdrawals	Funding Source	Quality Rating
Paolini, 2011	All chronic, duration <12 months in 85% vs. 62% Vs. 69%	4 weeks (at end of therapy)	A vs. B vs. C Pain (mean, 0-10): 3.1 vs. 3.5 vs. 3.7 at 3 w (p>0.05) RDQ (mean, 0-24): 9.5 vs. 5.4 vs. 7.3 at 3 w (p>0.05)	Not reported	Not reported	Fair
Silva Parreira, 2014	Chronic: All chronic, mean duration 24 vs. 36 months	12 weeks (8 weeks after completion of therapy)	A vs. B Pain (mean difference from baseline, 0-10 NRS): -0.4 (95% CI -1.3 to 0.4) at 4 w, -0.5 (95% CI -1.4 to 0.4) at 12 w RDQ (mean difference from baseline, 0-24): -0.3 (95% CI -1.9 to 1.3) at 4 w, 0.3 (95% CI -1.3 to 1.9) at 12 w Global Perceived Effect (mean difference from baseline, -5 to 5): 1.4 (95% CI 0.3 to 2.5) at 4 w, 0.4 (95% CI -0.7 to 1.5) at 12 w	Not reported	Fundacao de Amparao a Pesquia do Estado de Sao Paulo and Conselho Nacional de Desenvolvimento Cientifico e Tecnologico	Good

Please see Appendix C. Included Studies for full study references.

Appendix F. Quality Assessment

Table F1. Quality assessment of systematic reviews of acetaminophen

Study, Year	(1) 'A priori' design provided?	(2) Duplicate study selection and data extraction? a. Study selection b. Data extraction	(3) Comprehensive literature search performed?	(4) Status of publication used as an inclusion criteria?	(5) List of studies (included and excluded) provided?	(6) Characteristics of the included studies provided?
Roelofs, 2008	Yes	a. Yes b. Yes	Yes	Unclear	Yes	Yes

Study, Year	(7) Scientific quality of included studies assessed and documented?	(8) Scientific quality of the included studies used appropriately in formulating conclusions?	(9) Methods used to synthesize the findings of studies appropriate?	(10) Likelihood of publication bias assessed?	(11) Conflict of interest stated? a) Systematic Review b) Individual Studies	Quality Rating
Roelofs, 2008	Yes	Yes	Yes	Yes	a. Yes b. No	Good

Please see Appendix C. Included Studies for full study references.

Table F2. Quality assessment of randomized controlled trials of acetaminophen

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Williams, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Author, Year	Compliance Acceptable in All Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Williams, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F3. Quality assessment of systematic reviews of NSAIDs

Study, Year	(1) 'A priori' design provided?	(2) Duplicate study selection and data extraction? a. Study selection b. Data extraction	(3) Comprehensive literature search performed?	(4) Status of publication used as an inclusion criteria?	(5) List of studies (included and excluded) provided?	(6) Characteristics of the included studies provided?
Roelofs, 2008	Yes	a. Yes b. Yes	Yes	Unclear	Yes	Yes

Study, Year	(7) Scientific quality of included studies assessed and documented?	(8) Scientific quality of the included studies used appropriately in formulating conclusions?	(9) Methods used to synthesize the findings of studies appropriate?	(10) Likelihood of publication bias assessed?	(11) Conflict of interest stated? a) Systematic Review b) Individual Studies	Quality Rating
Roelofs, 2008	Yes	Yes	Yes	Yes	a. Yes b. No	Good

Please see Appendix C. Included Studies for full study references.

Table F4. Quality assessment of randomized controlled trials of NSAIDs

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in All Groups
Herrmann, 2009	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Majchrzycki, 2014	Yes	No	Yes	No	No	Unclear	Unclear	Yes
Shirado, 2010	Yes	No	Yes	No	No	Yes	Yes	Yes

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Herrmann, 2009	Yes	Yes	Yes	Yes	No	Yes	Fair
Majchrzycki, 2014	Yes	Yes	Yes	Yes	No	Yes	Fair
Shirado, 2010	Yes	Yes	Yes	Yes	No	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F5. Quality assessment of systematic reviews of opioids

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
Carson, 2011	Yes	a. Unclear b. Yes	Yes	No	No	Yes	No- only 4 of 38 excluded full text articles were listed in Appendix D	Yes
Chaparro, 2013	Yes	Yes to both	Yes	Yes	No	Yes	Yes- but only for 36 of 76 excluded articles	Yes

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
Carson, 2011	a. Yes	Qualitatively, yes	Yes	a. Systematic review: Yes	Unclear	Good
Chaparro, 2013	Yes to both	No, except for analysis 4.1, examining results of studies with "enhanced enrollment", meaning patients were enrolled only if they benefitted from opioids and tolerated side effects, then were randomized to opioid withdrawal.	Yes	a. Systematic review: Yes b. Individual studies: only for strong opioids	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F6. Quality assessment of randomized controlled trials of opioids

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in all Groups
Cloutier, 2013	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear
Hyup Lee, 2013	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Rauck, 2014	Unclear	Unclear	No; not sex	Yes	Yes	Unclear	Yes	Yes
Schiphorst Preuper, 2014	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Yes

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in All Groups Similar	Intention-to-Treat Analysis	Is There A Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Cloutier, 2013	Yes	No; <20%	Yes	Yes	Unclear	Unclear	Good
Hyup Lee, 2013	Yes	No; 21%	Yes	Yes	Yes	Yes	Good
Rauck, 2014	Yes	No; 39%	Yes	Yes	No	Yes	Poor
Schiphorst Preuper, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Fair

Please see Appendix C. Included Studies for full study references.

Table F7. Quality assessment of randomized controlled trials of SMRs

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Pareek, 2009	Unclear	Unclear	Yes	Yes	Unclear	Yes	Unclear
Ralph, 2008	Unclear	Unclear	Yes	Yes	Unclear	Yes	Yes

Author, Year	Compliance Acceptable in all Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment In All Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Pareek, 2009	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair
Ralph, 2008	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair

Please see Appendix C. Included Studies for full study references.

Table F8. Quality assessment of randomized controlled trials of benzodiazepines

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in All Groups
Brotz, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes	Quality Rating
Brotz, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F9. Quality assessment of systematic reviews of antidepressants

Study, Year	(1) 'A priori' design provided?	(2) Duplicate study selection and data extraction? a. Study selection b. Data extraction	(3) Comprehensive literature search performed?	(4) Status of publication used as an inclusion criteria?	(5) List of studies (included and excluded) provided?	(6) Characteristics of the included studies provided?
Urquhart, 2010	Yes	a. Yes b. No	Yes	Unclear	Yes	Yes

Study, Year	(7) Scientific quality of included studies assessed and documented?	(8) Scientific quality of the included studies used appropriately in formulating conclusions?	(9) Methods used to synthesize the findings of studies appropriate?	(10) Likelihood of publication bias assessed?	(11) Conflict of interest stated? a) Systematic Review b) Individual Studies	Quality Rating
Urquhart, 2010	Yes	Yes	Yes	Yes	a. Yes b. No	Good

Please see Appendix C. Included Studies for full study references.

Table F10. Quality assessment of randomized controlled trials of antidepressants

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in All Groups
Farajirad, 2013	Unclear	Unclear	Yes	Unclear	No	No	Unclear	Unclear
Mazza, 2010	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Unclear
Skljarevski, 2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Skljarevski, 2010 (Journal of Pain)	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes
Skljarevski, 2010 (Spine)	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Farajirad, 2013	No	Unclear	Unclear	Unclear	Unclear	Unclear	Poor
Mazza, 2010	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair
Skljarevski, 2009	Yes	Yes	Yes	No	Unclear	Unclear	Good
Skljarevski, 2010 (Journal of Pain)	Yes	Yes	Yes	No	Unclear	Unclear	Fair
Skljarevski, 2010 (Spine)	Yes	Yes	Yes	No	Unclear	Unclear	Fair

Please see Appendix C. Included Studies for full study references.

Table F11. Quality assessment of randomized controlled trials of antiseizure medications

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in All Groups
Baron, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Baron, 2014	Unclear	Unclear	Yes	Yes	Yes	Unclear	Yes	Yes
Kalita, 2014	Yes	Unclear	Yes	No	No	No	Yes	Unclear
Markman, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes
Pota, 2012	Unclear	No	Yes	Yes	Unclear	Unclear	Unclear	Unclear
Romano, 2009	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Yes	Unclear
Yaksi, 2007	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Unclear

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Baron, 2010	Yes	Yes	Yes	Yes	Unclear	Yes	Fair
Baron, 2014	Yes	Yes	Yes	Yes	Unclear	Yes	Fair
Kalita, 2014	Yes	No	Yes	Yes	Yes	Yes	Poor
Markman, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Pota, 2012	Yes	Yes	Yes	Yes	No	Yes	Fair
Romano, 2009	Yes	Yes	Yes	No	Unclear	Yes	Fair
Yaksi, 2007	No	Unclear	Yes	Unclear	Unclear	Yes	Poor

Please see Appendix C. Included Studies for full study references.

Table F12. Quality assessment of randomized controlled trials of corticosteroids

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Eskin, 2014	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
Friedman, 2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hedeboe, 1982	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Yes
Holve, 2008	No (sequential allocation)	No	Unclear	Yes	Yes	Yes	Yes
Rodrigues, 2014	Yes	Yes	Yes	Yes	Unclear	Yes	Yes

Author, Year	Compliance Acceptable in All Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Eskin, 2014	Yes	Yes	Yes	Yes	No	Unclear	Yes	Fair
Friedman, 2008	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Good
Hedeboe, 1982	Unclear	No	Unclear	Yes	Yes	Unclear	Unclear	Fair
Holve, 2008	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Poor
Rodrigues, 2014	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Fair

Please see Appendix C. Included Studies for full study references.

Table F13. Quality assessment of systematic reviews of exercise

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
Bystrom, 2013	Yes	a. Yes; b. no	>2 databases through October 2011; no mention of "plus" sources	No	Not stated	Yes	No	Yes
Oesch, 2010	Yes	a. Yes; b. No	Yes , >2 databases through Aug 2008; checked refs	No	Not stated	Yes	No	Yes
van Middelkoop, 2010	Yes	a. Yes; b. Yes	Data bases through 2008 for CLBP only; unclear if additional sources	Cite Cochrane Back group strategy used - assume no restriction?	Cite Cochrane Back group strategy used - assume so?	Not explicitly; references provided	No	No

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
Bystrom, 2013	a. 10-point PEDro scale b. marginally - score out of 10 provided; areas of methodological concern for studies not described	No; no information on heterogeneity provided	Yes	a. Systematic review: Yes, however 1 author is also author of one of the included trials b. Individual studies: No	Unclear	Fair
Oesch, 2010	a. According to Juni b. Not by study	Metaregresion-NS Effect of specific exercise characteristics; sensitivity by study quality; funnel plot	Yes	a. Funding source stated b. No	Yes	Fair
van Middelkoop, 2010	a. Yes b. Yes	No	Yes	a. No b. No	Unclear	Fair

Please see Appendix C. Included Studies for full study references.

