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Noninvasive Treatments for Low Back Pain

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

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 e-mail list to learn about new program products and opportunities for input.

We welcome 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, 540 Gaither Road, Rockville, MD 20850, 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.

The list of Key Informants who participated in developing this report will be added for the final version.

Technical Expert Panel

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.

Technical Experts 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 conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

The list of Technical Experts who participated in developing this report will be added for the final version

Peer Reviewers

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 does 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 non-financial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential non-financial conflicts of interest identified.

The list of Peer Reviewers who participated in reviewing this report will be added for the final version.

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 August 2014), 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 [NSAID]s, 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 2,990 citations identified at the title and abstract level, a total of 134 studies were included. 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 analogue scale [VAS]) to moderate (10 to 20 points) range; effects on function were generally smaller than effects on pain, or not observed. Benefits were mostly observed at short-term followup. For acute low back pain, evidence suggested that skeletal muscle relaxants (strength of evidence [SOE]: moderate), NSAIDs (SOE: low to moderate), and superficial heat (SOE: moderate) are more effective than placebo or no heat and that acetaminophen and systemic corticosteroids 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 analgesics, benzodiazepines, pregabalin, duloxetine, multidisciplinary rehabilitation (SOE: moderate), psychological therapies (SOE: low), massage (SOE: low), acupuncture (SOE: moderate), yoga (SOE: low), and exercise (SOE: moderate); spinal manipulation was as effective as other active interventions (ultrasound and transcutaneous electrical nerve stimulation [TENS] were no more effective than sham interventions) (SOE: low). Few trials evaluated the effectiveness of treatments for radicular low back pain, but the available evidence found that pregabalin, benzodiazepines, corticosteroids, traction, and spinal manipulation were not effective or associated small effects (SOE: low). Relatively few trials directly compared the effectiveness of different medications, different nonpharmacological therapies, or compared pharmacological versus nonpharmacological therapies, and found no clear differences.

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—in 1998, total U.S. 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 and 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 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 encompass 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 interdisciplinary 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).

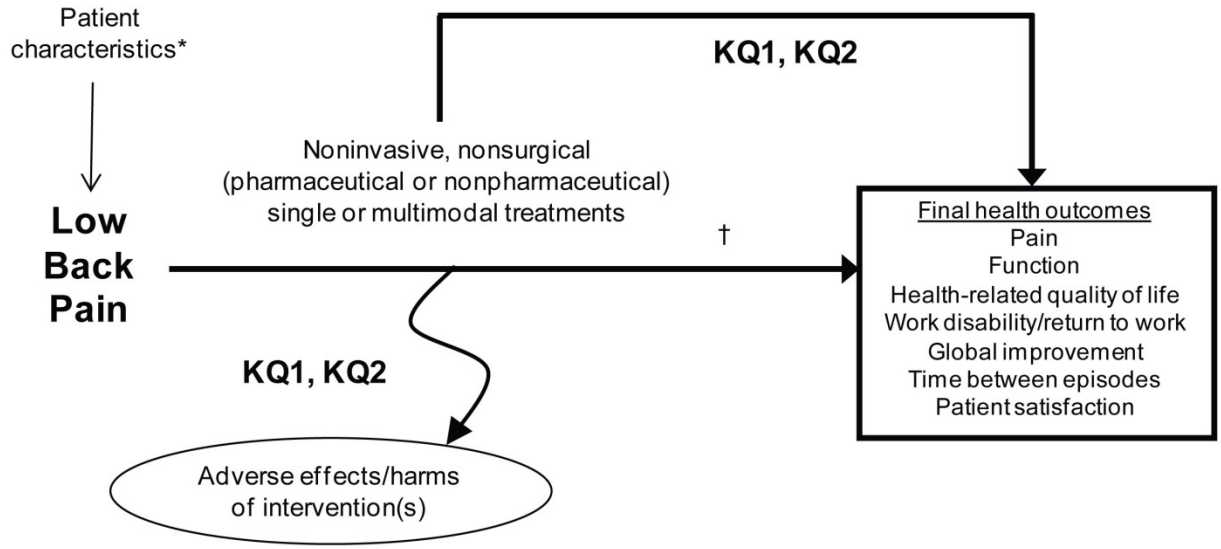
Scope of Review and Key Questions

The provisional Key Questions, population, intervention, comparator, outcomes, timing, settings, and study designs (PICOTS), and analytic framework for this topic 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? (Including NSAIDs, acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, corticosteroids, and topicals /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? (Including but not limited to interdisciplinary rehabilitation, exercise (various types), physical modalities (ultrasound, transcutaneous electrical nerve stimulation [TENS], electrical muscle stimulation [EMS], interferential therapy [IFT], 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 are typically not measured (e.g., inflammation).

Methods

This comparative effectiveness review (CER) follows the methods suggested in the AHRQ *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* (hereafter "AHRQ Methods Guide").[19]

Searching for the Evidence

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 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. 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.

Study Selection

We developed criteria for inclusion and exclusion of studies based on the Key Questions and the defined population, interventions, comparators, outcomes, timing, settings, and study designs (PICOTS). Inclusion and exclusion criteria are summarized below. 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.

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 pharmacologic and noninvasive, nonpharmacological therapies for low back pain. Pharmacological therapies were restricted to those administered orally or topically; we evaluated NSAIDs, acetaminophen, opioids, tramadol and tapentadol, antidepressants, skeletal muscle relaxants, benzodiazepines, corticosteroids, antiepileptic medications, capsaicin, and lidocaine. We excluded studies of medications administered intravenously but included studies of medications administered intramuscularly if the therapeutic effects were felt to be similar to oral administration. Nonpharmacological therapies were multidisciplinary rehabilitation (defined as an intervention consisting at a minimum of physical therapy plus psychological therapy, with some coordination); 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. 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, and 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, 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. 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, 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 tool.[23] 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 quality of studies but did not report details regarding specific methodological shortcomings, we assessed the quality 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. 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.

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 as 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.

Assessment of the Risk of Bias 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 AHRQ Methods Guide.[21] 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.[23]

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.

Studies rated "good" are considered to have no more than very minor methodological shortcomings and their results are likely to be valid. Studies rated "fair" have some methodological shortcomings, but no flaw or combination of flaws judged likely to cause major bias. Studies rated "poor" have significant flaws that may invalidate the results. They have a serious or "fatal" flaw or combination of flaws in design, analysis, or reporting; large amounts of missing information, or serious discrepancies in reporting. We did not exclude studies rated poor quality *a priori*, but they were considered the least reliable when synthesizing the evidence, particularly when discrepancies between 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 risk of bias 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).

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.[26] We classified the magnitude of effects for pain and function using the same system as in the APS/ACP review.[14, 27] A small/slight effect was defined for pain as a mean difference of 5 to 10 points on a 100-point visual analogue scale (VAS) or equivalent; for function as a mean difference of 5 to 10 point difference on the Oswestry Disability Index (ODI) or 1 to 2 points on the 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 100 point VAS, for function as a mean difference of 10 to 20 points on the ODI or 2 to 5 points on the RDQ, and for any outcome as an SMD Of 0.5 to 0.8. Large/substantial effects were defined as greater than moderate. We 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.

Data Synthesis

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 low back pain, radicular low back pain, spinal stenosis), 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).

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 between reviews. When findings between 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,[19] 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 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.[19] 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.

Results

Database searches resulted in 2,990 potentially relevant articles. After dual review of abstracts and titles, 1,204 articles were selected for full-text dual review and 134 publications were determined to meet inclusion criteria and were included in this review.

Key Question 1. Pharmacological therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis

Acetaminophen

The acetaminophen section included the APS/ACP review and one additional trial not included in the review.

- 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]: moderate).
- For acute low back pain, a systematic review 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 (SOE: low).
- 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.
- 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).

NSAIDs

The NSAIDs section included the APS/ACP review, one systematic review, and three trials not included in the systematic review.

- For acute low back pain, a systematic review found NSAIDs associated with greater improvement in pain intensity versus placebo (4 studies, 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 versus the other intervention alone to determine effectiveness (SOE: insufficient).
- There was insufficient evidence from two trials to determine the effects of NSAIDs versus interventions other than acetaminophen and opioids (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).

Opioids

The Opioids section included the APS/ACP review, two systematic reviews, and four trials not included in the systematic reviews.

- 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, I^2=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; I^2=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 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, I^2=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, I^2=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 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 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 between different long-acting opioids in pain or function (SOE: moderate).
- 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 opioid use 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.

Skeletal Muscle Relaxants

The skeletal muscle relaxants section included the APS/ACP review and two trials not in the review.

- 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; I^2=0%) and 5 to 7 days (3 trials; RR 1.72, 95% CI 1.32 to 2.22; I^2=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; I^2=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 between 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; I^2=50%); one additional placebo-controlled trial was consistent with these findings (SOE: moderate).

Benzodiazepines

The benzodiazepines section included the APS/ACP review and one additional trial.

- 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 failure to improve pain at 5 to 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 failure to experience 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 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).

Antidepressants

The antidepressants section included the APS/ACP review, one systematic review, and five trials not in the systematic review.

- For chronic low back pain, a systematic review found no difference between tricyclic antidepressants versus placebo in pain (4 trials; SMD −0.10, 95% CI −0.51 to 0.31; I^2=32%) or SSRIs versus placebo (3 trials; SMD 0.11, 95% CI −0.17 to 0.39; I^2=0%); there was also no difference between antidepressants versus placebo on function (2 trials, SMD −0.06, 95% CI −0.40 to 0.29; I^2=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).
- No study compared duloxetine with a tricyclic antidepressant.
- Antidepressants were associated with higher risk of any adverse events compared to placebo, with no difference in risk of serious adverse events (SOE: moderate).

Antiseizure medications

The antiseizure medication section included the APS/ACP review and six additional trials.

- 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 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).

Corticosteroids

The corticosteroids section of the report included four trials.

- 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 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).
- 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).

Topical Medications

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

Key Question 2. Different nonpharmacological, noninvasive therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis

Exercise

The exercise section included the APS/ACP review, 2 systematic reviews, and 15 trials not in the systematic reviews.

- For acute low back pain, a systematic review found no differences between exercise therapy versus usual care 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 −2.82 at short term, 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 chronic low back pain, a systematic review found exercise associated with greater pain relief versus usual care (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 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 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).
- There were no clear differences between different exercise regimens 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).

Motor Control Exercise [MCE]

The MCE section included one systematic review and two additional trials.

- 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 chronic low back pain, a systematic review included two trials that 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. 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 chronic low back pain, a systematic review found MCE associated with lower pain intensity versus multimodal PT at intermediate term (4 trials, WMD, −14.20, 95% CI −21.23 to −7.16) and two trials found MCE associated with decreased disability versus PT at intermediate term (WMD −12.98 on 0 to 100 scale, 95% CI −19.49 to −6.47) (SOE: low).
- Two trials found no clear differences between MCE plus another type of exercise versus the other type of exercise alone (SOE: low). Harms were poorly reported in trials of MCE, but few adverse events were reported, with no clear difference in risk (SOE: low).

Pilates

The Pilates section included one systematic review.

- 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 chronic low back pain, three trials found no clear differences between Pilates versus other types of exercises in pain or function (SOE: low).

Tai Chi

The Tai Chi section included two trials.

- 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 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).

Yoga

The yoga section included the APS/ACP review, two systematic reviews, and two trials not included in the systematic reviews.

- 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 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 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; I^2=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, I^2=47%); yoga was also associated with better function at short-term (5 trials, SMD 0.45, 95% CI −0.65 to −0.25; I^2=8%) and long-term followup (4 trials, SMD 0.39, 95% CI −0.66 to −0.11; I^2=40%) (SOE: moderate).
- Reporting of harms was suboptimal, but adverse events when reported were almost all classified as mild to moderate (SOE: low).

Psychological Therapies

The psychological therapies section included the APS/ACP review, one systematic review, and five trials (in six publications) not included in the systematic review.

- 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, I^2=57%) and functional status (3 trials, standardized mean difference −0.88, 95% CI −1.36 to −0.39, I^2=0%) (SOE: low).

- For chronic low back pain, a systematic review found EMG biofeedback associated with lower pain intensity at the end of treatment (3 trials, SMD −0.80, 95% CI −1.32 to −0.28, I^2=0%), with no clear effect on function (3 trials) (SOE: low).
- 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, I^2=0%), with no clear effect on function (2 trials) (SOE: low).
- 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: low).
- 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, I^2=40%), but effects on function were smaller and not statistically significant (4 trials, SMD −0.37, 95% CI −0.87 to 0.13, I^2=50%) (SOE: low).
- 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 (SOE: low).
- Ten trials found no clear differences between different psychological therapies in pain or function (SOE: moderate).
- Harms were not well-reported, but no trial included reported any adverse events associated with psychological therapies (SOE: low).

Multidisciplinary Rehabilitation

The multidisciplinary rehabilitation section included the APS/ACP review, one systematic review, and two additional trials.

- For chronic low back pain, a systematic review found multidisciplinary rehabilitation, versus usual care, associated with lower short-term pain intensity (9 trials, SMD −0.55, 95% CI −0.83 to −0.28, I^2=72%; or ~1.4-point mean difference on a 0- to 10-point numerical rating scale) and disability (9 trials, SMD −0.41, 95% CI −0.62 to −0.19, I^2=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, I^2=25% and 6 trials, SMD −0.23, 95% CI −0.40 to −0.06, I^2=19%, respectively), with no difference in likelihood of return to work (7 trials, OR 1.04, 95% CI 0.73 to 1.47, I^2=31%) (SOE: moderate).
- For chronic low back pain a systematic review found multidisciplinary rehabilitation, versus no multidisciplinary rehabilitation, associated with lower short-term pain intensity (3 trials, SMD −0.73, 95% CI −1.22 to −0.24, I^2=64%, or ~1.7 point mean difference on a 0 to 10 numerical rating scale) and disability (3 trials, pooled SMD −0.49, 95% CI −0.76 to −0.22, I^2=0%, or ~2.9 point mean difference on the RDQ); there was insufficient evidence to assess effects on long-term outcomes (SOE: low for short-term pain and disability).
- For chronic low back pain, a systematic review found multidisciplinary rehabilitation, versus nonmultidisciplinary physical therapy, associated with lower short-term pain intensity (12 trials, SMD −0.30, 95% CI −0.54 to −0.06, I^2=80%, or an approximate 0.6 point mean difference on a 0- to 10-point numerical rating scale) and disability (13 trials,

SMD −0.39, 95% CI −0.68 to −0.10, I^2=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, I^2=92%) and function (10 trials, SMD −0.68, 95% CI −1.19 to −0.16, I^2=94%) and greater likelihood for return to work (8 trials, OR 1.87, 95% CI 1.39 to 2.53, I^2=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: insufficient).

Acupuncture

The acupuncture section included the APS/ACP review, two systematic reviews, and five trials not included in the systematic review.

- 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, I^2=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. There were no clear effects on function in five trials (SOE: low).
- 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, I^2=90%) and at up to 12 weeks (3 trials, WMD −9.55, 95% CI −16.5 to −2.58, I^2=40%), but there were no differences in function. Four additional trials reported results consistent with these findings (SOE: moderate).
- 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, I^2=51%) and better function (3 trials, SMD −0.94, 95% CI −1.41 to −0.47, I^2=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 scale and the other two trials showed small or no clear differences at longer-term followup (SOE: moderate).
- 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, I^2=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, I^2=0%) and improvement in function (3 trials, SMD −0.36, 95% CI −0.67 to −0.04, I^2=7%) immediately postintervention (SOE: low).
- Harms of acupuncture were poorly reported in the trials, though no serious adverse events were reported (SOE: low).

Massage

The massage section included the APS/ACP review, one systematic review and four trials not in the systematic review.

- 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 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 subacute to chronic low back pain, a systematic review found massage associated with better effects on short-term pain in seven of nine trials (mean differences −0.6 to −0.94 points on a 0 to 10 scale) and better effects on short-term function in three of four trials (SOE: moderate).
- For subacute to chronic low back pain, a systematic review included five 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 (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).

Spinal Manipulation

The spinal manipulation section included the APS/ACP review, two systematic reviews and 13 additional trials.

- 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, I^2=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 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, I^2=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, I^2=0%) or at 3 months (1 trial, SMD −0.28, 95% CI −0.59 to 0.02) (SOE: low).
- For chronic low back pain, one good 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 high 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, I^2=0%), 1 month (3 trials, WMD −0.15, 95% CI −0.49 to 0.18, I^2=0%), 3 to 6 months (2 trials, WMD −0.20, 95% CI −1.13 to 0.73, I^2=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 timepoint (SOE: moderate).
- For chronic low back pain, a systematic review found spinal manipulation 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, I^2=27%) and 6 months (7 comparisons from 4 trials, WMD −3.07, 95% CI −5.42 to −0.71, I^2=0%); effects were smaller and no longer statistically significant at 12 months (3 trials, WMD −0.76, 95% CI −3.19 to 1.66, I^2=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, I^2=3%); effects were smaller and no longer statistically significant at 6 and 12 months. Two trials not included in the systematic reviews reported results consistent with these findings (SOE: moderate).
- 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, I^2=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, I^2=37%) or 3 months (2 trials, SMD −0.22, 95% CI −0.61 to 0.16, I^2=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, I^2=0%), 3 months (2 trials, MD −7.23, 95% CI −11.72 to −2.74, I^2=43%), and 12 months (2 trials, MD −3.31, 95% CI −6.60 to −0.02, I^2=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, I^2=0%), 3 months (2 trials, SMD −0.22, −0.38 to −0.06, I^2=33%), and 12 months (2 trials, SMD −0.21, 95% CI −0.34 to −0.09, I^2=0%). One trial not included in the systematic review reported results consistent with these findings (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).

Ultrasound

The ultrasound section included the APS/ACP review, one systematic review, and two trials not in the systematic review.

- 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, I^2=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, I^2=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 chronic low back pain, evidence from three 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).
- 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 one small trial with serious 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).

Transcutaneous Electrical Nerve Stimulation [TENS]

The TENS section included the APS/ACP review, one systematic review, and five additional trials.

- 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 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 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 suggested an increased risk of skin site reactions without an increased risk of serious adverse events (SOE: low).

Electrical Muscle Stimulation

The electrical muscle stimulation section included five trials.

- 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).

Percutaneous Electrical Nerve Stimulation [28]

The PENS section included the APS/ACP review and two additional trials.

- There was insufficient evidence from six trials to determine effects of PENS versus sham, PENS plus exercise versus exercise alone, or PENS versus other interventions, due to methodological limitations and imprecision (SOE: insufficient).
- No study evaluated harms of PENS (SOE: insufficient).

Interferential Therapy

The interferential therapy section included the APS/ACP review and one additional trial.

- 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).

Superficial Heat or Cold

The superficial heat or cold section included the APS/ACP review and four additional trials.

- 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). One subsequent trial 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). 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 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) (SOE: low).
- 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 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.
- There was insufficient evidence from two 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).

Low-Level Laser Therapy

The low-level laser therapy section included the APS/ACP review and four additional trials.

- 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 trials found low-level laser therapy more effective than sham laser for pain, though methods for assessing pain and duration of followup varied; one trial found low-level laser therapy more effective than sham laser for function (mean difference −8.20 on the ODI, 95% CI −13.44 to −2.96) (SOE: low).
- 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 another intervention versus the other intervention alone, due to methodological shortcomings and imprecision (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.

Short-wave Diathermy

The short-wave diathermy section included the APS/ACP review and two additional trials.

- 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.

Lumbar Supports

The lumbar supports section included one systematic review and three trials not in the systematic review.

- 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 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 chronic low back pain, one trial found no difference between a lumbar support plus exercise (muscle strengthening) versus exercise alone in short-term (8 week) or long-term (6 month) pain or function (SOE: low).
- Three trials found no clear differences between lumbar supports versus other active treatments in pain or function (SOE: low).

- There was insufficient evidence from two trials to determine comparative effects of different types of lumbar supports, due to methodological shortcomings and imprecision (SOE: insufficient)
- Trials reported no harms associated with use of lumbar supports (SOE: low).

Traction

The traction section included the APS/ACP review, one systematic review, and three trials (in four publications) not in the systematic review.

- 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 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 differences between traction versus other active interventions in pain or function (SOE: low).
- 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).

Taping

The taping section included five trials.

- For chronic low back pain, two 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 one 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).
- No trial of taping reported harms.

Discussion

Key Findings and Strength of Evidence

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

Table A. Summary of evidence

Key Question Outcome	Strength of Evidence Grade	Conclusion
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? (Including NSAIDs, acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, corticosteroids and topicals/patch-delivered medications)		
Acetaminophen		
Acetaminophen vs. Placebo, acute LBP Pain and function	Moderate	One good-quality trial found no difference between acetaminophen versus placebo in pain intensity or function through 3 weeks.
Acetaminophen vs. NSAID, acute LBP Pain and global improvement	Low	A systematic review 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.
Acetaminophen vs. Placebo, chronic LBP	Insufficient	No study evaluated acetaminophen versus placebo.
Acetaminophen vs. NSAID, chronic LBP	Insufficient	There was insufficient evidence from one trial to determine effects of acetaminophen versus NSAIDs.
Acetaminophen vs. other interventions, acute LBP	Insufficient	There was insufficient evidence from four trials to determine effects of acetaminophen versus 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 acetaminophen associated with lower risk of side effects versus 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, function	Moderate for pain, low for function	A systematic review found NSAIDs associated with greater improvement in pain intensity versus placebo (4 studies, 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.
NSAIDs vs. Placebo, chronic LBP: Pain, function	Moderate for pain, low for function	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.
NSAIDs vs. Placebo, radicular LBP: Pain	Low	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).

Key Question Outcome	Strength of Evidence Grade	Conclusion
NSAID plus another intervention vs. Other intervention alone	Insufficient	There was insufficient evidence from two trials of an NSAID plus another intervention versus the other intervention alone to determine effectiveness.
NSAIDs vs. Interventions other than acetaminophen and opioids	Insufficient	There was insufficient evidence from two trials to determine the effects of NSAIDs versus interventions other than acetaminophen and opioids.
NSAID vs. NSAID, acute or chronic LBP: Pain	Moderate	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).
NSAIDs vs. Placebo: Adverse events	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 vs. nonselective NSAIDs: Adverse events	Moderate	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).
Opioids		
Opioids vs. Placebo, chronic LBP: Pain and function	Moderate	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, I^2=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; I^2=0.0%, for a mean difference of ~1 point on the RDQ) versus placebo; three additional trials reported results consistent with the systematic review.
Tramadol vs. Placebo, chronic LBP: Pain and function	Moderate	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, I^2=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, I^2=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.
Buprenorphine patch vs. Placebo, subacute or chronic LBP: Pain and function	Low for pain Insufficient for function	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.
Opioids vs. NSAIDs, chronic LBP: Pain relief, function	Insufficient	Three trials reported inconsistent effects of opioids versus NSAIDs for pain relief, one 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 versus acetaminophen in days to return to work; pain was not reported.
Long acting opioids vs. Long acting opioids: Pain, function	Moderate	Four trials found no clear differences between different long-acting opioids in pain or function.
Long acting opioids vs. Short acting opioids: Pain	Low	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.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Opioids vs. Placebo: Adverse events	Moderate	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.
Skeletal Muscle Relaxants (SMR)		
SMRs vs Placebo, acute LBP: Pain	Moderate	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; I^2=0%) and 5 to 7 days (3 trials; RR 1.72, 95% CI 1.32 to 2.22; I^2=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 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; I^2=84%); one other trial (n=197) also reported results that favored combination therapy.
SMR vs. Placebo, chronic LBP: Pain	Insufficient	Evidence from three 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 between different skeletal muscle relaxants for acute or chronic low back pain.
SMR vs. Placebo, acute LBP: Adverse events	Moderate	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; I^2=50%); one additional placebo-controlled trial was consistent with these findings.
Benzodiazepines		
Benzodiazepines vs. Placebo, acute LBP: Pain, function	Insufficient	There was insufficient evidence from two trials with inconsistent results to determine effectiveness of benzodiazepines versus placebo.
Tetrazepam vs. Placebo, chronic LBP: Pain, overall improvement	Low	A systematic review included two trials that found tetrazepam associated with lower likelihood of failure to improve 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) versus placebo, and lower likelihood of failure to experience overall improvement at 10-14 days (RR 0.63, 95% CI 0.42 to 0.97).

Key Question Outcome	Strength of Evidence Grade	Conclusion
Diazepam vs. Placebo, acute or subacute radicular pain: Pain, function	Low	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 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. Skeletal muscle relaxants, chronic LBP: Pain, function	Insufficient	There was insufficient evidence from two trials with inconsistent results to determine effects of benzodiazepines versus skeletal muscle relaxants.
Diazepam vs. Cyclobenzaprine, chronic LBP: Muscle spasms	Low	One trial found no difference between diazepam versus cyclobenzaprine in outcomes related to muscle spasm.
Benzodiazepines vs. Placebo: Adverse events	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.
Antidepressants		
Tricyclic antidepressants or SSRI vs. Placebo, chronic LBP: Pain, function	Moderate for pain, low for function	A systematic review found no difference between tricyclic antidepressants versus placebo in pain (4 trials; SMD −0.10, 95% CI −0.51 to 0.31; I^2=32%) or SSRIs versus placebo (3 trials; SMD 0.11, 95% CI −0.17 to 0.39; I^2=0%); there was also no difference between antidepressants versus placebo on function (2 trials, SMD −0.06, 95% CI −0.40 to 0.29; I^2=0%).
Duloxetine vs. Placebo, chronic LBP: Pain, Function	Moderate	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.
Duloxetine vs. Tricyclic antidepressants	Insufficient	No study compared duloxetine versus a tricyclic antidepressant.
Antidepressants vs. Placebo: Adverse events, Serious adverse events	Moderate	Antidepressants were associated with higher risk of any adverse events compared to 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 low back pain.
Gabapentin vs. Placebo, chronic nonradicular LBP	Insufficient	One trial found no difference between gabapentin (up to 3600 mg/day) versus placebo, but did not meet inclusion criteria because it was only published as an abstract.
Gabapentin vs. Placebo, chronic radicular LBP: Pain and function	Insufficient	There was insufficient evidence from three poor-quality trials with inconsistent findings to determine effects of gabapentin versus placebo.
Topiramate vs. Placebo, chronic radicular or mixed radicular and nonradicular LBP: Pain	Insufficient	Two trials reported inconsistent results for effects of topiramate versus placebo.
Pregabalin vs. Placebo, chronic radicular LBP: pain, function	Insufficient	Two trials reported inconsistent effects of pregabalin versus placebo for pain or function.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Pregabalin plus transdermal buprenorphine vs. transdermal buprenorphine, chronic nonradicular LBP: Pain	Insufficient	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.
Pregabalin plus another analgesic vs. the other analgesic alone: Pain	Insufficient	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.
Gabapentin vs. Placebo: Adverse events	Low	Two trials of gabapentin versus 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 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.
Pregabalin vs. Placebo: Withdrawal due to adverse events, somnolence, dizziness	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.
Corticosteroids		
Systemic corticosteroids vs. Placebo, acute nonradicular LBP: Pain, function	Low	Two trials found no differences between a single intramuscular injection or a 5 day course of systemic corticosteroids versus placebo for pain or function.
Systematic corticosteroids vs. Placebo, radicular LBP: Pain, function	Moderate	Five trials consistently found no differences between systemic corticosteroids (administered a single bolus or as a short taper) versus placebo in pain or function for acute or unspecified duration LBP; one trial found no effect on need for spine surgery.
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. 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?		

Key Question Outcome	Strength of Evidence Grade	Conclusion
Exercise		
Exercise vs. Usual care, acute to subacute LBP: Pain, function	Low	A systematic review found no differences between exercise therapy versus usual care 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.
Exercise vs. Usual care, chronic LBP: Pain, Function	Moderate	A systematic review found exercise associated with greater pain relief versus usual care (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.
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, function	Low	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.
Exercise vs. Exercise, acute or chronic LBP	Moderate	There were no clear differences between different exercise regimens in >20 head-to-head trials of patients with acute or chronic low back pain.
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 Outcome	Strength of Evidence Grade	Conclusion
Motor Control Exercise		
MCE vs. General exercise, chronic LBP: Pain, function	Low	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.
MCE vs. Minimal intervention, chronic LBP: Pain, function	Low	A systematic review included two trials that 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. 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).
MCE vs. Multimodal PT, chronic LBP: Pain, function	Low	A systematic review found MCE associated with lower pain intensity versus multimodal PT at intermediate term (4 trials, WMD, −14.20, 95% CI−21.23 to −7.16) and two trials found MCE associated with decreased disability versus PT at intermediate term (WMD −12.98 on 0 to 100 scale, 95% CI −19.49 to −6.47).
MCE plus exercise vs. Exercise alone	Low	Two trials found no clear differences between MCE plus another type of exercise versus the other type of exercise alone.
MCE: Adverse events	Low	Harms were poorly reported in trials of MCE, but few adverse events were reported, with no clear difference in risk.
Pilates		
Pilates vs. usual care plus physical activity, chronic LBP: Pain, function	Low	A systematic review included 7 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.
Pilates vs. other exercise, chronic LBP: Pain, function	Low	Three trials found no clear differences between Pilates versus other types of exercises in pain or function.
Tai Chi		
Tai Chi vs. waitlist or no Tai Chi, chronic LBP: Pain, function	Low	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).

Key Question Outcome	Strength of Evidence Grade	Conclusion
Tai Chi vs. other exercise, chronic LBP: Pain	Low	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.
Tai Chi: Adverse events	Low	One trial of Tai Chi reported a small temporary increase in back pain symptoms and one trial reported no harms.
Yoga		
Yoga vs. Usual care, chronic LBP: Pain, Function	Low	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.
Yoga vs. Exercise, chronic LBP: Pain, Function	Low	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 statistically significant (5 trials).
Yoga vs. Education, chronic LBP: Pain, function	Moderate	Yoga was associated with lower short-term pain intensity versus education (5 trials, SMD −0.45,- 95% CI −0.63 to −0.26; I^2=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' I^2=47%); yoga was also associated with better function at short-term (5 trials, SMD 0.45, 95% CI−0.65 to −0.25; I^2=8%) and long-term followup (4 trials, SMD 0.39, 95% CI −0.66 to −0.11; I^2=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, 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, I^2=57%) and functional status (3 trials, standardized mean difference −0.88, 95% CI −1.36 to −0.39, I^2=0%).
EMG biofeedback, chronic LBP: Pain, Function	Low	A systematic review found EMG biofeedback associated with lower pain intensity at the end of treatment (3 trials, SMD −0.80, 95% CI −1.32 to −0.28, I^2=0%), with no clear effect on function (3 trials).
Operant therapy, chronic LBP: Pain, Function	Low	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, I^2=0%), with no clear effect on function (2 trials).
Cognitive therapy vs. Wait list control, chronic LBP	Insufficient	There was insufficient evidence from two trials to determine effects of cognitive therapy versus wait list control, due to inconsistency and imprecision.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Cognitive-behavioral and other combined therapy vs. Wait list control, chronic LBP: Pain, Function	Low	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, I^2=40%), but effects on function were smaller and not statistically significant (4 trials, SMD −0.37, 95% CI −0.87 to 0.13, I^2=50%).
Psychological therapies vs. exercise or physical therapy, chronic LBP: Pain	Low	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.
Psychological therapies vs. Psychological therapies: Pain, Function	Moderate	Ten trials found no clear differences between different psychological therapies in pain or function.
Psychological therapies: Adverse events	Low	Harms were not well-reported, but no trial included 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, versus usual care, associated with lower short-term pain intensity (9 trials, standardized mean difference −0.55, 95% CI −0.83 to −0.28, I^2=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, I^2=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, I^2=25% and 6 trials, standardized mean difference −0.23, 95% CI −0.40 to −0.06, I^2=19%, respectively), with no difference in likelihood of return to work (7 trials, OR 1.04, 95% CI 0.73 to 1.47, I^2=31%).
Multidisciplinary rehabilitation vs. No multidisciplinary rehabilitation, chronic LBP: Pain, function	Low	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, I^2=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, I^2=0%, or ~2.9 point mean difference on the RDQ); there was insufficient evidence to assess effects on long-term outcomes.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Multidisciplinary rehabilitation vs. Physical therapy, chronic LBP: Pain, function	Moderate	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, I^2=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, I^2=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, I^2=92%) and function (10 trials, standardized mean difference −0.68, 95% CI −1.19 to −0.16, I^2=94%) and greater likelihood for return to work (8 trials, OR 1.87, 95% CI 1.39 to 2.53, I^2=0%).
Multidisciplinary rehabilitation, acute LBP, radicular LBP	Insufficient	No study evaluated the effectiveness of multidisciplinary rehabilitation for acute low back pain or for radicular low back pain.
Multidisciplinary rehabilitation: Adverse events	Insufficient	Harms were poorly reported in trials of multidisciplinary rehabilitation, though no serious harms were reported.
Acupuncture		
Acupuncture vs. Sham acupuncture, subacute LBP: Pain	Low	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, I^2=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.
Acupuncture vs. Sham acupuncture, chronic LBP: Pain, function	Low	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], I^2=90%) and at up to 12 weeks (3 trials, WMD −9.55, 95% CI −16.5 to −2.58], I^2=40%), but there were no differences in function. Four additional trials reported results consistent with these findings.
Acupuncture vs. No acupuncture, chronic low back pain	Moderate	A systematic review found acupuncture associated with lower pain intensity (4 trials, SMD −0.72, 95% CI −0.94 to −0.49, I^2=51%) and better function (3 trials, SMD −0.94, 95% CI −1.41 to −0.47, I^2=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 scale and the other two trials; two trials showed small or no clear differences at longer-term followup.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Acupuncture vs. NSAIDs, acute LBP: Overall improvement	Low	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, I^2=0%).
Acupuncture vs. Medications, chronic LBP: Pain, Function	Low	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, I^2=0%) and improvement in function (3 trials, SMD −0.36, 95% CI −0.67 to −0.04, I^2=7%) immediately postintervention.
Acupuncture: Adverse events	Low	Harms of acupuncture were poorly reported in the trials, though no serious adverse events were reported.
Massage		
Massage vs. Sham massage, acute LBP: Pain, function	Low	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.
Massage vs. Usual care, chronic LBP: Pain, function	Low	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.
Massage vs. Other interventions, subacute to chronic LBP: Pain, function	Moderate	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.
Massage plus another active intervention vs. the Other intervention alone, subacute to chronic low back pain: Pain, function	Low	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.
Massage vs. massage: Pain, function	Insufficient	Comparisons of difference massage techniques were too heterogeneous and effects were too small from six trials to determine effects on pain and function.
Massage: Adverse events	Low	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.
Spinal manipulation		
Spinal manipulation, acute LBP: Pain, function	Low for function Insufficient for 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).