Table F14. Quality assessment of randomized controlled trials of exercise

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in All Groups
Albaladejo, 2010	Yes	Yes	Yes	No	No	Yes	Unclear	Unclear
Albert, 2012	Yes	No	Yes	No	No	Yes	Unclear	Unclear
Bronfort, 2011	Yes	Yes	Yes	No	No	Yes	Unclear	Yes
Garcia, 2013	Yes	Yes	Yes	No	No	Yes	Unclear	Unclear
George, 2008	Yes	No	No	No	No	Yes	Unclear	Unclear
Hagen, 2010	Yes	No	Yes	No	No	Yes	Unclear	Unclear
Hartvigsen, 2010	Unclear	Yes	Yes	No	No	Unclear	Unclear	Unclear
Helmhout, 2008	Yes	Unclear	No	No	No	Unclear	Unclear	Unclear
Henchoz, 2010	Unclear	Unclear	Yes	No	No	No	Unclear	No
Hofstee, 2002	Yes	No	No	No	No	No	No	Unclear
Hurley, 2015	Yes	Yes	Yes	No	No	Yes	Unclear	No
Jensen, 2012	Yes	Yes	Yes	No	No	Yes	Unclear	Yes
Kell, 2011	Unclear	Unclear	Yes	No	No	Unclear	Unclear	Unclear
Little, 2008	Yes	Yes	Yes	No	No	Yes	Unclear	Yes
Macedo, 2012	Yes	Yes	Yes	No	No	Yes	Unclear	Unclear
Machado, 2010	Yes	Yes	Yes	No	No	Yes	Unclear	Yes
Pengel, 2007	Yes	Yes	Yes	Unclear/ sham	No	Yes	No	Unclear

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in All Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Albaladejo, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Fair (but results reporting poor)
Albert, 2012	Yes	Yes	Yes	Yes	Yes	Unclear	Fair
Bronfort, 2011	Yes	Yes	Yes	Yes	Yes	Yes	Good
Garcia, 2013	Yes	Yes	Yes	Yes	Yes	Yes	Good
George, 2008	Yes	No	Yes	Yes	Yes	Unclear	Poor
Hagen, 2010	Yes	Yes	Yes	Yes	No	Unclear	Fair
Hartvigsen, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Helmhout, 2008	Yes	Yes	Yes	Yes	Yes	Unclear	Poor
Henchoz, 2010	Yes	Yes	Yes	Yes	No	Yes	Poor
Hofstee, 2002	Yes	Yes	Yes	Yes	No	Unclear	Poor
Hurley, 2015	Yes	No	Yes	Yes	Yes	Yes	Fair
Jensen, 2012	Yes	Yes	Yes	Yes	Yes	Yes	Good
Kell, 2011	No	Unclear	Yes	Unclear	No	Yes	Poor
Little, 2008	Yes	Yes	Yes	Unclear	Yes	Yes	Good
Macedo, 2012	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear/fair
Machado, 2010	Yes	Yes	Yes	Yes	Yes	Unclear	Fair
Pengel, 2007	Yes	Yes	Yes	Yes	Yes	Unclear	Fair

Please see Appendix C. Included Studies for full study references.

Table F15. Quality assessment of systematic reviews of Pilates

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
Wells, 2014	Yes	a. Yes; b. No	Yes, >2 databases including CINAHL, Cochrane Library, Scopus	No	Yes (Proquest - dissertations and theses; Nursing and Allied Health Source; hand search of bibliographies	Yes	No	Yes

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
Wells, 2014	Yes: Modified Guidelines for use of the McMasters Critical Appraisal Form for Quantitative Studies	No; no metaanalysis done; quality rating	No ; Study quality (high vs. low quality) described w/results; conclusions regarding pain short term - may be over stated;	a. Yes b. No	Unclear	Fair

Please see Appendix C. Included Studies for full study references.

Table F16. Quality assessment of randomized controlled trials of tai chi

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Hall, 2011	Yes	Yes	Yes	No	No	No	Unclear
Weifen, 2013	Unclear	Unclear	Yes	No	No	Yes	Unclear

Author, Year	Compliance Acceptable in All Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in All Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Hall, 2011	Yes	Yes	Yes	Yes	Yes	No	Yes	Fair
Weifen, 2013	Yes	No	Unclear	Yes	Unclear	No	Yes	Fair

Please see Appendix C. Included Studies for full study references.

Table F17. Quality assessment of systematic reviews of yoga

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
Cramer, 2013	Yes	a. Not stated explicitly; Stated used PRISMA and Cochrane methods b. Yes	January 2012: Medline, EMBASE, the Cochrane Library, PsycINFO, and CAMBASE	Yes	No	Yes	Yes - full text; reason with citation	Yes

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
Cramer, 2013	a. 2009 Updated Method Guidelines for Systematic Reviews in the Cochrane Back Review Group b. Yes	Yes; high vs. low ROB; if heterogeneity	Study quality considered; Conclusions regarding pain, disability are supported; HRQOL conclusions - seem to be downgraded more (short term) than rating scheme might suggest? Limited info on adverse events available, but conclude that Yoga not associated with serious adverse events	a. Systematic review: Yes b. Individual studies: No	Unclear	Good

Please see Appendix C. Included Studies for full study references.

Table F18. Quality assessment of randomized controlled trials of yoga

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Nambi, 2014	Yes	Unclear	Yes	No	Unclear	Unclear	Unclear
Saper, 2013	Yes	Unclear	No (But adjusted estimates for baseline differences were essentially the same as crude estimates)	No	Unclear	Yes	Yes use of other treatments overall: 53% (26/47) vs.. 61% (28/44); similar % for massage, PH, acupuncture, chiropractic, epidural injections

Author, Year	Compliance Acceptable in All Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in All Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Nambi, 2014	Unclear	Yes	Yes	Yes	Yes	No	unclear	Poor
Saper, 2013	No; attendance: 65% for once weekly class, 44% for twice weekly classes	Yes	Yes	Yes	Yes	Yes	Yes	Fair

Please see Appendix C. Included Studies for full study references.

Table F19. Quality assessment of systematic reviews of psychological therapies

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?
Henschke, 2010	Yes	a. Yes b. Yes	Yes	Yes	Unclear	Yes	Yes

Author, Year	Characteristics of the included studies provided?	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
Henschke, 2010	Yes	a. Yes b. Yes	No	Yes (yes)	a. Yes b. No	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F20. Quality assessment of randomized controlled trials of psychological therapy

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Kahn, 2014	Yes	Unclear	Unclear (age, sex, duration of pain NR, slight differences in pain and function at baseline)	Yes (statement that patients were blind to the study)	No (but blinding not possible for these interventions)	Yes (outcomes patient reported)	Unclear
Lamb 2010/2012	Yes	Yes	Yes	No	No (but blinding not possible for these interventions)	Yes	No (control group free to seek any additional care on their own; additional treatments received not reported)
Siemonsma, 2013	Yes	Yes	Yes	No	No (but blinding not possible for these interventions)	Yes	Yes
Vong, 2011	Yes	Unclear	Yes	Yes (patients told they would receive one of two types of conventional patient treatment but did not know anything about motivational enhancement therapy)	No (but blinding not possible for these interventions)	Yes (outcomes patient reported)	Yes

Table F21. Quality assessment of systematic reviews of multidisciplinary rehabilitation

Author, Year	Compliance Acceptable in All Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in All Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Kahn, 2014	Unclear	Yes	Yes (100%)	Yes	Unclear	No	Yes	Fair
Lamb 2010/2012	No Intervention group: 63% (294/468) Control group: 100% (233/233)	Yes	Yes (85% in both groups)	Yes	No	Yes	Yes	Fair
Siemonsma, 2013	No Intervention group: 81.7% Control group (waiting list, no interventions permitted): Unclear	Yes	Yes (89% was lowest f/u reported (for activity-specific pain, 139/156)	Yes	No (Their fig 1 makes it look like all pts randomized were included in the primary analysis but the paragraph under "Primary Outcome" contradicts this.)	Yes	Yes	Fair
Vong, 2011	No Intervention group: 62% Control group: 63% (% of patients who participated fully)	Yes	yes (86%)	Yes	No (they said they used ITT but 12 patients who were randomized did not receive treatment and were excluded from all analyses)	No	Yes	Fair

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
Kamper, 2014	Yes	a. Yes b. Yes	Yes	Yes	No	Yes	No	Yes

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic review b) Individual studies	Multidisciplinary systematic review team?	Quality Rating
Kamper, 2014	a. Yes b. Yes	Yes	Yes	a. Yes b. No	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F22. Quality assessment of randomized controlled trials of multidisciplinary rehabilitation

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Eisenberg, 2012	Yes	Unclear	Yes	No	No	Unclear	NA
Gatchel, 2003	Yes	Unclear	Unclear	No	No	Unclear	NA
Monticone, 2014	Yes	Unclear	Yes	Yes	No	Unclear	NA

Author, Year	Compliance Acceptable in All Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in All Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Eisenberg, 2012	Yes	Yes	Yes	Yes	Yes	No	Unclear	Good
Gatchel, 2003	Yes	No	NA	Yes	Unclear	Yes	Unclear	Fair
Monticone, 2014	Yes	Yes	Yes	Yes	Yes	No	Unclear	Good

Please see Appendix C. Included Studies for full study references.

Table F23. Quality assessment of systematic reviews of acupuncture

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
Lam, 2013	Unclear	a. Yes b. Yes	Yes	Yes	No	Yes	No	Yes
Lee, 2013	Unclear	a. Yes b. Yes	Yes	Yes	Yes	Yes	No	Yes

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
Lam, 2013	a. Yes b. Yes	No	Unclear	a. Yes b. No	No	Fair
Lee, 2013	a. Yes b. Yes	Yes	Yes	a. Yes b. No	No	Fair

Please see Appendix C. Included Studies for full study references.