Key Question Outcome	Strength of Evidence Grade	Conclusion
Spinal manipulation vs. Sham manipulation, chronic LBP: Pain, function	Low for pain Insufficient for function	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, I^2=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.
Spinal manipulation vs. Intert treatment, acute LBP: Pain, Function	Low	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, I^2=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, I^2=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 low risk of bias 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 high 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.
Spinal manipulation vs. Other active interventions, acute LBP: Pain, function	Moderate	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, I^2=0%), 1 month (3 trials, WMD −0.15, 95% CI −0.49 to 0.18, I^2=0%), 3 to 6 months (2 trials, WMD −0.20, 95% CI −1.13 to 0.73, I^2=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 timepoint.
Spinal manipulation vs. Other interventions, chronic LBP: Pain, function	Moderate	A systematic review found spinal manipulation 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, I^2=27%) and 6 months (7 comparisons from 4 trials, WMD −3.07, 95% CI −5.42 to −0.71, I^2=0%); effects were smaller and no longer statistically significant at 12 months (3 trials, WMD −0.76, 95% CI −3.19 to 1.66, I^2=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, I^2=3%); effects were smaller and no longer statistically significant at 6 and 12 months. Two trials not included in the systematic reviews reported results consistent with these findings.

Key Question Outcome	Strength of Evidence Grade	Conclusion
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 associated with greater improvement in function at 1 week (SMD −0.41, 95% CI −0.73 to −0.10, I^2=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, I^2=37%) or 3 months (2 trials, SMD −0.22, 95% CI −0.61 to 0.16, I^2=41%).
Spinal manipulation plus another active treatment, chronic LBP: Pain, function	Low	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, I^2=0%), 3 months (2 trials, MD −7.23, 95% CI −11.72 to −2.74, I^2=43%), and 12 months (2 trials, MD −3.31, 95% CI −6.60 to −0.02, I^2=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, I^2=0%), 3 months (2 trials, SMD −0.22, −0.38 to −0.06, I^2=33%), and 12 months (2 trials, SMD −0.21, 95% CI −0.34 to −0.09, I^2=0%). One trial not included in the systematic review reported results consistent with these findings.
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, function	Low for pain Insufficient for function	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, I^2=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.
Ultrasound vs. No ultrasound, chronic LBP: Pain, function	Low	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, I^2=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, Function	Insufficient	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.
Ultrasound vs. Other interventions	Insufficient	There was insufficient evidence from three small trials with methodological shortcomings to determine effects of ultrasound versus other interventions.
Ultrasound vs. Other interventions, radiculopathy	Insufficient	There was insufficient evidence from one small trial with serious methodological shortcomings to determine effects of ultrasound versus other interventions.
Ultrasound, acute nonradicular LBP	Insufficient	No study evaluated the effectiveness of ultrasound for acute nonradicular low back pain.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Ultrasound vs. Sham ultrasound: Adverse events	Low	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).
Transcutaneous electrical nerve stimulation		
TENS vs. Sham TENS, acute or subacute LBP: Pain, 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, function	Low	A systematic review found no differences between 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.
TENS vs. Acupuncture, chronic LBP: Pain	Low	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.
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]		
EMS plus exercise vs. Exercise, EMS vs. Other interventions, acute or chronic LBP: Pain, function	Insufficient	There was insufficient evidence from 5 RCTs to determine effects of electrical muscle stimulation plus exercise versus exercise alone or versus other interventions, due to methodological limitations and imprecision.
EMS: Adverse events	Insufficient	There was insufficient evidence to determine harms of electrical muscle stimulation.
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 6 trials to determine effects of PENS versus sham, PENS plus exercise versus exercise alone, or PENS versus other interventions, due to methodological limitations and imprecision.
PENS: Adverse events	Insufficient	No study evaluated harms of PENS.
Interferential therapy [IFT]		
IFT vs. other interventions, IFT plus another intervention vs. the other intervention, subacute to chronic LBP: Pain, function	Insufficient	There was insufficient evidence from 4 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.
IFT: Adverse events	Insufficient	No study evaluated harms of interferential therapy.
Superficial Heat or Cold		

Key Question Outcome	Strength of Evidence Grade	Conclusion
Heat wrap vs. Placebo, acute or subacute LBP: Pain, function	Moderate	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). One subsequent trial 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). Another trial found a heat wrap during emergency transport associated with substantially lower pain intensity versus an unheated blanket upon arrival to the hospital.
Heat plus exercise vs. exercise alone, acute LBP: Pain, function	Low	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).
Heat vs. Simple analgesics, acute or subacute LBP: Pain, function	Low	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).
Heat vs. Exercise, acute LBP: Pain, Function	Low	A systematic review included one trial that found no clear differences between heat versus exercise in pain relief or function.
Superficial Cold vs. Placebo	Insufficient	No study compared superficial cold versus placebo or no cold treatment.
Heat vs. Cold	Insufficient	There was insufficient evidence from two trials to determine effects of heat versus 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 versus no heat or placebo in two trials; no serious adverse events were reported with use of heat.
Low- Level Laser Therapy		
LLLT vs. Sham laser, acute LBP	Insufficient	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.
LLLT vs. Sham laser, chronic LBP: Pain, Function	Low	Three trials found low-level laser therapy more effective than sham laser for pain, though methods for assessing pain and duration of followup varied; one trial found low-level laser therapy more effective than sham laser for function (mean difference −8.20 on the ODI, 95% CI −13.44 to −2.96).

Key Question Outcome	Strength of Evidence Grade	Conclusion
LLLT plus NSAID vs. Sham plus NSAID, acute or subacute LBP: Pain, function	Low	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).
LLLT plus another intervention vs. the other intervention alone, chronic LBP: Pain, function	Insufficient	There was insufficient evidence from 3 trials to determine effects of low-level laser therapy plus another intervention versus the other intervention alone, due to methodological shortcomings and imprecision.
LLLT vs. another intervention: Pain, function	Insufficient	There was insufficient evidence to determine effects of low-level laser therapy versus another intervention, due to methodological shortcomings and imprecision.
LLLT differing wavelengths or doses	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.
LLLT: Adverse events	Insufficient	Harms were not well-reported in trials of low-level laser therapy, but no serious adverse events and no harms were reported.
Short-wave Diathermy		
Short-wave diathermy vs. Sham diathermy, mixed duration LBP: Effectiveness, Adverse events	Insufficient	There was insufficient evidence from 5 RCTs to determine effects of short-wave diathermy versus 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, function	Insufficient	There was insufficient evidence from 5 trials to determine effects of lumbar supports versus 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 versus no lumbar supports, due to methodological shortcomings and inconsistent results.
Lumbar support plus education vs. education, acute or subacute LBP: Pain, function	Low	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.
Lumbar support plus exercise vs. exercise alone, chronic LBP: Pain, function	Low	One trial found no difference between a lumbar support plus exercise (muscle strengthening) versus exercise alone in short-term (8 week) or long-term (6 month) pain or function.
Lumbar support vs. other active treatments: Pain, Function	Low	Three trials found no clear differences between lumbar supports versus other active treatments in pain or function.
Lumbar supports vs. Lumbar supports: Pain, function	Insufficient	There was insufficient evidence from 2 trials to determine comparative effects of different types of lumbar supports, due to methodological shortcomings and imprecision.
Lumbar supports: Adverse events	Low	Trials reported no harms associated with use of lumbar supports.

Key Question Outcome	Strength of Evidence Grade	Conclusion
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 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.
Traction vs. physiotherapy, LBP with or without radicular symptoms	Low	A systematic review included five trials that found no clear differences between traction versus physiotherapy versus physiotherapy alone.
Traction vs. other interventions, LBP with or without radicular symptoms: pain, function	Low	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.
Traction vs. Traction	Low	A systematic review included five trials that found no clear differences between 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 versus placebo or other interventions. Three subsequent trials reported findings consistent with the systematic review.
Taping		
Kinesio Taping vs. Sham taping, chronic LBP: Pain, function	Insufficient for pain Low for function	Two 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.
Functional Fascial Taping plus exercise vs. Sham taping plus exercise, chronic LBP: Pain, function	Insufficient	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.
Kinesio Taping vs. exercise therapy, chronic LBP: Pain, Function	Low	Two trials found no differences between Kinesio Taping versus exercise therapy in pain or function.
Taping: Adverse events	Insufficient	No trial of taping reported harms.

CI=confidence interval, EMS=electrical muscle stimulation, LBP=low back pain, LLLT=low-level laser therapy, MCE=motor control exercise, NSAID=nonsteroidal anti-inflammatory drug, ODI= Oswestry Disability Index, PENS=percutaneous electrical nerve stimulation, RDQ= Roland-Morris Disability Questionnaire, RR=relative risk, SMD=standardized mean difference, SSRI=selective serotonin reuptake inhibitor, TENS= transcutaneous electrical nerve stimulation, VAS=visual analogue scale, WMD=weighted mean difference

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). It 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 RDQ or the

ODI). When present, observed benefits were generally in the small (5 to 10 point on a 100-point VAS or equivalent, or 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 showed no clear effects; 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 (SOE: moderate).[29] 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).[30-32] 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 the effects of pregabalin for radicular low back pain, but did not show beneficial effects (SOE: low).[33, 34] 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).[35] 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; I^2=32%) (SOE: moderate).[36] 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.

There remain no placebo-controlled trials of acetaminophen for chronic low back pain and only one small trial of acetaminophen versus NSAIDs.[37] Evidence indicates that 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).

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[38] (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 between different long-acting opioids or between 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. 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 the commonly

implemented enriched enrollment and withdrawal design.[39] 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.

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 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 function[40] (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 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 TENS was previously classified as insufficient, additional evidence now supports the findings that ultrasound is not effective versus sham ultrasound[41] and that TENS is not effective versus sham TENS,[42] though the strength of evidence remains low due to methodological limitations in the trials and imprecision. Based on three trials,[43-45] 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, 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).[46] 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).[47] 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,[46] 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[48, 49] and spinal manipulation[50, 51] than for massage,[52] 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.[52] Although acupuncture was more effective than sham acupuncture for chronic low back pain,[48] 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.[51] 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 utilized 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.[53, 54] 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).[55] 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.[56] 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[57, 58] indicates that such patients are more likely to be prescribed opioids in clinical practice than patients without risk factors.[53, 59]

Our finding that acetaminophen is not effective for acute low back pain is based on a recent, well-conducted RCT[29] 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.[60]

Our prior report and other previous systematic reviews[61, 62] 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; I^2=32%) or function.[36] One potential reasons for the discrepancy between this finding and prior reviews are that some of the prior reviews did not conduct a meta-analysis.[62, 63] A review[61] that did conduct meta-analysis included a study that did not report being randomized and reported the largest effect in favor of antidepressant,[64] did not include relevant studies that were in the more current review,[65-67] and included two relevant studies in the meta-analysis for which data had to be imputed,[68, 69] but did not report methods for imputation.

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.[70] 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.[71]

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.[53, 72-75] 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.[48, 49] As in prior reviews, we found no clear evidence to support one specific type of massage, manipulation, or acupuncture over another.[76-79]

Findings regarding the effectiveness of exercise are similar to our prior review and other reviews.[80, 81] Our findings are also consistent with more specific reviews that focused on specific types of exercise such as aquatic exercise,[82] sling exercise,[83] stability exercises,[84] modifying patterns of movement,[85] Additional evidence published since our prior review strengthens conclusions that yoga is effective for low back pain,[86, 87] a finding consistent with other recent systematic reviews, and support 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).[88]

Our findings that psychological therapies and multidisciplinary rehabilitation were both effective are consistent with our prior review and other reviews.[89] 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.[59, 90, 91] Although there was insufficient evidence to determine which patients are most likely to benefit from psychological therapies and multidisciplinary rehabilitation, a recent randomized trial[92] 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 patients. 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 evidence[47] 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.[93]

As in other reviews, we found that evidence the effectiveness of therapies for radicular low back pain was quite limited.[94, 95] Like other reviews, including our prior report, we found that systematic corticosteroids are not effective for radicular low back pain.[95, 96] 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.[97]

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. 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 nonpharmacological treatments, the applicability of our findings is affected by the variability between trials in the interventions 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.[48, 49] 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,[98, 99] 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.

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).[27] 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. When present, most beneficial effects were observed at shorter-term followup; effects were typically attenuated or no longer present at longer-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, 100] New evidence[29] that acetaminophen is ineffective for acute low back pain call into question its appropriateness as a recommended therapy, though other factors such as low cost, favorable side-effect profile, and effectiveness for other acute pain conditions could also impact decisions regarding its use.[101] 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.[56] 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.[102]

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 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, and the continued use of systemic corticosteroids for this indication, despite trials showing that they are ineffective.

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 patients.[92] 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,[98, 99] 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.[103] 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.[23] 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,[104] educational interventions,[105, 106] advice to remain active,[105, 107] mattresses, shoe insoles,[108] and others.[109, 110] We also did not include comparisons of noninvasive therapies versus surgery or interventional procedures, though 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, 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 of 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 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,[111] 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 was 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, 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. More research is needed to determine effective treatments for low back pain with radicular symptoms. Trials should be designed to not just evaluate patients 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 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. 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 is lacking.[56] For systemic corticosteroids, the largest trial to date was recently completed and should help further characterize the effectiveness (or lack thereof) of this treatment.[112]

More research is needed to help understand which patients are most likely to benefit from specific therapies.[113-117] Trials are also needed to confirm whether effects of risk-stratified approaches are reproducible in the United States,[118, 119] and to optimize their implementation.[120] 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 healthcare 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 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 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.

References

1. Deyo RA, Mirza SK, Martin BI. Back pain prevalence and visit rates. Spine (Phila Pa 1976). 2006 Nov 1;31(23):2724-7. PMID: 17077742.
2. Walker BF. The prevalence of low back pain: a systematic review of the literature from 1966 to 1998. J Spinal Disord. 2000;13(3):205-17. PMID: 10872758.
3. Luo X, Pietrobon R, Sun SX, et al. Estimates and patterns of direct health care expenditures among individuals with back pain in the United States. Spine (Phila Pa 1976). 2004;29(1):79-86. PMID: 14699281.
4. Martin BI, Deyo RA, Mirza SK, et al. Expenditures and health status among adults with back and neck problems. JAMA. 2008 Feb 13;299(6):656-64. PMID: 18270354.
5. Stewart WF, Ricci JA, Chee E, et al. Lost productive time and cost due to common pain conditions in the US workforce. JAMA. 2003;290(18):2443-54. PMID: 14612481.
6. Pengel LHM, Herbert RD, Maher CG, et al. Acute low back pain: systematic review of its prognosis. BMJ. 2003;327(7410):323-7. PMID: 12907487.
7. Chou R, Shekelle P. Will this patient develop persistent disabling low back pain? JAMA. 2010 Apr 7;303(13):1295-302. PMID: 20371789.
8. Deyo RA, Dworkin SF, Amtmann D, et al. Report of the NIH Task Force on Research Standards for Chronic Low Back Pain. Spine (Phila Pa 1976). 2014 Jun 15;39(14):1128-43. PMID: 24887571.
9. Frymoyer JW. Predictors of low back pain disability. J Clinical Orthop Relat Res. 1987 August;22:89-98. PMID: 2955993.
10. Engel CC, Von Korff M, Katon WJ. Back pain in primary care: predictors of high health-care costs. Pain. 1996;65:197-204. PMID: 8826507.
11. Waddell G, McCulloch JA, Kummel E, et al. Nonorganic physical signs in low-back pain. Spine (Phila Pa 1976). 1980 Mar-Apr;5(2):117-25. PMID: 6446157.
12. Jarvik JG, Deyo RA. Diagnostic evaluation of low back pain with emphasis on imaging. Ann Intern Med. 2002;137(7):586-97. PMID: 12353946.
13. van Tulder MW, Assendelft WJ, Koes BW, et al. Spinal radiographic findings and nonspecific low back pain: a systematic review of observational studies. Spine. 1997;22(4):427-34. PMID: 9055372.
14. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: A joint clinical practice guideline from the American College of Physicians and the American Pain Society. Ann Intern Med. 2007;147(7):478-91. PMID: 17909209.
15. Chou R, Huffman LH, American Pain S, et al. Medications for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Annals of Internal Medicine. 2007 Oct 2;147(7):505-14. PMID: 17909211.
16. Chou R, Huffman LH, American Pain Society, et al. Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Annals of Internal Medicine. 2007 Oct 2;147(7):492-504. PMID: 17909210.
17. Chou R, Atlas SJ, Stanos SP, et al. Nonsurgical interventional therapies for low back pain: a review of the evidence for an American Pain Society clinical practice guideline. Spine. 2009 May 1;34(10):1078-93. PMID: 19363456.
18. Chou R, Baisden J, Carragee EJ, et al. Surgery for low back pain: A review of the evidence for an American pain society clinical practice guideline. Spine (Phila Pa 1976). 2009;34(10):1094-109. PMID: 19363455.
19. Agency for Healthcare Research and Quality. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. AHRQ Publication No. 10(13)-EHC063-EF. Rockville, MD; 2014.

20. Chou R, Huffman L, eds. Guideline for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. Evidence Review. American Pain Society in Conjunction with American Academy of Pain Medicine. Glenview, IL; 2009.

21. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. AHRQ Publication No. 10(12)-EHC063-EF. Rockville, MD: Agency for Healthcare Research and Quality; January 2014. Chapters available at: www.effectivehealthcare.ahrq.gov.

22. Shea BJ, Hamel C, Wells GA, et al. AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. J Clin Epidemiol. 2009 Oct;62(10):1013-20. PMID: 19230606.

23. Agency for Healthcare Research and Quality. Integrating Bodies of Evidence: Existing Systematic Reviews and Primary Studies. www.ahrq.org; 2015. http://effectivehealthcare.ahrq.gov/ehc/products/597/1964/Integrating-evidence-draft-140910.pdf

24. Furlan AD, Reardon R, Weppler C. Opioids for chronic noncancer pain: a new Canadian practice guideline. CMAJ. 2010 Jun 15;182(9):923-30. PMID: 20439443.

25. U.S. Preventive Services Task Force Procedure Manual. AHRQ Publication No. 08-05118-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2008. http://www.uspreventiveservicestaskforce.org/uspstf08/methods/procmanual.htm

26. Atkins D, Chang SM, Gartlehner G, et al. Assessing applicability when comparing medical interventions: AHRQ and the Effective Health Care Program. J Clin Epidemiol. 2011 Nov;64(11):1198-207. PMID: 21463926.

27. Ostelo RW, Deyo RA, Stratford P, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine (Phila Pa 1976). 2008 Jan 1;33(1):90-4. PMID: 18165753.

28. Purepong N, Jitvimonrat A, Boonyong S, et al. Effect of flexibility exercise on lumbar angle: a study among non-specific low back pain patients. Journal of Bodywork & Movement Therapies. 2012 Apr;16(2):236-43. PMID: 22464123.

29. Williams CM, Maher CG, Latimer J, et al. Efficacy of paracetamol for acute low-back pain: a double-blind, randomised controlled trial. Lancet. 2014;384(9954):1586-96. PMID: No PMID.

30. Skljarevski V, Ossanna M, Liu-Seifert H, et al. A double-blind, randomized trial of duloxetine versus placebo in the management of chronic low back pain. European Journal of Neurology. 2009 Sep;16(9):1041-8. PMID: 19469829.

31. Skljarevski V, Zhang S, Desaiah D, et al. Duloxetine versus placebo in patients with chronic low back pain: a 12-week, fixed-dose, randomized, double-blind trial. Journal of Pain. 2010 Dec;11(12):1282-90. PMID: 20472510.

32. Skljarevski V, Desaiah D, Liu-Seifert H, et al. Efficacy and safety of duloxetine in patients with chronic low back pain. Spine. 2010 Jun 1;35(13):E578-85. PMID: 20461028.

33. Baron R, Freynhagen R, Tolle TR, et al. The efficacy and safety of pregabalin in the treatment of neuropathic pain associated with chronic lumbosacral radiculopathy. Pain. 2010 Sep;150(3):420-7. PMID: 20493632.

34. Markman JD, Frazer ME, Rast SA, et al. Double-blind, randomized, controlled, crossover trial of pregabalin for neurogenic claudication. Neurology. 2014 Dec 10PMID: 25503625.

35. Brotz D, Maschke E, Burkard S, et al. Is there a role for benzodiazepines in the management of lumbar disc prolapse with acute sciatica? Pain. 2010 Jun;149(3):470-5. PMID: 20362397.

36. Urquhart DM, Hoving JL, Assendelft JJW, et al. Antidepressants for non-specific low back pain. Cochrane Database of Systematic Reviews. 2010(10). PMID: No PMID.

37. Hickey RF. Chronic low back pain: a comparison of diflunisal with paracetamol. New Zealand Medical Journal. 1982 May 12;95(707):312-4. PMID: 6212783.

38. Chaparro EL, Furlan AD, Deshpande A, et al. Opioids compared to placebo or other treatments for chronic low-back pain. Cochrane Database of Systematic Reviews. 2014(5)PMID: No PMID.

39. Furlan A, Chaparro LE, Irvin E, et al. A comparison between enriched and nonenriched enrollment randomized withdrawal trials of opioids for chronic noncancer pain. Pain Research & Management. 2011 Sep-Oct;16(5):337-51. PMID: 22059206.

40. Hall AM, Maher CG, Lam P, et al. Tai chi exercise for treatment of pain and disability in people with persistent low back pain: a randomized controlled trial. Arthritis care & research. 2011 Nov;63(11):1576-83. PMID: 22034119.

41. Ebadi S, Henschke N, Nakhostin Ansari N, et al. Therapeutic ultrasound for chronic low-back pain. Cochrane Database of Systematic Reviews. 2014;3:CD009169. PMID: 24627326.

42. van Middelkoop M, Rubinstein SM, Kuijpers T, et al. A systematic review on the effectiveness of physical and rehabilitation interventions for chronic non-specific low back pain. European Spine Journal; 2011. p. 19-39.

43. Toya S, Motegi M, Inomata K, et al. Report on a computer-randomized double blind clinical trial to determine the effectiveness of the GaAlAs (830 nm) diode laser for pain attenuation in selected pain groups. Laser Therapy. 1994;6:143-. PMID: No PMID.

44. Soriano F, Rios R. Gallium Arsenide laser treatment of chronic low back pain: a prospective, randomized and double blind study. Laser Therapy. 1998;10:175-80. PMID: No PMID.

45. Basford JR, Sheffield CG, Harmsen WS. Laser therapy: a randomized, controlled trial of the effects of low-intensity Nd:YAG laser irradiation on musculoskeletal back pain. Archives of Physical Medicine & Rehabilitation. 1999 Jun;80(6):647-52. PMID: 10378490.

46. Henschke N, Ostelo WJGR, van Tulder MW, et al. Behavioural treatment for chronic low-back pain. Cochrane Database of Systematic Reviews. 2011(2)PMID: No PMID.

47. Kamper SJ, Apeldoorn AT, Chiarotto A, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. Cochrane Database of Systematic Reviews. 2014;9:CD000963. PMID: 25180773.

48. Lam M, Galvin R, Curry P. Effectiveness of acupuncture for nonspecific chronic low back pain: a systematic review and meta-analysis. Spine. 2013 Nov 15;38(24):2124-38. PMID: 24026151.

49. Lee J-H, Choi T-Y, Lee MS, et al. Acupuncture for acute low back pain: a systematic review. Clinical Journal of Pain. 2013 Feb;29(2):172-85. PMID: 23269281.

50. Rubinstein SM, Terwee CB, Assendelft WJJ, et al. Spinal manipulative therapy for acute low-back pain. Cochrane Database of Systematic Reviews. 2012;9:CD008880. PMID: 22972127.

51. Rubinstein SM, van Middelkoop M, Assendelft WJ, et al. Spinal manipulative therapy for chronic low-back pain. Cochrane Database of Systematic Reviews. 2011(2):CD008112. PMID: 21328304.

52. Furlan AD, Imamura M, Dryden T, et al. Massage for low-back pain. Cochrane Database of Systematic Reviews. 2010(6)PMID: No PMID.

53. Machado LAC, Kamper SJ, Herbert RD, et al. Analgesic effects of treatments for non-specific low back pain: a meta-analysis of placebo-controlled randomized trials. Rheumatology. 2009 May;48(5):520-7. PMID: 19109315.

54. Kuijpers T, van Middelkoop M, Rubinstein SM, et al. A systematic review on the effectiveness of pharmacological interventions for chronic non-specific low-back pain. European Spine Journal. 2011 Jan;20(1):40-50. PMID: 20680369.

55. Martell BA, O'Connor PG, Kerns RD, et al. Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. Annals of Internal Medicine. 2007 Jan 16;146(2):116-27. PMID: 17227935.

56. Chou R, Turner JA, Devine EB, et al. The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention WorkshopEffectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain. Annals of Internal Medicine. 2015;162(4):276-86. PMID: 25581257.

57. Morasco BJ, Duckart JP, Carr TP, et al. Clinical characteristics of veterans prescribed high doses of opioid medications for chronic non-cancer pain. Pain. 2010 Dec;151(3):625-32. PMID: 20801580.

58. Weisner CM, Campbell CI, Ray GT, et al. Trends in prescribed opioid therapy for non-cancer pain for individuals with prior substance use disorders. Pain. 2009 Oct;145(3):287-93. PMID: 19581051.

59. Richards MC, Ford JJ, Slater SL, et al. The effectiveness of physiotherapy functional restoration for post-acute low back pain: a systematic review. Manual Therapy. 2013 Feb;18(1):4-25. PMID: 22796390.

60. Davies RA, Maher CG, Hancock MJ. A systematic review of paracetamol for non-specific low back pain. European Spine Journal. 2008 Nov;17(11):1423-30. PMID: 18797937.

61. Salerno SM, Browning R, Jackson JL. The effect of antidepressant treatment on chronic back pain: a meta-analysis. Arch Intern Med. 2002 162(1):19-24. PMID: 11784215.

62. Staiger TO, Gaster B, Sullivan MD, et al. Systematic review of antidepressants in the treatment of chronic low back pain. Spine. 2003;28(22):2540-5. PMID: 14624092.

63. Schnitzer TJ, Ferraro A, Hunsche E, et al. A comprehensive review of clinical trials on the efficacy and safety of drugs for the treatment of low back pain. J Pain & Sympt Mgmt. 2004;28(1):72-95. PMID: 15223086.

64. Ward N. Tricyclic antidepressants for chronic low-back pain. Mechanisms of ation and predictors of response. Spine (Phila Pa 1976). 1986;11(7):661-5. PMID: 2947334.

65. Treves R, Montaine de la Roque P, Dumond JJ, et al. [Prospective study of the analgesic action of clomipramine versus placebo in refractory lumbosciatica (68 cases)]. Revue du Rhumatisme et des Maladies Osteo-Articulaires. 1991 Jul-Sep;58(7):549-52. PMID: 1833813.

66. Atkinson JH, Slater MA, Capparelli EV, et al. Efficacy of noradrenergic and serotonergic antidepressants in chronic back pain: a preliminary concentration-controlled trial. J Clin Psychopharmacol. 2007 Apr;27(2):135-42. PMID: 17414235.

67. Jenkins DG, Ebbutt AF, Evans CD. Tofranil in the treatment of low back pain. Journal of International Medical Research. 1976;4(2 Suppl):28-40. PMID: 140827.

68. Alcoff J, Jones E, Rust P, et al. Controlled trial of imipramine for chronic low back pain. Journal of Family Practice. 1982 May;14(5):841-6. PMID: 6210751.

69. Pheasant H, Bursk A, Goldfarb J, et al. Amitriptyline and chronic low back pain: a randomized double-blind crossover study. Spine (Phila Pa 1976). 1983;8:552-7. PMID: 6228015.

70. U.S. Food and Drug Administration. FDA clears Cymbalta to treat chronic musculoskeletal pain [Press Release]. Silver Spring, MD: U.S. Food and Drug Adminstration; 2010. Accessed on March 10th, 2015 2015.

71. Cawston H, Davie A, Paget M-A, et al. Efficacy of duloxetine versus alternative oral therapies: an indirect comparison of randomised clinical trials in chronic low back pain. European Spine Journal. 2013 Sep;22(9):1996-2009. PMID: 23686477.

72. Goertz CM, Pohlman KA, Vining RD, et al. Patient-centered outcomes of high-velocity, low-amplitude spinal manipulation for low back pain: a systematic review. Journal of Electromyography & Kinesiology. 2012 Oct;22(5):670-91. PMID: 22534288.

73. Brosseau L, Wells GA, Poitras S, et al. Ottawa Panel evidence-based clinical practice guidelines on therapeutic massage for low back pain. Journal of Bodywork & Movement Therapies. 2012 Oct;16(4):424-55. PMID: 23036876.

74. Hutchinson AJP, Ball S, Andrews JCH, et al. The effectiveness of acupuncture in treating chronic non-specific low back pain: a systematic review of the literature. Journal of Orthopaedic Surgery. 2012;7:36. PMID: 23111099.

75. Xu M, Yan S, Yin X, et al. Acupuncture for chronic low back pain in long-term follow-up: a meta-analysis of 13 randomized controlled trials. American Journal of Chinese Medicine. 2013;41(1):1-19. PMID: 23336503.

76. Netchanok S, Wendy M, Marie C, et al. The effectiveness of Swedish massage and traditional Thai massage in treating chronic low back pain: a review of the literature. Complementary Therapies in Clinical Practice. 2012 Nov;18(4):227-34. PMID: 23059437.

77. Furlan AD, van Tulder MW, Cherkin DC, et al. Acupuncture and dry-needling for low back pain. Cochrane Database of Systematic Reviews. 2005(1):CD001351. PMID: 15674876.

78. Assendelft WJJ, Morton SC, Yu EI, et al. Spinal manipulative therapy for low-back pain Cochrane Database of Systematic Reviews. 2004(1)PMID: 14973958.

79. Furlan AD, Brosseau L, Imamura M, et al. Massage for low-back pain: a systematic review within the framework of the Cochrane Collaboration Back Review Group. Spine (Phila Pa 1976). 2002 Sep 1;27(17):1896-910. PMID: 12221356.

80. Hidalgo B, Detrembleur C, Hall T, et al. The efficacy of manual therapy and exercise for different stages of non-specific low back pain: an update of systematic reviews. Journal of Manual & Manipulative Therapy. 2014 May;22(2):59-74. PMID: 24976749.

81. Ferreira ML, Smeets RJEM, Kamper SJ, et al. Can we explain heterogeneity among randomized clinical trials of exercise for chronic back pain? A meta-regression analysis of randomized controlled trials. Physical Therapy. 2010 Oct;90(10):1383-403. PMID: 20671101.

82. Waller B, Lambeck J, Daly D. Therapeutic aquatic exercise in the treatment of low back pain: a systematic review. Clinical Rehabilitation. 2009 Jan;23(1):3-14. PMID: 19114433.

83. Yue Y-S, Wang X-D, Xie B, et al. Sling exercise for chronic low back pain: a systematic review and meta-analysis. PLoS ONE [Electronic Resource]. 2014;9(6):e99307. PMID: 24919119.

84. Wang X-Q, Zheng J-J, Yu Z-W, et al. A meta-analysis of core stability exercise versus general exercise for chronic low back pain. PLoS ONE [Electronic Resource]. 2012;7(12):e52082. PMID: 23284879.

85. Laird RA, Kent P, Keating JL. Modifying patterns of movement in people with low back pain -does it help? A systematic review. BMC Musculoskeletal Disorders. 2012;13:169. PMID: 22958597.

86. Ward L, Stebbings S, Cherkin D, et al. Yoga for functional ability, pain and psychosocial outcomes in musculoskeletal conditions: a systematic review and meta-analysis. Musculoskeletal Care. 2013 Dec;11(4):203-17. PMID: 23300142.

87. Holtzman S, Beggs RT. Yoga for chronic low back pain: a meta-analysis of randomized controlled trials. Pain Research & Management. 2013 Sep-Oct;18(5):267-72. PMID: 23894731.

88. Machado LA, de Souza M, Ferreira PH, et al. The McKenzie method for low back pain: a systematic review of the literature with a meta-analysis approach. Spine (Phila Pa 1976). 2006 Apr 20;31(9):E254-62. PMID: 16641766.