Table F24. Quality assessment of randomized controlled trials of acupuncture

Author, Year	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Patients masked?	Care provider masked?
Cho, 2013	Yes	Yes	Yes	Yes	Yes	No
Hasagawa, 2014	Yes	Yes	Yes	Yes	Yes	No
Vas, 2012	Yes	Yes	Yes	Yes	Yes (for acupuncture and sham groups only)	No
Yun, 2012 (back points)	Yes	Unclear, but likely ok - just says "central randomization with random block sizes"	Yes	Yes	Yes (only for acupuncture groups, not for usual care group)	No
Weiss, 2013	Unclear	Unclear	Yes	Yes	Unclear	Unclear

Author, Year	Outcomes assessors masked?	Attrition and withdrawals reported?	Attrition acceptable and comparable?	Analyze people in the groups in which they were randomized	Primary outcome specified and reported?	Other issues	Quality Rating
Cho, 2013	Yes	Yes	Yes	Yes	Yes	None	Good
Hasagawa, 2014	Yes	Yes	Yes	Yes	Yes	None	Good
Vas, 2012	Yes	Yes	Yes	Yes	Yes	None	Good
Yun, 2012 (back points)	Yes	Yes	Yes	Yes	Yes	None	Fair
Weiss, 2013	Unclear	Yes	Yes	Yes	Unclear	Exploratory only	Poor

Please see Appendix C. Included Studies for full study references.

Table F25. Quality assessment of systematic reviews of massage

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?
Furlan, 2010	Yes	a. Yes b. Yes	Yes	Yes	Yes	Yes	Yes

Author, Year	Characteristics of the included studies provided?	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
Furlan, 2010	Yes	a. Yes b. Yes	Yes	Yes	a. Yes b. No	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F26. Quality assessment of randomized controlled trials of massage

Author, Year	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?
Ajimsha, 2014	Unclear	No	Yes	Yes	Yes	No
Borges, 2014	Yes	Unclear	Yes	Yes	Unclear	No
Cherkin, 2011	Yes	Yes	Yes	Yes	Yes - for the two massage groups only	No
Kong, 2012	Yes	Yes	Yes	Yes	Yes	No
Romanowski, 2012	Unclear	Unclear	Yes	Yes	Yes	No
Sritooma, 2014	Yes	Unclear	Yes	Yes	No	No
Zhang, 2015	No	No	Yes	Yes	Yes	No
Zheng, 2012	Yes	Unknown	Yes	Yes	Unclear	Unclear

Author, Year	Patient masked?	Attrition and withdrawals reported?	Attrition acceptable and comparable?	Analyze people in the groups in which they were randomized	Primary outcome specified and reported?	Other issues?	Quality Rating
Ajimsha, 2014	Yes	Yes	Yes	Yes	Yes	None	Fair
Borges, 2014	Unclear	Yes	Yes	Yes	Yes	None	Fair
Cherkin, 2011	Yes	Yes	Yes	Yes	Yes	None	Good
Kong, 2012	Yes	Yes	Yes	Yes	Yes	None	Good
Romanowski, 2012	Yes	Yes	Yes	Yes	Yes	None	Poor
Sritooma, 2014	No - not described	Yes	Yes	Yes	Yes	None	Fair
Zhang, 2015	Unclear	Yes	Yes	Yes	Yes	None	Fair
Zheng, 2012	Unclear	Yes	Yes	Yes	Yes	None	Fair

Please see Appendix C. Included Studies for full study references.

Table F27. Quality assessment of systematic reviews of spinal manipulation

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?
Rubinstein, 2011	Yes	a. Yes b. Yes	Yes	Yes	Yes	Yes	Yes
Rubinstein, 2012	Yes	a. Yes b. Yes	Yes	Unclear	Yes, but excluded from analysis	Yes	Yes

Author, Year	Characteristics of the included studies provided?	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
Rubinstein, 2011	Yes	a. Yes b. Yes	Yes	Yes	a. Yes b. Yes	Yes	Good
Rubinstein, 2012	Yes	a. Yes b. Yes	Yes	Yes	a. Yes b. Yes	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F28. Quality assessment of randomized controlled trials of SMT

Author, Year	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Patient masked?	Care provider masked?
Balthazard, 2012	Yes	Unclear	Yes - although pain slightly higher in sham group (53 vs. 62) but not statistically significant	Yes	No	No
Bicahlo, 2010	Yes	Unclear	Yes	Yes	No	No
Bronfort, 2004	Yes	No	Yes	Yes	No	No
Bronfort, 2011	Yes	Yes	Yes	No	No	Yes
Bronfort, 2014	Yes - minimization used, not randomization	Yes	Yes	Yes	No	No
Burton, 2000	Yes	Yes	Yes	Yes	No	No
Cecchi, 2010	Yes	Unclear	No - sick leave higher in back school group compared to other groups	Yes	No	No
De Oliviera, 2013	Yes	Yes	Yes	Yes	Yes	No
Goertz, 2013	Yes	Yes	Yes	Yes	No	No
Haas, 2014	Yes	Yes	Yes	Yes	No	No
Paatelma, 2008	Yes	Yes	Yes	Yes	No	No
Petersen, 2011	Yes	Yes	Yes	Yes	No	No
Santilli, 2006	Yes	Yes	Yes	Yes	Yes	Yes

Author, Year	Outcomes assessor masked?	Attrition and withdrawals reported?	Attrition acceptable and comparable?	Analyze people in the groups in which they were randomized	Primary outcome specified and reported?	Other issues	Quality Rating
Balthazard, 2012	Unclear	Yes	Yes	Yes	Yes	None	Fair
Bicahlo, 2010	Unclear	Yes	Yes	Yes	Yes	Incomplete reporting of outcomes (function)	Fair
Bronfort, 2004	No	No	Unclear	Yes	No	Primary outcome not specified	Poor
Bronfort, 2011	Unclear	Yes	Yes	Yes	Yes	Yes	Good
Bronfort, 2014	No	Yes	Yes	Yes	Yes	None	Fair - not blinded
Burton, 2000	No	Yes	Unclear	Yes	Yes	None	Poor
Cecchi, 2010	Unclear	Yes	Yes	Yes	Yes	None	Fair
De Oliviera, 2013	Yes	Yes	Yes	Yes	Yes	None	Good
Goertz, 2013	Yes	Yes	No - low followup rate in the SMC group	Yes	Yes	None	Fair
Haas, 2014	Yes	Yes	Yes	Yes	Yes	None	Good
Paatelma, 2008	Yes	Yes	No - high drop out rate	Yes	Yes	None	Fair
Petersen, 2011	Yes	Yes	Yes	Yes	Yes	None	Good
Santilli, 2006	Unclear	Yes	Yes	Yes	Yes	None	Good

Author, Year	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Patient masked?	Care provider masked?
Schneider, 2015	Yes	Yes	Yes	Yes	No	No
Senna, 2011	Yes	Yes	Yes	Yes	Yes	No
Von Heymann, 2013	Yes	Yes	Yes	Yes	Yes	No

Author, Year	Outcomes assessor masked?	Attrition and withdrawals reported?	Attrition acceptable and comparable?	Analyze people in the groups in which they were randomized	Primary outcome specified and reported?	Other issues	Quality Rating
Schneider, 2015	Yes	Yes	Yes	Yes	Yes	None	Good
Senna, 2011	Yes	Yes	No - low followup rate in sham SMT group	Yes	Yes	None	Fair
Von Heymann, 2013	Yes	Yes	No - low followup rate	Yes	Yes	Unclear intervention (Single treatment?), small sample size with high drop out rate	Fair

Please see Appendix C. Included Studies for full study references.

Table F29. Quality assessment of systematic reviews of ultrasound

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
Ebadi, 2014	Yes	Yes/Yes	Yes	Yes	Yes	Yes	Yes	Yes

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
Ebadi, 2014	Yes	Yes (considered in SOE analyses)	Yes	Yes/No	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F30. Quality assessment of randomized controlled trials of ultrasound

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Bronfort, 2011	Yes	Yes	Yes	No	No	Yes	Unclear
Fiore, 2011	Yes	Yes	Unclear	No	No	Yes	Unclear
Goren, 2010	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Licciardone, 2013	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Unlu, 2008	Unclear	Unclear	Yes	No	No	Unclear	Unclear

Author, Year	Compliance Acceptable in all Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality (Cochrane Back Group)
Bronfort, 2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good
Fiore, 2011	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair
Goren, 2010	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair
Licciardone, 2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good
Unlu, 2008	Unclear	No	Unclear	Yes	Unclear	Unclear	Unclear	Poor

Please see Appendix C. Included Studies for full study references.

Table F31. Quality assessment of systematic reviews of TENS

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
van Middelkoop, 2011	Yes	a. Yes b. Yes	Yes	Yes	Unclear	Yes	No	Yes

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
van Middelkoop, 2011	a. Yes b. Yes	Unclear	Yes	a. Yes b. Yes	Unclear	Good

Please see Appendix C. Included Studies for full study references.

Table F32. Quality assessment of randomized controlled trials of TENS

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in All Groups
Buchmuller, 2012	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Facci, 2011	Yes	Yes	No; significant difference between TENS and control in pain intensity at baseline (p=0.009)	Yes	Unclear	Yes	Yes	Yes
Shimoji, 2007	Unclear	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes
Tsukayama, 2002	Yes	Unclear	Yes	No	No	Yes	Yes	Yes

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Buchmuller, 2012	Yes	No	Yes	Unclear	Unclear	Unclear	Fair
Facci, 2011	Yes	Yes	Yes	Yes	Unclear	Unclear	Good
Shimoji, 2007	No	Unclear	Yes	Unclear	Unclear	Unclear	Fair
Tsukayama, 2002	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair

Please see Appendix C. Included Studies for full study references.

Table F33. Quality assessment of randomized controlled trials of electrical stimulation

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in all Groups
Durmus, 2009	Unclear	Unclear	Yes	No	No	Unclear	Unclear	Unclear
Durmus, 2010	Unclear	Unclear	Yes	No	No	Unclear	Unclear	Unclear
Glaser, 2001	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Unclear
Moore, 1997	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Unclear
Pope, 1994	Yes	Unclear	Unclear	No	No	Yes	Unclear	No

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality (Cochrane Back Group)	Comments
Durmus, 2009	No	Unclear	Yes	Unclear	Unclear	Yes	Poor	Some outcomes assessed as means and others as medians, no explanation provided
Durmus, 2010	Yes	Yes	Yes	No	Unclear	Yes	Poor	Some outcomes assessed as means and others as medians, no explanation provided
Glaser, 2001	Yes	No	Yes	No	Unclear	Yes	Poor	Very high loss to followup
Moore, 1997	Yes	Yes	Yes	No	Unclear	Yes	Poor	Crossover design, results of first intervention not reported and carryover effects not assessed
Pope, 1994	Yes	Yes	Yes	Unclear	Yes	Yes	Fair	

Please see Appendix C. Included Studies for full study references.

Table F34. Quality assessment of randomized controlled trials of PENS

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Hamza, 1999	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Pérez-Palomares, 2010	Yes	Unclear	Unclear	No	No	Yes	Unclear
Weiner, 2008	Yes	Unclear	Yes	Yes	No	Yes	Unclear

Author, Year	Compliance Acceptable in all Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Hamza, 1999	Unclear	Yes	No	Yes	Unclear	Unclear	Unclear	Poor
Pérez-Palomares, 2010	Unclear	Yes	Yes	Yes	Unclear	Unclear	Unclear	Poor
Weiner, 2008	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Fair

Please see Appendix C. Included Studies for full study references.

Table F35. Quality assessment of randomized controlled trials of interferential therapy

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Lara-Palomo, 2013	Yes	Yes	Yes	No	No	Unclear	Unclear

Author, Year	Compliance Acceptable in all Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Lara-Palomo, 2013	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Fair

Please see Appendix C. Included Studies for full study references.

Table F36. Quality assessment of systematic reviews of heat-cold

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
French, 2006 Updated in French, 2011	Yes	a. Yes b. Yes	Yes	Unclear	Unclear	Yes	Yes (no reasons for exclusion provided)	Yes

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
French, 2006 Updated in French, 2011	a. Yes b. Yes	No	Yes	a. Yes b. No	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F37. Quality assessment of randomized controlled trials of heat-cold

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in All Groups
Dehgan, 2014	Unclear	Unclear	Unclear	No	Unclear	Unclear	Unclear	Unclear
Kettenmann, 2007	Unclear	Unclear	Yes	No	Unclear	Unclear	Yes	Unclear
Stark, 2014	Unclear	Unclear	Yes	No	Unclear	Unclear	Yes	Unclear
Tao, 2005	Unclear	Unclear	Yes	No	Unclear	Unclear	Unclear	Unclear

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality
Dehgan, 2014	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair
Kettenmann, 2007	Yes	No	Yes	No	Unclear	Unclear	Fair
Stark, 2014	No	Unclear	Yes	Yes	Yes	Unclear	Fair
Tao, 2005	No	Unclear	Yes	Unclear	Unclear	Unclear	Poor

Please see Appendix C. Included Studies for full study references.

Table F38. Quality assessment of randomized controlled trials of LLLT

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in All Groups
Ay, 2010	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes
Djavid, 2007	Unclear	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes
Hsieh, 2014	Yes	Yes	Yes	Yes	No	Unclear	Unclear	Unclear
Jovicic, 2012	Unclear	Unclear	Yes	Yes	Unclear	Unclear	Yes	Yes
Konstantinovic, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Vallone, 2014	Yes	Yes	Unclear	Yes	Unclear	Unclear	Yes	Unclear

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Ay, 2010	Yes	Yes	Yes	Yes	Unclear	Unclear	Good
Djavid, 2007	Yes	Yes	Yes	No	Unclear	Unclear	Fair
Hsieh, 2014	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair
Jovicic, 2012	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair
Konstantinovic, 2010	Yes	Yes	Yes	Yes	Unclear	Unclear	Good
Vallone, 2014	No	Unclear	Yes	Unclear	Unclear	Unclear	Fair

Please see Appendix C. Included Studies for full study references.

Table F39. Quality assessment of randomized controlled trials of diathermy

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Ahmed, 2009	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	Unclear
Shakoor, 2008	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	Yes

Author, Year	Compliance Acceptable in all Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Ahmed, 2009	Unclear	No	Unclear	Yes	No	Unclear	Unclear	Poor
Shakoor, 2008	Unclear	No	Unclear	Yes	No	Unclear	Unclear	Poor

Please see Appendix C. Included Studies for full study references.

Table F40. Quality assessment of systematic reviews of lumbar supports

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
van Duijvenbode, 2011	Yes	a. Yes b. Yes	Yes	Yes	Unclear	Yes	Yes	Yes

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
van Duijvenbode, 2011	a. Yes b. Yes	Yes	Yes	a. Yes b. No	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F41. Quality assessment of randomized controlled trials of lumbar support

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar
Calmels, 2009	Yes	Unclear	Yes (reported in text; data not shown for some characteristics)	No	No	Unclear	Yes
Morrisette, 2014	Yes	Yes	Yes	No	No	Unclear	Unclear
Oleske, 2007	Yes	Yes	Yes	No	No	Yes	Yes
Sato, 2012	Yes	Unclear	Yes (reported in text; data not shown)	No	No	Unclear	Yes

Author, Year	Compliance Acceptable in all Groups	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment In All Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Calmels, 2009	Unclear	Yes	Yes	Yes	No	Unclear	Unclear	Fair
Morrisette, 2014	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair
Oleske, 2007	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair
Sato, 2012	Unclear	Yes	Yes	Yes	No	Unclear	Unclear	Fair

Please see Appendix C. Included Studies for full study references.

Table F42. Quality assessment of systematic reviews of traction

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction? a. Study selection b. Data abstraction	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?
Wegner, 2013	Yes	a. Yes b. Yes	Yes	Yes	Yes	Yes	Yes	Yes

Author, Year	Scientific quality of included studies: a. Assessed? b. Documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence? (Was study quality considered in the synthesis?)	Conflict of interest stated? a) Systematic Review b) Individual Studies	Multidisciplinary systematic review team?	Quality Rating
Wegner, 2013	a. Yes b. Yes	Yes	Yes	a. Yes b. No	Yes	Good

Please see Appendix C. Included Studies for full study references.

Table F43. Quality assessment of randomized controlled trials of traction

Author, year	Randomization	Concealed treatment allocation	Baseline group similarity	Patient blinded	Care provider blinded	Outcome assessor / Data analyst blinded	Cointerventions avoided or similar	Compliance acceptable in all groups
Diab, 2012 and Diab, 2013	Yes	Yes	Yes	No	No	No	Yes	Yes
Moustafa, 2013	Yes	Yes	Yes	No	Unclear	Unclear	Yes	Yes
Prasad, 2013	Unclear	Unclear	Yes	No	Yes	Unclear	Yes	Unclear

Author, year	Attrition reported	Attrition acceptable	Timing of outcome assessment in all groups similia	Intention-to-treat analysis	Is there a registered or published protocol	Avoidance of selective outcomes	Quality Rating
Diab, 2012 and Diab, 2013	Yes	Yes	Yes	Unclear	Yes	Yes	Fair
Moustafa, 2013	Yes	Yes	Yes	Yes	Unclear	Unclear	Fair
Prasad, 2013	Yes	No	Yes	No	Unclear	Unclear	Poor

Please see Appendix C. Included Studies for full study references.

Table F44. Quality assessment of randomized controlled trials of taping

Author, Year	Randomization	Concealed Treatment Allocation	Baseline Group Similarity	Patient Blinded	Care Provider Blinded	Outcome Assessor / Data Analyst Blinded	Cointerventions Avoided or Similar	Compliance Acceptable in All Groups
Bae, 2013	Unclear	Unclear	Yes	No	No	Unclear	Yes	Unclear
Castro-Sanchez, 2012	Yes	Yes	P	Yes	No	Yes	Unclear	Yes
Chen, 2012	Unclear	Unclear	Yes	No	No	Yes	Unclear	Unclear
Kachanathu, 2014	Unclear	Unclear	Unclear	No	No	Unclear	Unclear	Unclear
Paolini, 2011	Yes	Unclear	Yes	No	No	Unclear	Unclear	Unclear
Silva Parreira, 2014	Yes	Yes	Yes	Yes	No	Yes	Unclear	Yes

Author, Year	Attrition Reported	Attrition Acceptable	Timing of Outcome Assessment in all Groups Similar	Intention-to-Treat Analysis	Is There a Registered or Published Protocol	Avoidance of Selective Outcomes Reporting	Quality Rating
Bae, 2013	No	Unclear	Yes	Yes	Unclear	Yes	Fair
Castro-Sanchez, 2012	Yes	Yes	Yes	Yes	Unclear	Yes	Good
Chen, 2012	Yes	Yes	Yes	Yes	Unclear	Yes	Fair
Kachanathu, 2014	No	Unclear	Yes	Unclear	Unclear	Yes	Poor
Paolini, 2011	No	Unclear	Yes	Unclear	Unclear	Yes	Fair
Silva Parreira, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Good

Please see Appendix C. Included Studies for full study references.

Appendix G. Outcome Measures

Table G1. Outcome measures

Outcome Measure	Measure Description	Score Range and Direction	Section of Current Report
SF-12® Health Survey	• Short form survey with 12 questions from the SF-36 Health Survey • Two scales: mental and physical functioning and overall health-related-quality of life • 4-week recall of symptoms	• Scores range from 0 to 100 (zero score indicates the lowest level of health and 100 indicates the highest level of health)	Antiseizure Medications; Opioids; Psychological Therapies
Athens Insomnia Scale (AIS)	• Assesses the severity of insomnia; evaluates sleep onset, night and early-morning waking, sleep time, sleep quality, frequency and duration of complaints, distress caused by the experience of insomnia, and interference with daily functioning.	• Likert-type scales to show how severely certain sleep difficulties have affected them during the past month. • Scores range from 0 (meaning that the item in question has not been a problem) to 3 (indicating more acute sleep difficulties)	Antidepressants
Beck Depression Inventory (BDI)	The BDI is a 21-item measure of depressive symptomatology, including items assessing both cognitive and somatic complaints associated with depression. Survey is completed by patient	Scored on 0 to 3 scale Minimal: 0 Severe: 3 Each item represents a symptom or belief that is rated from 0 to 3 in terms of intensity. The BDI consists of 21 groups of statements, and after reading each group of statements, participants mark the statement in each group that best describes the way they have been feeling over the previous week.	Electrical Stimulation
BPI- Short Form (BPI-SF)	A 9 item self-administered questionnaire used to evaluate the severity of a patient's pain and the impact of this pain on the patient's daily functioning	Rating of: worst, least, average, and current pain intensity, list current treatments and their perceived effectiveness, and rate the degree that pain interferes with general activity, mood, walking ability, normal work, relations with other persons, sleep, and enjoyment of life on a 10 point scale. (Higher score indicates higher level of pain)	Antiseizure Medications
Brief Pain Inventory (BPI)	To assess the severity of pain and the impact of pain on daily functions	The BPI assesses pain at its “worst,” “least,” “average,” and “now” (current pain). In clinical trials, the items “worst” and “average” have each been used singly to represent pain severity. A composite of the four pain items (a mean severity score) is sometimes presented as supplemental information.	Antidepressants; Opioids
Center for Disease Control and Prevention health-related quality of life Questionnaire (CDC HRQOL– 4)	4 item questionnaire to measure General health and the number of recent days when a person was physically unhealthy, mentally unhealthy, or limited in usual activities.	Responses to questions 2 and 3 are combined to calculate a summary index of overall unhealthy days, with a logical maximum of 30 unhealthy days. Healthy days are the positive complementary form of unhealthy days.	Yoga