89. van Geen J-W, Edelaar MJA, Janssen M, et al. The long-term effect of multidisciplinary back training: a systematic review. Spine. 2007 Jan 15;32(2):249-55. PMID: 17224822.

90. Bunzli S, Gillham D, Esterman A. Physiotherapy-provided operant conditioning in the management of low back pain disability: A systematic review. Physiotherapy Research International. 2011 Mar;16(1):4-19. PMID: 20310071.

91. Schonstein E, Kenny DT, Keating J, et al. Work conditioning, work hardening and functional restoration for workers with back and neck pain. Cochrane Database of Systematic Reviews. 2003(1):CD001822. PMID: 12535416.

92. Hill JC, Whitehurst DG, Lewis M, et al. Comparison of stratified primary care management for low back pain with current best practice (STarT Back): a randomised controlled trial. Lancet. 2011 Oct 29;378(9802):1560-71. PMID: 21963002.

93. Dubinsky RM, Miyasaki J. Assessment: Efficacy of transcutaneous electric nerve stimulation in the treatment of pain in neurologic disorders (an evidence-based review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2010 January 12, 2010;74(2):173-6. PMID: 20042705.

94. Vroomen PC, de Krom MC, Slofstra PD, et al. Conservative treatment of sciatica: a systematic review. J Spinal Disord. 2000 Dec;13(6):463-9. PMID: 11132976.

95. Luijsterburg PAJ, Verhagen AP, Ostelo RWJG, et al. Effectiveness of conservative treatments for the lumbosacral radicular syndrome: a systematic review. European Spine Journal. 2007 Jul;16(7):881-99. PMID: 17415595.

96. Johnson M, Neher JO, St Anna L. Clinical inquiries. How effective--and safe--are systemic steroids for acute low back pain? J Fam Pract. 2011 May;60(5):297-8. PMID: 21544281.

97. Lewis RA, Williams NH, Sutton AJ, et al. Comparative clinical effectiveness of management strategies for sciatica: systematic review and network meta-analyses. Spine Journal: Official Journal of the North American Spine Society. 2013 Oct 4PMID: 24412033.

98. Kalauokalani D, Cherkin DC, Sherman KJ, et al. Lessons from a trial of acupuncture and massage for low back pain: Patient expectations and treatment effects. Spine. 2001;26(13):1418-24. PMID: 11458142.

99. Linde K, Witt CM, Streng A, et al. The impact of patient expectations on outcomes in four randomized controlled trials of acupuncture in patients with chronic pain. Pain. 2007 Apr;128(3):264-71. PMID: 17257756.

100. National Institute for Health and Care Excellence. Low back pain: Early management of persistent non-specific low back pain. 2009. http://www.nice.org.uk/guidance/cg88/chapter/1-guidance. Accessed on March, 10th 2015.

101. Koes BW, Enthoven WT. Do patients with acute low-back pain need paracetamol? Lancet. 2014 Nov 1;384(9954):1556-7. PMID: 25064595.

102. Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. Journal of Pain. 2009 Feb;10(2):113-30. PMID: 19187889.

103. Whitlock EP, Lin JS, Chou R, et al. Using Existing Systematic Reviews in Complex Systematic Reviews. Annals of Internal Medicine. 2008;148(10):776-82. PMID: 18490690.

104. Gagnier JJ, van Tulder M, Berman B, et al. Herbal medicine for low back pain. Cochrane Database of Systematic Reviews. 2006(2):CD004504. PMID: 16625605.

105. Abdel Shaheed C, Maher CG, Williams KA, et al. Interventions available over the counter and advice for acute low back pain: systematic review and meta-analysis. Journal of Pain. 2014 Jan;15(1):2-15. PMID: 24373568.

106. Dupeyron A, Ribinik P, Gelis A, et al. Education in the management of low back pain: literature review and recall of key recommendations for practice. Annals of Physical & Rehabilitation Medicine. 2011 Jul;54(5):319-35. PMID: 21782541.

107. Dahm KT, Brurberg KG, Jamtvedt G, et al. Advice to rest in bed versus advice to stay active for acute low-back pain and sciatica. Cochrane Database of Systematic Reviews. 2010(6):CD007612. PMID: 20556780.

108. Chuter V, Spink M, Searle A, et al. The effectiveness of shoe insoles for the prevention and treatment of low back pain: a systematic review and meta-analysis of randomised controlled trials. BMC Musculoskeletal Disorders. 2014;15:140. PMID: 24775807.

109. Huang C-Y, Choong M-Y, Li T-S. Effectiveness of cupping therapy for low back pain: a systematic review. Acupuncture in Medicine. 2013 Sep;31(3):336-7. PMID: 23886511.

110. Oliveira VC, Ferreira PH, Maher CG, et al. Effectiveness of self-management of low back pain: systematic review with meta-analysis. Arthritis care & research. 2012 Nov;64(11):1739-48. PMID: 22623349.

111. Moore RA, Derry S, Wiffen PJ. Challenges in design and interpretation of chronic pain trials. Br J Anaesth. 2013 Jul;111(1):38-45. PMID: 23794643.

112. National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). Effectiveness of Oral Prednisone in Improving Physical Functioning and Decreasing Pain in People with Sciatica (ACT FAST). Kaiser Permanente; 2008.

113. Pincus T, McCracken LM. Psychological factors and treatment opportunities in low back pain. Best Practice & Research in Clinical Rheumatology. 2013 Oct;27(5):625-35. PMID: 24315144.

114. Patel S, Friede T, Froud R, et al. Systematic review of randomized controlled trials of clinical prediction rules for physical therapy in low back pain. Spine (Phila Pa 1976). 2013 Apr 20;38(9):762-9. PMID: 23132535.

115. Kent P, Kjaer P. The efficacy of targeted interventions for modifiable psychosocial risk factors of persistent nonspecific low back pain - a systematic review. Manual Therapy. 2012 Oct;17(5):385-401. PMID: 22421188.

116. van der Giessen RN, Speksnijder CM, Helders PJM. The effectiveness of graded activity in patients with non-specific low-back pain: a systematic review. Disability & Rehabilitation. 2012;34(13):1070-6. PMID: 22148906.

117. Balague F, Piguet V, Dudler J. Steroids for LBP - from rationale to inconvenient truth. Swiss Medical Weekly. 2012;142:w13566. PMID: 22495738.

118. Group Health Cooperative. Matching Appropriate Treatments to Consumers' Healthcare Needs, MATCH. 2014.

119. Delitto A. Targeted interventions to Prevent Chronic Low Back Pain in High Risk Patients: A Multi-Site Pragmatic RCT. 2015. http://www.pcori.org/research-results/2015/targeted-interventions-prevent-chronic-low-back-pain-high-risk-patients-multi. Accessed on March, 10th 2015.

120. Foster NE, Hill JC, O'Sullivan P, et al. Stratified models of care. Best Pract Res Clin Rheumatol. 2013 Oct;27(5):649-61. PMID: 24315146.

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 U.S. 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 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 interdisciplinary 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).

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 provisional Key Questions, population, intervention, comparator, outcomes, timing, settings, and study designs (PICOTS), and analytic framework for this topic were posted on the Agency for Healthcare Research and Quality (AHRQ) Web site for public comment from December 17, 2013, through January 17, 2014. Some changes were made in response to public comments. The PICOTS were revised to include Tai Chi as an intervention and time between back pain episodes as an outcome, and the Key Questions and PICOTS were 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 (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.

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? (Including NSAIDs, acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, corticosteroids, and topicals/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? (Including but not limited to interdisciplinary rehabilitation, exercise (various types), physical modalities (ultrasound, transcutaneous electrical nerve stimulation [TENS], electrical muscle stimulation [EMS], interferential therapy [IFT], 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

<u>KQ1: Oral or topical pharmacologic therapies (or combinations thereof)</u>

- 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

<u>KQ2: Noninvasive, nonpharmacological therapies (or combinations thereof)</u>

- 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)

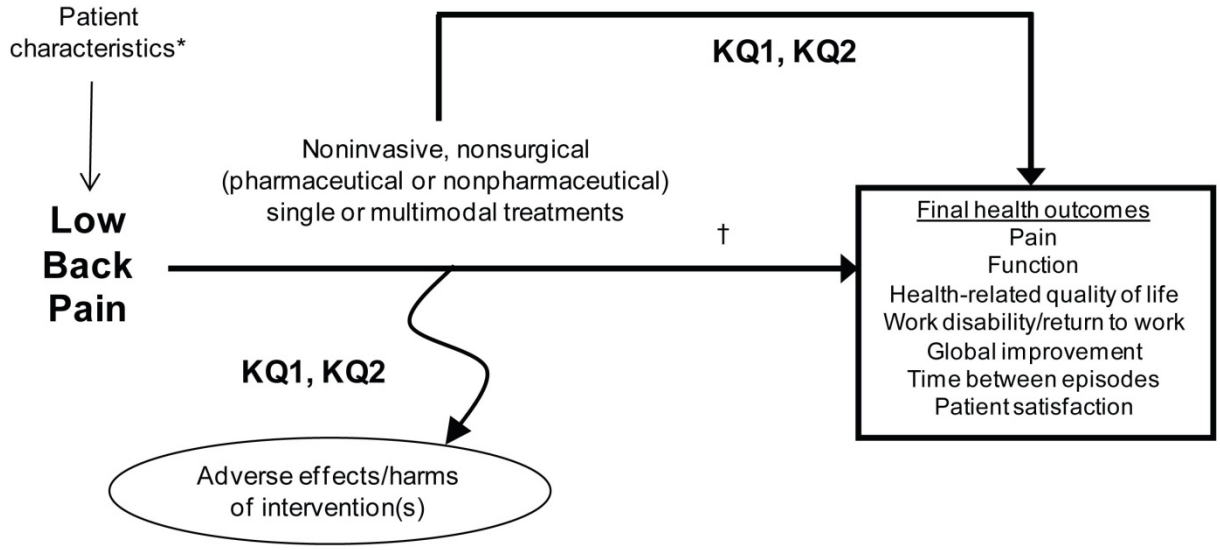
Setting

- Any nonhospital setting or in self-directed care

Analytic Framework

The analytic framework 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).

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 (SRC) developed preliminary Key Questions based on input from the topic nominator. An Evidence-based Practice Center (EPC) 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 EPC 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.

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 low back pain, radicular low back pain (e.g., due to herniated disc), and symptomatic 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 if the therapeutic effects were felt to be similar to oral administration. Nonpharmacological therapies were interdisciplinary rehabilitation (defined as an intervention consisting at a minimum of physical therapy plus psychological therapy, with some coordination); 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. 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, 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 interdisciplinary 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. 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 as 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 U.S. 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 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 between 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 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 difference of 5 to 10 points on a 100-point visual analogue scale (VAS) or equivalent; for function as a mean difference of 5- to 10-point difference on the Oswestry Disability Index (ODI) or 1 to 2 points on the 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 100-point VAS, for function as a mean difference of 10 to 20 points on the ODI or 2 to 5 points on the RDQ, and for any outcome as an SMD of 0.5 to 0.8. Large/substantial effects were defined as greater than moderate. We 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 low back pain, radicular low back pain, spinal stenosis), 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).

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 between reviews. When findings between 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 G** for the strength of evidence table.

Peer Review and Public Commentary

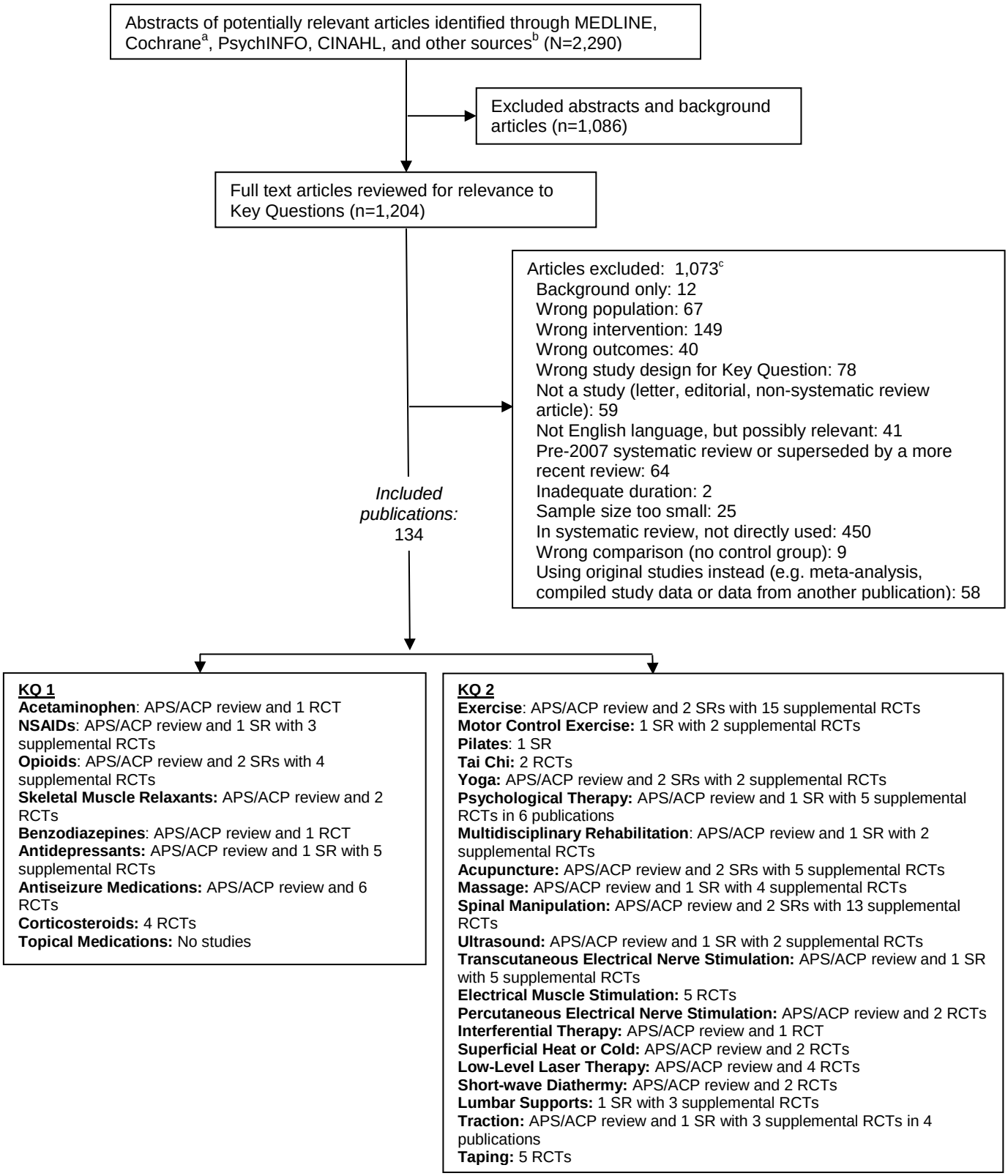
Peer reviewers with expertise in primary care and back pain have been invited to provide written comments on the draft report. The AHRQ Task Order Officer and an Evidence-based Practice Center Associate Editor will also provide comments and editorial review. The draft report will be posted on the AHRQ 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 2,990 potentially relevant articles. After dual review of abstracts and titles, 1,204 articles were selected for full-text dual review and 134 studies 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



[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] Three publications were included in one or more interventions and also excluded for one or more other interventions

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? (Including NSAIDs, acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, corticosteroids and topicals/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 (SOE: moderate).
- For acute low back pain, a systematic review found no difference between acetaminophen versus NSAIDs in pain intensity (3 trials, pooled SMD 0.21, 95% confidence interval [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 (SOE: low)
- 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.
- 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 included eight trials of acetaminophen **(Appendix E1)**. One trial evaluated acetaminophen versus no treatment,[29] five trials included in a systematic review[30, 31] evaluated acetaminophen versus various NSAIDs,[29, 32-35] and three trials evaluated acetaminophen versus other interventions (amitriptyline,[36] electroacupuncture,[37] and manipulation, corset, or physical therapy[38]). The sample size was 70 in the trial of acetaminophen versus no treatment, sample sizes ranged from 45 to 70 in the trials of acetaminophen versus NSAIDs, and sample sizes were 39, 40 and 456 in the trials of acetaminophen versus other interventions. One trial evaluated acetaminophen for chronic low back pain,[33] one mixed acute to chronic low back pain,[38] and the remainder acute low back pain. No trial specifically focused on patients with radiculopathy. Acetaminophen doses were 4 g/day in 3 trials,[32-34] 3 g/day in 1 trial,[29] 2 g/day in one trial,[36] and unclear in 3 trials.[36-38] Duration of treatment ranged from 1 to 5 weeks. Four trials evaluated patients at 3 to 9 weeks after the completion of therapy[29, 34, 37, 38] and the remainder evaluated patients at the end of therapy. Two trials[33, 36] 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[39, 40] to the systematic review[31] of acetaminophen versus NSAIDs included one additional high-quality trial (n=371) of patients with acute pain **(Table 1)**.[41] 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 E2, F1)**.[42] 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.[42] Differences between acetaminophen and placebo were ≤0.2 points on a 0-10 pain scale and ≤0.6 on the 0-24 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.[29] 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.[40] Another low quality trial (n=50) that was not included in the meta-analysis also found no differences.[34]

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).[33]

Acetaminophen Versus Other Interventions

Acute Low Back Pain

Four trials found no clear differences between acetaminophen versus nonpharmacologic therapies (heart wrap therapy, electroacupuncture, physical therapy, corset, or spinal manipulation)[37, 38, 41] or amitriptyline,[36] but there was insufficient evidence to reach reliable conclusions because each comparison was only evaluated in one trial and due to methodological shortcomings in the studies.

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).[42] 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).[40] 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.[41] Adverse events were not reported in other trials of acetaminophen versus other interventions.[36-38]

NSAIDs

Key Points

- For acute low back pain, a systematic review found NSAIDs associated with greater improvement in pain intensity versus placebo (4 studies, 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 versus the other intervention alone to determine effectiveness (SOE: insufficient).
- There was insufficient evidence from two trials to determine the effects of NSAIDs versus interventions other than acetaminophen and opioids (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[43] included a good-quality systematic review with 51 trials of NSAIDs **(Appendix E3)**.[30, 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, Appendixes E4, F2)**.[40] 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 were 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 mg per day to 2400 mg per day, diclofenac doses ranged from 48 mg per day 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 and 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.[40]

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; Appendixes E5, F3).** 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 pain;[45, 53-62] studies that focused on patients with acute sciatica are discussed separately. In studies 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).[40] 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 timepoint versus placebo), as measured on a 100 mm 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).[40] 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, 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.[40] 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.[40]

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).[40] 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

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,

I^2=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; I^2=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 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, I^2=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, I^2=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 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 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 between different long-acting opioids in pain or function (SOE: moderate).
- 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 **(Appendix E6)**.[14] 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 RCTs (reported in 15 publications) **(Table 1; Appendixes E7, F4)**.[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, 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[35, 86] from the APS/ACP review that were not included in the systematic review and 4 additional newer trials **(Table 4; Appendixes E8, F5)**.[87-90] Sample sizes ranged from 36 to 302 subjects. One trial evaluated patients with acute low back pain[35] 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. One of the newer trials was rated good-quality,[88] two fair-quality,[87,90] 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.

Of the 23 total trials, 8 employed an enriched enrollment and withdrawal design. In this approach, 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.[91]

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] Finally, 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.[92] 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 review[93] of opioids for chronic noncancer pain that included three head-to-head trials of different long-acting opioids

for low back pain[85, 94, 95] and five trials of long-acting versus short-acting opioids,[86, 96-99] and two other trials that evaluated comparisons among opioids.[100, 101]

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 (I^2=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; I^2=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]

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, I^2=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, I^2=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).[35] 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. In the trials, patients were titrated for effective pain relief in both arms.[93] One trial[94] 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.[95] One other trial found no differences between extended-release morphine versus controlled-release oxycodone in pain or function.[100]

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.[93] Three trials found no differences between long-acting versus immediate-release preparations in pain control.[96, 97, 99] 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.[101]

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% of patients randomized to opioids versus 9% randomized to placebo among trials that did not use an enrichment design (difference 17%, 95% CI 13 to 21), 26% vs. 7% for constipation (difference 20%, 95% CI 15 to 25), 24% vs. 7% for somnolence/drowsiness (difference 14%, 95% CI 10 to 18), and 15% vs. 2% for pruritus (difference 10%, 95% CI 5 to 15).[91] In trials that used an enrichment design, rates were 16% vs. 8% for nausea (difference 7%, 95% CI 0% to 14%), 15% vs. 3% for constipation (difference 11%, 95% CI 6 to 16), 10% vs. 5% for somnolence/drowsiness (difference 3%, 95% CI 1 to 7), 10% vs. 5% for dizziness/vertigo (difference 5%, 95% CI 2 to 8), and 5% vs. 2% 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 serious adverse events, including overdose, 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; I^2=0%) and 5 to 7 days (3 trials; RR 1.72, 95% CI 1.32 to 2.22; I^2=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; I^2=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 between 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; I^2=50%); one additional placebo-controlled trial was consistent with these findings (SOE: moderate).

Detailed Synthesis

The APS/ACP review[43] included a good-quality systematic review of skeletal muscle relaxants[102] with 22 studies **(Appendix E9)**.[103-124] Twelve trials compared a skeletal muscle relaxant versus placebo,[103-106, 108, 111, 113-115, 117, 118, 120] four compared a skeletal muscle relaxant plus an NSAID versus an NSAID alone,[109, 112, 122, 124] two compared a skeletal muscle relaxant versus another active treatment,[116, 123] and three compared one skeletal muscle relaxant versus another.[110, 119, 121] 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.[117] Only three trials followed patients after treatment had been completed.[105, 122, 124] Sample sizes ranged from 20 to 405 (median n=80). Eighteen of the trials enrolled patients with acute back pain and four[105, 111, 119, 120] enrolled patients with chronic back pain. The review classified 17 trials[103, 104, 106-108, 110-113, 115-122, 124] as high quality based on meeting at least 6 of 11 Cochrane Back Review criteria; the other five trials were classified as low quality.[105, 109, 114, 119, 123] 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 ACP/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 E10, F6)**.[125, 126] One trial evaluated carisoprodol 1000 mg/day (250 mg three times daily) versus placebo (n=562)[126]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.[125] 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; I^2=0%) and 5 to 7 days of treatment (3 trials; RR 1.72, 95% CI 1.32 to 2.22; I^2=0%.)[102] 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 (I^2=89%); the difference was no longer statistically significant after 5 to 7 days (RR 1.47, 95% CI 0.88 to 2.44; I^2=34%)

A more recent fair-quality trial of carisoprodol versus placebo (n=562) was consistent with the systematic review. It 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.)[126]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[111] found dantrolene associated with better pain-related outcomes versus placebo and one low-quality trial (n=69)[105] 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).[120]

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; I^2=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; I^2=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; I^2=34%).[102]

One fair-quality (n=197) trial not included in the systematic review compared tizanidine plus aceclofenac with aceclofenac alone.[125] 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).[125]Results 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[105, 127, 128] 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 review[102] found no differences in any outcome between carisoprodol versus cyclobenzaprine (1 trial [n=78]),[121] or tizanidine versus chlorzoxazone (1 trial [n=27]),[110] for acute back pain or pridinol versus thiocolchicoside (1 trial [n=120]) for chronic back pain.[119]

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; I^2=50%).[102] 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; I^2=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; I^2=50%), or when added to an NSAID (3 trials; RR 2.77, 95% CI 1.18 to 6.46; I^2=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; I^2=50%) or when added to an NSAID (3 trials; RR 0.48, 95% CI 0.23 to 1.00; I^2=50%).[102]

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).[125] 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.[126] No serious adverse events were reported in either study.[125, 126]

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; I^2=0%).[102] 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 failure to improve 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 failure to experience 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 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 included a systematic review of skeletal muscle relaxants for low back pain[102] that included eight trials of benzodiazepines.[105, 127-133] The sample size was 152 in one trial;[132] and ranged from 30 to 80 in the other trials. Four trials compared a benzodiazepine versus placebo,[105, 129-131] one trial compared a benzodiazepine plus physical therapy versus placebo plus physical therapy,[132] and three trials compared a benzodiazepine versus a skeletal muscle relaxant (carisoprodol,[127] cyclobenzaprine,[105] or tizanidine[128]). One other trial evaluated a benzodiazepine versus drugs that are not available in the United States.[133] Four trials in the systematic review evaluated benzodiazepines for acute low back pain[127, 128, 130, 131] and three for chronic low back pain.[105, 129, 132] Two trials specifically enrolled patients with muscle spasms.[105, 128] No trial focused on patients with radiculopathy; in one trial the proportion of patients with radiculopathy was 40%.[130] Five trials evaluated diazepam[105, 127, 128, 130, 131] and two trials evaluated tetrazepam (not available in the United States).[129, 132] Diazepam was administered orally at doses of 5 to 10 mg three or four times daily in three trials;[105, 127, 128] two trials evaluated regimens that included initial intramuscular diazepam and oral doses.[130, 131] In both trials of tetrazepam, the dose was 50 mg by mouth three times daily.[129, 132] The duration of therapy ranged from 6 to 14 days; two trials[105, 129] 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[127-130, 132] based on meeting at least 6 of 11 Cochrane Back Review group criteria; the other two trials were classified as low quality.[105, 131] All trials utilized 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 was 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 tid for 5 days versus placebo for acute radiculopathy due to prolapse lumbar disc (with CT or MRI confirmation) **(Table 6; Appendix E11, F7)**.[134] 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)[130] included in the APS/ACP review found no differences between diazepam and placebo in likelihood of improvement in 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)[131] 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)[129, 132] included in the APS/ACP review found tetrazepam associated with lower likelihood of failure to improve 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 failure to experience 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.[132] One low-quality trial (n=76) found no difference between diazepam versus placebo in outcomes related to muscle spasm.[105]

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.[134] 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.[127, 128] One trial (n=30) found no differences between diazepam versus tizanidine in measures of pain relief or daily activities.[128] 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).[127]

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.[105]

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 compared to placebo, though harms were not reported well.[102] No trial was designed to evaluated 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.[134]

Antidepressants

Key Points

- For chronic low back pain, a systematic review found no difference between tricyclic antidepressants versus placebo in pain (4 trials; SMD −0.10, 95% CI −0.51 to 0.31; I^2=32%) or SSRIs versus placebo (3 trials; SMD 0.11, 95% CI −0.17 to 0.39; I^2=0%); there was also no difference between antidepressants versus placebo on function (2 trials, SMD −0.06, 95% CI −0.40 to 0.29; I^2=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).
- No study compared duloxetine versus a tricyclic antidepressant.
- Antidepressants were associated with higher risk of any adverse events compared to placebo, with no difference in risk of serious adverse events (SOE: moderate).

Detailed Synthesis

The APS/ACP review[43] included three higher-quality systematic reviews[135-137] of antidepressants for low back pain. The reviews included a total of 10 unique trials (8 placebo controlled). Based on the evidence in the systematic reviews, the APS/ACP review[43] 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[138] on antidepressants for low back pain published subsequent to the APS/ACP review **(Table 1; Appendix E12, F8)**. The review included 10 trials (n=16 to 121);[139-148] seven of the trials were included in one or more of the older systematic reviews.[139, 141-144, 146, 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[148] 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,[141] benztropine,[140] or atropine[147]) 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).[141] 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.[139] Seven trials were assessed as high quality based on meeting at least 6 Cochrane Back Review Group criteria. Methodological limitations in the 3 lower-quality trials included inadequate description of randomization and allocation concealment methods and high rates of attrition.[138]

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 E13, F9**).[149-153] Three trials compared duloxetine (a serotonin-norepinephrine reuptake inhibitor) versus placebo,[151-153] one trial duloxetine versus escitalopram,[150] and one trial amitriptyline versus bupropion.[149] One trial was rated good quality,[151] three trials fair quality,[150, 152, 153] and one trial poor quality.[149] 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; I^2=0%), with a point estimate close to 0 (no effect).[138] 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; I^2=32%) or SSRIs (3 trials; SMD 0.11, 95% CI −0.17 to 0.39; I^2=0%). The review also found that antidepressants were not associated with reduced depression (SMD 0.06, 95% CI −0.29 to 0.40; I^2=0%) or improved function (SMD −0.06, 95% CI −0.40 to 0.29; I^2=0%), but each of these outcomes was only evaluated in two trials.

One good-quality[151] and two fair-quality[152, 153] trials evaluated duloxetine versus placebo for chronic low back pain a 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.[151] 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% versus 35%; RR 1.41, 95% CI 1.11 to 1.78).[152]

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 versus −2.22; p=0.26).[152] 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).[151] Two other fair-quality trials found no differences between duloxetine and placebo in mean change in CGI-S scores.[152, 153]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).[153]

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[36] included in the APS/ACP review[43] 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).[141] 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.)[154]

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.[150, 151] 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.[149]

Harms

The APS/ACP review[43] found antidepressant use associated with a higher risk for any adverse event compared to placebo (22% vs. 14%; RR 1.73, 95% CI 1.17 to 2.55) based on an older systematic review.[136] 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 and placebo in risk of serious adverse events, with no deaths reported.[151-153] 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; I^2=0%]; duloxetine 60 mg versus placebo [OR 2.52, 95% CI 1.58 to 4.03; I^2=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[150] or amitriptyline versus bupropion[149] 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 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 included four trials of antiseizure medications for low back pain **(Appendix E14)**.[155-158] Two trials (n=50 and 65)[156, 158] evaluated gabapentin and two trials (n=29 and 96)[155, 157] evaluated topiramate. All trials compared antiseizure medications versus placebo, with one trial[155] utilizing an "active" placebo (diphenhydramine). Three trials[155, 156, 158] evaluated patients with radicular symptoms and one trial (of topiramate)[157] evaluated a mixed population of patients with radicular or nonradicular pain.

We identified six trials of antiseizure medications for low back pain published subsequent to the APS/ACP review **(Table 8; Appendix E15, F10)**.[159-164] Sample sizes were 211 and 309 in the two largest trials[159, 160] and ranged from 26 to 55 in the other four trials. Five trials[159-163] evaluated pregabalin and one trial[164] evaluated gabapentin. Two trials compared pregabalin versus placebo[159] or active placebo (diphenhydramine)[161] and one trial[164] compared gabapentin versus no gabapentin. The other trials compared pregabalin plus another medication (tapentadol,[160] transdermal buprenorphine,[162] or celecoxib[163]) versus the other medication without pregabalin. The celecoxib trial also compared pregabalin alone versus celecoxib alone.[163] Five trials evaluated patients with radicular symptoms,[159-161, 163, 164] with two trials[161, 164] focusing on patients with spinal stenosis. One trial enrolled patients with nonradicular back pain.[162]

Including the trials in the APS/ACP review, all of the trials evaluated patients with chronic symptoms. Dosing of antiseizure medications varied. One trial evaluated fixed-dose pregabalin 300 mg/day in combination with transdermal buprenorphine.[162] In the other pregabalin trials, doses were titrated, though titration protocols and maximum doses varied. Two trials[155, 157] 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.[156, 158, 164] 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,[160] which evaluated patients 1-2 weeks after completing 8 weeks of therapy.

Three trials[155, 161, 163] used a crossover design and the rest were parallel-group trials. Six trials[157, 159-163] were rated fair-quality and four[155, 156, 158, 164] 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 utilized an enrichment/withdrawal design.[159] None of the crossover trials reported results of the first intervention period and two of the crossover trials[161, 163] 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.[165]

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.[165] 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.[156, 158] One trial (n=80) found no clear differences between gabapentin (titrated up to 1200 mg/day) versus placebo in back 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).[156] 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).[158]

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%).[164] 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.[155, 157] 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).[157] 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)[155] 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.[159] Pregabalin was superior for outcomes related to sleep and HADS depression and anxiety, but effects appeared 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.[161] 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).[163]

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, $p<0.05$).[162]

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[163] 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.[160] 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.[158] 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.[156] One subsequent trial of gabapentin versus placebo also reported no withdrawals, though ataxia (7%) was reported with gabapentin.[164]

Harms were reported in two trials of topiramate versus placebo.[155, 157] One trial found topiramate associated with higher likelihood of withdrawal due to adverse events versus diphenhydramine (33% vs. 15%),[155] but there was no difference between topiramate versus placebo in rates of withdrawal due to adverse events in the other (4% vs. 4%).[157] 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 to diphenhydramine in one trial.[155]

Two trials published reported harms associated with pregabalin versus placebo.[159, 161] One trial[161] found pregabalin associated with greater risk of any adverse event versus diphenhydramine (active placebo) (64% vs. 35%), though the other trial[159] 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[161] reporting increased risk and the other[159] 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).[159]

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.[160, 162, 163]

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 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).
- 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 included four trials of systemic corticosteroids **(Appendix E16)**.[166-169] Three trials (n=49 to 60)[166, 168, 169] evaluated systemic corticosteroids in patients with radiculopathy and one trial (n=86)[167] 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 three trials[170-172] of systemic corticosteroids published subsequent to the APS/ACP review and one older trial[173] that was not included in the APS/ACP review **(Table 9; Appendix E17, F11)**. Three trials (n=27 to 78)[171-173] evaluated patients with radicular pain and one trial (n=67)[170] evaluated patients with nonradicular pain.

All of the trials were placebo-controlled. Five trials[166, 167, 170-172] evaluated patients with acute low back pain (including the two trials of nonradicular back pain)[167, 170] and the other three[168, 169, 173] did not specify the duration of symptoms. Three trials were conducted in emergency department settings,[167, 170, 171] one trial in an inpatient setting,[166] 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).[166, 167, 171] In the other trials, the duration of treatment ranged from 5 to 9 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]).[168, 169, 173] The other two trials evaluated different courses of oral prednisone (50 mg for 5 days,[170] or 60 mg for 3 days, 40 mg for 3 days, and 20 mg for 3 days[172]). 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[169, 170] to 1 to 4 years after a 1-week course of therapy.[168]

Among the trials of systemic corticosteroids for radiculopathy, two trials(Friedman)[172] required a positive straight leg raise for inclusion and four others[166, 168, 169, 173] 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.[166]

Three trials[166, 167, 171] were rated good-quality, four trials fair-quality,[168-170, 173] and one trial poor-quality.[172] 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.[172]

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.[174]

Systemic Corticosteroids Versus Placebo

Acute Low Back Pain

Two trials evaluated the effects of systemic corticosteroids versus placebo for acute nonradicular low back pain.[167, 170] The APS/ACP review included one good-quality trial (n=86) that found no differences between a single intramuscular injection of 160 mg po methylprednisolone versus placebo in pain relief or improvement in the RDQ at 1 week or 1 month.[167] 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.[170]

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.[174]

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.[166, 168, 169] 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.[166] 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.[168, 169]

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.[171, 172] A good-quality trial (n=78)[171] evaluated outcomes through 1 month after a single dose of intramuscular methylprednisolone 160 mg and one poor-quality trial (n=27)[172] 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.[173]

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.[166] In two trials, a smaller (160 mg) intramuscular methylprednisolone injection was associated with no cases of hyperglycemia requiring medical attention, infection, or gastrointestinal bleeding.[167, 171] 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.[173] 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? (Including but not limited to interdisciplinary rehabilitation, exercise (various types), physical modalities (ultrasound, transcutaneous electrical nerve stimulation [TENS], electrical muscle stimulation [EMS], interferential therapy [IFT], 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 usual care 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 chronic low back pain, a systematic review found exercise associated with greater pain relief versus usual care (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 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 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).
- There were no clear differences between different exercise regimens 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[43] included six systematic reviews[175-181] with a total of 79 unique trials and one additional large, lower quality trial **(Appendix E18)**.[182] The most comprehensive systematic review in the 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).[183] 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 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). 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 two systematic reviews of exercise for low back pain published subsequent to the APS/ACP review **(Table 10; Appendix E19, F12)**.[184, 185] One focused on exercise for nonspecific chronic low back pain[184] and the other review evaluated effects of exercise on work disability in patients with nonacute, nonspecific low back pain (duration >4 weeks).[185]

The review of exercise therapy for chronic low back pain included 37 RCTs (n = 3957).[184] 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[183] plus 29 additional trials; it excluded a number of trials in the previous review because it applied more strict criteria for 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 (ATEP).[184] Comparisons of exercise versus other active interventions (behavioral treatment, passive modalities [TENS, laser, ultrasound, massage], spinal manipulations and psychotherapy), are discussed in other sections in the results 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,[186-212] 11 (41%) were rated low risk of bias, based on meeting ≥6 of 11 Cochrane Back Review Group criteria.[188-190, 194, 195, 198-200, 204, 206, 211, 213] 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% of trials did not report blinding of outcome assessors.

The second, fair quality review evaluated effects of exercise specifically on work disability in patients with nonacute (>4 weeks), nonspecific low back pain.[185] 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[203, 214-221] (39%) were rated high quality and the remainder were considered low quality, based on risk of bias criteria by June et al. Methodological shortcomings included detection bias in 12 trials (52%), selection bias in 9 trials (39%), and attrition bias in 8 trials (35%).

We identified 15 trials of exercise for low back pain not included in the systematic reviews with sample sizes >100 (**Table 11; Appendix E20, F13)**.[222-236] Three trials evaluated exercise versus no exercise or usual care for acute to subacute low back pain,[226, 235, 236] two trials compared different types of exercise for patients primarily with subacute low back pain ,[225, 228] four trials compared exercise versus no exercise or usual care for chronic low back pain,[232-234, 237] three trials compared different types of exercise for chronic low back pain,[224, 231, 233] and three trials evaluated exercise versus various other interventions for radicular low back pain.[222, 223, 230] 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, and others. Three trials were rated good-quality,[224, 232, 234] six trials fair-quality[222, 223, 226, 227, 231, 235, 236] and five poor-quality.[225, 228, 230, 233, 237] Methodological shortcomings included inadequate allocation concealment, failure to clearly described cointerventions, and failure to report compliance to treatment. Patients and caregivers were not blinded in trial.

We also identified 24 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[194, 197, 238-253] and 11 compared different forms of exercise.[194, 197, 239, 242, 252, 254-259] 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).[183] 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.[226, 235, 236] For acute or subacute low back pain, a good-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).[236] Exercise plus advice was also associated with better scores on the Patient-Specific Functional Scale (PSFS) (differences 1.1 to 1.3 on an 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.[235] There were no differences in disability at either timepoint (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.[226]

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).[183] A more recent systematic review[184] 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)[190, 197, 207] and better function (3 RCTs, WMD −12.35 on a 0 to 100 scale, 95% CI –23.0 to –1.69)[190, 197, 207] 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).[190, 200, 211]

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.[234] 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 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 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 timepoints (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 session without exercise with respect to the effect on the number of low back pain days and function.

A poor-quality trials (n=240) not included in the systematic review 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).[233] 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 trials (n=100 and 105) of exercise for subacute to chronic low back pain (mean duration of symptoms not reported).[232, 237] 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).[232] 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.[237]

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).[185] 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.[194, 197, 238-248, 251-253] For pain, 11 trials reported differences favoring exercise;[238, 239, 241, 242, 244, 245, 247, 248, 251-253] the other five found no differences between groups.[194, 197, 240, 243, 246] Of the 12 trials that reported on function, results favored exercise in nine[239, 241, 242, 244-246, 251-253] and three found no differences.[194, 197, 243] Quality of life was reported by five trials, three of which favored exercise[241-243] and two of which found no difference between groups.[194, 197] Global improvement was reported by two studies with results favoring exercise in one[245] but not the other.[194]

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.[227, 249] 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.[227] No differences between treatments were seen on the EQ5D. 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.[249]

Efficacy of Exercise Therapy Versus Education or Back School

Chronic Low Back Pain

The systematic review[184] included three trials of exercise (yoga, Pilates and MCE) versus education or back school.[187, 193, 210] One small trial (n=53) found no differences between 10- to 60-minute sessions of Pilates versus back school (n =53) in post-intervention pain (mean difference 0.2 on a 0 to10 scale) or function (mean difference 0.8 the ODI).[187] The trials of yoga[210] and MCE[193] are discussed in those sections of this report.

One other small trial (n= 61) reported no differences between exercise therapy versus a single education session or between exercise versus conventional PT in pain of function for subacute to chronic low back pain at 6 or 12 months.[250]

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.[222, 223, 230] 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% of the sample had lower extremity motor deficits.[223] 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%).[223]

In one fair quality trial, the difference in median pain scores at 6 months for education plus four PT 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.[222] Education plus PT was also associated with better function versus usual care (mean difference in improvement 2.3, 95% CI 1.7 to 2.9 on the RDQ) 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.[230] Mean differences between PT 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 Exercise

Acute And Subacute Low Back Pain

The APS/ACP review included a higher-quality systematic review[180] 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 between different types of exercise.[225, 228] One trial compared PT based on a treatment based classification system (TBC) plus graded exposure (GX), TBC plus graded activity (GA), and TBC only[225] and one trial compared lumbar extensor strength training versus "regular" PT.[228]

Chronic Low Back Pain

The APS/ACP review[43] found few trials that directly compared different types of exercise for chronic low back pain, with no clear differences.[16] The APS/ACP review also included a meta-regression that was conducted in conjunction with a higher-quality systematic review.[260] 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 to no treatment. and improve function by 5.5 points (95% CI 0.5 to 10.5) compared to

no treatment. However, trials to directly confirm the incremental benefits of exercise therapies utilizing these factors are not available.

A more recent systematic review[184] included 11 trials that compared different exercise interventions[188, 189, 194, 196, 198, 199, 202-204, 208, 212] Results could not be pooled because of differences in the exercise regimens and comparisons evaluated. Only two trials reported statistically significant differences between 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.[189] 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.[208]

Two subsequent trials that compared various forms of exercise in patients with chronic low back pain found no differences in pain relief.[224, 231] One good-quality trial (n=201) compared supervised exercise focused on core strengthening versus home exercise[224] and the other compared exercise therapy, a walking program or usual physical therapy.[231]

One poor quality trial (n=180 for exercise groups) that evaluated different intensities of exercise found the greatest intensity of periodized musculoskeletal rehabilitation (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).[233]

Eleven smaller trials (n<100) also compared different forms of exercise for chronic low back pain. In three trials, results for pain favored global postural reeducation versus stabilization exercises; exercise and stabilization training versus routine exercises; or periodized resistance training versus periodized aerobic exercise.[242, 254, 258] Six other trials found no differences between different types of exercises in outcomes related to pain.[197, 239, 252, 256, 257, 259] Similar results were reported for other outcomes, with most trials reporting no clear differences.

Harms

Harms were poorly reported in trials of exercise.[43, 184] When reported, harms were typically related to muscle soreness and increased pain,[224, 228, 231, 236, 261] or no harms were reported.[222, 225, 232, 234] Serious harms were not reported in patients who underwent exercise therapy.[230]

Motor Control Exercise (MCE)

Key Points

- 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 chronic low back pain, a systematic review included two trials that 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. 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 chronic low back pain, a systematic review found MCE associated with lower pain intensity versus multimodal PT at intermediate term (4 trials, WMD, −14.20, 95% CI−21.23 to −7.16) and two trials found MCE associated with decreased disability versus PT at intermediate-term (WMD −12.98 on 0 to 100 scale, 95% CI −19.49 to −6.47) (SOE: low).
- Two trials found no clear differences between MCE plus another type of exercise versus the other type of exercise alone (SOE: low). Harms were poorly reported in trials of MCE, but few adverse events were reported, with no clear difference in risk (SOE: low).

Detailed Synthesis

The APS/ACP review did not specifically evaluate motor control exercises (MCE) and a systematic review[183] on exercise therapies in the APS/ACP review did not include any studies of MCE.

We identified a recent systematic review that included 16 trials of MCE (sample size range 30 to 346, total n =1993) **(Table 10; E21,F14)**.[262] 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. However, 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),[189, 263-268] three trials of MCE versus a minimal intervention (no intervention, advice/education or placebo short-wave therapy and ultrasound),[193, 269, 270] and four trials of MCE versus multimodal physical therapy (including ultrasound, electrotherapy, lumbar strengthening, passive physical therapy and general exercise).[267, 271-273] Two trials evaluated MCE as part of a multimodal intervention versus other components of that intervention.[274, 275] Eight trials included only chronic low back pain patients;[189, 193, 263, 265-267, 269, 270] three trials also included patients with subacute low back pain, but mean duration of symptoms was 25 to 34 months.[268, 271, 273]Three trials focused on patients with recurrent low back pain, with duration of the current episode ranging from >6 weeks to >3 months.[268, 272, 274] 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[189, 263, 264, 266, 267, 269-275] and six low quality.[193, 264, 266, 268, 270, 271] 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).

Two trials published subsequent to the systematic review also evaluated MCE for low back pain **(Table 12; Appendix E22, F15)**.[276] One fair quality trial (n=172) compared MCE versus graded activity (12 individualized sessions over 8 weeks supplemented with 2 booster sessions and home practice) for chronic low back pain, with followup through 12 months.[276] A small (n=30), poor quality trial compared 4 weeks of MCE versus conventional exercise (stretching, isometric back muscle exercises, graded flexion/extension of spine) with followup for 2 months after the end of treatment.[277] Patients could not be blinded in either trial.

MCE Versus General Exercise

Chronic Low Back Pain

The 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)[189, 263-266, 268] and at intermediate-term (3 trials, WMD −6.06, 95% CI −10.94 to −1.18),[189, 264, 267] but effects were smaller and no longer statistically significant at long-term (4 trials, WMD −3.10, 95% CI −7.03 to 0.83).[189, 264, 265, 267] Individual trial estimates at all timepoints 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)[189, 263-266, 268] intermediate term (3 trials, WMD −4.86 95% CI−8.59 to −1.13)[189, 264, 267] and long term (3 trials, WMD −4.72, 95% CI −8.81 to −0.63).[189, 264, 267] Individual trials estimates generally favored MCE at all timepoints, with one trial reporting a statistically significant effect.[264]

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).[276] 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 SF36 mental or physical component summary scores.[276] A small (n=30), poor-quality trial found MCE associated with decreased pain (mean difference −0.9 on 0 to 10 scale, p value and CI not reported) and better function (mean difference −3.6, on 0 to 100 ODI, p value and CI not reported) at 3 months versus conventional exercise (mean difference −0.9 on 0-10 scale, CI and p-value not reported).[277]

MCE Versus Minimal Intervention

Chronic Low Back Pain

Based on two trials[193, 269] included in the systematic review,[262] versus a minimal intervention, MCE was 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). Each trial favored MCE at all timepoints.

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).[193, 269, 270] 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.[193, 269] Across trials, estimates consistently favored MCE.

MCE Versus Multimodal PT

Four trials in the systematic review compared MCE versus multimodal PT.[267, 271-273] One trial (n=44) found MCE associated with lower pain intensity versus multimodal PT in the short term (mean difference −32.00 on 0 to 100 scale, 95% CI −47.00 to −17.00).[272] MCE was also associated with lower pain intensity at intermediate term (WMD, −14.20, 95% CI−21.23 to −7.16), based on 4 trials.[267, 271-273] Results were consistent across trials. One trial reported a difference between MCE versus multimodal PT in long-term pain that was smaller and not statistically significant (mean difference, −7.00, 95% CI −16.27 to 2.27).[267]

Two trials both found MCE associated with better function versus PT at intermediate-term (WMD −12.98 on 0 to 100 scale, 95% CI −19.49 to −6.47).[267, 272] Effects on function also favored MCE at short-term and long-term, but was only evaluated in one trial at each timepoints (mean difference −10.0 on 0 to 100 scale at short term, 95% CI −19 to −0.47[272] and −9.17 at long term, 95% CI −18.36 to 0.02[267]).

MCE as Part of Multimodal Intervention Versus Other Components of That Intervention

Two trials evaluated MCE plus another type of exercise versus the other exercise without MCE.[274, 275] One trial (n=152) found general trunk strengthening alone associated with better short-term function versus a combination of MCE and trunk strengthening (mean difference 10.62 on a 0 to 100 scale, 95% CI 1.25 to 19,99)[274] In both trials, there were no differences between MCE plus another type of exercise versus the other exercise alone in pain or function, though outcomes were measured at different timepoints.

Harms

Adverse events were poorly reported in trials of MCE. Mild adverse effects were similar between MCE and graded activity in one trial: 22.1% (19/86) vs. 19.8% (17/86), RR 1.12,95% CI 0.62 to 2.00) and withdrawal was more common in the MCE group (8.1% [7/86] vs. 2.3% [2/86], RR 3.50, 95% CI 0.75 to 16.4).[276] In another trial, three patients in the MCE group and two receiving placebo ultrasound and short-wave therapy reported temporary exacerbation of pain which did not result in trial withdrawal.[269] One trial reported a single patient with an unspecified adverse event leading to withdrawal following sling exercise.[265] Three trials reported that no adverse events occurred;[189, 267, 273] none of the other trials reported adverse events.

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 chronic low back pain, three trials found no clear differences between Pilates versus other types of exercises in pain or function (SOE: low).

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[278] included seven trials of Pilates versus usual care (sample size range17 to 86, total n=301)[192, 279-284] and four trials of Pilates versus other exercise techniques (sample size range 12 to 83, total n =199) **(Table 10; Appendix E23; F16)**.[285-288] The trials exclusively or primarily (~75%)[284, 285] 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[281] and another provided an educational booklet on low back pain.[282] 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.[281, 285, 289] 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),[281, 282, 286, 288] four very good (13-14 points),[192, 279, 283, 284] one fair (9-10 points)[285] and four poor (0-8 points).[280, 288-290] Methodological shortcomings included inability to blind patients (most trials blinded outcomes assessors) and high attrition in trials with longer followup.[286, 288]

Pilates Versus Usual Care And Physical Activity

Chronic Low Back Pain

Seven trials[192, 279-284] included in the systematic review evaluated the effects of Pilates on pain.[278] 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), 3 trials found no significant difference (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 to the effects at the end of therapy (mean difference −2.2, 95% CI −2.2, 95% CI −3.2 to −1.1).[282] 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).[279] 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[192, 281-284, 289, 290] included in the systematic review evaluated effects of Pilates on function.[278] 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[192] or 12-week course of therapy[289] (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).[282] 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[284] and −2.6, 95% CI −5.2 to −0.1[281]) 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) .[290]

Pilates Versus Other Exercise

Chronic Low Back Pain

There were no differences between Pilates versus traditional lumbar stabilization exercises (1 trial, n=12),[285] Pilates versus McKenzie and daily postural correction exercises (1 trial, n=40[287]), or Pilates versus general exercise (including aerobics, stretching, and strengthening) (1 trial, n=83[288]) 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.[286] Attrition was high in this trial and greater in patients randomized to cycling.

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 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 13; Appendix E24, F17**;[261, 291] one of the trials also evaluated Tai Chi versus other exercise interventions including backward walking, jogging and swimming.[291] Tai Chi sessions were eighteen 40-minute sessions over 10 weeks in one trial[261] and 45-minute sessions 5 days a week for 6 months in the other.[291] Both trials were rated fair quality. One trial did not adequately report allocation concealment and attrition[291] and adherence was unclear in both trials. The nature of the intervention precluded blinding of participants and persons 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.[261, 291] 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% improvement in pain intensity was 46% vs. 15% and the proportion who experienced ≥30% improvement in RDQ was 50% vs. 24%.[261] 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%).[261] 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 versus 3.6 on a 0 to 10 scale).[291]

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 timepoints).[291]

Harms

One trial reported a small increase in back pain symptoms that resolved by 3-4 weeks in three patients who underwent Tai Chi,[261] the other trial reported no harms.[291]

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 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 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; I^2=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, I^2=47%); yoga was also associated with better function at short-term (5 trials, SMD 0.45, 95% CI −0.65 to −0.25; I^2=8%) and long-term followup (4 trials, SMD 0.39, 95% CI −0.66 to −0.11; I^2=40%) (SOE: moderate).
- 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[43] included three trials (n=22 to 101)of yoga for chronic low back pain **(Appendix E25)**.[191, 204, 210] One trial evaluated Viniyoga[191] and two trials Iyengar yoga;[204, 210] 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 published subsequent to the APS/ACP review included 10 trials,[191, 204, 207, 210, 292-297] including the 3 trials described above **(Table 10; Appendix E26, F18)**. 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[207] 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,[207, 293] one in the United Kingdom,[292] and the remainder in the United States. Two trials[210, 293] 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[298, 299] not included in the systematic review of yoga for chronic low back pain **(Table 14; Appendix E27; F19)**.[298, 299] 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)[298] and a U.S. trial (n=95) compared once versus twice weekly 75-minute hatha yoga classes over 12 weeks.[299] 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.[191, 297] 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.[297] 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 between groups, precluding reliable conclusions.[191]

Yoga Versus Exercise

Chronic Low Back Pain

Effects of yoga versus exercise on pain were reported in four trials, with somewhat inconsistent results.[204, 295, 298, 300] 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),[204] 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.[295] 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).[300] 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).[298]

Effects of yoga versus exercise on back-specific disability were reported in three trials, with somewhat inconsistent effects.[204, 207, 295] 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,[295] 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.[204] 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).[207]

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.[204] 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).[298, 301] One trial found no statistically significant differences between yoga and exercise in 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).[295] 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).[300]

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; I^2=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; I^2=47%).[302] 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).[295] 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).[294]

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; I^2=8%) and long-term followup (4 trials, SMD 0.39,

95% CI −0.66 to −0.11; I^2=40%).[302] 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.[204, 295, 296] 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).[296] 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).[295] 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).[294]

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; I^2=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; I^2=0%).[302] 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 timepoint. [296]

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; I^2=0%).[302] 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).[295] 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.[299] 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.[302] 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[298] and one trial of once versus twice weekly yoga classes reported no differences in risk of any adverse event, which were primarily musculoskeletal.[299]

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, I^2=57%) and functional status (3 trials, standardized mean difference −0.88, 95% CI −1.36 to −0.39, I^2=0%) (SOE: low).
- For chronic low back pain, a systematic review found EMG biofeedback associated with lower pain intensity at the end of treatment (3 trials, SMD −0.80, 95% CI −1.32 to −0.28, I^2=0%), with no clear effect on function (3 trials) (SOE: low).

- 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, I^2=0%), with no clear effect on function (2 trials) (SOE: low).
- 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: low).
- 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, I^2=40%), but effects on function were smaller and not statistically significant (4 trials, SMD −0.37, 95% CI −0.87 to 0.13, I^2=50%) (SOE: low).
- 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 (SOE: low).
- Ten trials found no clear differences between different psychological therapies in pain or function (SOE: moderate).
- 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 included two higher-quality systematic reviews on psychological therapies for chronic low back pain.[303, 304] One review included 22 trials (6 assessed as higher quality)[303] and the other included 21 trials (7 assessed as higher quality).[304] 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[304] included in the APS/ACP review has been published **(Table 10; Appendix E28, F20)**.[305] 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).[305] Operant therapies refer to psychological therapies that encourage healthy behaviors such as exercise and work while discouraging positive reinforcement of pain re-enforcing behaviors. Cognitive therapies address and attempt to redirect maladaptive thoughts patients may have about their low back pain. Respondent therapy is based on the premise that the psychological response to pain is linked to muscle tension in a negative feedback loop, and that this cycle can be interrupted by reducing muscle tension through techniques such as relaxation or biofeedback. 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 between groups. The majority of trials used an unblinded design.[305]

We identified five additional trials of psychological therapies for chronic low back pain not included in the systematic review **(Table 15; Appendix E29; F21)**.[306-311] Two trials evaluated psychological therapies versus wait list control,[308, 310] one trial psychological therapy versus another noninvasive intervention,[309] and three trials psychological therapies plus another noninvasive intervention versus the other intervention alone.[306, 307, 311] 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 intention-to-treat analysis.[306-311] One trial also had high (>20%) attrition.[308]

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.[305] All were assessed as high risk of bias. No information was provided regarding treatment duration except that one study offered eight 45-minute sessions.[312] 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, I^2=57%) and functional status (3 trials, standardized mean difference −0.88, 95% CI −1.36 to −0.39, I^2=0%).[312-314] For function, one trial reported a 0.5-point difference in favor of progressive relaxation on a 7-point function scale[312] and two trials reported a 4.8 to 11.1-point difference on the 100-point Sickness Impact Profile.[313, 314] Two small studies reported post-treatment depression using the 63-point Beck Depression Inventory. One study[313] (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),[314] with no difference when results were pooled (2 trials, mean difference −6.80 on 0 to 63 scale, 95% CI −20 to 6.12, I^2=85%).[313, 314] One additional trial (n=37) not included in the systematic review found no difference between 8 weeks of meditation versus wait list control for post-treatment pain (McGill Pain Questionnaire, SF-36 pain subscale), function (RDQ or SF-36 physical function subscales), or quality of life (SF-36 mental health, and global health subscales).[308]

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.[305] 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, I^2=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.[312, 315, 316] A fourth trial could not be pooled, but reported no effect of biofeedback on pain.[317] There was no clear difference between biofeedback versus wait list control for function, with inconsistent results from three trials.[312, 315, 317]

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).[305] 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, I^2=0%).[209, 318, 319] Results favored operant therapy in all three trials (13 points on a 0 to 100 VAS scale in one trial[318] or 3.3 to 3.6 points on the 78-point McGill Pain Questionnaire in two trials,[209, 319] though the difference was statistically significant in only one[318] 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, I^2=0%).[209, 319] Operant therapy also had no effect on depression, based on two trials.[209, 318]

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.[305] In one trial, cognitive therapy consisted of graded exposure to fearful activities plus psychological education over 13 sessions in addition to usual care;[320] treatment details were not reported for the other trial.[314] 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.[314, 320] 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).[310] 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.[305] 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.[206, 313, 315] 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, I^2=40%).[206, 313-315, 319] Effects were statistically significant in two[206, 313] 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;[313, 314] one low risk of bias trial (n=45) found a 6.2-point difference between treatment groups in the 78-point McGill Pain Questionnaire;[319] 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).[206, 315] 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, I^2=50%).[313-315, 319] 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,[313] the remaining three trials (n=28 to 45) found no differences.[314, 315, 319] 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, I^2=70%),[206, 313-315] with only one small (n=22) trial showing an effect that favored treatment.[313]

Psychological Therapy Versus Usual Care

Two high risk of bias trials in the systematic review compared behavioral therapy versus usual care.[305] One trial (n=100) compared 6 weeks of progressive muscle relaxation versus usual care (not otherwise described)[321] 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).[322] 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, I^2=20%), there was no difference at 6-month followup (2 trials, mean difference −4.3, 95% CI −9.3 to 0.7, I^2=0%).[321, 322] 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, I^2=0% and SMD −0.12 at 6 months, 95% CI −0.3 to 0.1, I^2=0%), though results slightly favored behavioral therapy.[321, 322]

Psychological Therapy Versus Other Noninvasive Treatments

Five trials included in the systematic review[206, 209, 323-325] and one additional trial[309] not included in the systematic review 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.[305] 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[206] 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.[209] 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, I^2=0%) or at 12 months (2 trials, N=136, mean difference 0.14, 95% CI −4.4 to 4.7, I^2=0%). Similarly, there were no differences

in depression at the end of therapy at any timepoint measured through 12 months in either study or when results were pooled.[206, 209]

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).[325] There were no differences between 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.[323] A small (n=40), fair-quality trial not included in the systematic review found no difference between eight 90-minute weekly sessions of respondent therapy focused on mindfulness meditation versus health education in pain (as measured by the McGill Pain Questionnaire or the SF-36 pain subscale), function (as measured by the RDQ), or global improvement either at the end of therapy or at 2 months. Although behavioral therapy was associated with greater improvements in quality of life, measured by the SF-36 role limitations emotional subscale at the end of treatment, the differences were no longer statistically meaningful at 2 months.[309] Results for other SF-36 subscales were not reported.

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.[324]

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)[206, 209, 326-328] in the systematic review[305] 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.[206] 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)[329] and two high risk of bias (n=45 and 409)[330, 331] trials.[305] 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.[332]

Two fair-quality trials not included in the systematic review also evaluated the effects of combining psychological therapies with another noninvasive intervention.[306, 307, 311] 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.[311] 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.[306, 307]

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.[305] Sample sizes ranged from 16 to 90 patients. In general, trials found no differences between 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,[319, 327, 333, 334] four trials compared various combinations of psychological therapies versus respondent therapy,[313-315, 335] one trial compared different types of respondent therapy (EMG biofeedback vs. progressive relaxation),[323] two trials compared cognitive therapy versus operant therapy,[327, 336] one trial compared cognitive therapy versus respondent therapy (progressive muscle relaxation), and two trials compared combined psychological therapy versus cognitive therapy.[314, 327] 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, I^2=0%),[313-315] 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, I^2=28%),[314, 315] with no differences at either timepoint in one low risk of bias trial.[315]

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, I^2=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, I^2=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, I^2=25% and 6 trials, standardized mean difference −0.23, 95% CI −0.40 to −0.06, I^2=19%, respectively), with no difference in likelihood of return to work (7 trials, OR 1.04, 95% CI 0.73 to 1.47, I^2=31%) (SOE: moderate).
- 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, I^2=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, I^2=0%, or ~2.9-point mean difference on the RDQ); there was insufficient evidence to assess effects on long-term outcomes (SOE: low for short-term pain and disability).

- 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, I^2=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, I^2=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, I^2=92%) and function (10 trials, standardized mean difference −0.68, 95% CI −1.19 to −0.16, I^2=94%) and greater likelihood for return to work (8 trials, OR 1.87, 95% CI 1.39 to 2.53, I^2=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: insufficient).

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[43] 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.[337-340] 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.[337-340]

We identified a subsequent high-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 E30; F22)**.[341] 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).

Two additional trials not included in the systematic review evaluated multidisciplinary rehabilitation for subacute (<12 weeks duration) low back pain **(Table 16; Appendix E31, F23)**.[342, 343] 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.[342] 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.[343]

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, I^2=72%; ~1.4-point mean difference on a 0- to 10-point numerical rating scale).[341] Multidisciplinary rehabilitation was also associated with better short-term disability (9 trials, standardized mean difference −0.41, 95% CI −0.62 to −0.19, I^2=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, I^2=0%). The odds ratios for return to work in the two included studies were 0.91 and 1.14.[322, 344]

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, I^2=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, I^2=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, I^2=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, I^2=73%), with no effect on the SF-36 physical component subscale (mean difference 13.45, 95% CI −9.07 to 35.96, I^2=94%).[345, 346] 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.[342] 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.[343] 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, I^2=64%; ~1.7-point mean differences on a 0 to 10 NRS).[341] 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, I^2=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, I^2=80%; ~0.6-point mean difference on a 0- to 10-point NRS).[341] Multidisciplinary rehabilitation was also associated with better short-term disability (13 trials, standardized mean difference −0.39, 95% CI −0.68 to −0.10, I^2=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, I^2=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).[347]

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, I^2=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, I^2=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, I^2=0%).

Three trials found no differences between multidisciplinary rehabilitation versus physical therapy in the short or long term for quality of life measures[206, 331, 348-350] and seven trials found no differences in short- or long-term depression or anxiety, or self-efficacy.[206, 209, 327, 328, 331, 348-351]

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[352] and one trial reported one case of pain due to acupuncture.[342]

Acupuncture, Massage, and Spinal Manipulation

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, I^2 = 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 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], I^2= 90%) and at up to 12 weeks (3 trials, WMD −9.55, 95% CI −16.5 to −2.58], I^2=40%), but there were no differences in function. Four additional trials reported results consistent with these findings (SOE: moderate).
- 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, I^2=51%) and better function (3 trials, SMD −0.94, 95% CI −1.41 to −0.47, I^2=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 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, I^2=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, I 2= 0%) and improvement in function (3 trials, SMD −0.36, 95% CI −0.67 to −0.04, I^2=7%) immediately post-intervention (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[16] included three systematic reviews[353-355] with a total of 51 unique trials of acupuncture **(Appendix E32)**. 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 recent systematic reviews of acupuncture for low back pain; one evaluated acupuncture for acute or subacute low back pain[356] and the other evaluated acupuncture for chronic low back pain (**Table 10; Appendix E33, F24**).[357]

The systematic review[356] 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).[358-366] 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[363, 367] 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.[366, 368, 369] Five trials were rated low risk of bias,[358, 363, 366-368] 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.[363, 366, 367]

The systematic review[357] on acupuncture for chronic low back pain included 32 trials (9 not included in the APS/ACP review).[370-377] 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).[378] 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[370-373, 375, 379, 380] 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[381, 382] or chronic[383] low back pain (**Table 17; Appendix E34;F25**). 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.[381] 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.[382] 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.[383] 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.[384] 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.[385]

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[356] evaluated acupuncture versus a sham procedure involving nonpenetrating needles to acupuncture points.[363, 366, 367] 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, I^2 = 27%).[363, 367] 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% 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).[382] 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 RMDQ).[381]

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)[386] and the other trials evaluated acupuncture to the body versus superficial needling at acupuncture points,[380, 387] nonpenetrating pressure with a needling tube,[388] or superficial needling at nonacupuncture points.[371, 389, 390] Four trials could be included in pooled analyses.[380, 387-389] 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, I^2=90%) and at up to 12 weeks (3 trials, WMD −9.55, 95% CI −16.5 to −2.58, I^2=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,[371, 386, 390] 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.[389]

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.[383] There was no difference in function (ODI) at any timepoint through 6 months.

Acupuncture Versus No Acupuncture

Chronic Low Back Pain

The systematic review of acupuncture for chronic low back pain[357] included five trials of acupuncture versus no acupuncture. One trial was rated low risk of bias[370] and the others unclear risk of bias.[376, 389, 391, 392] The systematic review found acupuncture associated with lower pain intensity (4 trials, SMD −0.72, 95% CI −0.94 to −0.49, I^2=51%)[376, 389, 391, 392] and better function (3 trials, SMD −0.94, 95% CI −1.41 to −0.47, I^2=78%)[370, 389, 392] 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[389] and the other two trials[370, 392] 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).[370] 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).[376]

Acupuncture Versus Medications

Acute Low Back Pain

Five trials[358-361, 365] in the systematic review of acupuncture for acute low back pain[356] 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, I^2=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; I^2=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)[361] or versus ibuprofen (94% vs. 75% "cured", p<0.05).[358] The three high risk of bias trials reported inconsistent effects of acupuncture versus medications on pain intensity. One trial favored acupuncture over ibuprofen[360] immediately following each treatment, but two other trials found no significant differences between acupuncture versus naproxen[369] or diclofenac.[364]

Chronic Low Back Pain

Three trials in a systematic review of acupuncture for chronic low back pain[357] compared acupuncture versus medications (NSAIDs, muscle relaxants and analgesics).[392-394] Two of the trials were rated high risk of bias[393, 394] and the other unclear risk of bias.[392] 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, I 2= 0%) and function (SMD −0.36, 95% CI −0.67 to −0.04, I^2=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.[364, 365] One trial (n=200) found 7 days of acupuncture plus nimesulide (an NSAID) associated with better short-term overall improvement the NSAID alone.[365] 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.[364]

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 persons receiving acupuncture were gastrointestinal problems, changes in energy,[369] mild bleeding at the needling site,[363] and temporarily increased low back pain.[383]

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 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 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 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 (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 included two good-quality systematic reviews with a total of eight unique trials of massage.[395, 396] 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[396] has been updated to include 13 trials (total n=1596, range 39 to 262) **(Table 10; Appendix E35, F26)**.[397] 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.