Outcome Measure	Measure Description	Score Range and Direction	Section of Current Report
Chronic Pain Acceptance Questionnaire (CPAQ)	A 20-item inventory measuring acceptance of pain	Two subscales: activity engagement (AE) and pain willingness (PW). Participants rate items on a scale from 0 (never true) to 6 (always true). Higher scores denote greater activity engagement and pain willingness (pain willingness items are reverse scored	Psychological Therapies
Chronic Pain Self Efficacy Scale (PSEQ)	A 10-item questionnaire to assess the confidence people with ongoing pain have in performing activities while in pain.	A 7-point Likert scale (0-6) 0= not at all confident 6= completely confident A total score ranging from 0 to 60 is calculated by adding the scores for each item. Higher score reflect stronger self-efficacy beliefs	Psychological Therapies
Clinical Global Impressions of Severity Scale (CGI-S)	Provides an overall clinician-determined summary measure that takes into account all available information, including a knowledge of the patient's history, psychosocial circumstances, symptoms, behavior, and the impact of the symptoms on the patient's ability to function	Scale: 1-7 Ranging from 1 (normal) to 7 (extremely ill)	Antidepressants
Dallas Pain Questionnaire (DPQ)	Assess the amount of chronic spinal pain that affects four aspects of the patients' lives: Daily activities, work-leisure activities, anxiety-depression, and social interest/	A 16-item visual analog scale, with each item broken down into 5 to 8 small segments; each item contains its own visual analog scale. Each segment is marked with an 'x' by the subject – this indicates where their pain impact falls on that continuum. The scales range from "no pain" or 0%, to "some" pain, to "all the time" and 100% impact of pain. Each item in assigned a value, then individual rating are summed and multiplies bay a constant for a percentage of pain impact for each of the four aspects of the patients' lives.	TENS
EuroQoL (EQ-5D)	Designed for the collection of health state values using a VAS rating scale. It's only distributed in instances where researchers specifically wish to elicit valuations of health.	A vertical 20 cm visual analogue scale with the end points labelled best imaginable health state at the top and worst imaginable health state at the bottom having numeric values of 100 and 0 respectively.	Antidepressants; Antiseizure Medications; Interferential therapy; Opioids; Psychological Therapies
Fear Avoidance Beliefs Questionnaire (FABQ)	Measures patients' fear of pain and consequent avoidance of physical activity because of their fear	This questionnaire consists of 16 items, with 2 subscales, the Work Subscale and the Physical Activity Subscale; each item is scored from 0-6. Higher scores on the FABQ are indicative of greater fear and avoidance beliefs.	Psychological Therapies

Outcome Measure	Measure Description	Score Range and Direction	Section of Current Report
Functional Rating Index (FRI)	An instrument specifically designed to quantitatively measure the subjective perception of function and pain of the spinal musculoskeletal system in a clinical environment	A 10-item assessment with a 5 point scale ranked by the patient; 0 = no pain or full ability to function; 4 = worst possible pain and/or unable to perform this function at all. The index score is achieved by simply summing up the equally weighted scores, dividing by the total number of possible points, and multiplying by one hundred percent. The range of scores is zero percent (no disability) to 100% (severe disability). {(total score/40) x 3 100%}	Ultrasound
Geriatric Depression Scale (GDS)	Developed as a basic screening measure for depression in older adults	normal-0-9; mild depressives-10-19; severe depressives-20-30	PENS
The Hospital Anxiety and Depression Scale (HADS)	Instrument for detecting states of depression and anxiety in the setting of an hospital medical outpatient clinic	There are 14 items; 7 regarding depression and 7 regarding anxiety. Score for each subscale (anxiety and depression) can range from 0-21 with scores categorized as follows: normal (0-7), mild (8-10), moderate (11-14), severe (15-21). Scores for the entire scale (emotional distress) range from 0-42, with higher scores indicating more distress	Antiseizure Medications
Illness Perceptions Questionnaire-Revised (IPQ-R)	An 84-item self-completed instrument developed to provide a quantitative measurement of the components of illness representations, as described by Leventhal's Common-Sense Model (CSM) of self regulation.	Divided into three sections: identity subscale (14 symptoms), causal subscale (18 causes), and a third section which contains 7 subscales, including consequences, timeline acute/chronic and cyclical, personal and treatment control/cure, illness coherence, and emotional representations. For the identity subscale, patients respond by circling 'yes' or 'no' to each question. For the causal subscale, patients respond to each of the listed causes using a 5-point Likert style scale, ranging from strongly disagree to strongly agree. The third section (7 subscales) is scored by summing responses to each item is on a 5-point Likert style scale, ranging from strongly disagree to strongly agree. All items for each of the subscales are summed to give an overall score.	Psychological Therapies
Isotechnologies B-200	A computerized isodynamic system providing information about the functional characteristics of the low back	Parameters measured included: Range of motion, isometric torque, and isodynamic velocities in all three major axes.	LLLT
Japanese Orthopedic Association (JOA)	An objective assessment scale quantitating the severity of the spondylotic myelopathy.	Results are scored on a 23 point scale. Total is based on the sum 2 sub scales: 'Subjective systems' (0-9); (ADL) Activities of daily living, (0-14). Higher point scores indicate improved symptoms.	Lumbar Supports

Outcome Measure	Measure Description	Score Range and Direction	Section of Current Report
Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)	Tool used in identifying patients in whom neuropathic mechanisms dominate their pain experience.	If score < 12, neuropathic mechanisms are unlikely to be contributing to the patient's pain. If score ≥ 12, neuropathic mechanisms are likely to be contributing to the patient's pain	Antiseizure Medications
Low Back Pain Outcome Instrument (LBPOI)	A comprehensive back pain Questionnaire designed to be applicable to a varied population of patients with back pain	6 summative subscales based on 34 items: back pain, neurogenic symptoms, job exertion, job stress/satisfaction, expectations for treatment, and additionally the Short Form 36 (SF36) mental health subscale Discrete, linear values are calculated for each Subscale. The numeric range of response is 1 through 6.	Electrical Stimulation
McGill Pain Questionnaire Pain Rating Index (MPQ)	consists primarily of 3 major classes of word descriptors--sensory, affective and evaluative--that are used by patients to specify subjective pain experience	(0 to 78) minimum pain score: 0 (would not be seen in a person with true pain) maximum pain score: 78 The higher the pain score the greater the pain	Interferential therapy; PENS; TENS
McGill Pain Questionnaire Pain Rating Index- Short-Form (SF-MPQ)	A self-report measure of pain quality consisting of 15 descriptors of pain, representing both the sensory (e.g., 'throbbing', 'aching') and affective (e.g., 'sickening', 'fearful') components of pain quality. Participants are asked to indicate the extent to which each descriptor describes the severity of their pain experience.	Responses are made on a four-point Likert scale, ranging from 0 (none) to 3 (severe). Three subscale scores are calculated: sensory, affective and total pain responses	Antiseizure Medications; Psychological Therapies
Medical Outcome Study Sleep Scale (MOS Sleep Scale)	Measures six dimensions of sleep, including initiation, maintenance, quantity, adequacy, somnolence, and respiratory impairments	Ten of the scale's 12 items are scored using a six-point response scale, one item uses a five-point Likert scale, and sleep quantity is an open-ended question recording the actual number of hours slept. Sleep quantity are recalibrated on a 0–100 scale that represents the percentage of a particular sleep domain; sleep quantity is recorded as 0–24 h. Higher scores for the domains of sleep disturbance, somnolence and the sleep indices indicate worse sleep problems, whereas lower scores for sleep quantity and sleep adequacy indicate worse sleep problems	Antiseizure Medications
Multidimensional Pain Inventory (Pain Severity Scale)	A self-report instrument that measures the impact of pain on an individual's life. Pain Severity Scale, a sub-scale of the Multidimensional Pain Inventory focuses on the average pain the subject has had in the past week and the corresponding Amount of suffering experienced.	Rated on a 7-point scale (0-6). Scale scores are computed by summing over all items and then the mean is composed based on the number of scale items.	PENS

Outcome Measure	Measure Description	Score Range and Direction	Section of Current Report
Oswestry disability index (ODI)	A self-administered outcome-measure questionnaire for low back pain in a hospital setting; divided into ten sections designed to assess limitations of various activities of daily living	For each section of six statements the total score is 5; if the first statement is marked the score = 0; if the last statement is marked it = 5. Intervening statements are scored according to rank. If more than one box is marked in each section, take the highest score. If all 10 sections are completed the score is calculated as follows: total scored/ 50 (total possible score) x 100= %	Antiseizure Medications; Electrical Stimulation; Interferential therapy; Opioids; PENS; Taping; Traction; Ultrasound
Pain Disability Index (PDI)	A seven-item self-report measure that assesses disability in seven areas: family, occupation, sexual relations, social activities, recreation, self-care and life support. Participants are asked to indicate their disability in each of the seven areas.	Each of the seven subscales is graded from zero to 10; zero (no disability) to 10 (total disability). A total disability score is determined by summing the numerical ratings of the seven disability scales (range zero to 70).	Acetaminophen; Electrical Stimulation
Pain Self Efficacy Scale (PSEQ)	A 10-item questionnaire to assess the confidence people with ongoing pain have in performing activities while in pain.	A 7-point Likert scale (0-6) 0= not at all confident 6= completely confident A total score ranging from 0 to 60 is calculated by adding the scores for each item. Higher score reflect stronger self-efficacy beliefs	Psychological Therapies
Patient Specific Functional Scale (PSFS)	Patients rate their ability to complete an activity on a 11-point scale at a level experienced prior to injury or change in functional status	mean, 0-10 (0" represents “unable to perform” "10" represents “able to perform at prior level”)	Acetaminophen
Patients' Global Impression (PGIC)	A self-reported measure which reflects a patient's belief about the efficacy of treatment	A 7 point scale depicting a patient's rating of overall improvement. (Patients rate their change as “very much improved,” “much improved,” “minimally improved,” “no change,” “minimally worse,” “much worse,” or “very much worse.”)	Antidepressants
Pittsburgh Sleep Quality Index (PSQI)	An instrument used to measure the quality and patterns of sleep in the older adults.	Based on a 0 to 3 scale, whereby 3 reflects the negative extreme on the Likert Scale. A global sum of “5”or greater indicates a “poor” sleeper	PENS
Profile of Mood States (POMS)	To assess affective mood state fluctuation	Measures six identifiable mood or affective states: 1) Tension-Anxiety 2) Vigor-Activity 3) Depression-Dejection 4) Fatigue-Inertia 5) Anger-Hostility 6) Confusion-Bewilderment; Requires respondents to indicate how well each item describes their mood over the past week using a five-point scale (0-4) ranging from “not at all” to “extremely.”	Antidepressants
Quebec Back Pain disability scale (QBPDS)	A condition-specific questionnaire developed to measure the level of functional disability for patients with low back pain	There are 6 answer categories, measured by using a Likert scale from 0-5 (0 = no effort, 5 = not able to)	Opioids; Psychological Therapies