One additional good quality trial (n=401) not included in the systematic review evaluated two different types of massage (structural or relaxation) versus usual care for chronic low back pain **(Table 18; Appendix E36, F27)**.[398] Patients randomized to massage received 10 weekly treatments including up to 3 home exercises from a predefined list of 7 exercises, 6 of which were common to both treatments, as well as stretching. The relaxation massage group was also given 2.5-minute home relaxation exercises. Three additional smaller trials (n=26 to 140) not included in the systematic review compared different massage techniques with one another. One of these trials was rated as good quality,[399] one fair[400] and one poor quality[401]. Methodological shortcomings of the poor quality trial included unclear randomization technique, allocation concealment methods, and 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.[402, 403] 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.[402] 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)[403] 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 to 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).[402, 403] However, one trial that evaluated longer-term outcomes found no statistically significant effects on pain and back-related function at 5 weeks.[403]

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.[321] A recent, good quality, larger (n=401) trial[398] 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 RMDQ −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),[404] exercise therapy (1 trial),[402] relaxation therapy (3 trials),[321, 405, 406] acupuncture (1

trial),[395] or physiotherapy (2 trials).[407, 408] 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.[404] 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.[321] 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[395] 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);[402] 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.[407]

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],[402, 409] exercise and education [1 trial],[410] or usual care [2 trials][321, 411]) versus the other intervention without massage; three of these trials[321, 410, 411] were not in the prior APS/ACP review. Three trials were assessed as being at low risk of bias.[321, 402, 409] The two studies that included usual care interventions either did not define usual care[411] or included a broad range of possible treatments including no treatment, medications, physical therapy, herbal remedies and aromatherapy.[321] Only one trial included patients with subacute low back pain;[411] 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 heterogenous 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.[402, 409, 410]

Comparisons Of Different Types Of Massage

Six trials compared different types of massage;[398-401, 409, 412] two of these[409, 412] were included in the systematic review.[397] The massage techniques that were compared varied. Although most trials found statistically significant differences between 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).[409] 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).[398] Other, smaller (n=26 to 140) trials also found small

differences that favored Chinese massage with oils vs. standard massage,[399] Swedish massage with oils versus Thai massage,[400] traditional Thai versus Swedish massage[412] and deep tissue versus standard massage.[401]

Harms

Harms were not well-reported in trials of massage, though no serious adverse events were reported. In two trials that reported adverse events,[408, 412] 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, I^2=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, I^2=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, I^2=0%) or at 3 months (1 trial, SMD −0.28, 95% CI −0.59 to 0.02) (SOE: low).
- 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, I^2 = 0%), 1 month (3 trials, WMD −0.15, 95% CI −0.49 to 0.18, I^2 = 0%), 3 to 6 months (2 trials, WMD−0.20, 95%CI −1.13 to 0.73, I^2=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 timepoint (SOE: moderate).
- For chronic low back pain, a systematic review found spinal manipulation 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, I^2=27%) and 6 months (7 comparisons from 4 trials, WMD −3.07, 95% CI −5.42 to −0.71, I^2=0%);

effects were smaller and no longer statistically significant at 12 months (3 trials, WMD −0.76, 95% CI −3.19 to 1.66, I^2=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, I^2=3%); effects were smaller and no longer statistically significant at 6 and 12 months. Two trials not included in the systematic reviews reported results consistent with these findings (SOE: moderate).

- 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, I^2=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, I^2 =37%) or 3 months (2 trials, SMD −0.22, 95% CI −0.61 to 0.16, I^2=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, I^2=0%), 3 months (2 trials, MD −7.23, 95% CI −11.72 to −2.74, I^2=43%), and 12 months (2 trials, MD −3.31, 95% CI −6.60 to −0.02, I^2=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, I^2=0%), 3 months (2 trials, SMD −0.22, −0.38 to −0.06, I^2=33%), and 12 months (2 trials, SMD −0.21, 95% CI −0.34 to −0.09, I^2=0%). One trial not included in the systematic review reported results consistent with these findings (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[43] included 12 systematic reviews[353, 413-424] 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 **(Appendix E37)**.[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 reviews for acute low back pain[425] and chronic low back pain **(Table 10; Appendix E38, F28)**[426] The acute low back pain review included 19 randomized trials; eight of these trials were not included in the APS/ACP review.[427-434] 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,[430-433, 435-439] four included patients with a mix of acute and subacute back pain[427, 429, 434, 440] and six included patients with acute to chronic low back pain.[428, 441-445]

A separate review[426] 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.[182, 189, 193, 394, 446-459] Only 8 trials restricted inclusion to patients with symptoms longer than 3 months.[189, 193, 394, 446, 448, 452, 453, 455, 458] 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[429-431, 433, 434, 441] and nine studies of chronic low back pain were rated as low risk of bias.[182, 189, 449, 450, 457, 460-462] 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[463] significant baseline differences between 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.[434]

We identified 10 additional trials published subsequent to the updated reviews, 8 of which were trials for chronic low back pain,[464-471] one for acute low back pain[472] and one which included patients with acute to chronic low back pain **(Table 19; Appendixes E39, F29)**.[454] We also included 3 trials that were excluded from the systematic reviews because they enrolled patients with sciatica/radiculopathy.[473-475] These additional trials varied in terms of the comparators including epidural steroid injections,[473] chemonucleolysis,[474] McKensie,[454, 470] PT,[466] usual care[468] and inactive or sham treatments including detuned ultrasound,[464] simulated manipulation,[475] side lying,[465] light massage.[469] The duration of treatment ranged from a single treatment[467] on 1 day to 18 sessions over a period of 9 months.

Spinal Manipulation Versus Sham

Acute Low Back Pain

The systematic review of spinal manipulation for acute low back pain[425] included one high risk of bias trial (n=192) of SMT versus sham SMT.[432] 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[472] (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.[447, 452, 476] 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, I^2=53%). Two of the trials (n=64 and 19)[447, 476] reported a nonsignificant effects in favor of SMT, while the third trial (n=65)[452] reported a nonsignificant effect that favored sham SMT. One trial that reported 3- and 6-month outcomes[452] 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.[467, 471] 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.[467] 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.[471] 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 to 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[425] compared SMT versus inert interventions (an educational booklet,[441] detuned ultrasound and cold packs,[435] detuned ultrasound,[431] detuned short-wave diathermy,[477] antiedema gel spread,[444] bed rest,[444] and short-wave diathermy[438, 440]). Two trials were rated low risk of bias.[431, 441] 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, I^2=27%),[435, 440, 441] one trial found SMT associated with better longer-term pain relief (MD −1.20 at 3 months, 95% CI 2.11 to −0.29).[441] 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, I^2=0%)[435, 441] or at 3 months (1 trial, SMD −0.28, 95% CI −0.59 to 0.02).[441]

Chronic Low Back Pain

The systematic review of manipulation for chronic low back pain[426] 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]).[444, 462, 463, 478] One trial (n=76) was rated low risk of bias.[462] 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 timepoints were smaller not statistically significant. Three high risk of bias trials found no clear differences between SMT verus various inert interventions in pain or other outcomes.[444, 463, 478]

Three additional trials (n=42, 40, and 400)[464, 465, 469] 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[469] and two were rated fair-quality.[464, 465] The inactive comparators were detuned ultrasound,[464] side lying without SMT,[465] and light massage for 5 minutes.[469] One trial evaluated effects of a single treatment session immediately after treatment.[465]

The good-quality trial[469] 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).[465] 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).[464] 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 Low Back Pain

Eight trials in the systematic review compared SMT versus another active intervention (exercise;[427, 439] physical therapy [according to McKenzie principles];[436, 440, 441, 444, 445] massage;[442] standard general practitioner [GP] care consisting primarily of prescription [diclofenac or codeine] or nonprescription medication (paracetamol), or both;[439, 444] or back school[440, 444]). One trial was rated as a low risk of bias.[441] 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; I^2=0%), 1 month (3 trials, MD −0.15, 95% CI −0.49 to 0.18; I^2 = 0%), 3 to 6 months (2 trials MD −0.20, 95% CI −1.13 to 0.73, I^2=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 timepoint. Among the trials included in the pooled analyses, the active comparators were exercise or PT in all trials except for one, which evaluated back school.[440] The only low risk of bias trial[441] compared SMT (n=122) versus PT/McKenzie (n=133) versus a minimal intervention (an educational booklet). It found no differences between SMT versus PT/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).

Chronic Low Back Pain

Fifteen studies in the systematic review of SMT for chronic low back pain compared SMT with another active intervention.[182, 189, 448-451, 453, 454, 456-461, 463] 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, I^2=27%) and 6 months (7 comparisons from 4 trials, WMD −3.07, 95% CI −5.42 to −0.71, I^2=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, I^2=0%).[182, 189, 451] 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, I^2=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, I^2=0% and 9 comparisons from 5 trials, SMD −0.06, 95% CI −0.16 to 0.05, I^2=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.

Two additional trials compared SMT versus other active treatments for chronic low back pain.[466, 470] One good-quality trial (n=350) found SMT (maximum of 15 sessions over 12 weeks) associated with worse function at 12 months (mean difference 1.5 on the RDQ, 95% CI 0.2 to 2.9), though the effect was small.[470] 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 high risk of bias 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.[466]

Low Back Pain Of Mixed Duration

One fair quality trial (n=134)[454] of patients with acute to chronic low back pain was not included in the systematic reviews. It 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 results 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,[443] analgesic medication (parecetamol, diclofenac or dihydrocodeine),[433] exercise,[428] or physiotherapy[430]). One trial was rated low risk of bias.[433] 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[428, 443] 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, I^2=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, I^2=37%) or 3 months (2 trials, SMD −0.22, 95% CI −0.61 to 0.16, I^2 =41%).

Chronic Low Back Pain

The systematic review of spinal manipulation for chronic low back pain.[426] included five studies[182, 450, 452, 455, 479] of SMT plus another active treatment versus the other active treatment alone. Two trials were rated low risk of bias.[182, 450] The comparators were extension exercises,[455] best care + exercise,[182] myofascial therapy,[450] or usual care.[452] 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, I^2=0%),[450, 452, 455] 3 months (2 trials, MD −7.23, 95% CI −11.72 to −2.74, I^2=43%),[182, 452] and 12 months (2 trials, MD −3.31, 95% CI −6.60 to −0.02, I^2=12%).[182, 455] 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, I^2=0%), 3 months (2 trials, SMD −0.22, −0.38 to −0.06, I^2=33%), and 12 months (2 trials, SMD −0.21, 95% CI −0.34 to −0.09, I^2=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.[468]

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.[426] 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, I^2=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, I^2=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 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).
- 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 one small trial with serious 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 included three small (n=15 to 73) trials of therapeutic ultrasound for low back pain **(Appendix E40)**.[480-482] 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).[481] 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.[480] 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.[482] 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 E41, F30)**.[483] It included seven trials, including one of the trials described above[480] and six subsequent trials.[453, 480, 484-488] All trials enrolled patients with chronic nonradicular low back pain. Sample sizes ranged from 15 to 120 subjects. One trial was published in Croatian.[488] 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[487] and 6 months[453] after the end of treatment. Four trials evaluated ultrasound versus sham ultrasound,[480, 484, 487, 488] two trials ultrasound versus no ultrasound,[485, 486] and three trials ultrasound versus other treatments (spinal manipulation,[453] electrical stimulation,[485] and phonophoresis[486]). In all of the trials except for one,[480] patients in all treatment groups also underwent exercise therapy. Although all trials had methodological shortcomings, two trials[484, 487] 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 4 trials,[480, 484, 487, 488] care providers were blinded in none of the trials, and intention-to-treat analysis was reported in 2 trials.[484, 487]

The largest randomized trial (n=455) of ultrasound was published after the systematic review **(Table 20; Appendix E42, F31)**.[489] 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 one poor-quality trial (n=60) of ultrasound versus traction or low-level laser therapy for acute radiculopathy due to herniated disc that was not included in the systematic review.[490]

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, I^2=77%).[483] Statistical heterogeneity was high, with one trial[484] reporting an effect favoring ultrasound (mean difference −20.0, 95% CI −31.1 to −8.81) and two trials[487, 488] 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, I^2=0%).[483] Although statistical heterogeneity was not present, only one[487] 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).[480, 484] 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.[489]

Two trials of ultrasound versus sham ultrasound reported no effects on pain 4 weeks after the end of treatment.[487, 489] In a fair-quality trial,[487] there was no difference in pain scores (28 vs. 26, p=0.48) and in a good-quality trial[489] there was no difference in the likelihood of experiencing ≥30% (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[487] found that ultrasound was superior to sham ultrasound on the Functional Rating Index (23 vs. 30, p=0.04), but the good-quality trial[489] 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[483] 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, I^2=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.[485, 486] Neither individual trial found a statistically significant effect on either outcome.

Ultrasound Versus Other Interventions

Chronic Low Back Pain

Three nonblinded trials compared ultrasound versus other interventions.[453, 485, 486] 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).[453] 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[485] or ultrasound versus phonophoresis[486] in pain or function.

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.[490]

Harms

Harms were only reported in one good-quality trial of therapeutic ultrasound. It 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).[489]

TENS

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 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 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[43] included a good-quality systematic review[491] of TENS versus sham that included one good-quality trial,[492] and one poor-quality trial.[493] The first (good-quality) trial

(n=145) compared 4 weeks of treatment with followup 2 months after treatment cessation.[492] 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.[493] The APS/ACP review also included evidence from systematic reviews of acupuncture,[355] massage,[494] spinal manipulation,[414] traction, and superficial heat and cold[495] 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[496] that included the good-quality trial described above[492] and four other trials **(Table 10; Appendix E43, F32)**.[492, 497-500] The poor-quality study discussed above[493] 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[492, 497, 498, 500] and duration of followup ranged from 2 to 11 weeks in three trials;[492, 497, 500] duration of followup was not reported in one crossover study.[499] One trial also included an exercise comparison group and one trial[497] included a PENS comparison group. Three trials were classified as higher-quality[492, 498, 500] 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[501, 502] or interventional therapy[503] **(Table 21; Appendix E44, F33)**. Two fair-quality trials (n=236[501] and n=21[502]), one of which included patients with or without radicular symptoms[501] 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.[503] 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.[492] 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.[493]

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).[496] 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.[501, 502] Both trials found no differences between TENS versus sham TENS on any outcome after 6 weeks of treatment, including mean pain scores,[502] patient satisfaction, and functional improvement.[501] 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% 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).[501] 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 subacute low back pain, a fair-quality trial (n=164) found spinal manipulation superior to TENS for pain (VAS mean difference, scale 0-100: −24.1 vs. −9.6, p=0.04).[478] For acute low back pain, one small 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).[504]

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)[355] or between TENS versus gentle ice massage (1 trial),[505] though the quality of evidence was fair to poor for both comparisons.[43] Evidence for TENS versus other interventions was limited and mixed. Based on one trial traction was superior to TENS,[506] and minimal ice massage was inferior in one trial[507] with no difference in another trial.[505]

A systematic review[496] published subsequent to the APS/ACP review included one trial of TENS versus exercise[492] and one trial of TENS versus PENS[497] 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).[503]

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).[501] 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.

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 22; Appendix E45, F34)**.[478, 485, 508-510] The sample size ranged from 28 to 80 in four trials and was 164 in the fifth trial.[478] Four trials enrolled patients with chronic low back pain and the fifth trial[478] enrolled patients with back pain of 3 weeks to 6 months in duration. Two trials compared electrical muscle stimulation plus exercise versus exercise,[485, 508] one trial electrical muscle stimulation plus exercise versus sham stimulation plus exercise,[509] and three trials electrical muscle stimulation versus other interventions (ultrasound,[485] TENS or sham TENS,[510] and massage, manipulation, or lumbar supports[478]), 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.[509] One trial was rated fair-quality[478] 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.[485, 508]

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.[509] 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.[485, 508]

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.[478]

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).[510] 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.[485]

Harms

One trial of electrical muscle stimulation reported no adverse treatment effects.[510] The other trials did not report harms.

Percutaneous Electrical Nerve Stimulation

Key Points

- There was insufficient evidence from six 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 and imprecision (SOE: insufficient).
- No study evaluated harms of PENS (SOE: insufficient).

Detailed Synthesis

The APS/ACP review included four trials (n=34 to 64) of percutaneous electrical nerve stimulation (PENS) for low back pain **(Appendix E46)**.[497, 511, 512] Two trials compared PENS versus sham PENS,[497, 511] one trial compared PENS plus physical therapy versus sham PENS plus physical therapy,[512] three trials compared PENS versus TENS,[497, 511, 513] and one trial compared PENS versus exercise.[497] Two trials enrolled patients with nonradicular low back pain,[497, 512] one trial enrolled patients with radicular back pain,[511] and one trial did not specify presence or absence of radicular symptoms.[513] 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.[497] 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,[497, 511] and 8 weeks[513] or 3 months[512] 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 two trials not included in the APS/ACP review **(Table 23; Appendix E47, F35)**. One trial (n=112) compared PENS (three 30-minute sessions weekly for 3 weeks) versus dry needling for chronic low back pain.[514] 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).[515] Outcomes were assessed at the end of treatment in both trials.

One trial was rated fair quality[512] and the rest were rated poor quality. Methodological shortcomings included inadequate description of randomization and allocation concealment methods, failure to report attrition, 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.[497, 511, 515]

PENS Versus Sham PENS

Chronic Low Back Pain

One poor-quality trial (n=60) of patients with nonradicular low back pain[497] 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.[515] 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[511] 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 Physical Therapy Versus Sham PENS Plus Physical 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.[512] 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.

PENS Versus TENS

Chronic Low Back Pain

Three trials included in the APS/ACP review evaluated PENS versus TENS for chronic low back pain.[497, 511, 513] 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.[497] 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.[513] 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).[497]

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, $p<0.01$).[511] 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.[497] PENS was also more effective than exercise on the SF-36 physical and mental component scores, but differences were small.

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.[514]

Harms

No trial of PENS reported harms.

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 included three trials (n=151 to 240) of interferential therapy for low back pain **(Appendix E48)**.[516-518] No trial compared interferential therapy versus sham therapy. One trial each compared interferential therapy versus spinal manipulation[516] or traction.[518] One of these trials also compared interferential therapy versus the combination of interferential therapy plus spinal manipulation.[516] 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.[517] The trials focused on patients with nonradicular low back pain. The duration of symptoms was 4 to 12 weeks in two trials[516, 517] and unspecified (mainly chronic) in the third.[518] 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[517] 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 24; Appendix E49, F36)**.[519] 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[516] or interferential therapy versus traction[518] 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.[519] 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.[517] 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.[516]

Harms

No trial of interferential therapy reported harms.

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). One subsequent trial 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). 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 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) (SOE: low).
- 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 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.
- There was insufficient evidence from two 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[43] included a good-quality systematic (Cochrane) review[495] of nine controlled clinical trials on the effects of heat or cold on low back pain **(Appendix E50)**. An updated version of the review was published in 2011, but included no additional trials (**Table 2; Appendix E51, F37)**.[520] Of the studies included in the systematic review, five were randomized parallel-group trials.[41, 521-524] The other four used alternate allocation or did not describe the

allocation method;[505, 525-527] one was a parallel group trial[525] and the other three used a crossover design.[505, 526, 527] Four trials evaluated hot packs or heated wraps versus placebo or nonheated wraps,[41, 522-524, 527] one trial heat plus exercise versus heat or exercise alone,[521] one trial heat versus ibuprofen or acetaminophen,[41] and two trials hot packs versus ice massage.[525, 526] One trial[505] 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.[524]

The systematic review rated the five RCTs[41, 521-524] higher quality, based on meeting at least 6 of 11 Cochrane Back Review Group criteria,[528] and the remaining studies were rated lower quality.[505, 525-527] All studies had methodological limitations, including unblinded design and failure to adequately report methods of randomization and allocation concealment.[495] Four trials reported funding by manufacturers of heat wraps.

We identified one small, fair-quality trial (n=30) published subsequent to the systematic review of heat therapy (4 hours daily for 4 days) versus no heat therapy (**Table 25; Appendix E52, F38)**.[529] Patients with chronic pain (>3 months in duration) were excluded from the study, but mean duration of back pain was not reported. Methodological shortcomings included inadequate description of randomization and allocation concealment methods and high (21%) attrition. Both trials were funded by a manufacturer of heat wraps. Another small (n=43), poor-quality trial of patients with acute low back pain in an occupational health setting evaluated effects of 3 days of heat-wrap therapy plus education versus education only through 14 days.[530] Methodological shortcomings included inadequate description of randomization and allocation concealment and failure to report attrition.

Heat Versus Placebo

Acute or Subacute Low Back Pain

For acute or subacute low back pain, the systematic review[495] 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.[522, 523] 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).[524] A fourth trial did not report effects on pain or disability.[527]

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.[529] 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)

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.[521] 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).

A poor-quality trial (n=43) not included in the systematic review 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.[530]

Heat Versus Other Active Treatments

For acute or subacute pain, the systematic review[520] 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.[41] 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).[41]

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).[521]

Cold Versus Placebo

No study compared cold versus placebo or no cold.

Cold Versus Another Intervention Versus The Other Intervention Without Heat

No study compared cold plus another intervention versus the other intervention alone.

Cold Versus Other Active Treatments

One lower-quality trial included in the systematic review[520] found no differences between ice massage versus TENS (see the TENS section of this report.)[505]

Heat Versus Cold

Two lower-quality trials (n=117 and 36) included in the systematic review[520] evaluated heat versus cold.[525, 526] One trial found no difference between hot packs versus ice massage for back pain of mixed duration (treatment duration and followup not reported)[525] and one trial found ice massage superior to hot packs for chronic pain following two 20-minute treatments.[526]

Harms

The only adverse events reported in the systematic review[520] 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; **Evidence Table Heat-cold SR**).[522, 523] No serious adverse events were reported.

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 trials found low-level laser therapy more effective than sham laser for pain, though methods for assessing pain and duration of followup varied; one trial found low-level laser therapy more effective than sham laser for function (mean difference −8.20 on the ODI, 95% CI −13.44 to −2.96) (SOE: low).
- 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 3 trials to determine effects of low-level laser therapy plus another intervention versus the other intervention alone, due to methodological shortcomings and imprecision (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.

Detailed Synthesis

The APS/ACP review[43] included seven trials[531-537] of low-level laser therapy for low back pain **(Appendix E53)**. 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[538] included six[531-536] of the trials included in the APS/ACP review plus one additional trial **(Table 2)**.[539] We also identified three recently published trials not included in prior reviews **(Table 26; Appendix E54, F39)**.[540-542]

In total, after excluding one poor-quality trial with uninterpretable findings,[537] 10 trials assessed low-level laser therapy for low back pain.[531-536, 539-542] Laser wavelengths ranged from

830 to 10600 nm and five of the trials used a 904 nm laser.[532, 533, 536, 540, 542] Duration of treatment ranged from 1 day to 6 weeks, followup was from 1 day to 1 year, and there were 10 to 20 laser treatment sessions (1 trial[536] did not report the treatment protocol and 1 trial[534] assessed outcomes after a single treatment). Four trials compared laser versus sham[531-534] and two trials compared different laser doses, either with[536] or without[542] a sham group. The remaining four trials compared laser plus another treatment (heat, exercise, or NSAID) versus the other treatment, either alone or in combination with sham laser.[535, 539-541] Sample sizes in nine of the trials ranged from 20 to 120 and in the tenth (largest) study was 546.[540] Patients had chronic low back pain in five trials[531-533, 535, 539] and acute low back pain in three trials.[536,542,540] One trial enrolled both subacute and chronic pain patients[541] and one trial did not report the duration of pain.[534] Two trials[540, 541] were rated good quality, two[535, 536] poor quality, and six 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 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.[536] A higher proportion of patients in both active laser groups reported effective (undefined) treatment versus sham, with no difference between 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[531, 533, 534] included in the APS/ACP review found laser more effective than sham treatment for pain and disability. All three trials (n=41 to 71)[531, 533, 534] 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)[533] and another found that more laser-treated patients had “effective” (undefined) treatment (94% [15/16] vs 48% [12/25]; RR 1.95, 95% CI 1.27 to 2.99).[534] 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).[531]

One 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).[531]

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)[540, 541] 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).[540] 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.)[541]

Chronic Low Back Pain

Three trials evaluated low-level laser therapy for chronic low back pain compared low-level laser therapy plus another intervention versus the other intervention alone.[532, 539, 541] 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,[541] but differences were small (less than 1 point on a 0 to 10 scale).[543] 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. A small, fair-quality trial (n=20) found no difference between low-level laser therapy plus exercise versus sham plus exercise 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.[532] The third, fair-quality trial (n=54), found low-level laser therapy plus exercise associated with lower pain intensity (2.4 vs. 4.4 on 0 to 10 VAS; p=0.0005) and disability (16.8 vs. 24.1 on the 0 to 50 modified ODI; p=0.0001) versus sham laser plus exercise.[539]

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.[537] 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).[535] 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.[542] 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.)[536]

Harms

Harms were not well-reported in trials of low-level laser therapy. The APS/ACP review[43] reported no harms associated with low-level laser therapy. Three subsequent trials described no

adverse events (including local adverse events), without providing further data.[539, 540, 542] One trial reported two withdrawals due to worsening pain across groups.[542]

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 included three trials (n=24 to 400) of short-wave diathermy for low back pain **(Appendix E55)**.[438, 463, 544] Two trials[463, 544] compared short-wave diathermy versus sham diathermy and all three trials compared short-wave diathermy versus other interventions (exercises,[544] traction,[544] or manipulation[438 , 463]). The trials focused on patients with nonradicular low back pain. One trial enrolled patients with acute (<3 weeks) back pain,[438] one trial patients with low back pain for 2 to 12 months,(Gibson) and the third patients with back pain for >1 week.[544] The trials varied in the number of sessions (6, 12, or not specified); only one trial[544] specified the duration of each session (20 minutes). Outcomes were assessed at the end of a 2-week course of therapy in two trials[438, 544] and at 12 weeks (8 weeks after the end of therapy) in the third trial.[463] Two trials[463, 544] were rated fair quality and one trial[438] 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 27; Appendix E56, F40)**.[545, 546] 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.[463] 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).[544]

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.[545, 546] 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[463] in pain, use of analgesics, or work or activity limitations through 12 weeks or versus extension exercises or traction[544] 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).[438]

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 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 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).
- Three trials found no clear differences between lumbar supports versus other active treatments in pain or function (SOE: low).
- There was insufficient evidence from 2 trials to determine comparative effects of different types of lumbar supports, due to methodological shortcomings and imprecision (SOE: insufficient).
- Trials reported no harms associated with use of lumbar supports (SOE: low).

Detailed Synthesis

The APS/ACP review[43] included a good-quality systematic review[44] with six trials[38, 547-551] of lumbar supports for low back pain. Sample sizes ranged from 19 to 456 subjects. One of the

trials was classified as high-quality.[548] 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[552] with two additional trials[553, 554] (eight total) has since been published (**Table 2; Appendix E57, F41**). Six trials compared lumbar supports versus no lumbar supports,[38, 547, 548, 550, 551, 554] three trials lumbar supports versus other active interventions (e.g. spinal manipulation therapy, exercise, massage),[38, 547, 548, 554] and two trials compared different types of lumbar supports[549, 553] 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[38, 547, 553] also evaluated patients 6 to 16 months after the end of treatment. Three trials enrolled patients with chronic pain[549, 553, 554] and four enrolled patients with low back pain of mixed duration;[38, 547, 548, 551] one trial[550] 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[548] were rated lower quality by the systematic review, based on meeting at least 5 of 10 Cochrane Back Review Group criteria.[528] 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.[552]

We identified two trials (n=50 and 217) published since the updated Cochrane review of lumbar supports versus no support for subacute low back pain[555] or chronic low back pain[556] and one trial (n=433) of lumbar supports plus education versus education alone for acute or subacute low back pain[557] (**Table 28; Appendix E58, F42**). Treatment duration was 3 or 6 months in two trials, with followup up through the end of treatment. The third trial did not report treatment duration, but followed patients for 1 year. All three trials were rated fair -quality due to methodological limitations regarding treatment allocation and compliance and blinding.

Lumbar Support Versus No Lumbar Support or an Inactive Therapy

Acute Or Subacute Low Back Pain

The systematic review[552] included four trials of lumbar supports versus no lumbar support or an inactive therapy (light massage)[548] for acute or subacute low back pain. Meta-analysis was not performed due to clinical heterogeneity. One higher-quality trial (n=164)[548] and two lower-quality trials (n=334 and 456)[38, 547] 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).[551] Only one trial evaluated function using standardized measures; it found no differences between a corset versus light message on the RDQ or ODI.[548] 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,[547] 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).[551] Two lower-quality trials (n=790) reported no difference in measures of global improvement.[38, 547]

A fair-quality trial (n=217) published subsequent to the systematic review evaluated lumbar supports versus no lumbar support for subacute low back pain.[555] 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).

Chronic Low Back Pain

One lower-quality trial (n=79)[554] of lumbar supports versus no support for chronic pain found no differences in pain or functional outcomes after 2 months of treatment.[552] 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.[556]

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.[557]

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.[553]

Lumbar Support Versus Other Treatments

Acute, Subacute, or Chronic Low Back Pain

The systematic review included one higher-quality (n=164)[548] and two lower-quality (n=334 and 456) trials[38, 547]of lumbar supports versus other active treatments.[552] None of the trials found a significant difference between 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,[548] 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).[552]

One Type of Lumbar Support Versus Another

Chronic Low Back Pain

For chronic low back pain, one trial (n=79; lower quality) included in the systematic review[552] found no differences between a flexible versus semi-rigid corset in pain or functional outcomes after 2 months of use.[554] 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.[549]

Harms

No harms associated with use of lumbar supports were reported in the systematic review, and none of the three subsequent trials.[555-557]

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 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).
- 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[43] included a large, good-quality systematic review[558] 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 E59, F43)**.[559] 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[448, 560, 561] 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 29; Appendix E60, F44)**.[562-565] 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[562-564] required 3 months or more of pain at baseline (subacute/chronic) and the third[565] 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[562,

[563]or hot packs and interferential therapy[564]) versus usual care alone. The third trial compared inversion traction plus physiotherapy with physiotherapy alone.[565] Study participants received treatment for 10 weeks in two trials[562-564] and for 4 weeks in the third,[565] with respective followup of 6 months and 56 weeks. Two trials were rated fair quality[562-564] and one poor quality.[565] Methodological shortcomings included unblinded design and in the case of the poor-quality study,[565] 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.[559] 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,[560, 566] functional status,[566] or global improvement.[566, 567]

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 timepoint.[559]

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.[562-564] 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).[562, 563] 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.[564] 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.)[565]

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.[559] 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.[559] 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)[568] and one trial (n=67) found autotraction superior to mechanical traction (risk difference 0.53, 95% CI 0.32 to 0.73.)[569] For radicular low back pain, there were no differences between 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[559] 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[562-564] or reported no adverse events.[565]

Taping

Key Points

- For chronic low back pain, two 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).

- No trial of taping reported harms.

Detailed Synthesis

The APS/ACP review did not evaluate taping for low back pain. We identified five trials on the effects of taping **(Table 30; Appendix E61, F45)**.[570-574] Sample sizes ranged from 39 to 60 in four trials and was 148 in the fifth trial.[574] Four trials evaluated Kinesio Taping[570, 572-574] and one trial Functional Fascial Taping.[571] Two trials of Kinesio Taping[570, 574] and the trial of Functional Fascial Taping[571] 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. One trial[572] compared Kinesio Taping versus exercise therapy without Kinesio Taping and another[573] compared Kinesio Taping versus exercise therapy or the combination of taping and exercise. The four 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 4 weeks) varied. Outcomes were assessed at the end of a 4-week course of therapy in two trials[572, 573] and at 5 to 12 weeks (4 to 10 weeks after the end of therapy) in the other three. Two trials were rated good quality,[570, 574] two fair quality,[571, 573] and one poor quality.[572] 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) 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)[570] or 12 weeks (following 4 weeks of therapy).[574] 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,[570] but the other trial found no effect of a 4-week course of taping after 12 weeks (mean difference, 0-10 VAS −0.5, 95% CI −1.4 to 0.4).[574]

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.[571]

Taping Versus Exercise

Chronic Low Back Pain

One fair-quality (n=39)[573] and one poor-quality (n=40) trial[572] 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 pharmacologic treatments for low back pain[a]

Author, year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Antidepressants			
Urquhart 2010	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	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.

Author, year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Opioids			
Chaparro, 2013	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 B. Tramadol, 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]) 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 (MD 0.58 lower, 95% CI 0.61 to 0.55; Function: very low quality evidence of no difference in function (MD 3 lower (95% CI 11.44 lower to 5.44 higher) D. 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])

[a] See evidence tables (Appendix XX, XX, XX etc.) for detailed results

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 12 weeks Acute *Not reported*	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)

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**
Majchrzycki, 2014 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: 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	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 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: -0.35 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Herrmann, 2009 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 LNX 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	

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**
Rauck, 2014 12 weeks Chronic *Poor*	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 Mean pain score before titration (NRS): 6.9 vs. 6.9 Mean pain score after titration (NRS): 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 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): 6.1 vs. 4.7	A vs. B 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 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Cloutier, 2013 4 weeks Subacute, chronic *Quality not reported*	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: Mean age: 50.6 years Female: 50% Baseline score on Pain and Disability Index (PDI): 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: 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)	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 29 days Subacute, chronic *Good*	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%	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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Hale, 2005 18 days LBP duration not specified *Quality not reported*	A: Long-acting oxymorphone (titrated) (Mean dose 79.4 mg/day) (n=71) B: Long acting oxycodone (titrated) (Mean dose 155 mg/day) (n=75) C: Placebo (n=67) 18 days	Median age: 46 years Female: 47%	A vs. B vs. C Pain Intensity (100 point VAS): A: -18.21 difference compared to C; B: 18.55 difference compared to C (p=0.0001 for each comparison) Pain Intensity Categorical scale: Proportion rating pain intensity "none" or "mild" similar for A and B (around 14%) vs. C (45%) Pain Relief: 56.8 vs. 54.1 vs. 39.1	A vs. B vs. C Pain Interference: A and B similar and superior to C for general activity, mood, normal work, relations with other people, and enjoyment of life (no difference for sleep and walking ability) Global Assessment "Good", "very good", or "excellent': 59% vs. 63% vs. 27% Discontinuation due to treatment failure (treatment phase): 20% vs. 16% vs. 57% Discontinuation due to treatment failure (dose titration phase): 7/166 (4.2%) vs. 4/164 (2.4%) Rescue medication use: 13.8 vs. 14.7 mg/day after first 4 days

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Jamison, 1998 26 weeks LBP duration not specified *Quality not reported*	A: Long acting morphine + short-acting oxycodone (titrated doses) + Naproxen B: Short-acting oxycodone (set dose) + Naproxen C: Naproxen Mean dose A: 41.1 mg morphine equivalent/day Mean dose B: Not reported, max 20 mg oxycodone/day Mean dose C: Not reported In all groups, max 1000 mg/day of naproxen 16 weeks	Average age: 43 years Female: 57%	A vs. B. vs. C Average pain (means, 0-100 VAS): 54.9 vs. 59.8 vs. 65.5 Current pain (means, 0-100 VAS): 51.3 vs. 55.3 vs. 62.7 Highest pain (means, 0-100 VAS): 71.4 vs. 75.5 vs. 78.9	A vs. B. vs. C Anxiety (means): 11.2 vs. 15.0 vs. 31.6 Depression (means): 10.8 vs. 16.4 vs. 26.9 Irritability (means): 17.7 vs. 20.5 vs. 33.7 Level of activity (means, 0-100 scale): 49.3 vs. 49.3 vs. 51.5 Hours of sleep (means): 5.9 vs. 5.9 vs. 6.1
Wiesel, 1980 15 days LBP duration not specified *Quality not reported*	A: Codeine 60 mg three times daily B: Oxycodone + aspirin 1 tablet three times daily (doses not specified) C: Acetaminophen 1 tablet twice daily (doses not specified) 14 days	Mean age: 23 years Female: not reported		A vs. B. vs. C Mean number of days before return to work: 10.67 vs. 12.0 vs. 13.0 (NS)

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**
Studies published since the APS/ACP review				
Pareek, 2009 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 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 RMDQ 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)

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**
Studies published since the APS/ACP review				
Brotz, 2010 1 year LBP duration not specified *Quality not reported*	A: Diazepam: 5 mg po twice daily x 5 d, 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 w, 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 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) 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

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 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 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 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 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, VAS mean change from baseline: -1.77 vs. -2.46 vs. -2.40 vs. -2.10; no significant differences between 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 between groups for other subscales 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention**	**Population**	**Pain Outcomes**	**Other Outcomes**
Skljarevski 2010 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 RMDQ 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, RMDQ 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 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) 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; RMDQ = Roland Morris Disability Questionnaire; 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**
Studies published since the APS/ACP review				
Baron, 2014 9-10 weeks Subacute, chronic *Quality not reported*	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)	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 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
Markman, 2014 10 days Subacute, chronic *Quality not reported*	A: Pregabalin: 75 mg po twice daily x 3 d, 150 mg twice daily x 7 d, 75 mg twice daily x 4 d (n=14) B: Placebo: Diphenhydramine 6.25 mg po twice daily x 3 d, 12.5 mg twice daily x 7 d, 6.25 mg twice daily x 4 d (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 w (p=0.46) 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)	A vs. B Walking distance (mean, m): 237 vs. 261 at 2 w (p=0.35) RDQ (mean, 0-24): 13 vs. 11 at 2 w (p=0.01) 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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Pota, 2012 3 weeks Chronic *Quality not reported*	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)	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 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	A vs. B 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)
Baron, 2010 5 weeks Subacute, chronic *Quality not reported*	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)	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 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Romano, 2009 4 weeks Chronic *Quality not reported*	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	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 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%	
Yaksi, 2007 4 months LBP duration not specified *Quality 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	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)

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**
Studies published since the APS/ACP review				
Eskin, 2014 5-7 days Acute *Quality not reported*	A: Prednisone: 50 mg po 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 d (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 1 month Acute *Quality not reported*	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 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)	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%)
Holve, 2008 6 months Acute *Quality not reported*	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 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 m (p>0.05)	A vs. B RDQ (mean, 0-24): 13 vs. 16 at 1 w, 8 vs. 13 at 2 w, 8 vs. 9 at 4 w, 3 vs. 2 at 3 m, 1 vs. 2 at 6 m (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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Hedeboe, 1982 3 month LBP duration not specified *Quality not reported*	A: Dexamethasone: 4 mg/ml, 16 mg IM three times daily x 1 d, 8 mg three times daily x 1 d, 8 mg tid x 1 d, 4 mg tid x 1 d, 4 mg twice daily on x 3 d (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

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

Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Acupuncture			
Lee, 2013	11 RCTs, Acute to subacute LBP (<12 weeks), 1139 patients (approximately 50 per arm), 5 LRoB	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 to 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	32 studies SR, 25 meta (n=6266 patients); 7 LRoB, 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 post-intervention 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.

Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Exercise			
van Middelkoop 2010	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)[190, 197, 207] and better function (3 RCTs, WMD −12.35 on a 0 to 100 scale, 95% CI –23.0 to –1.69)[190, 197, 207] 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).[190, 200, 211]
Oesch 2010	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).[185] 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).
Lumbar Supports			
van Duijvenbode 2008	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*	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.

Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Massage			
Furlan, 2010	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 to 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.

Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Motor Control Exercise			
Bystrom 2013	16 RCTs (1 with 2 arms) (n = 1933) 80% with CBLP; 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 PT (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)

Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Multidisciplinary Rehabilitation			
Kamper 2014 (Cochrane)	41 RCTs; all chronic low back pain; Multidisciplinary biopsychosocial rehab (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	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	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.
Karjalainen 2001	2 RCTs, subacute low back pain	Interdisciplinary rehab (2 trials, 233 patients)	Multidisciplinary rehabilitation with a work site visit or more comprehensive occupational health care intervention is more effective than usual care for return to work, sick leave, and subjective disability.
Tveito 2004	5 RCTs	Interdisciplinary rehab (5 RCTs, 1645 patients)	Evidence that interdisciplinary rehab has a positive effect on sick leave. No evidence of a positive effect on pain.

Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Pilates			
Wells, 2014	14 RCTS CLBP of > 3months duration; if studies included acute or subacute LPB with CLBP, 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

Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Psychological Therapies			
Henshcke 2011 (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) 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	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.

Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Spinal Manipulation			
Rubenstein, 2012	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. Intert 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 to inert interventions, sham SMT, or when added to another intervention, in terms of pain, function, QOL, work, global improvement. Low to mod no diff vs. other interventions, with the exception of moderate short-term effect of SMT on functional status when added to another intervention.
Rubenstein, 2011	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)	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.

Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Superficial Heat-Cold			
French 2006	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	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	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.

Author, Year	Number and Type of Studies	Interventions and Number of Patients	Conclusions
Ultrasound			
Ebadi, 2014	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, I^2=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, I^2=0%) or back-specific function (2 trials, mean difference -0.41, 95% CI -3.14 to 2.32), but estimates were imprecise.
Yoga			
Cramer 2013	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; I^2=0%) Effects were smaller and not statistically significant at longer-term followup (4 trials, SMD -0.28, 95% CI-0.58 to -0.02' I^2=47%) Yoga was also associated with better function: Short-term (5 trials, SMD 0.45, 95% CI-0.65 to -0.25; I^2=8%) Long-term followup (4 trials, SMD 0.39, 95% CI -0.66 to -0.11; I^2=40%)

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**
Hurley, 2015 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: 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: 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
Albert, 2012 12 months Acute, subacute, chronic *Quality not reported*	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 (RMDQ), 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 calc 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 (RMDQ) (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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Jensen, 2012 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: 5.6 vs. 5.1 Mean RMQ: 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) <u>Posttreatment</u> Pain: 5.0 vs. 4.5; adjusted difference -0.07 (95% CI -0.9 to 0.7) <u>One-year followup</u> 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) <u>Posttreatment</u>) RMQ: 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) <u>One-year followup</u> RMQ: 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)
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).

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Kell, 2011 13 weeks Subacute, chronic *Quality not reported*	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 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: 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Albaladejo, 2010 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 RMQ: 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, low back pain: -2.0 vs. -2.0 vs. 0 Change in median VAS, referred pain: -2.0 vs. -2.0 vs. -0.5	A vs. B vs. C Improvement in RMQ: 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
Hagen, 2010 24 months LBP duration not reported *Quality not reported*	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 (RMDQ) Subjective health complaints Psychological distress (HSCL-25) Return to work

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Hartvigsen, 2010 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
Henchoz, 2010 52 weeks Subacute, chronic *Fair*	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: 5.3 vs. 5.1	A vs. B VAS: 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 (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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Machado, 2010 3 months Acute *Quality not reported*	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	A vs. B Mean age: 47.5 vs. 45.9 years Female: 52% vs. 48% Baseline Pain (NRS): 6.6 ± 1.8 vs. 6.3 ± 1.9 Function (PSFS): 3.7 ± 1.6 vs. 3.4 ± 1.8 Disability (RMDQ): 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) 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 (RMDQ) 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
George, 2008B 6 months Acute, subacute *Quality not reported*	A: TBC + 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: TBC + 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 (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): 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) <u>High fear</u> 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 <u>Low fear</u> 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) <u>High fear</u> 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 <u>Low fear</u> 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Helmhout, 2008 62 weeks Acute, subacute, chronic *Quality not reported*	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 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	A vs. B Mean age: 37 vs. 35 years Female: 3% vs. 4% Baseline Function (PSFS): 178 ± 65 vs. 178 ± 52 Disability (RMDQ): 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 (RMDQ, 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 timepoints

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Little, 2008 52 weeks Subacute, chronic *Fair*	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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Pengel, 2007 12 months Acute, subacute *Quality not reported*	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.	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): 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 (RMDQ): 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	A vs. B vs. C vs. D adjusted multivariable mixed model, relative change (95% CI) <u>Exercise vs. No Exercise</u> 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 <u>Exercise + Advice vs. No Exercise or Advice</u> 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	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 (RMDQ): 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 <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 (RMDQ): 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Hofstee, 2002 6 months Acute *Quality not reported*	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

Table 12. Characteristics and conclusions of included motor control exercise trials

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Inani, 2013 3 months LBP duration not specified *Quality not reported*	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 follow up 3x/wk 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): 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Macedo, 2012 12 months Subacute, chronic Quality not reported	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 wk for first 4 wks then 1x/wk for next 4 wks] 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 minutes/wk in first month and 1 hr/wk in second month.	A vs. B Mean age: 48.7 vs. 49.6 years Female: 66.3% vs 52.3% Baseline Pain intensity (NRS): 6.1 vs. 6.1 Function (PSFS): 3.7 vs. 3.6 Disability (RMDQ-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) 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 (RMDQ-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 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

Table 13. 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**
Weifen, 2013 26 weeks Chronic *Poor*	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: 5.3 vs. 5.2 vs. 5.0 vs. 5.2 vs. 5.1	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	
Hall, 2011 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: 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: 46.3% vs. 15%; NNT 4	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) PDI: 22.7-17.0 vs. 23.9-23.8; mean between-group difference 5.7 (95% CI 1.8 to 9.6) RMQ: 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 RMQ: 50% vs. 23.8%; NNT 4 QBPDS: 40% vs. 7.5%; NNT 4 PSFS: 43.8% vs. 16.3%; NNT 4

Table 14. 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 6 months Subacute, chronic *Quality not reported*	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): 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) *SMD calculated from means and SD based on sample before attrition	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;

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Saper, 2013 12 weeks Chronic *Quality not reported*	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 Back-specific function: (mean Roland-Morris Disability Questionnaire (RMDQ)) 13.7 vs. 13.6 SF-26 Physical: 37.5 vs 37.4; Mental 44.8 vs.44.	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 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;	A vs. B Change from baseline, *between group* difference in means: RMDQ: 6 weeks −0.6 (−2.7 to 1.6), p-0.62; 12 weeks, −0.1 (−1.4 to 1.2), p= 0.83 RMDQ 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. 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 RMDQ -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

Table 15. 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**
Morone, 2008 Post-treatment Chronic *Fair*	A. Respondent therapy (mindfulness meditation) (n=19) B. Wait list control (no interventions, could be treated as group A at end of 8 weeks) (n=18) Treatment protocol (group A): 1x90 minute session/week for 8 weeks	A vs B Mean age 74 vs 76 years 53% vs 61% female Pain (McGill): 15.2 vs 15.2 Pain (SF-36 Pain): 35.5 vs 35.7 Pain acceptance (CPAQ Total Score): 72.2 vs 68.1 Pain acceptance (CPAQ Activities Engagement Subscore): 47.7 vs 47.9 Function (RDQ): 11.5 vs 11.8 Function (SF-36 Physical Function): 42.0 vs 45.1 Quality of life (SF-36 Physical Health): 41.4 vs 41.2 Quality of life (SF-36 Mental Health): 41.7 vs 40.8 Quality of life (SF-36 Global Health): 40.4 vs 40.3	A vs B Pain (mean 0-90 McGill): 13.7 vs 15.7 post-treatment (p=0.16), 16.5 vs NR at 1 month Pain (mean 0-100 SF-36 Pain Scale): 39.9 vs 38.8 post-treatment (p=0.31), 39.9 vs NR at 1 month Pain acceptance (mean 0-120 CPAQ Total Score): 75.5 vs 64.8 post-treatment (p=0.008), 74.5 vs NR at 1 month Pain acceptance (mean 0-66 CPAQ Activities Engagement Subscore): 50.3 vs 43.4 post-treatment (p=0.004), 48.1 vs NR at 1 month	A vs B Function (mean 0-24 RDQ): 9.4 vs 10.6 post-treatment (p=0.25), 8.9 vs NR at 1 month Function (mean 0-100 SF-36 Physical Function Scale): 45.7 vs 44.5 post-treatment (p=0.03), 45.8 vs NR at 1 month Quality of life (mean 0-100 SF-36 Physical Health): 43.9 vs 42.9 post-treatment (p=0.36), 44.6 vs NR at 1 month Quality of life (mean 0-100 SF-36 Mental Health): 45.7 vs 43.2 post-treatment (p=0.30), 45.1 vs NR at 1 month Quality of life (mean 0-100 SF-36 Global Health): 44.7 vs 42.9 post-treatment (p=0.27), 43.9 vs NR at 1 month

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Siemonsma, 2013 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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Morone, 2009 Post-treatment and 2 months Chronic *Fair*	A. Respondent therapy (mindfulness meditation) (n=20) B. Health education program (n=20) Treatment protocol: 1x90 minute session/week for 8 weeks	A vs B Mean age 78 vs 73 years (p=0.03)* 69% vs 58% female All data estimated from graphs: Pain (McGill): ~15.5 vs ~16.0 Pain (McGill Current Pain): ~3.0 vs ~4.5 Pain (SF-36 Pain Scale): ~39.5 vs ~40 Chronic Pain Self Efficacy: ~63 vs ~64 Function (RDQ): ~9.0 vs ~11.5 Quality of life (SF-36 Role Limitation Emotional): ~33 vs ~30	A vs B (all data estimated from graphs) Pain (mean 0-90 McGill Total Score): ~11.5 vs ~11.5 post-treatment, ~12 vs ~11.5 at 2 months (p>0.05 for both) Pain (mean 0-45 McGill Current Pain Score): ~2.5 vs ~4 post-treatment, ~2 vs ~3.5 at 2 months (p>0.05 for both) Pain (mean 0-100 SF-36 Pain Scale): ~42.5 vs ~39.5 post-treatment, ~41.5 vs ~40.5 at 2 months (p>0.05 for both) Chronic Pain Self Efficacy (mean 0-100): ~71 vs ~66 post-treatment, ~78 vs ~70 at 2 months (p>0.05 for both)	A vs B (all data estimated from graphs) Function (mean 0-24 RDQ): ~7.5 vs ~9 post-treatment, ~7.5 vs ~10 at 2 months (p>0.05 for both) Quality of life (mean 0-100 SF-36 Role Limitation Emotional): ~34 vs ~26 post-treatment (p<0.05), ~34 vs ~28 at 2 months (p>0.05) Global improvement (% of patients who consider themselves "much improved"): 31% (5/16) vs 11% (2/18) post-treatment (p=0.26)

Author, Year Duration of Followup LBP Duration *Quality*	Intervention and Duration of Treatment	Population	Pain Outcomes	Other Outcomes
Lamb, 2010/2012 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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Vong, 2011 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)

* Morone 2009: all subsequent analyses adjusted for age

Table 16. 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 2, 5, 12, and 26 weeks LBP duration not specified *Quality not reported*	A: Integrative Care (IC) (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 RMDQ: 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 RMDQ 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 RMDQ, pain, and bothersomeness at 12 weeks, but not at 26 weeks
Gatchel, 2003 3,6,9,12 months Acute *Quality not reported*	A: Intensive Multidisciplinary rehabilitation (physician evaluation, psychology, physical therapy, biofeedback, case management, occupational therapy) B: Usual care	Mean age: 38 years Female: 35%	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

Table 17. 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**
Hasagawa, 2014 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: 6.6 vs 6.7 Disability, RDQ: 14.9 vs 14.6	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
Vas, 2012 Primary: 3 weeks F/U 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 RMQ (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**
Cho, 2013 Primary: 8 weeks F/U 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 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)*
Yun, 2012 Chronic 24 weeks Fair* Unclear allocation concealment, patients and providers not blinded	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, VAS 6.1 vs 6.1 vs. 6.1 Disability, RMDQ: 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 RMDQ mean change from baseline: 6.2 vs. 5.3 vs. 4.1 (p<0.0001)
Weiss, 2013 3 months after end of treatment Chronic Poor[a] Unclear randomization and concealment methods, no primary outcome identified (exploratory only), unclear blinding	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

[a]Δ 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 18. 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**
Cherkin, 2011 10 weeks (primary) 52 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: 5.6 vs 5.6 vs 5.8 Disability, RDQ: 10.1 vs 11.6 vs 10.5	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
Sritoomma, 2014 15 weeks Chronic *Fair** **no blinding of patients, providers or assessors described*	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: 66.66 vs. 63.27 Disability, ODQ: 26.9 vs. 29.5	A vs B: Pain, VAS 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Romanowski, 2012 10 days F/U to 48 weeks Chronic *Poor** *No randomization or allocation concealment described, no blinding described, baseline demographics not described*	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 gender	A vs B Mean change in 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

Author, year **Duration of followup** **LBP duration** ***Quality***	**Intervention** **Treatment protocol**	**Population**	**Pain outcomes**	**Other outcomes**
Kong, 2012 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

Table 19. 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**
Studies published since the APS/ACP review				
Bronfort, 2004 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
Burton, 2000 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
Pareek, 2009 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 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 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 Female:49% vs. 55% Baseline pain severity: mild 0.4% vs 0.4%; moderate 74% vs 74%; severe 25% vs 26% Baseline RMDQ 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)
Santilli, 2006 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

Table 20. 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**
Studies published since the APS/ACP review				
Licciardone, 2013 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 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)	A vs. B 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)
Ebadi, 2012 8 weeks Chronic *Fair*	A: Ultrasound 1.5 W/cm2 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 ultrasound (n=222)	A vs. B Mean age: 31 vs. 37 years Female: 25% vs. 50% Pain intensity (mean, 0-100 VAS): 47 vs. 49 Functional Rating Index (mean, 0-100): 41 vs. 44	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)	A vs. B 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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Unlu, 2008 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 m after end of treatment, 27 vs. 31 vs. 30 3 m 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 m after end of treatment, 25 vs. 30 vs. 24 3 m 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 m after end of treatment, 8.6 vs. 8.9 vs. 6.7 3 m after end of treatment Modified ODI (0-50): 14 vs. 15 vs. 15 at end of treatment, 14 vs. 14 vs. 14 1 m after end of treatment, 14 vs. 15 vs. 14 3 m after end of treatment	

Table 21. 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**
Studies published since the APS/ACP review				
Buchmuller, 2012 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 63 vs. 66 Roland-Morris disability score: 15 vs. 15	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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Facci, 2011 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, 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 RMDQ, 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 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: 4.5 vs. 5.0	A vs. B Pain, mean change from baseline: -1.4 vs. -1.1; p=0.4	

Table 22. 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**
Studies published since the APS/ACP review				
Durmus, 2010 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/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)	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 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) SF-36 Pain (median): 88.0 vs. 88.0 vs. 77.0 at 6 w (p=0.28)	A vs. B vs. C 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 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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Durmus, 2009 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 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) SF-36 Pain (mean): 87 vs. 64 at 8 w (p=0.001)	A vs. B 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 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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Glazer, 2001 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 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Moore, 1997 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)	

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Pope, 1994 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)	

Table 23. 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**
Pérez-Palomares, 2010 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)

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Hamza, 1999 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)

Table 24. 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, 2012 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)

Table 25. 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**
Studies published since the APS/ACP and Cochrane reviews				
Kettenmann, 2007 5 days Acute *Quality: Not reported*	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 (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)

Table 26. 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 3 weeks Subacute and chronic *Good*	Subacute LBP A. GaA1As laser, 850 nm + heat (n=20) B. Sham laser + heat (n=20) Chronic LBP A. GaA1As 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: 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	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 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	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 12 weeks Chronic *Fair*	A. GaA1As laser, 810 nm (n=16) B. GaA1As 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 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Jovicic 2012 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 Gender, race not reported Lumbar pain, VAS: 7 vs 7 vs 6.5	A vs B vs C Lumbar pain, VAS 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 2010[a] 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: 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 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

[a] Population characteristics for entire study population, including 74 participants with chronic cervical and extremity pain.

Table 27. 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 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 6 weeks	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)	

Table 28. 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**
Studies published since the APS/ACP and Cochrane review				
Sato, 2012 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	
Calmels, 2009 3 months Acute *Fair*	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)	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, 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	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
Oleske, 2007 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

Table 29. 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**
Studies published since the APS/ACP and Cochrane reviews				
Moustafa, 2013 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: 6.2 vs. 5.9 Disability, ODI: 32.4 vs. 31.7	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)	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)
Diab, 2012; Diab, 2013 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: 6.0 vs. 5.5 Disability, ODI: 32.4 vs. 31.1	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)	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)
Prasad, 2012 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: 3.2 vs. 2.8 Disability, ODI: 50 vs. 48 Disability, RMDQ: 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: 0.9 (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, RMDQ: 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)

Table 30. 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**
Kachanathu, 2014 4 weeks Chronic *Quality 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)	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 w (p=0.57)	A vs. B RDQ (mean, 0-24): 4.7 vs. 7.0 at 4 w (p=0.67)
Parreira, 2014 12 weeks Chronic *Quality not reported*	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 w, -0.5 (95% CI -1.4 to 0.4) at 12 w	A vs. B 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Castro-Sanchez, 2012 5 weeks Chronic *Quality not reported*	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 w, -1.0 (95% CI -1.7 to -0.2) at 5 w	A vs. B 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
Chen, 2012 12 weeks Acute *Quality not reported*	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 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	A vs. B 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

Author, Year **Duration of Followup** **LBP Duration** ***Quality***	**Intervention and Duration of Treatment**	**Population**	**Pain Outcomes**	**Other Outcomes**
Paolini, 2011 4 weeks Acute, subacute, chronic *Quality 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% 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 w (p>0.05) RDQ (mean, 0-24): 9.5 vs. 5.4 vs. 7.3 at 3 w (p>0.05)	A vs. B vs. C RDQ (mean, 0-24): 9.5 vs. 5.4 vs. 7.3 at 3 w (p>0.05)

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 31**); the factors used to determine the overall strength of evidence are summarized in Appendix G. 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). It 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 RDQ or the ODI). When present, observed benefits were generally in the small (5 to 10 point on a 100-point VAS or equivalent, or 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 showed no clear effects; 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 (SOE: moderate).[42] 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).[151-153] 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 the effects of pregabalin for radicular low back pain, but did not show beneficial effects (SOE: low).[159, 161] 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).[134] 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; I^2=32%) (SOE: moderate).[138] 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.

There remain no placebo-controlled trials of acetaminophen for chronic low back pain and only one small trial of acetaminophen versus NSAIDs.[33] Evidence indicates that 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).

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[69] (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 between different long-acting opioids or between 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. 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 the commonly implemented enriched enrollment and withdrawal design.[91] 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.

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 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 function[261] (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 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 TENS was previously classified as insufficient, additional evidence now supports the findings that ultrasound is not effective versus sham ultrasound[483] and that TENS is not effective versus sham TENS,[496] though the strength of evidence remains low due to methodological limitations in the trials and imprecision. Based on three trials,[531, 533, 534] 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, 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).[305] 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).[341] 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,[305] 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[356, 357] and spinal manipulation[425, 426] than for massage,[397] 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.[397] Although acupuncture was more effective than sham acupuncture for chronic low back pain,[357] 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.[426] 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 utilized 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.[575, 576] 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).[577] 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.[578] 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[579, 580] indicates that such patients are more likely to be prescribed opioids in clinical practice than persons without risk factors.[575, 581]

Our finding that acetaminophen is not effective for acute low back pain is based on a recent, well-conducted RCT[42] 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.[582]

Our prior report and other previous systematic reviews[136, 137] 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; I^2=32%) or function.[138] One potential reasons for the discrepancy between this finding and prior reviews are that some of the prior reviews did not conduct a meta-analysis.[135, 137] A review[136] that did conduct meta-analysis included a study that did not report being randomized and reported the largest effect in favor of antidepressant,[583] did not include relevant studies that were in the more current review,[140, 145, 148] and included two relevant studies in the meta-analysis for which data had to be imputed,[139, 147] but did not report methods for imputation.

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.[584] 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.[585]

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.[575, 586-589] 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.[356, 357] As in prior reviews, we found no clear evidence to support one specific type of massage, manipulation, or acupuncture over another.[354, 396, 414, 590]

Findings regarding the effectiveness of exercise are similar to our prior review and other reviews.[591, 592] Our findings are also consistent with more specific reviews that focused on specific types of exercise such as aquatic exercise,[593] sling exercise,[594] stability exercises,[595] modifying patterns of movement,[596] Additional evidence published since our prior review strengthens conclusions that yoga is effective for low back pain,[597, 598] a finding consistent with other recent systematic reviews, and support 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).[180]

Our findings that psychological therapies and multidisciplinary rehabilitation were both effective are consistent with our prior review and other reviews.[599] 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.[581, 600, 601] Although there was insufficient evidence to determine which patients are most likely to benefit from psychological therapies and multidisciplinary rehabilitation, a recent randomized trial[602] 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 persons. 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 evidence[341] 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.[603]

As in other reviews, we found that evidence the effectiveness of therapies for radicular low back pain was quite limited.[423, 604] Like other reviews, including our prior report, we found that systematic corticosteroids are not effective for radicular low back pain.[604, 605] 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.[606]

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. 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 nonpharmacological treatments, the applicability of our findings is affected by the variability between trials in the interventions 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.[356, 357] 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., U.S. 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,[607, 608] 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.

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. When present, most beneficial effects were observed at shorter-term followup; effects were typically attenuated or no longer present at longer 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, 609] New evidence[42] that acetaminophen is ineffective for acute low back pain call into question its appropriateness as a recommended therapy, though other factors such as low cost, favorable side-effect profile, and effectiveness for other acute pain conditions could also impact decisions regarding its use.[610] 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.[578] 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.[611]

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 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, and the continued use of systemic corticosteroids for this indication, despite trials showing that they are ineffective.

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 persons.[602] 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,[607, 608] 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.[612] 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,[613] educational interventions,[614, 615] advice to remain active,[614, 616] mattresses, shoe insoles,[617] and others.[618, 619] We also did not include comparisons of noninvasive therapies versus surgery or interventional procedures, though 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, 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 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,[620] 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 was 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, 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.[621-624] More research is needed to determine effective treatments for low back pain with radicular symptoms. Trials should be designed to not just evaluate patients 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 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. 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 is lacking.[578] For systemic corticosteroids, the largest trial to date was recently completed and should help further characterize the effectiveness (or lack thereof) of this treatment.[625]

More research is needed to help understand which patients are most likely to benefit from specific therapies.[626-630] Trials are also needed to confirm whether effects of risk-stratified approaches are reproducible in the United States,[631, 632] and to optimize their implementation.[633] 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 healthcare 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 order to provide balanced assessments of low back pain interventions, trials should more consistently and rigorously evaluate and report harms.

Table 31. Summary of evidence

Key Question **Outcome**	**Strength of Evidence Grade**	**Conclusion**
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? (Including NSAIDs, acetaminophen, opioids, muscle relaxants, antiseizure medications, antidepressants, corticosteroids and topicals/patch-delivered medications)		
Acetaminophen		
Acetaminophen vs. Placebo, acute LBP Pain and function	Moderate	One good-quality trial found no difference between acetaminophen versus placebo in pain intensity or function through 3 weeks.
Acetaminophen vs. NSAID, acute LBP Pain and global improvement	Low	A systematic review 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.
Acetaminophen vs. Placebo, chronic LBP	Insufficient	No study evaluated acetaminophen versus placebo.
Acetaminophen vs. NSAID, chronic LBP	Insufficient	There was insufficient evidence from one trial to determine effects of acetaminophen versus NSAIDs.
Acetaminophen vs. other interventions, acute LBP	Insufficient	There was insufficient evidence from four trials to determine effects of acetaminophen versus 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 acetaminophen associated with lower risk of side effects versus 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, function	Moderate for pain, low for function	A systematic review found NSAIDs associated with greater improvement in pain intensity versus placebo (4 studies, 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.