Outcome Measure	Measure Description	Score Range and Direction	Section of Current Report
Roland Morris Back Pain disability questionnaire (RMDQ)	A self-administered disability questionnaire designed for back pain.	A 24 item questionnaire, with and individual's score ranging from 0 (no disability) to 24 (maximum disability).	Acetaminophen; Antidepressants; Antiseizure Medications; Benzodiazepine; Corticosteroids; Interferential therapy; LLLT; Opioids; PENS; Psychological Therapies; Taping; TENS; Traction; Ultrasound;
Schober test	Assesses the amount of lumbar flexion.	A mark is made at the level of the posterior iliac spine on the vertebral column, i.e. approximately at the level of L5. The examiner then places one finger 5cm below this mark and another finger at about 10cm above this mark. The patient is then instructed to touch his toes. If the increase in distance between the two fingers on the patients spine is less than 5cm then this is indicative of a limitation of lumbar flexion.	LLLT
SF12 Mental score (MCS-12)	The SF-12 is a multipurpose short form survey with 12 questions, all selected from the SF-36 Health Survey The questions are combined, scored, and weighted to create two scales that provide glimpses into mental functioning and overall health-related-quality of life	mean, 0-100 (zero score indicates the lowest level of health measured by the scales and 100 indicates the highest level of health)	Acetaminophen
SF12 Physical score (PCS-12)	The SF-12 is a multipurpose short form survey with 12 questions, all selected from the SF-36 Health Survey The questions are combined, scored, and weighted to create two scales that provide glimpses into physical functioning and overall health-related-quality of life	mean, 0-100 (zero score indicates the lowest level of health measured by the scales and 100 indicates the highest level of health)	Acetaminophen
Short Form-36 (SF-36)	36 item questionnaire which measures Quality of Life (QoL) across eight domains, which are both physically and emotionally based	0–100 (higher score indicates worse disability)	Antidepressants; Electrical Stimulation; Antidepressants; Electrical Stimulation; Interferential therapy; Opioids; PENS; Psychological Therapies; TENS; Traction; Ultrasound; Yoga
Short Opioid Withdrawal Scale (SOWS)	A 10 item scale as a measure of the opiate withdrawal response.	Four point scale: (0) none to (3) severe.	Opioids

Outcome Measure	Measure Description	Score Range and Direction	Section of Current Report
State-trait Anxiety Inventory (STAI)	Measure of trait and state anxiety It can be used to diagnose anxiety and to distinguish it from depressive syndromes.	20 items for assessing trait anxiety and 20 for state anxiety 4-point scale. Higher score indicates greater anxiety.	Yoga
Swiss Spinal Stenosis Questionnaire (SSS)	A disease-specific self-report outcome instrument designed to complement generic measures of lumbar spine disability and health status in patients with lumbar spinal stenosis.	Symptom severity scale: the range of the scales: 1 to 5 (higher score indicates higher severity) Physical function scale: the range of the scale is 1 to 4 (higher score indicates lower function) Patient's satisfaction with treatment scale: the range of the scale is 1 to 4 (higher score indicates greater dissatisfaction)	Antiseizure Medications
Symptom Checklist-90	Helps evaluate a broad range of psychological problems and symptoms of psychopathology. The instrument is also useful in measuring patient progress or treatment outcomes	The 90 items in the questionnaire are scored on a five-point Likert scale, indicating the rate of occurrence of the symptom during the time reference. It is intended to measure symptom intensity on nine different subscales	Opioids
Visual Analogue Scale (VAS)	A unidimensional measure of pain intensity. It's a continuous scale comprised of a horizontal (HVAS) or vertical (VVAS) line, usually 10 centimeters (100 mm) in length, anchored by 2 verbal descriptors, one for each symptom extreme.	For pain intensity, the scale is most commonly anchored by "no pain" (score of 0) and "pain as bad as it could be" or "worst imaginable pain" (score of 100 [100-mm scale])	Antidepressants
Von Korff pain scale	A system for grading chronic pain and chronic disability resulting from different causes	scale 0–100%; lower scores indicate less severe pain or disability	Psychological Therapies

Appendix H. Strength of Evidence

Table H1. Strength of evidence

Key Question Outcome	Study Design Number of Studies	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Strength of Evidence
1. What are the comparative benefits and harms of different pharmacological therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis? (Including NSAIDs, acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, corticosteroids, and topicals/patch-delivered medications)							
Acetaminophen							
Acetaminophen vs. Placebo, acute LBP : Pain and function	1 RCT	Low	Unable to determine	Direct	Precise	Undetected	Low
Acetaminophen vs. NSAID, acute LBP: Pain and global improvement	3 RCTs	High	Consistent	Direct	Precise	Undetected	Low
Acetaminophen vs. Placebo, chronic LBP	No studies	-	-	-	-	-	Insufficient
Acetaminophen vs. NSAID, chronic LBP	1 RCT	High	Unable to determine	Direct	Imprecise	Undetected	Insufficient
Acetaminophen vs. other interventions, acute LBP	4 RCTs	High	Consistent	Direct	Imprecise	Undetected	Insufficient
Acetaminophen vs. placebo: Adverse events (serious adverse events)	1 RCT	Low	Consistent	Direct	Imprecise	Undetected	Moderate
Acetaminophen vs. NSAIDs : Adverse events	3 RCTs in systematic revie	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Acetaminophen vs. Placebo, NSAID or Other intervention, radicular LBP	No studies	-	-	-	-	-	Insufficient
NSAIDs							
NSAIDs vs. Placebo, acute LBP : Pain, function	4 RCTs in systematic review and 1 RCT for pain; 1 RCT for function	Moderate	Consistent for pain Unable to determine for function	Direct	Precise for pain Imprecise for function	Undetected	Moderate for pain, low for function
NSAIDs vs. Placebo, chronic LBP : Pain, function	4 RCTs in systematic review for pain 2 RCTs for function	Moderate	Consistent	Direct	Precise for pain Imprecise for function	Undetected	Moderate for pain, low for function
NSAIDs vs. Placebo, radicular LBP : Pain	2 RCTs in systemtic review	Moderate	Inconsistent	Direct	Imprecise	Undetected	Low
NSAID plus another intervention vs. Other intervention alone	2 RCTs	High	Inconsistent	Direct	Imprecise	Undetected	Insufficient
NSAIDs vs. Interventions other than acetaminophen and opioids	2 RCTs	High	Inconsistent	Direct	Imprecise	Undetected	Insufficient

Key Question Outcome	Study Design Number of Studies	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Strength of Evidence
NSAID vs. NSAID, acute or chronic LBP : Pain	27 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
NSAIDs vs. Placebo : Adverse events	10 RCTs	Moderate	C onsistent	Direct	Precise	Undetected	Moderate
COX-2-selective NSAIDs vs. nonselective NSAIDs : Adverse events	4 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Opioids, Tramadol and Tapentadol							
Opioids vs. Placebo, chronic LBP : Pain and function	6 RCTs in systematic review and 3 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Tramadol vs. Placebo, chronic LBP : Pain and function	5 RCTs in systematic review and 2 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Buprenorphine patch vs. Placebo, subacute or chronic LBP : Pain and function	2 RCTs in systematic review	Moderate	Consistent for pain Inconsistent for function	Direct	Imprecise	Undetected	Low for pain Insufficient for function
Opioids vs. NSAIDs, chronic LBP : Pain relief, function	3 RCTs for pain 1RCT for function	Moderate	Inconsistent for pain Unable to determine for function	Direct	Imprecise	Undetected	Insufficient
Opioids vs. Acetaminophen, acute LBP : Days to return to work, pain	1 RCT for return to work No studies for pain	Moderate	Unable to determine	Direct	Imprecise	Undetected	Insufficient
Long acting opioids vs. Long acting opioids : Pain, function	4 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Long acting opioids vs. Short acting opioids : Pain	6 RCTs	Moderate	Inconsistent	Direct	Precise	Undetected	Low
Opioids vs. Placebo: Adverse events	16 RC Ts in systematic review	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Skeletal Muscle Relaxants (SMR)							
SMRs vs. Placebo, acute LBP : Pain	4 RCTs in a systematic review and 1 RCT	Moderate	Consistent	Direct	Precise	Undetected	Moderate
SMR plus NSAID vs. NSAID alone, acute LBP : Pain	2 RCTs in systematic review and 1 RCT	Moderate	Consistent	Direct	Imprecise	Undetected	Low
SMR vs. Placebo, chronic LBP : Pain	3 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
SMR vs. SMR, acute or chronic LBP : Pain	3 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
SMR vs. Placebo, acute LBP : Adverse events	8 RCTs in systematic review and 1 RCT	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Benzodiazepines							
Benzodiazepines vs. Placebo, acute LBP : Pain, function	2 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient

Key Question Outcome	Study Design Number of Studies	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Strength of Evidence
Tetrazepam vs. Placebo, chronic LBP:Pain, overall improvement	2 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Diazepam vs. Placebo, acute or subacute radicular pain : Pain, function	1 RCT	Low	Unable to determine	Direct	Precise	Undetected	Low
Benzodiazepines vs. Skeletal muscle relaxants, chronic LBP: Pain, function	2 RCTs	Low	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Diazepam vs. Cyclobenzaprine, chronic LBP : Muscle spasms	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Undetected	Low
Benzodiazepines vs. Placebo: Adverse events	8 RCTs in systematic review and 1 RCT	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Antidepressants							
Tricyclic antidepressants or SSRI vs. Placebo, chronic LBP : Pain, function	4 RCTs of tricyclics and 3 RCTs of SSRIs in systematic review for pain; 2 RCTs evaluated function	Moderate	Consistent	Direct	Imprecise	Undetected	Moderate for pain, low for function
Duloxetine vs. Placebo, chronic LBP : Pain, Function	3 RCTs	Low	Consistent	Direct	Precise	Undetected	Moderate
Duloxetine vs. Tricyclic antidepressants	No studies	-	-	-	-	-	Insufficient
Antidepressants vs. Placebo : Adverse events, Serious adverse events	9 RCTs in systematic review and 3 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Antiseizure medications							
Antiseizure medications, acute non-radicular LBP	No studies	-	-	-	-	-	Insufficient
Gabapentin vs. Placebo, chronic non-radicular LBP	1 RCT (abstract only, excluded)	-	-	-	-	Suspected	Insufficient
Gabapentin vs. Placebo, chronic radicular LBP: Pain and function	3 RCTs	High	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Topiramate vs. Placebo, chronic radicular or mixed radicular and non-radicular LBP: Pain	2 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Pregabalin vs. Placebo, chronic radicular LBP : pain, function	2 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Pregabalin plus transdermal buprenorphine vs. transdermal buprenorphine, chronic non-radicular LBP : Pain	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Undetected	Insufficient
Pregabalin plus another anaglesic vs. the other analgesica alone: Pain	2 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Gabapentin vs. Placebo : Adverse events	2 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Topiramate vs. Placebo : Withdrawal due to adverse events, sedation, diarrhea	2 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient

Key Question Outcome	Study Design Number of Studies	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Strength of Evidence
Pregabalin vs. Placebo : Withdrawal due to adverse events, somnolence, dizziness	2 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Corticosteroids							
Systemic corticosteroids vs. Placebo, acute non-radicular LBP : Pain, function	2 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Systematic corticosteroids vs. Placebo, radicular LBP : Pain, function	5 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Systemic corticosteroids vs. Placebo, spinal stenosis: Pain, function	1 RCT	Moderate	Unable to determine	Direct	Precise	Undetected	Low
Systemic corticosteroids : Adverse events	12 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
2. What are the comparative benefits and harms of different nonpharmacological, noninvasive therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis?							
Exercise							
Exercise vs. Usual care, acute to subacute LBP : Pain, function	8 RCTs in systematic review and 3 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Exercise vs. Usual care, chronic LBP: Pain, Function	19 RCTs in systematic review 3 RCTs in another systematic review, and 20 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
MCE vs. Minimal intervention, chronic LBP : Pain, function	2 RCTs for pain and 3 RCTs for function in systematic review	Modeate	Consistent	Direct	Imprecise	Undetected	Low
Exercise vs. Usual care, non- acute LBP: Work disability	8 RCTs in systematic review	Moderate	Consistent	Direct	Precise	Undetected`	Moderate
Exercise vs. Usual care, radicular LBP: Pain, function	3 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Exercise vs. Exercise, acute or chronic LBP	>20 RCTs	Moderate	Consistent	Direct	Precise	Suspected	Moderate
Exercise : Adverse events							Low
MCE vs. General exercise, chronic LBP : Pain, function	6 RCTs in systematic review and 2 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
MCE vs. Multimodal PT, chronic LBP : Pain, function	4 RCTs for pain and 2 RCTs for function in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
MCE plus exercise vs. Exercise alone	2 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
MCE : Adverse events	6 RCTs	Moderate	Consistent	Direct	Precise	Suspected	Low

Key Question Outcome	Study Design Number of Studies	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Strength of Evidence
Pilates							
Pilates vs. usual care plus physical activity, chronic LBP: Pain, function	7 RCTs in systematic review	Moderate	Inconsistent	Direct	Precise	Undetected	Low
Pilates vs. other exercise, chronic LBP: Pain, function	3 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Tai Chi							
Tai Chi vs. waitlist or no Tai Chi, chronic LBP : Pain, function	2 RCTs for pain, 1 RCT for function	Moderate	Consistent for pain Unable to determine for function	Direct	Imprecise	Undetected	Low
Tai Chi vs. other exercise, chronic LBP : Pain	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Undetected	Low
Tai Chi : Adverse events	2 RCTs	Moderate	Unable to determine	Direct	Imprecise	Undetected	Low
Yoga							
Yoga vs. Usual care, chronic LBP :Pain, Function	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Undetected	Low
Yoga vs. Exercise, chronic LBP : Pain, Function	5 RCTs in sytematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Yoga vs. Education, chronic LBP : Pain, function	5 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Yoga : Adverse events	5 RC Ts	Moderate	Consistent	Direct	Imprecise	Suspected	Low
Psychological Therapies							
Progressive relaxation vs. wait list control, chronic LBP : Pain, Function	3 RCTs in systematic review	Moderate	Inconsistent	Direct	Precise	Undetected	Low
EMG biofeedback, chronic LBP : Pain, Function	3 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Operant therapy, chronic LBP : Pain, Function	3 RCTs for pain, 2 RCTs for function in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Cognitive therapy vs. Wait list control, chronic LBP	2 RCTs in systematic review	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Cognitive-behavioral and other combined therapy vs. Wait list control, chronic LBP : Pain, Function	5 RCTs for pain, 4 RCTs for function in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Psychological therapies vs. exercise or physical therapy, chronic LBP : Pain	8 RCTs	Moderate	Inconsistent	Direct	Precise	Undetected	Low
Psychological therapies vs. Psychological therapies : Pain, Function	10 RCTs	Modeate	Inconsistent	Direct	Precise	Undetected	Moderate

Key Question Outcome	Study Design Number of Studies	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Strength of Evidence
Psychological therapies : Adverse events	28 RCTs in systematic review	High	Consisent	Direct	Imprecise	Suspected	Low
Multidisciplinary rehabilitation							
Multidisciplinary rehabilitation vs. Usual care, chronic LBP : Pain, function, return to work	9 RCTs in systematic review	Moderate	Inconsistent	Direct	Precise	Undetected	Moderate
Multidisciplinary rehabilitation vs. No multidisciplinary rehabilitation, chronic LBP : Pain, function	3 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Multidisciplinary rehabilitation vs. Physical therapy, chronic LBP : Pain, function	13 RCTs in systematic review	Moderate	Inconsistent	Direct	Precise	Undetected	Moderate
Multidisciplinary rehabilitation, acute LBP, radicular LBP	No studies						Insufficient
Multidisciplinary rehabilitation : Adverse events	2 RCTs	High	Consistent	Direct	Imprecise	Suspected	Low
Acupuncture							
Acupuncture vs. Sham acupuncture, subacute LBP : Pain	3 RCTs in systematic review and 2 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Acupuncture vs. Sham acupuncture, chronic LBP : Pain, function	7 RCTs in systematic review and 1 RCT	Moderate	Inconsistent	Direct	Precise	Undetected	Moderate
Acupuncture vs. No acupuncture, chronic low back pain	5 RCTs in systematic review	Moderate	Inconsistent	Direct	Precise	Undetected	Moderate
Acupuncture vs. NSAIDs, acute LBP : Overall improvement	5 RCTs in systematic review	Moderate	Consistent	Direc t	Imprecise	Undetected	Low
Acupuncture vs. Medications, chronic LBP : Pain, Function	3 RCTs in systematic review	High	Consistent	Direct	Precise	Undetected	Low
Acupuncture : Adverse events	3 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Massage							
Massage vs. Sham massage, acute LBP: Pain, function	2 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Massage vs. Usual care, chronic LBP: Pain, function	2 RCTs	Moderate	Inconsistent	Direct	Precise	Undetected	Low
Massage vs. Other interventions, subacute to chronic LBP: Pain, function	9 RCTs for pain and 4 RCTs for function in systematic review	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Massage plus another active intervention vs. the Other intervention alone, subacute to chronic low back pain: Pain, function	5 RCTs in systematic review and 2 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Massage vs. massage: Pain, function	6 RCTs	High	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Massage: Adverse events	12 RCTs	High	Consistent	Direct	Prec ise	Suspected	Low

Key Question Outcome	Study Design Number of Studies	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Strength of Evidence
Spinal manipulation							
Spinal manipulation, acute LBP : Pain, function	1 RCT for pain and 2 RCTs for function	High	Unable to determine for pain Consistent for function	Direct	Imprecise	Undetected	Low for function Insufficient for pain
Spinal manipulation vs. Sham manipulation, chronic LBP : Pain, function	3 RCTs in systematic review and 1 RCT	Moderate	Inconsistent	Direct	Precise	Undetected	Low for pain Insufficient for function
Spinal manipulation vs. Intert treatment, acute LBP : Pain, Function	3 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Spinal manipulation vs. Inert treatment, chronic LBP	4 RCTs in systematic review and 3 RCTs	Modeate	Inconsistent	Direct	Precise	Undetected	Low
Spinal manipulation vs. Other active interventions, acute LBP : Pain, function	3 RCTS in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Moderate
Spinal manipulation vs. Other interventions, chronic LBP : Pain, function	6 RCTs in systematic review and 3 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Spinal manipulation plus exercise or advice vs. exercise or advice alone, acute LBP : Function	4 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Spinal manipulation plus another active treatment, chronic LBP : Pain, function	3 RCTS in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Spinal manipulation : Adverse events	55 RCTs	Moderate	Consistent	Direct	Precise	Suspected	Low
Ultrasound							
Ultrasound vs. Sham ultrasound, chronic LBP : Pain, function	5 RCTs	Moderate	Consistent for pain Inconsistent for function	Direct	Imprecise	Undetected	Low for pain Insufficient for function
Ultrasound vs. No ultrasound, chronic LBP : Pain, function	2 RCTs	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Ultrasound plus exercise vs. Exercise, chronic LBP : Pain, Function	2 RCTs	High	Consistent	Direct	Imprecise	Undetected	Insufficient
Ultrasound plus exercise vs. Exercise, Radicular LBP: Back pain, leg pain	1 RCT	Moderate	Unable to determine	Direct	Precise	Undetected	Moderate
Ultrasound vs. Other interventions	3 RCTs	High	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Ultrasound vs. Other interventions, radiculopathy	2 RCT	High	Unable to determine	Direct	Imprecise	Undetected	Insufficient
Ultrasound, acute non-radicular LBP	No studies						Insufficient
Spinal manipulation plus home exercise and advice, radicular LBP	1 RCT	Moderate	Unable to determine	Direct	Precise	Suspected	Low

Key Question Outcome	Study Design Number of Studies	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Strength of Evidence
Ultrasound vs. Sham ultrasound : Adverse events	1 RCT	Low	Unable to determine	Direct	Imprecise	Suspected	Low
Transcutaneous electrical nerve stimulation [TENS]							
TENS vs. Sham TENS, acute or subacute LBP: Pain, function	2 RCTs	High	Unable to determine	Direct	Imprecise	Undetected	Insufficient
TENS vs. Sham TENS, chronic LBP : Pain, function	4 RCTs for pain and 2 RCTs for function in systematic review	Moderate	Consistent	Direct	Iimprecise	Undetected	Low
TENS vs. Acupuncture, chronic LBP : Pain	4 RCTs for pain and 2 RCTs for function in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
TENS : Adverse events	8 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Suspected	Low
Electrical muscle stimulation [EMS]							
EMS plus exercise vs. Exercise, EMS vs. Other interventions, acute or chronic LBP: Pain, function	5 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
EMS: Adverse events	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Suspected	Insufficient
Percutaneous Electrical Nerve Stimulation [PENS]							
PENS vs. Sham PENS, PENS plus exercise vs. exercise, PENS vs. other interventions, chronic LBP (with or without radiculopathy)	7 RCTs	High	Inconsistent	Direct	Imprecise	Undetected	Insufficient
PENS : Adverse events	1 RCT	High	Unable to determine	Direct	--	Suspected	Insufficient
Interferential therapy [IFT]							
IFT vs. other interventions, IFT plus another intervention vs. the other intervention,subacute to chronic LBP: Pain, function	4 RCTs	High	Inconsistent	Direct	Imprecise	Undetected	Insufficient
IFT : Adverse events	No studies					Suspected	Insufficient
Superficial Heat or Cold							
Heat wrap vs. Placebo, acute or subacute LBP : Pain, function	2 RCTs in systematic review and 2 RCTs	Moderate	Consistent	Direct	Precise	Undetected	Moderate
Heat plus exercise vs. exercise alone, acute LBP : Pain, function	1 RCT	Low	Unable to determine	Direct	Imprecise	Undetected	Low
Heat plus NSAID vs. NSAID alone, acute LBP:Pain	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Undetected	Insufficient
Heat vs. Simple analgesics, acute or subacute LBP : Pain, function	1 RCT in systematic review	Low	Unable to determine	Direct	Imprecise	Undetected	Low

Key Question Outcome	Study Design Number of Studies	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Strength of Evidence
Heat vs. Exercise, acute LBP : Pain, Function	1 RCT in systematic review	Low	Unable to determine	Direct	Imprecise	Undetected	Low
Cold plus naproxen vs. naproxen alone, acute LBP: Pain	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Undetected	Insufficient
Superficial Cold vs. Placebo	No studies						Insufficient
Heat vs. Cold	3 RCTs	High	Consistent	Direct	Imprecise	Undetected	Insufficient
Heat vs. No heat or placebo : Adverse events, flushing	2 RCTs	Low	Consistent	Direct	Imprecise	Suspected	Low
Low Level Laser Therapy [LLLT]							
LLLT vs. Sham laser, acute LBP	1 RCT	High	Unable to determine	Direct	Imprecise	Undetected	Insufficient
LLLT vs. Sham laser, chronic LBP : Pain, Function	3 RCTs for pain, 1 RCT for function	Moderate	Consistent	Direct	Imprecise	Undetected	Low
LLLT plus NSAID vs. Sham plus NSAID, acute or subacute LBP : Pain, function	1 RCT	Low	Unable to determine	Direct	Imprecise	Undetected	Low
LLLT plus another intervention vs. the other intervention alons, chronic LBP: Pain, function	3 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
LLLT vs. anotehr intervention: Pain, function	2 RCTs	High	Unable to determine	Direct	Imprecise	Undetected	Insufficient
LLLT differing wavelengths or doses	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Undetected	Insufficient
LLLT : Adverse events	10 RCTs	High	Consistent	Direct	Imprecise	Suspected	Low
Short-wave Diathermy							
Short-wave diathermy vs. Sham diathermy, mixed duration LBP : Effectiveness, Adverse events	4 RCTs	High	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Short-wave diathermy: Adverse events	No studies					Suspected	Insufficient
Lumbar Supports							
Lumbar supports vs. no lumbar supports or an inactive treatment, acute or subacute LBP: Pain, function	4 RCTs in systematic review and 1 RCT	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Lumbar supports vs. no lumbar supports, chronic LBP	2 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Lumbar supports vs. no lumbar supports, mixed duration LBP: Pain and function	1 RCT	Moderate	Unable to determine	Direct	Precise	Undetected	Low
Lumbar support plus education vs. education, acute or subacute LBP : Pain, function	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Undetected	Low
Lumbar support plus exercise vs. exercise alone, chronic LBP : Pain, function	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Undetected	Low
Lumbar support vs. other active treaatments : Pain, Function	3 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Low

Key Question Outcome	Study Design Number of Studies	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Strength of Evidence
Lumbar supports vs. Lumbar supports: Pain, function	2 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Lumbar supports : Adverse events	8 RCTs in systematic review and 3 RCTs	Moderate	Consistent	Direct	Imprecise	Suspected	Low
Traction							
Traction vs. placebo, sham or no treatment, LBP with or without radicular symptoms : Pain, function	13 RCTs in systematic review and 2 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Insufficient
Traction vs. physiotherapy, LBP with or without radicular symptoms: Pain, function	5 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Traction vs. other interventions, LBP with or without radicular symptoms : Pain, function	15 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Traction vs. Traction: Pain, function	5 RCTs in systematic review	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Traction : Adverse events	11 RCTs in systematic reviews	Moderate	Consistent	Direct	Imprecise	Undetected	Low
Taping							
Kinesio Taping vs. Sham taping, chronic LBP : Pain, Function	2 RCTs	Low	Inconsistent for pain Consistent for function	Direct	Imprecise	Undetected	Insufficient for pain Low for function
Functional Fascial Taping plus exercise vs. Sham taping plus exercise, chronic LBP: Pain, function	1 RCT	Moderate	Unable to determine	Direct	Imprecise	Undetected	Insufficient
Kinesio Taping vs. exercise therapy, chronic LBP : Pain, Function	2 RCTs	Moderate	Inconsistent	Direct	Imprecise	Undetected	Low
Taping : Adverse events							Insufficient

Appendix I. Abbreviations Used in the Appendixes

Abbreviation	Term
ADL	Activities of daily living
AE	Adverse event
AIS	Athens Insomnia Scale
BDI	Beck Depression Inventory
bid	Twice daily
BMI	Body mass index
BPI	Brief Pain Inventory
BPI-SF	Brief Pain Inventory-Short Form
BRLP	Back-related leg pain
CBT	Cognitive behavioral therapy
CCRCT	Cochrane Central Register of Controlled Trials
CCT	Controlled clinical trial
CDC HRQOL-4	Centers for Disease Control and Prevention's Health-Related Quality of Life Questionnaire
CGI-S	Clinical Global Impressions of Severity Scale
CI	Confidence interval
CLBP	Chronic low back pain
CMT	Chiropractic Manipulative Therapy
CPAQ	Chronic Pain Acceptance Questionnaire
CSFMPQ	Chinese Short Form McGill Pain Questionnaire
CSQ	Coping Strategies Questionnaire
CT	Computed tomography scan
D	Day
DASS	Depression Anxiety Stress Scales
DPQ	Dallas Pain Questionnaire
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th edition
EERW	Enriched enrolment with randomized withdrawal
EIFEL	French translation of Roland-Morris Disability Questionnaire
EMG	Electromyography
EPC	Evidence-based Practice Center
ER	Emergency room
FABQ	Fear Avoidance Beliefs Questionnaire
FAPESP	Fundacao de Amparo a Pesquisa do Estado de Sao Paulo
FRI	Functional Rating Index
GA	Graded activity
GDS	Geriatric Depression Scale
GI	Gastrointestinal
GPE	Global Perceived Effect Scale
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
GX	Graded exposure

Abbreviation	Term
H	Hour
HADS	The Hospital Anxiety and Depression Scale
HEA	Home exercise with advice
HR	Hazard ratio
HRoB	High risk of bias
HRQOL	Health-related quality of life
HSCL-25	Hopkin's Symptom Checklist
HVLA	High-velocity low-amplitude
I^2	Statistic that describes the percentage of the variability in effect estimates that is due to heterogeneity
IC	Integrative Care
IM	Intramuscular
IPAQ	International Physical Activity Questionnaire
IPQ	Illness Perception Questionnaire
IPQ-R	Illness Perceptions Questionnaire-Revised
IQR	Interquartile range
ITT	Intention-to-treat
IV	Intravenous therapy
JLEQ	Japan Low Back Pain Evaluation Questionnaire
JOA	Japanese Orthopedic Association
L2	2nd lumbar vertebra
L4	4th lumbar vertebra
L5-S1	Lumbosacral joint
LANSS	Leeds Assessment of Neuropathic Symptoms and Signs
LBP	Low back pain
LBPOI	Low Back Pain Outcome Instrument
LBPRS	Low back pain rating scale
LRoB	Low risk of bias
mA	Milliampere
MBR	Multidisciplinary biopsychosocial rehabilitation
MCE	Motor control exercise
MCS	Mental component score of the SF-36
MCS-12	Mental component score of the SF-12
MD	Mean difference
MOS	Medical outcome study
Mos	Months
MPI	Multidimensional Pain Inventory
MPQ	McGill Pain Questionnaire
MRI	Magnetic resonance imaging
NCCAM	National Center for Complementary and Integrative Health
Nd:YAG	Neodymium-doped yttrium aluminium garnet laser
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases

Abbreviation	Term
NIH	National Institute of Health
NIOSHTIC-2	The National Institute for Occupational Safety and Health database
NMT	Measure of back extension strength
NPRS	Numerical pain rating scale
NR	Not reported
NRS	Numeric rating scale
NS	Not significant
NSAID	Nonsteroidal anti-inflammatory drug
OA	Osteoarthritis
ODI	Oswestry Disability Index
OMT	Osteopathic manipulative treatment
PA	Placebo acupuncture
PCS	Pain Catastrophizing Scale
PCS-12	SF12 Physical score
PDI	Pain Disability Index
PEDro	Physiotherapy Evidence Database
PENS	Percutaneous electrical nerve stimulation
PGIC	Patients' Global Impression
PMR	Periodized musculoskeletal rehabilitation
PO	Oral route of medication administration
POMS	Profile of Mood States
PR	Partial response
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSC	Patient Specific Complaints
PSEQ	Chronic Pain Self Efficacy Scale
PSFS	Patient-Specific Functional Scale
PSQI	Pittsburgh Sleep Quality Index
PT	Physical therapy
pts	Patients
QBPDS	Quebec Back Pain Disability Scale
QD	Once daily
QHS	Each night at bedtime
QOL	Quality of life
RA	Rheumatoid arthritis
RCT	Randomized controlled trail
RDQ	Roland-Morris Disability Questionnaire
ROB	Risk of bias
RR	Relative risk
S	Second
SA	Sham acupuncture
SAE	Serious adverse event
SCL-90	Symptom Checklist 90

Abbreviation	Term
SD	Standard deviation
SF-12	Short Form-12
SF-36	Short Form-36
SF-MPQ	McGill Pain Questionnaire Pain Rating Index- Short-Form
SHCI	Subjective Health Complaint Inventory
SMD	Standardized mean differences
SMR	Skeletal muscle relaxant
SMT	Spinal manipulation therapy
SOE	Summary of evidence
SOWS	Short Opioid Withdrawal Scale
SSRI	Selective serotonin reuptake inhibitor
SSS	Swiss Spinal Stenosis Questionnaire
STAI	State-trait Anxiety Inventory
TA	True acupuncture
TENS	Transcutaneous electrical nerve stimulation
tid	Three times daily
TSK	Tampa Scale of Kinesiophobia
UAW-GM	United Auto Workers- General Motors
UK	United Kingdom
USA	United States of America
USPSTF	United States Preventive Services Task Force
VAS	Visual analog scale
VRS	Visual rating scale
vs.	Versus
w	Week
WHO	World Health Organization
WHOQOL-BREF	World Health Organization Quality of Life-BREF instrument
WMD	Weighted mean difference
WPAI	Work activity impairment subscale
y	Year