Key Question Outcome	Strength of Evidence Grade	Conclusion
NSAIDs vs. Placebo, chronic LBP: Pain, function	Moderate for pain, low for function	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.
NSAIDs vs. Placebo, radicular LBP: Pain	Low	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).
NSAID plus another intervention vs. Other intervention alone	Insufficient	There was insufficient evidence from two trials of an NSAID plus another intervention versus the other intervention alone to determine effectiveness.
NSAIDs vs. Interventions other than acetaminophen and opioids	Insufficient	There was insufficient evidence from two trials to determine the effects of NSAIDs versus interventions other than acetaminophen and opioids.
NSAID vs. NSAID, acute or chronic LBP: Pain	Moderate	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).
NSAIDs vs. Placebo: Adverse events	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 vs. nonselective NSAIDs: Adverse events	Moderate	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).
Opioids		
Opioids vs. Placebo, chronic LBP: Pain and function	Moderate	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, I^2=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; I^2=0.0%, for a mean difference of ~1 point on the RDQ) versus placebo; three additional trials reported results consistent with the systematic review.
Tramadol vs. Placebo, chronic LBP: Pain and function	Moderate	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, I^2=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, I^2=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.
Buprenorphine patch vs. Placebo, subacute or chronic LBP: Pain and function	Low for pain Insufficient for function	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.
Opioids vs. NSAIDs, chronic LBP: Pain relief, function	Insufficient	Three trials reported inconsistent effects of opioids versus NSAIDs for pain relief, one 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 versus acetaminophen in days to return to work; pain was not reported.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Long acting opioids vs. Long acting opioids: Pain, function	Moderate	Four trials found no clear differences between different long-acting opioids in pain or function.
Long acting opioids vs. Short acting opioids: Pain	Low	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.
Opioids vs. Placebo: Adverse events	Moderate	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.
Skeletal Muscle Relaxants (SMR)		
SMRs vs Placebo, acute LBP: Pain	Moderate	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; I^2=0%) and 5 to 7 days (3 trials; RR 1.72, 95% CI 1.32 to 2.22; I^2=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 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; I^2=84%); one other trial (n=197) also reported results that favored combination therapy.
SMR vs. Placebo, chronic LBP: Pain	Insufficient	Evidence from three 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 between different skeletal muscle relaxants for acute or chronic low back pain.
SMR vs. Placebo, acute LBP: Adverse events	Moderate	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; I^2=50%); one additional placebo-controlled trial was consistent with these findings.
Benzodiazepines		
Benzodiazepines vs. Placebo, acute LBP: Pain, function	Insufficient	There was insufficient evidence from two trials with inconsistent results to determine effectiveness of benzodiazepines versus placebo.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Tetrazepam vs. Placebo, chronic LBP: Pain, overall improvement	Low	A systematic review included two trials that found tetrazepam associated with lower likelihood of failure to improve 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) versus placebo, and lower likelihood of failure to experience 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, function	Low	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 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. Skeletal muscle relaxants, chronic LBP: Pain, function	Insufficient	There was insufficient evidence from two trials with inconsistent results to determine effects of benzodiazepines versus skeletal muscle relaxants.
Diazepam vs. Cyclobenzaprine, chronic LBP: Muscle spasms	Low	One trial found no difference between diazepam versus cyclobenzaprine in outcomes related to muscle spasm.
Benzodiazepines vs. Placebo: Adverse events	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.
Antidepressants		
Tricyclic antidepressants or SSRI vs. Placebo, chronic LBP: Pain, function	Moderate for pain, low for function	A systematic review found no difference between tricyclic antidepressants versus placebo in pain (4 trials; SMD −0.10, 95% CI −0.51 to 0.31; I^2=32%) or SSRIs versus placebo (3 trials; SMD 0.11, 95% CI −0.17 to 0.39; I^2=0%); there was also no difference between antidepressants versus placebo on function (2 trials, SMD −0.06, 95% CI −0.40 to 0.29; I^2=0%).
Duloxetine vs. Placebo, chronic LBP: Pain, Function	Moderate	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.
Duloxetine vs. Tricyclic antidepressants	Insufficient	No study compared duloxetine versus a tricyclic antidepressant.
Antidepressants vs. Placebo: Adverse events, Serious adverse events	Moderate	Antidepressants were associated with higher risk of any adverse events compared to 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 low back pain.
Gabapentin vs. Placebo, chronic nonradicular LBP	Insufficient	One trial found no difference between gabapentin (up to 3600 mg/day) versus placebo, but did not meet inclusion criteria because it was only published as an abstract.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Gabapentin vs. Placebo, chronic radicular LBP: Pain and function	Insufficient	There was insufficient evidence from three poor-quality trials with inconsistent findings to determine effects of gabapentin versus placebo.
Topiramate vs. Placebo, chronic radicular or mixed radicular and nonradicular LBP: Pain	Insufficient	Two trials reported inconsistent results for effects of topiramate versus placebo.
Pregabalin vs. Placebo, chronic radicular LBP: pain, function	Insufficient	Two trials reported inconsistent effects of pregabalin versus placebo for pain or function.
Pregabalin plus transdermal buprenorphine vs. transdermal buprenorphine, chronic nonradicular LBP: Pain	Insufficient	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.
Pregabalin plus another analgesic vs. the other analgesic alone: Pain	Insufficient	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.
Gabapentin vs. Placebo: Adverse events	Low	Two trials of gabapentin versus 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 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.
Pregabalin vs. Placebo: Withdrawal due to adverse events, somnolence, dizziness	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.
Corticosteroids		
Systemic corticosteroids vs. Placebo, acute nonradicular LBP: Pain, function	Low	Two trials found no differences between a single intramuscular injection or a 5 day course of systemic corticosteroids versus placebo for pain or function.
Systematic corticosteroids vs. Placebo, radicular LBP: Pain, function	Moderate	Five trials consistently found no differences between systemic corticosteroids (administered a single bolus or as a short taper) versus placebo in pain or function for acute or unspecified duration LBP; one trial found no effect on need for spine surgery.
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. 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?		

Key Question Outcome	Strength of Evidence Grade	Conclusion
Exercise		
Exercise vs. Usual care, acute to subacute LBP: Pain, function	Low	A systematic review found no differences between exercise therapy versus usual care 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.
Exercise vs. Usual care, chronic LBP: Pain, Function	Moderate	A systematic review found exercise associated with greater pain relief versus usual care (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.
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, function	Low	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.
Exercise vs. Exercise, acute or chronic LBP	Moderate	There were no clear differences between different exercise regimens in >20 head-to-head trials of patients with acute or chronic low back pain.
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 Outcome	Strength of Evidence Grade	Conclusion
Motor Control Exercise		
MCE vs. General exercise, chronic LBP: Pain, function	Low	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.
MCE vs. Minimal intervention, chronic LBP: Pain, function	Low	A systematic review included two trials that 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. 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).
MCE vs. Multimodal PT, chronic LBP: Pain, function	Low	A systematic review found MCE associated with lower pain intensity versus multimodal PT at intermediate term (4 trials, WMD, −14.20, 95% CI−21.23 to −7.16) and two trials found MCE associated with decreased disability versus PT at intermediate term (WMD −12.98 on 0 to 100 scale, 95% CI −19.49 to −6.47).
MCE plus exercise vs. Exercise alone	Low	Two trials found no clear differences between MCE plus another type of exercise versus the other type of exercise alone.
MCE: Adverse events	Low	Harms were poorly reported in trials of MCE, but few adverse events were reported, with no clear difference in risk.
Pilates		
Pilates vs. usual care plus physical activity, chronic LBP: Pain, function	Low	A systematic review included 7 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.
Pilates vs. other exercise, chronic LBP: Pain, function	Low	Three trials found no clear differences between Pilates versus other types of exercises in pain or function.
Tai Chi		
Tai Chi vs. waitlist or no Tai Chi, chronic LBP: Pain, function	Low	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).

Key Question Outcome	Strength of Evidence Grade	Conclusion
Tai Chi vs. other exercise, chronic LBP: Pain	Low	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.
Tai Chi: Adverse events	Low	One trial of Tai Chi reported a small temporary increase in back pain symptoms and one trial reported no harms.
Yoga		
Yoga vs. Usual care, chronic LBP: Pain, Function	Low	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.
Yoga vs. Exercise, chronic LBP: Pain, Function	Low	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 statistically significant (5 trials).
Yoga vs. Education, chronic LBP: Pain, function	Moderate	Yoga was associated with lower short-term pain intensity versus education (5 trials, SMD −0.45,- 95% CI −0.63 to −0.26; I^2=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' I^2=47%); yoga was also associated with better function at short-term (5 trials, SMD 0.45, 95% CI−0.65 to −0.25; I^2=8%) and long-term followup (4 trials, SMD 0.39, 95% CI −0.66 to −0.11; I^2=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, 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, I^2=57%) and functional status (3 trials, standardized mean difference −0.88, 95% CI −1.36 to −0.39, I^2=0%).
EMG biofeedback, chronic LBP: Pain, Function	Low	A systematic review found EMG biofeedback associated with lower pain intensity at the end of treatment (3 trials, SMD −0.80, 95% CI −1.32 to −0.28, I^2=0%), with no clear effect on function (3 trials).
Operant therapy, chronic LBP: Pain, Function	Low	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, I^2=0%), with no clear effect on function (2 trials).
Cognitive therapy vs. Wait list control, chronic LBP	Insufficient	There was insufficient evidence from two trials to determine effects of cognitive therapy versus wait list control, due to inconsistency and imprecision.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Cognitive-behavioral and other combined therapy vs. Wait list control, chronic LBP: Pain, Function	Low	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, I^2=40%), but effects on function were smaller and not statistically significant (4 trials, SMD −0.37, 95% CI −0.87 to 0.13, I^2=50%).
Psychological therapies vs. exercise or physical therapy, chronic LBP: Pain	Low	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.
Psychological therapies vs. Psychological therapies: Pain, Function	Moderate	Ten trials found no clear differences between different psychological therapies in pain or function.
Psychological therapies: Adverse events	Low	Harms were not well-reported, but no trial included 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, versus usual care, associated with lower short-term pain intensity (9 trials, standardized mean difference −0.55, 95% CI −0.83 to −0.28, I^2=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, I^2=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, I^2=25% and 6 trials, standardized mean difference −0.23, 95% CI −0.40 to −0.06, I^2=19%, respectively), with no difference in likelihood of return to work (7 trials, OR 1.04, 95% CI 0.73 to 1.47, I^2=31%).
Multidisciplinary rehabilitation vs. No multidisciplinary rehabilitation, chronic LBP: Pain, function	Low	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, I^2=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, I^2=0%, or ~2.9 point mean difference on the RDQ); there was insufficient evidence to assess effects on long-term outcomes.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Multidisciplinary rehabilitation vs. Physical therapy, chronic LBP: Pain, function	Moderate	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, I^2=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, I^2=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, I^2=92%) and function (10 trials, standardized mean difference −0.68, 95% CI −1.19 to −0.16, I^2=94%) and greater likelihood for return to work (8 trials, OR 1.87, 95% CI 1.39 to 2.53, I^2=0%).
Multidisciplinary rehabilitation, acute LBP, radicular LBP	Insufficient	No study evaluated the effectiveness of multidisciplinary rehabilitation for acute low back pain or for radicular low back pain.
Multidisciplinary rehabilitation: Adverse events	Insufficient	Harms were poorly reported in trials of multidisciplinary rehabilitation, though no serious harms were reported.
Acupuncture		
Acupuncture vs. Sham acupuncture, subacute LBP: Pain	Low	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, I^2=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.
Acupuncture vs. Sham acupuncture, chronic LBP: Pain, function	Low	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], I^2=90%) and at up to 12 weeks (3 trials, WMD −9.55, 95% CI −16.5 to −2.58], I^2=40%), but there were no differences in function. Four additional trials reported results consistent with these findings.
Acupuncture vs. No acupuncture, chronic low back pain	Moderate	A systematic review found acupuncture associated with lower pain intensity (4 trials, SMD −0.72, 95% CI −0.94 to −0.49, I^2=51%) and better function (3 trials, SMD −0.94, 95% CI −1.41 to −0.47, I^2=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 scale and the other two trials; two trials showed small or no clear differences at longer-term followup.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Acupuncture vs. NSAIDs, acute LBP: Overall improvement	Low	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, I^2=0%).
Acupuncture vs. Medications, chronic LBP: Pain, Function	Low	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, I^2=0%) and improvement in function (3 trials, SMD −0.36, 95% CI −0.67 to −0.04, I^2=7%) immediately postintervention.
Acupuncture: Adverse events	Low	Harms of acupuncture were poorly reported in the trials, though no serious adverse events were reported.
Massage		
Massage vs. Sham massage, acute LBP: Pain, function	Low	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.
Massage vs. Usual care, chronic LBP: Pain, function	Low	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.
Massage vs. Other interventions, subacute to chronic LBP: Pain, function	Moderate	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.
Massage plus another active intervention vs. the Other intervention alone, subacute to chronic low back pain: Pain, function	Low	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.
Massage vs. massage: Pain, function	Insufficient	Comparisons of difference massage techniques were too heterogeneous and effects were too small from six trials to determine effects on pain and function.
Massage: Adverse events	Low	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.
Spinal manipulation		
Spinal manipulation, acute LBP: Pain, function	Low for function Insufficient for 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).

Key Question Outcome	Strength of Evidence Grade	Conclusion
Spinal manipulation vs. Sham manipulation, chronic LBP: Pain, function	Low for pain Insufficient for function	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, I^2=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.
Spinal manipulation vs. Intert treatment, acute LBP: Pain, Function	Low	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, I^2=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, I^2=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 low risk of bias 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 high 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.
Spinal manipulation vs. Other active interventions, acute LBP: Pain, function	Moderate	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, I^2=0%), 1 month (3 trials, WMD −0.15, 95% CI −0.49 to 0.18, I^2=0%), 3 to 6 months (2 trials, WMD −0.20, 95% CI −1.13 to 0.73, I^2=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 timepoint.
Spinal manipulation vs. Other interventions, chronic LBP: Pain, function	Moderate	A systematic review found spinal manipulation 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, I^2=27%) and 6 months (7 comparisons from 4 trials, WMD −3.07, 95% CI −5.42 to −0.71, I^2=0%); effects were smaller and no longer statistically significant at 12 months (3 trials, WMD −0.76, 95% CI −3.19 to 1.66, I^2=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, I^2=3%); effects were smaller and no longer statistically significant at 6 and 12 months. Two trials not included in the systematic reviews reported results consistent with these findings.

Key Question Outcome	Strength of Evidence Grade	Conclusion
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 associated with greater improvement in function at 1 week (SMD −0.41, 95% CI −0.73 to −0.10, I^2=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, I^2=37%) or 3 months (2 trials, SMD −0.22, 95% CI −0.61 to 0.16, I^2=41%).
Spinal manipulation plus another active treatment, chronic LBP: Pain, function	Low	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, I^2=0%), 3 months (2 trials, MD −7.23, 95% CI −11.72 to −2.74, I^2=43%), and 12 months (2 trials, MD −3.31, 95% CI −6.60 to −0.02, I^2=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, I^2=0%), 3 months (2 trials, SMD −0.22, −0.38 to −0.06, I^2=33%), and 12 months (2 trials, SMD −0.21, 95% CI −0.34 to −0.09, I^2=0%). One trial not included in the systematic review reported results consistent with these findings.
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, function	Low for pain Insufficient for function	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, I^2=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.
Ultrasound vs. No ultrasound, chronic LBP: Pain, function	Low	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, I^2=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, Function	Insufficient	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.
Ultrasound vs. Other interventions	Insufficient	There was insufficient evidence from three small trials with methodological shortcomings to determine effects of ultrasound versus other interventions.
Ultrasound vs. Other interventions, radiculopathy	Insufficient	There was insufficient evidence from one small trial with serious methodological shortcomings to determine effects of ultrasound versus other interventions.
Ultrasound, acute nonradicular LBP	Insufficient	No study evaluated the effectiveness of ultrasound for acute nonradicular low back pain.

Key Question Outcome	Strength of Evidence Grade	Conclusion
Ultrasound vs. Sham ultrasound: Adverse events	Low	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).
Transcutaneous electrical nerve stimulation		
TENS vs. Sham TENS, acute or subacute LBP: Pain, 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, function	Low	A systematic review found no differences between 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.
TENS vs. Acupuncture, chronic LBP: Pain	Low	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.
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]		
EMS plus exercise vs. Exercise, EMS vs. Other interventions, acute or chronic LBP: Pain, function	Insufficient	There was insufficient evidence from 5 RCTs to determine effects of electrical muscle stimulation plus exercise versus exercise alone or versus other interventions, due to methodological limitations and imprecision.
EMS: Adverse events	Insufficient	There was insufficient evidence to determine harms of electrical muscle stimulation.
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 6 trials to determine effects of PENS versus sham, PENS plus exercise versus exercise alone, or PENS versus other interventions, due to methodological limitations and imprecision.
PENS: Adverse events	Insufficient	No study evaluated harms of PENS.
Interferential therapy [IFT]		
IFT vs. other interventions, IFT plus another intervention vs. the other intervention, subacute to chronic LBP: Pain, function	Insufficient	There was insufficient evidence from 4 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.
IFT: Adverse events	Insufficient	No study evaluated harms of interferential therapy.
Superficial Heat or Cold		

Key Question Outcome	Strength of Evidence Grade	Conclusion
Heat wrap vs. Placebo, acute or subacute LBP: Pain, function	Moderate	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). One subsequent trial 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). Another trial found a heat wrap during emergency transport associated with substantially lower pain intensity versus an unheated blanket upon arrival to the hospital.
Heat plus exercise vs. exercise alone, acute LBP: Pain, function	Low	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).
Heat vs. Simple analgesics, acute or subacute LBP: Pain, function	Low	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).
Heat vs. Exercise, acute LBP: Pain, Function	Low	A systematic review included one trial that found no clear differences between heat versus exercise in pain relief or function.
Superficial Cold vs. Placebo	Insufficient	No study compared superficial cold versus placebo or no cold treatment.
Heat vs. Cold	Insufficient	There was insufficient evidence from two trials to determine effects of heat versus 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 versus no heat or placebo in two trials; no serious adverse events were reported with use of heat.
Low- Level Laser Therapy		
LLLT vs. Sham laser, acute LBP	Insufficient	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.
LLLT vs. Sham laser, chronic LBP: Pain, Function	Low	Three trials found low-level laser therapy more effective than sham laser for pain, though methods for assessing pain and duration of followup varied; one trial found low-level laser therapy more effective than sham laser for function (mean difference −8.20 on the ODI, 95% CI −13.44 to −2.96).

Key Question Outcome	Strength of Evidence Grade	Conclusion
LLLT plus NSAID vs. Sham plus NSAID, acute or subacute LBP: Pain, function	Low	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).
LLLT plus another intervention vs. the other intervention alone, chronic LBP: Pain, function	Insufficient	There was insufficient evidence from 3 trials to determine effects of low-level laser therapy plus another intervention versus the other intervention alone, due to methodological shortcomings and imprecision.
LLLT vs. another intervention: Pain, function	Insufficient	There was insufficient evidence to determine effects of low-level laser therapy versus another intervention, due to methodological shortcomings and imprecision.
LLLT differing wavelengths or doses	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.
LLLT: Adverse events	Insufficient	Harms were not well-reported in trials of low-level laser therapy, but no serious adverse events and no harms were reported.
Short-wave Diathermy		
Short-wave diathermy vs. Sham diathermy, mixed duration LBP: Effectiveness, Adverse events	Insufficient	There was insufficient evidence from 5 RCTs to determine effects of short-wave diathermy versus 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, function	Insufficient	There was insufficient evidence from 5 trials to determine effects of lumbar supports versus 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 versus no lumbar supports, due to methodological shortcomings and inconsistent results.
Lumbar support plus education vs. education, acute or subacute LBP: Pain, function	Low	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.
Lumbar support plus exercise vs. exercise alone, chronic LBP: Pain, function	Low	One trial found no difference between a lumbar support plus exercise (muscle strengthening) versus exercise alone in short-term (8 week) or long-term (6 month) pain or function.
Lumbar support vs. other active treatments: Pain, Function	Low	Three trials found no clear differences between lumbar supports versus other active treatments in pain or function.
Lumbar supports vs. Lumbar supports: Pain, function	Insufficient	There was insufficient evidence from 2 trials to determine comparative effects of different types of lumbar supports, due to methodological shortcomings and imprecision.
Lumbar supports: Adverse events	Low	Trials reported no harms associated with use of lumbar supports.

Key Question Outcome	Strength of Evidence Grade	Conclusion
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 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.
Traction vs. physiotherapy, LBP with or without radicular symptoms	Low	A systematic review included five trials that found no clear differences between traction versus physiotherapy versus physiotherapy alone.
Traction vs. other interventions, LBP with or without radicular symptoms: pain, function	Low	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.
Traction vs. Traction	Low	A systematic review included five trials that found no clear differences between 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 versus placebo or other interventions. Three subsequent trials reported findings consistent with the systematic review.
Taping		
Kinesio Taping vs. Sham taping, chronic LBP: Pain, function	Insufficient for pain Low for function	Two 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.
Functional Fascial Taping plus exercise vs. Sham taping plus exercise, chronic LBP: Pain, function	Insufficient	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.
Kinesio Taping vs. exercise therapy, chronic LBP: Pain, Function	Low	Two trials found no differences between Kinesio Taping versus exercise therapy in pain or function.
Taping: Adverse events	Insufficient	No trial of taping reported harms.

CI=confidence interval, EMS=electrical muscle stimulation, LBP=low back pain, LLLT=low-level laser therapy, MCE=motor control exercise, NSAID=nonsteroidal anti-inflammatory drug, ODI= Oswestry Disability Index, PENS=percutaneous electrical nerve stimulation, RDQ= Roland-Morris Disability Questionnaire, RR=relative risk, SMD=standardized mean difference, SSRI=selective serotonin reuptake inhibitor, TENS= transcutaneous electrical nerve stimulation, VAS=visual analogue scale, WMD=weighted mean difference

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.

References

1. Deyo RA, Mirza SK, Martin BI. Back pain prevalence and visit rates. Spine (Phila Pa 1976). 2006 Nov 1;31(23):2724-7. PMID: 17077742.

2. Walker BF. The prevalence of low back pain: a systematic review of the literature from 1966 to 1998. J Spinal Disord. 2000;13(3):205-17. PMID: 10872758.

3. Luo X, Pietrobon R, Sun SX, et al. Estimates and patterns of direct health care expenditures among individuals with back pain in the United States. Spine (Phila Pa 1976). 2004;29(1):79-86. PMID: 14699281.

4. Martin BI, Deyo RA, Mirza SK, et al. Expenditures and health status among adults with back and neck problems. JAMA. 2008 Feb 13;299(6):656-64. PMID: 18270354.

5. Stewart WF, Ricci JA, Chee E, et al. Lost productive time and cost due to common pain conditions in the US workforce. JAMA. 2003;290(18):2443-54. PMID: 14612481.

6. Pengel LHM, Herbert RD, Maher CG, et al. Acute low back pain: systematic review of its prognosis. BMJ. 2003;327(7410):323-7. PMID: 12907487.

7. Chou R, Shekelle P. Will this patient develop persistent disabling low back pain? JAMA. 2010 Apr 7;303(13):1295-302. PMID: 20371789.

8. Deyo RA, Dworkin SF, Amtmann D, et al. Report of the NIH Task Force on Research Standards for Chronic Low Back Pain. Spine (Phila Pa 1976). 2014 Jun 15;39(14):1128-43. PMID: 24887571.

9. Frymoyer JW. Predictors of low back pain disability. J Clinical Orthop Relat Res. 1987 August;22:89-98. PMID: 2955993.

10. Engel CC, Von Korff M, Katon WJ. Back pain in primary care: predictors of high health-care costs. Pain. 1996;65:197-204. PMID: 8826507.

11. Waddell G, McCulloch JA, Kummel E, et al. Nonorganic physical signs in low-back pain. Spine (Phila Pa 1976). 1980 Mar-Apr;5(2):117-25. PMID: 6446157.

12. Jarvik JG, Deyo RA. Diagnostic evaluation of low back pain with emphasis on imaging. Ann Intern Med. 2002;137(7):586-97. PMID: 12353946.

13. van Tulder MW, Assendelft WJ, Koes BW, et al. Spinal radiographic findings and nonspecific low back pain: a systematic review of observational studies. Spine. 1997;22(4):427-34. PMID: 9055372.

14. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: A joint clinical practice guideline from the American College of Physicians and the American Pain Society. Ann Intern Med. 2007;147(7):478-91. PMID: 17909209.

15. Chou R, Huffman LH, American Pain S, et al. Medications for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Annals of Internal Medicine. 2007 Oct 2;147(7):505-14. PMID: 17909211.

16. Chou R, Huffman LH, American Pain Society, et al. Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Annals of Internal Medicine. 2007 Oct 2;147(7):492-504. PMID: 17909210.

17. Chou R, Atlas SJ, Stanos SP, et al. Nonsurgical interventional therapies for low back pain: a review of the evidence for an American Pain Society clinical practice guideline. Spine. 2009 May 1;34(10):1078-93. PMID: 19363456.

18. Chou R, Baisden J, Carragee EJ, et al. Surgery for low back pain: A review of the evidence for an American pain society clinical practice guideline. Spine (Phila Pa 1976). 2009;34(10):1094-109. PMID: 19363455.

19. Owens D, Lohr KN, Atkins D, et al. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville, MD: Agency for Healthcare Research and Quality. 2011PMID: No PMID.

20. Chou R, Huffman L, eds. Guideline for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. Evidence Review. American Pain Society in Conjunction with American Academy of Pain Medicine. Glenview, IL; 2009.

21. Agency for Healthcare Research and Quality. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. AHRQ Publication No. 10(13)-EHC063-EF. Rockville, MD; 2014.

22. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. AHRQ Publication No. 10(12)-EHC063-EF. Rockville, MD: Agency for Healthcare Research and Quality; January 2014. Chapters available at: www.effectivehealthcare.ahrq.gov.

23. Shea BJ, Hamel C, Wells GA, et al. AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. J Clin Epidemiol. 2009 Oct;62(10):1013-20. PMID: 19230606.

24. Agency for Healthcare Research and Quality. Integrating Bodies of Evidence: Existing Systematic Reviews and Primary Studies. www.ahrq.org; 2015. http://effectivehealthcare.ahrq.gov/ehc/products/597/1964/Integrating-evidence-draft-140910.pdf

25. Furlan AD, Reardon R, Weppler C. Opioids for chronic noncancer pain: a new Canadian practice guideline. CMAJ. 2010 Jun 15;182(9):923-30. PMID: 20439443.

26. U.S. Preventive Services Task Force Procedure Manual. AHRQ Publication No. 08-05118-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2008. http://www.uspreventiveservicestaskforce.org/uspstf08/methods/procmanual.htm

27. Atkins D, Chang SM, Gartlehner G, et al. Assessing applicability when comparing medical interventions: AHRQ and the Effective Health Care Program. J Clin Epidemiol. 2011 Nov;64(11):1198-207. PMID: 21463926.

28. Ostelo RW, Deyo RA, Stratford P, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine (Phila Pa 1976). 2008 Jan 1;33(1):90-4. PMID: 18165753.

29. Milgrom C, Finestone A, Lev B, et al. Overexertional lumbar and thoracic back pain among recruits: a prospective study of risk factors and treatment regimens. J Spinal Disord. 1993 Jun;6(3):187-93. PMID: 8347966.

30. van Tulder MW, Scholten RJ, Koes BW, et al. Nonsteroidal anti-inflammatory drugs for low back pain: a systematic review within the framework of the Cochrane Collaboration Back Review Group. Spine (Phila Pa 1976). 2000 Oct 1;25(19):2501-13. PMID: 11013503.

31. van Tulder MW, Scholten RJ, Koes BW, et al. Non-steroidal anti-inflammatory drugs for low back pain. Cochrane Database of Systematic Reviews. 2000(2):CD000396. PMID: 10796356.

32. Evans DP, Burke MS, Newcombe RG. Medicines of choice in low back pain. Current Medical Research & Opinion. 1980;6(8):540-7. PMID: 6446445.

33. Hickey RF. Chronic low back pain: a comparison of diflunisal with paracetamol. New Zealand Medical Journal. 1982 May 12;95(707):312-4. PMID: 6212783.

34. Muckle DS. Flurbiprofen for the treatment of soft tissue trauma. American Journal of Medicine. 1986 Mar 24;80(3A):76-80. PMID: 2938471.

35. Wiesel SW, Cuckler JM, Deluca F, et al. Acute low-back pain. An objective analysis of conservative therapy. Spine (Phila Pa 1976). 1980 Jul-Aug;5(4):324-30. PMID: 6450448.

36. Stein D, Peri T, Edelstein E, et al. The efficacy of amitriptyline and acetaminophen in the management of acute low back pain. Psychosomatics. 1996 Jan-Feb;37(1):63-70. PMID: 8600497.

37. Hackett GI, Seddon D, Kaminski D. Electroacupuncture compared with paracetamol for acute low back pain. Practitioner. 1988 Feb 22;232(1443):163-4. PMID: 2973008.

38. Doran DM, Newell DJ. Manipulation in treatment of low back pain: a multicentre study. Br Med J. 1975 Apr 26;2(5964):161-4. PMID: 123815.

39. Roelofs PDDM, Deyo RA, Koes BW, et al. Nonsteroidal anti-inflammatory drugs for low back pain: an updated Cochrane review. Spine. 2008 Jul 15;33(16):1766-74. PMID: 18580547.

40. Roelofs PDDM, Deyo RA, Koes BW, et al. Non-steroidal anti-inflammatory drugs for low back pain. Cochrane Database of Systematic Reviews. 2008(1):CD000396. PMID: 18253976.

41. Nadler SF, Steiner DJ, Erasala GN, et al. Continuous low-level heat wrap therapy provides more efficacy than Ibuprofen and acetaminophen for acute low back pain. Spine (Phila Pa 1976). 2002 May 15;27(10):1012-7. PMID: 12004166.

42. Williams CM, Maher CG, Latimer J, et al. Efficacy of paracetamol for acute low-back pain: a double-blind, randomised controlled trial. Lancet. 2014;384(9954):1586-96. PMID: No PMID.

43. Chou R, Huffman L. Guideline for the evaluation and management of low back pain: evidence review American Pain Society. Glenview IL: 2007.

44. van Tulder MW, Jellema P, van Poppel MNM, et al. Lumbar supports for prevention and treatment of low-back pain. Cochrane Database of Systematic Reviews. 2000(3):Art. No.: CD001823. PMID: 17636685.

45. Dreiser RL, Le Parc JM, Velicitat P, et al. Oral meloxicam is effective in acute sciatica: two randomised, double-blind trials versus placebo or diclofenac. Inflamm Res. 2001 Mar;50 Suppl 1:S17-23. PMID: 11339516.

46. Famaey JP, Bruhwyler J, Geczy J, et al. Open controlled randomized multicenter comparison of nimesulide and diclofenac in the treatment of subacute and chronic low back pain. Journal of Clinical Research. 1998;1(219-238):219-38. PMID: No PMID.

47. Pohjolainen T, Jekunen A, Autio L, et al. Treatment of acute low back pain with the COX-2-selective anti-inflammatory drug nimesulide: results of a randomized, double-blind comparative trial versus ibuprofen. Spine (Phila Pa 1976). 2000 Jun 15;25(12):1579-85. PMID: 10851109.

48. Ximenes A, Robles M, Sands G, et al. Valdecoxib is as efficacious as diclofenac in the treatment of acute low back pain. Clinical Journal of Pain. 2007 Mar-Apr;23(3):244-50. PMID: 17314584.

49. Zerbini C, Ozturk ZE, Grifka J, et al. Efficacy of etoricoxib 60 mg/day and diclofenac 150 mg/day in reduction of pain and disability in patients with chronic low back pain: results of a 4-week, multinational, randomized, double-blind study. Current Medical Research & Opinion. 2005 Dec;21(12):2037-49. PMID: 16368055.

50. Herrmann WA, Geertsen MS. Efficacy and safety of lornoxicam compared with placebo and diclofenac in acute sciatica/lumbo-sciatica: an analysis from a randomised, double-blind, multicentre, parallel-group study. International Journal of Clinical Practice. 2009 Nov;63(11):1613-21. PMID: 19832818.

51. Majchrzycki M, Kocur P, Kotwicki T. Deep tissue massage and nonsteroidal anti-inflammatory drugs for low back pain: a prospective randomized trial. Thescientificworldjournal. 2014;2014:287597. PMID: 24707200.

52. Shirado O, Doi T, Akai M, et al. Multicenter randomized controlled trial to evaluate the effect of home-based exercise on patients with chronic low back pain: the Japan low back pain exercise therapy study. Spine. 2010 Aug 1;35(17):E811-9. PMID: 20628332.

53. Amlie E, Weber H, Holme I. Treatment of acute low-back pain with piroxicam: results of a double-blind placebo-controlled trial. Spine (Phila Pa 1976). 1987 Jun;12(5):473-6. PMID: 2957801.

54. Babej-Dolle R, Freytag S, Eckmeyer J, et al. Parenteral dipyrone versus diclofenac and placebo in patients with acute lumbago or sciatic pain: randomized observer-blind multicenter study. Int J Clin Pharmacol Ther. 1994 Apr;32(4):204-9. PMID: 8032581.

55. Basmajian JV. Acute back pain and spasm. A controlled multicenter trial of combined analgesic and antispasm agents. Spine (Phila Pa 1976). 1989 Apr;14(4):438-9. PMID: 2524114.

56. Dreiser RL, Marty M, Ionescu E, et al. Relief of acute low back pain with diclofenac-K 12.5 mg tablets: a flexible dose, ibuprofen 200 mg and placebo-controlled clinical trial. Int J Clin Pharmacol Ther. 2003 Sep;41(9):375-85. PMID: 14518597.

57. Goldie I. A clinical trial with indomethacin (indomee(R)) in low back pain and sciatica. Acta Orthop Scand. 1968;39(1):117-28. PMID: 4239771.

58. Jacobs JH, Grayson MF. Trial of an anti-inflammatory agent (indomethacin) in low back pain with and without radicular involvement. Br Med J. 1968 Jul 20;3(5611):158-60. PMID: 4232743.

59. Lacey PH, Dodd GD, Shannon DJ. A double blind, placebo controlled study of piroxicam in the management of acute musculoskeletal disorders. Eur J Rheumatol Inflamm. 1984;7(3):95-104. PMID: 6443759.

60. Szpalski M, Hayez JP. Objective functional assessment of the efficacy of tenoxicam in the treatment of acute low back pain. A double-blind placebo-controlled study. Br J Rheumatol. 1994 Jan;33(1):74-8. PMID: 8162464.

61. Weber H, Aasand G. The effect of phenylbutazone on patients with acute lumbago-sciatica. A double blind trial. J Oslo City Hosp. 1980 May;30(5):69-72. PMID: 6446598.

62. Weber H, Holme I, Amlie E. The natural course of acute sciatica with nerve root symptoms in a double-blind placebo-controlled trial evaluating the effect of piroxicam. Spine (Phila Pa 1976). 1993 Sep 1;18(11):1433-8. PMID: 8235813.

63. Berry H, Bloom B, Hamilton EB, et al. Naproxen sodium, diflunisal, and placebo in the treatment of chronic back pain. Annals of the Rheumatic Diseases. 1982 Apr;41(2):129-32. PMID: 6462116.

64. Birbara CA, Puopolo AD, Munoz DR, et al. Treatment of chronic low back pain with etoricoxib, a new cyclo-oxygenase-2 selective inhibitor: improvement in pain and disability--a randomized, placebo-controlled, 3-month trial. Journal of Pain. 2003 Aug;4(6):307-15. PMID: 14622687.

65. Coats TL, Borenstein DG, Nangia NK, et al. Effects of valdecoxib in the treatment of chronic low back pain: results of a randomized, placebo-controlled trial. Clinical Therapeutics. 2004 Aug;26(8):1249-60. PMID: 15476906.

66. Katz N, Ju WD, Krupa DA, et al. Efficacy and safety of rofecoxib in patients with chronic low back pain: results from two 4-week, randomized, placebo-controlled, parallel-group, double-blind trials. Spine (Phila Pa 1976). 2003 May 1;28(9):851-8; discussion 9. PMID: 12941996.

67. Chrubasik S, Model A, Black A, et al. A randomized double-blind pilot study comparing Doloteffin and Vioxx in the treatment of low back pain. Rheumatology. 2003 Jan;42(1):141-8. PMID: 12509627.

68. Colberg K, Hettich M, Sigmund R, et al. The efficacy and tolerability of an 8-day administration of intravenous and oral meloxicam: a comparison with intramuscular and oral diclofenac in patients with acute lumbago. German Meloxicam Ampoule Study Group. Current Medical Research & Opinion. 1996;13(7):363-77. PMID: 8862936.

69. Chaparro EL, Furlan AD, Deshpande A, et al. Opioids compared to placebo or other treatments for chronic low-back pain. Cochrane Database of Systematic Reviews. 2014(5)PMID: No PMID.

70. Buynak R, Shapiro DY, Okamoto A, et al. Efficacy and safety of tapentadol extended release for the management of chronic low back pain: results of a prospective, randomized, double-blind, placebo- and active-controlled Phase III study.[Erratum appears in Expert Opin Pharmacother. 2010 Nov;11(16):2773]. Expert Opinion on Pharmacotherapy. 2010 Aug;11(11):1787-804. PMID: 20578811.

71. Chu LF, D'Arcy N, Brady C, et al. Analgesic tolerance without demonstrable opioid-induced hyperalgesia: a double-blinded, randomized, placebo-controlled trial of sustained-release morphine for treatment of chronic nonradicular low-back pain. Pain. 2012 Aug;153(8):1583-92. PMID: 22704854.

72. Hale M, Khan A, Kutch M, et al. Once-daily OROS hydromorphone ER compared with placebo in opioid-tolerant patients with chronic low back pain.[Erratum appears in Curr Med Res Opin. 2010 Aug;26(8):1904]. Current Medical Research & Opinion. 2010 Jun;26(6):1505-18. PMID: 20429852.

73. Hale ME, Ahdieh H, Ma T, et al. Efficacy and safety of OPANA ER (oxymorphone extended release) for relief of moderate to severe chronic low back pain in opioid-experienced patients: a 12-week, randomized, double-blind, placebo-controlled study. Journal of Pain. 2007 Feb;8(2):175-84. PMID: 17145204.

74. Katz N, Rauck R, Ahdieh H, et al. A 12-week, randomized, placebo-controlled trial assessing the safety and efficacy of oxymorphone extended release for opioid-naive patients with chronic low back pain. Current Medical Research & Opinion. 2007 Jan;23(1):117-28. PMID: 17257473.

75. Khoromi S, Cui L, Nackers L, et al. Morphine, nortriptyline and their combination vs. placebo in patients with chronic lumbar root pain. Pain. 2007 Jul;130(1-2):66-75. PMID: 17182183.

76. Webster LR, Butera PG, Moran LV, et al. Oxytrex minimizes physical dependence while providing effective analgesia: a randomized controlled trial in low back pain. Journal of Pain. 2006 Dec;7(12):937-46. PMID: 17157780.

77. Peloso PM, Fortin L, Beaulieu A, et al. Analgesic efficacy and safety of tramadol/ acetaminophen combination tablets (Ultracet) in treatment of chronic low back pain: a multicenter, outpatient, randomized, double blind, placebo controlled trial. Journal of Rheumatology. 2004 Dec;31(12):2454-63. PMID: 15570651.

78. Ruoff GE, Rosenthal N, Jordan D, et al. Tramadol/acetaminophen combination tablets for the treatment of chronic lower back pain: a multicenter, randomized, double-blind, placebo-controlled outpatient study. Clinical Therapeutics. 2003 Apr;25(4):1123-41. PMID: 12809961.

79. Schnitzer TJ, Gray WL, Paster RZ, et al. Efficacy of tramadol in treatment of chronic low back pain. Journal of Rheumatology. 2000 Mar;27(3):772-8. PMID: 10743823.

80. Uberall MA, Mueller-Schwefe GHH, Terhaag B. Efficacy and safety of flupirtine modified release for the management of moderate to severe chronic low back pain: results of SUPREME, a prospective randomized, double-blind, placebo- and active-controlled parallel-group phase IV study. Current Medical Research & Opinion. 2012 Oct;28(10):1617-34. PMID: 22970658.

81. Vorsanger GJ, Xiang J, Gana TJ, et al. Extended-release tramadol (tramadol ER) in the treatment of chronic low back pain. Journal of Opioid Management. 2008 Mar-Apr;4(2):87-97. PMID: 18557165.

82. Gordon A, Callaghan D, Spink D, et al. Buprenorphine transdermal system in adults with chronic low back pain: a randomized, double-blind, placebo-controlled crossover study, followed by an open-label extension phase. Clinical Therapeutics. 2010 May;32(5):844-60. PMID: 20685494.

83. O'Donnell JB, Ekman EF, Spalding WM, et al. The effectiveness of a weak opioid medication versus a cyclo-oxygenase-2 (COX-2) selective non-steroidal anti-inflammatory drug in treating flare-up of chronic low-back pain: results from two randomized, double-blind, 6-week studies. Journal of International Medical Research. 2009 Nov-Dec;37(6):1789-802. PMID: 20146877.

84. Steiner DJ, Sitar S, Wen W, et al. Efficacy and safety of the seven-day buprenorphine transdermal system in opioid-naive patients with moderate to severe chronic low back pain: an enriched, randomized, double-blind, placebo-controlled study. Journal of Pain & Symptom Management. 2011 Dec;42(6):903-17. PMID: 21945130.

85. Hale ME, Dvergsten C, Gimbel J. Efficacy and safety of oxymorphone extended release in chronic low back pain: results of a randomized, double-blind, placebo- and active-controlled phase III study. Journal of Pain. 2005 Jan;6(1):21-8. PMID: 15629415.

86. Jamison RN, Raymond SA, Slawsby EA, et al. Opioid therapy for chronic noncancer back pain. A randomized prospective study. Spine (Phila Pa 1976). 1998 Dec 1;23(23):2591-600. PMID: 9854758.

87. Cloutier C, Taliano J, O'Mahony W, et al. Controlled-release oxycodone and naloxone in the treatment of chronic low back pain: a placebo-controlled, randomized study. Pain Research & Management. 2013 Mar-Apr;18(2):75-82. PMID: 23662289.

88. Hyup Lee J, Lee C-S, Ultracet ERSG. A randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of the extended-release tramadol hydrochloride/acetaminophen fixed-dose combination tablet for the treatment of chronic low back pain. Clinical Therapeutics. 2013 Nov;35(11):1830-40. PMID: 24183364.

89. Rauck RL, Nalamachu S, Wild JE, et al. Single-entity hydrocodone extended-release capsules in opioid-tolerant subjects with moderate-to-severe chronic low back pain: a randomized double-blind, placebo-controlled study. Pain Medicine. 2014 Jun;15(6):975-85. PMID: 24517082.

90. Schiphorst Preuper HR, Geertzen JHB, van Wijhe M, et al. Do analgesics improve functioning in patients with chronic low back pain? An explorative triple-blinded RCT. European Spine Journal. 2014 Apr;23(4):800-6. PMID: 24526247.

91. Furlan A, Chaparro LE, Irvin E, et al. A comparison between enriched and nonenriched enrollment randomized withdrawal trials of opioids for chronic noncancer pain. Pain Research & Management. 2011 Sep-Oct;16(5):337-51. PMID: 22059206.

92. Sullivan MD, Howe CQ. Opioid therapy for chronic pain in the United States: promises and perils. Pain. 2013 Dec;154 Suppl 1:S94-100. PMID: 24036286.

93. Carson S, Thakurta S, Low A, et al. Drug Class Review: Long-Acting Opioid Analgesics: Final Update 6 Report [Internet]. Drug Class Reviews. 2011 JulPMID: 21977550.

94. Allan L, Richarz U, Simpson K, et al. Transdermal fentanyl versus sustained release oral morphine in strong-opioid naive patients with chronic low back pain. Spine (Phila Pa 1976). 2005 Nov 15;30(22):2484-90. PMID: 16284584.

95. Rauck RL, Bookbinder SA, Bunker TR, et al. The ACTION study: a randomized, open-label, multicenter trial comparing once-a-day extended-release morphine sulfate capsules (AVINZA) to twice-a-day controlled-release oxycodone hydrochloride tablets (OxyContin) for the treatment of chronic, moderate to severe low back pain. Journal of Opioid Management. 2006 May-Jun;2(3):155-66. PMID: 17319449.

96. Hale ME, Fleischmann R, Salzman R, et al. Efficacy and safety of controlled-release versus immediate-release oxycodone: randomized, double-blind evaluation in patients with chronic back pain. Clinical Journal of Pain. 1999 Sep;15(3):179-83. PMID: 10524470.

97. Salzman RT, Roberts MS, Wild J, et al. Can a controlled-release oral dose form of oxycodone be used as readily as an immediate-release form for the purpose of titrating to stable pain control? Journal of Pain & Symptom Management. 1999 Oct;18(4):271-9. PMID: 10534967.

98. Hale M, Speight K, Harsanyi Z, et al. Efficacy of 12 hourly controlled-release codeine compared with as required dosing of acetaminophen plus codeine in patients with chronic low back pain. Pain Res Manage. 1997;2(1):33-8. PMID: No PMID.

99. . A comparison of the efficacy and adverse effects of controlled-release dihydrocodeine and immediate-release dihydrocodeine in the treatment of pain in osteoarthritis and chronic back pain. Proceedings of The Edinburgh Symposium on Pain Control and Medical Education; 1989. Rick opioids.

100. Nicholson B, Ross E, Sasaki J, et al. Randomized trial comparing polymer-coated extended-release morphine sulfate to controlled-release oxycodone HCl in moderate to severe nonmalignant pain. Current Medical Research & Opinion. 2006 Aug;22(8):1503-14. PMID: 16870075.

101. Beaulieu AD, Peloso P, Bensen W, et al. A randomized, double-blind, 8-week crossover study of once-daily controlled-release tramadol versus immediate-release tramadol taken as needed for chronic noncancer pain. Clinical Therapeutics. 2007 Jan;29(1):49-60. PMID: 17379046.

102. van Tulder MW, Touray T, Furlan AD, et al. Muscle relaxants for non-specific low-back pain. Cochrane Database of Systematic Reviews. 2009(4)PMID: No PMID.

103. Baptista R, Brizzi J, Josef H, et al. [Terepeutica da lombalgia com a tizanidina]. Folha Medica. 1988PMID: No PMID.

104. Baratta RR. A double-blind comparative study of carisoprodol, propoxyphene, and placebo in the management of low back syndrome. Curr Ther Res Clin Exp. 1976 Sep;20(3):233-40. PMID: 134877.

105. Basmajian JV. Cyclobenzaprine hydrochloride effect on skeletal muscle spasm in the lumbar region and neck: two double-blind controlled clinical and laboratory studies. Archives of Physical Medicine & Rehabilitation. 1978 Feb;59(2):58-63. PMID: 623512.

106. Berry H, Hutchinson D. Tizanidine and ibuprofen in acute low-back pain: results of a double-blind multicentre study in general practice. J Int Med Res. 1988;16(2):83-91. PMID: 2967781.

107. Berry H, Hutchinson DR. A multicentre placebo-controlled study in general practice to evaluate the efficacy and safety of tizanidine in acute low-back pain. J Int Med Res. 1988;16:75-82. PMID: 2967780.

108. Bianchi M. Evaluation of cyclobenzaprine for skeletal muscle spasm of local origin. Postgraduate Medicine Communications. 1978:25-9. PMID: No PMID.

109. Borenstein D, Lacks S, Wiesel S. Cyclobenzarpine and naproxen versus naproxen alone in the treatment of acute low back pain and muscle spasm. Clinical Therapeutics. 1990;12:125-31. PMID: 2141299.

110. Bragstad A, Bilkra G. Evaluation of a new skeletal muscle relaxant in the treatment of low back pain (a comparison of DS 103-282 wiht chlorzoxazone). Current Therapeutic Research. 1979;26(1):39-43. PMID: No PMID.

111. Casale R. Acute low back pain: symptomatic treatment with a muscle relaxing drug. Clinical Journal of Pain 1988;4:81-8. PMID: No PMID.

112. Corts Giner JR. [Estudio DS 103-282: relajante muscular en lumbalgia aguda o lumbao (estudio doble ciego de tizanidina + paracetamol vs. placebo + paracetamol]. Rev Esp de Cir Ost. 1989:119-24. PMID: No PMID.

113. Dapas F, Hartman SF, Martinez L, et al. Baclofen for the treatment of acute low-back syndrome. A double-blind comparison with placebo. Spine. 1985 May;10(4):345-9. PMID: 2931831.

114. Gold R. Orphenadrine Citrate: Sedative or Muscle Relaxant? Clinical Therapeutics. 1978;1(6):451-3. PMID: No PMID.

115. Hindle TH, 3rd. Comparison of carisoprodol, butabarbital, and placebo in treatment of the low back syndrome. California Medicine. 1972 Aug;117(2):7-11. PMID: 4262210.

116. Hingorani K. Orphenadine/Paracetamol in backache: a double-blind controlled trial. The British Journal of Clinical Practice. 1971;25:227-31. PMID: 4253016.

117. Klinger N, Wilson R, Kanniainen C, et al. Intravenous orphenadrine for the treatment of lumbar paravertebral muscle strain. Current Therapeutic Research. 1988;43(2):247-54. PMID: No PMID.

118. Lepisto P. A comparative trial of ds 103-283 and placebo in the treatment of acute skeletal muscle spasms due to disorders of the back. Therapeutic Research. 1979;26(4):454-59. PMID: No PMID.

119. Pipino F, Menarini C, Lombardi G, et al. A direct myotonolytic (Pridinol Mesilate) for the mangement of chronic low back pain: A multicentre, comparitive clinical evaluation. European Journal of Clinical Research. 1991;1(1):55-70. PMID: No PMID.

120. Pratzel HG, Alken RG, Ramm S. Efficacy and tolerance of repeated oral doses of tolperisone hydrochloride in the treatment of painful reflex muscle spasm: results of a prospective placebo-controlled double-blind trial. Pain. 1996 Oct;67(2-3):417-25. PMID: 8951937.

121. Rollings H. Management of acute musculoskeletal conditions - Thoracolumbar strain or sprain: A doulbe-blind evaluation comparing the efficacy and safety of carisoprodol with cyclobenzaprene hydrochloride. Current Therapeutic Research. 1983;34(6):917-28. PMID: No PMID.

122. Sirdalud Ternelin Asia-Pacific Study Group. Efficacy and gastroprotective effects of tizanidine plus diclofenac versus placebo plus dicofenac in patients with painful muscle spasms. Curr Ther Res. 1998;59:13-22. PMID: No PMID.

123. Sweetman BJ, Baig A, Parsons DL. Mefenamic acid, chlormezanone-paracetamol, ethoheptazine-aspirin-meprobamate: a comparative study in acute low back pain. British Journal of Clinical Practice. 1987 Feb;41(2):619-24. PMID: 2960369.

124. Tervo T, Petaja L, Lepisto P. A controlled clinical trial of a muscle relaxants analgesic combination in the treatment of acute lumbago. The British Journal of Clinical Practice. 1976;30:62-4. PMID: No PMID.

125. Pareek A, Chandurkar N, Chandanwale AS, et al. Aceclofenac-tizanidine in the treatment of acute low back pain: a double-blind, double-dummy, randomized, multicentric, comparative study against aceclofenac alone. European Spine Journal. 2009 Dec;18(12):1836-42. PMID: 19421791.

126. Ralph L, Look M, Wheeler W, et al. Double-blind, placebo-controlled trial of carisoprodol 250-mg tablets in the treatment of acute lower-back spasm. Current Medical Research & Opinion. 2008 Feb;24(2):551-8. PMID: 18194591.

127. Boyles WF, Glassmann JM, Soyka JP. Management of acute musculoskeletal conditions: Thoracolumbar strain or sprain. A double-blind evaluation comparing the efficacy and safety of carisoprodol with diazepam. Today's Therapeutic Trends. 1983;1(1):1-16. PMID: No PMID.

128. Hennies OL. A new skeletal muscle relaxant (DS 103-282) compared to diazepam in the treatment of muscle spasm of local origin. Journal of International Medical Research. 1981;9(1):62-8. PMID: 6451461.

129. Arbus L, Fajadet B, Aubert D, et al. Activity of tetrazepam (Myolastan®)* * Myolastan® - tetrazepam; Sanofi Recherche, Toulouse, France. in low back pain. A double-blind trial v. placebo. Clinical Trials Journal. 1990;27(4):258-67. PMID: No PMID.

130. Hingorani K. Diazepam in backache. A double-blind controlled trial. Ann Phys Med. 1966 Nov;8(8):303-6. PMID: 4224750.

131. Moll W. [Therapy of acute lumbovertebral syndromes through optimal muscle relaxation using diazepam. Results of a double-blind study on 68 cases]. Med Welt. 1973 Nov 9;24(45):1747-51. PMID: 4272092.

132. Salzmann E, Pforringer W, Paal G, et al. Treatment of chronic low-back syndrome with tetrazepam in a placebo controlled double-blind trial. Journal of Drug Development. 1992;4(4):219-28. PMID: No PMID.

133. Weber H. Comparison of the effect of diazepam and levomepromazine on pain in patients with acute lumbago-sciatica. J Oslo City Hosp. 1980 May;30(5):65-8. PMID: 6446597.

134. Brotz D, Maschke E, Burkard S, et al. Is there a role for benzodiazepines in the management of lumbar disc prolapse with acute sciatica? Pain. 2010 Jun;149(3):470-5. PMID: 20362397.

135. Schnitzer TJ, Ferraro A, Hunsche E, et al. A comprehensive review of clinical trials on the efficacy and safety of drugs for the treatment of low back pain. J Pain & Sympt Mgmt. 2004;28(1):72-95. PMID: 15223086.

136. Salerno SM, Browning R, Jackson JL. The effect of antidepressant treatment on chronic back pain: a meta-analysis. Arch Intern Med. 2002 162(1):19-24. PMID: 11784215.

137. Staiger TO, Gaster B, Sullivan MD, et al. Systematic review of antidepressants in the treatment of chronic low back pain. Spine. 2003;28(22):2540-5. PMID: 14624092.

138. Urquhart DM, Hoving JL, Assendelft JJW, et al. Antidepressants for non-specific low back pain. Cochrane Database of Systematic Reviews. 2010(10)PMID: No PMID.

139. Alcoff J, Jones E, Rust P, et al. Controlled trial of imipramine for chronic low back pain. Journal of Family Practice. 1982 May;14(5):841-6. PMID: 6210751.

140. Atkinson JH, Slater MA, Capparelli EV, et al. Efficacy of noradrenergic and serotonergic antidepressants in chronic back pain: a preliminary concentration-controlled trial. J Clin Psychopharmacol. 2007 Apr;27(2):135-42. PMID: 17414235.

141. Atkinson JH, Slater MA, Wahlgren DR, et al. Effects of noradrenergic and serotonergic antidepressants on chronic low back pain intensity. Pain. 1999 Nov;83(2):137-45. PMID: 10534584.

142. Atkinson JH, Slater MA, Williams RA, et al. A placebo-controlled randomized clinical trial of nortriptyline for chronic low back pain. Pain. 1998 Jun;76(3):287-96. PMID: 9718247.

143. Dickens C, Jayson M, Sutton C, et al. The relationship between pain and depression in a trial using paroxetine in sufferers of chronic low back pain. Psychosomatics. 2000 Nov-Dec;41(6):490-9. PMID: 11110112.

144. Goodkin K, Gullion CM, Agras WS. A randomized, double-blind, placebo-controlled trial of trazodone hydrochloride in chronic low back pain syndrome. Journal of Clinical Psychopharmacology. 1990 Aug;10(4):269-78. PMID: 2149565.

145. Jenkins DG, Ebbutt AF, Evans CD. Tofranil in the treatment of low back pain. Journal of International Medical Research. 1976;4(2 Suppl):28-40. PMID: 140827.

146. Katz J, Pennella-Vaughan J, Hetzel RD, et al. A randomized, placebo-controlled trial of bupropion sustained release in chronic low back pain. Journal of Pain. 2005 Oct;6(10):656-61. PMID: 16202958.

147. Pheasant H, Bursk A, Goldfarb J, et al. Amitriptyline and chronic low back pain: a randomized double-blind crossover study. Spine (Phila Pa 1976). 1983;8:552-7. PMID: 6228015.

148. Treves R, Montaine de la Roque P, Dumond JJ, et al. [Prospective study of the analgesic action of clomipramine versus placebo in refractory lumbosciatica (68 cases)]. Revue du Rhumatisme et des Maladies Osteo-Articulaires. 1991 Jul-Sep;58(7):549-52. PMID: 1833813.

149. Farajirad S, Behdani F, Hebrani P, et al. Comparison between the effects of amitriptyline and bupropione on the quality of life and the reduction in the severity of pain in patients with chronic low-back pain. Neurosurgery quarterly. 2013;23(4):227-9. PMID: No PMID.

150. Mazza M, Mazza O, Pazzaglia C, et al. Escitalopram 20 mg versus duloxetine 60 mg for the treatment of chronic low back pain. Expert Opinion on Pharmacotherapy. 2010 May;11(7):1049-52. PMID: 20402551.

151. Skljarevski V, Ossanna M, Liu-Seifert H, et al. A double-blind, randomized trial of duloxetine versus placebo in the management of chronic low back pain. European Journal of Neurology. 2009 Sep;16(9):1041-8. PMID: 19469829.

152. Skljarevski V, Zhang S, Desaiah D, et al. Duloxetine versus placebo in patients with chronic low back pain: a 12-week, fixed-dose, randomized, double-blind trial. Journal of Pain. 2010 Dec;11(12):1282-90. PMID: 20472510.

153. Skljarevski V, Desaiah D, Liu-Seifert H, et al. Efficacy and safety of duloxetine in patients with chronic low back pain. Spine. 2010 Jun 1;35(13):E578-85. PMID: 20461028.

154. Schreiber S, Vinokur S, Shavelzon V, et al. A randomized trial of fluoxetine versus amitriptyline in musculo-skeletal pain. Israel Journal of Psychiatry & Related Sciences. 2001;38(2):88-94. PMID: 11475920.

155. Khoromi S, Patsalides A, Parada S, et al. Topiramate in chronic lumbar radicular pain. Journal of Pain. 2005 Dec;6(12):829-36. PMID: 16326371.

156. McCleane GJ. Does gabapentin have an analgesic effect on background, movement and referred pain? A randomised, double-blind, placebo controlled study. The Pain Clinic. 2001;13(2):103-7. PMID: No PMID.

157. Muehlbacher M, Nickel MK, Kettler C, et al. Topiramate in treatment of patients with chronic low back pain: a randomized, double-blind, placebo-controlled study. Clinical Journal of Pain. 2006 Jul-Aug;22(6):526-31. PMID: 16788338.

158. Yildirim K, Şışecıoğlu M, Karatay S, et al. The effectiveness of gabapentin in patients with chronic radiculopathy. The Pain Clinic. 2003;15(3):213-8. PMID: No PMID.

159. Baron R, Freynhagen R, Tolle TR, et al. The efficacy and safety of pregabalin in the treatment of neuropathic pain associated with chronic lumbosacral radiculopathy. Pain. 2010 Sep;150(3):420-7. PMID: 20493632.

160. Baron R, Martin-Mola E, Muller M, et al. Effectiveness and Safety of Tapentadol Prolonged Release (PR) Versus a Combination of Tapentadol PR and Pregabalin for the Management of Severe, Chronic Low Back Pain With a Neuropathic Component: A Randomized, Double-blind, Phase 3b Study. Pain Practice. 2014 Apr 17PMID: 24738609.

161. Markman JD, Frazer ME, Rast SA, et al. Double-blind, randomized, controlled, crossover trial of pregabalin for neurogenic claudication. Neurology. 2014 Dec 10PMID: 25503625.

162. Pota V, Barbarisi M, Sansone P, et al. Combination therapy with transdermal buprenorphine and pregabalin for chronic low back pain. Pain Management. 2012 Jan;2(1):23-31. PMID: 24654615.

163. Romano CL, Romano D, Bonora C, et al. Pregabalin, celecoxib, and their combination for treatment of chronic low-back pain. Journal of Orthopaedics & Traumatology. 2009 Dec;10(4):185-91. PMID: 19921480.

164. Yaksi A, Ozgonenel L, Ozgonenel B. The efficiency of gabapentin therapy in patients with lumbar spinal stenosis. Spine. 2007 Apr 20;32(9):939-42. PMID: 17450066.

165. Atkinson J, Slater M, Patel S, et al. Gabapentin for chronic back pain: a randomized clinical trial. The Journal of Pain. 2010;11(4, Supplement):S37. PMID: No PMID.

166. Finckh A, Zufferey P, Schurch MA, et al. Short-term efficacy of intravenous pulse glucocorticoids in acute discogenic sciatica. A randomized controlled trial. Spine (Phila Pa 1976). 2006 Feb 15;31(4):377-81. PMID: 16481946.

167. Friedman BW, Holden L, Esses D, et al. Parenteral corticosteroids for Emergency Department patients with non-radicular low back pain. Journal of Emergency Medicine. 2006 Nov;31(4):365-70. PMID: 17046475.

168. Haimovic IC, Beresford HR. Dexamethasone is not superior to placebo for treating lumbosacral radicular pain. Neurology. 1986 Dec;36(12):1593-4. PMID: 2946981.

169. Porsman O, Friis H. Prolapsed lumbar disc treated with intramuscularly administered dexamethasonephosphate. A prospectively planned, double-blind, controlled clinical trial in 52 patients. Scand J Rheumatol. 1979;8(3):142-4. PMID: 386492.

170. Eskin B, Shih RD, Fiesseler FW, et al. Prednisone for emergency department low back pain: a randomized controlled trial. Journal of Emergency Medicine. 2014 Jul;47(1):65-70. PMID: 24739318.

171. Friedman BW, Esses D, Solorzano C, et al. A randomized placebo-controlled trial of single-dose IM corticosteroid for radicular low back pain. Spine. 2008 Aug 15;33(18):E624-9. PMID: 18665021.

172. Holve RL, Barkan H. Oral steroids in initial treatment of acute sciatica. Journal of the American Board of Family Medicine: JABFM. 2008 Sep-Oct;21(5):469-74. PMID: 18772303.

173. Hedeboe J, Buhl M, Ramsing P. Effects of using dexamethasone and placebo in the treatment of prolapsed lumbar disc. Acta Neurol Scand. 1982 Jan;65(1):6-10. PMID: 7039210.

174. Hofferberth B, Gottschaldt M, Grass H, et al. [The usefulness of dexamethasonephosphate in the conservative treatment of lumbar pain--a double-blind study (author's transl)]. Arch Psychiatr Nervenkr. 1982;231(4):359-67. PMID: 6214237.

175. Clare HA, Adams R, Maher CG. A systematic review of efficacy of McKenzie therapy for spinal pain. Australian Journal of Physiotherapy. 2004;50(4):209-16. PMID: 15574109.

176. Hayden JA, van Tulder MW, Malmivaara A, et al. Exercise therapy for treatment of non-specific low back pain. Cochrane database of systematic reviews (Online). 2005(3)PMID: 16034851.

177. Hayden JA, van Tulder MW, Malmivaara AV, et al. Meta-analysis: exercise therapy for nonspecific low back pain. Annals of Internal Medicine. 2005 May 3;142(9):765-75. PMID: 15867409.

178. Kool J, de Bie R, Oesch P, et al. Exercise reduces sick leave in patients with non-acute non-specific low back pain: a meta-analysis. Journal of Rehabilitation Medicine. 2004 Mar;36(2):49-62. PMID: 15180219.

179. Liddle SD, Baxter GD, Gracey JH. Exercise and chronic low back pain: what works? Pain. 2004 Jan;107(1-2):176-90. PMID: 14715404.

180. Machado LA, de Souza M, Ferreira PH, et al. The McKenzie method for low back pain: a systematic review of the literature with a meta-analysis approach. Spine (Phila Pa 1976). 2006 Apr 20;31(9):E254-62. PMID: 16641766.

181. McNeely ML, Torrance G, Magee DJ. A systematic review of physiotherapy for spondylolysis and spondylolisthesis. Man Ther. 2003 May;8(2):80-91. PMID: 12890435.

182. UK BEAM Trial Team. United Kingdom back pain exercise and manipulation (UK BEAM) randomised trial: effectiveness of physical treatments for back pain in primary care. BMJ. 2004 Dec 11;329(7479):1377. PMID: 15556955.

183. Hayden J, van Tulder MW, Malmivaara A, et al. Exercise therapy for treatment of non-specific low back pain. Cochrane Database of Systematic Reviews. 2011(2)PMID: No PMID.

184. van Middelkoop M, Rubinstein SM, Verhagen AP, et al. Exercise therapy for chronic nonspecific low-back pain. Best Practice & Research in Clinical Rheumatology. 2010 Apr;24(2):193-204. PMID: 20227641.

185. Oesch P, Kool J, Hagen KB, et al. Effectiveness of exercise on work disability in patients with non-acute non-specific low back pain: Systematic review and meta-analysis of randomised controlled trials. Journal of Rehabilitation Medicine. 2010 Mar;42(3):193-205. PMID: 20411212.

186. Alexandre NM, de Moraes MA, Correa Filho HR, et al. Evaluation of a program to reduce back pain in nursing personnel. Rev Saude Publica. 2001 Aug;35(4):356-61. PMID: 11600924.

187. Donzelli S, Di Domenica E, Cova AM, et al. Two different techniques in the rehabilitation treatment of low back pain: a randomized controlled trial. Eura Medicophys. 2006 Sep;42(3):205-10. PMID: 17039216.

188. Elnaggar IM, Nordin M, Sheikhzadeh A, et al. Effects of spinal flexion and extension exercises on low-back pain and spinal mobility in chronic mechanical low-back pain patients. Spine (Phila Pa 1976). 1991 Aug;16(8):967-72. PMID: 1835157.

189. Ferreira ML, Ferreira PH, Latimer J, et al. Comparison of general exercise, motor control exercise and spinal manipulative therapy for chronic low back pain: A randomized trial. Pain. 2007 Sep;131(1-2):31-7. PMID: 17250965.

190. Frost H, Lamb SE, Doll HA, et al. Randomised controlled trial of physiotherapy compared with advice for low back pain. BMJ. 2004 Sep 25;329(7468):708. PMID: 15377573.

191. Galantino ML, Bzdewka TM, Eissler-Russo JL, et al. The impact of modified Hatha yoga on chronic low back pain: a pilot study. Alternative Therapies in Health & Medicine. 2004 Mar-Apr;10(2):56-9. PMID: 15055095.

192. Gladwell V, Head S, Haggar M, et al. Does a Program of Pilates Improve Chronic Non-Specific Low Back Pain? Journal of Sport Rehabilitation. 2006;15(4):338-50. PMID: 23128349.

193. Goldby LJ, Moore AP, Doust J, et al. A randomized controlled trial investigating the efficiency of musculoskeletal physiotherapy on chronic low back disorder. Spine (Phila Pa 1976). 2006 May 1;31(10):1083-93. PMID: 16648741.

194. Harts CC, Helmhout PH, de Bie RA, et al. A high-intensity lumbar extensor strengthening program is little better than a low-intensity program or a waiting list control group for chronic low back pain: a randomised clinical trial. Australian Journal of Physiotherapy. 2008;54(1):23-31. PMID: 18298356.

195. Hildebrandt VH, Proper KI, van den Berg R, et al. [Cesar therapy is temporarily more effective in patients with chronic low back pain than the standard treatment by family practitioner: randomized, controlled and blinded clinical trial with 1 year follow-up]. Nederlands Tijdschrift voor Geneeskunde. 2000 Nov 18;144(47):2258-64. PMID: 11109471.

196. Johannsen F, Remvig L, Kryger P, et al. Exercises for chronic low back pain: a clinical trial. Journal of Orthopaedic & Sports Physical Therapy. 1995 Aug;22(2):52-9. PMID: 7581431.

197. Koldas Dogan S, Sonel Tur B, Kurtais Y, et al. Comparison of three different approaches in the treatment of chronic low back pain. Clinical Rheumatology. 2008 Jul;27(7):873-81. PMID: 18188660.

198. Lewis JS, Hewitt JS, Billington L, et al. A randomized clinical trial comparing two physiotherapy interventions for chronic low back pain. Spine (Phila Pa 1976). 2005 Apr 1;30(7):711-21. PMID: 15803071.

199. Mannion AF, Muntener M, Taimela S, et al. A randomized clinical trial of three active therapies for chronic low back pain. Spine (Phila Pa 1976). 1999 Dec 1;24(23):2435-48. PMID: 10626305.

200. Niemisto L, Lahtinen-Suopanki T, Rissanen P, et al. A randomized trial of combined manipulation, stabilizing exercises, and physician consultation compared to physician consultation alone for chronic low back pain. Spine (Phila Pa 1976). 2003 Oct 1;28(19):2185-91. PMID: 14520029.

201. Risch SV, Norvell NK, Pollock ML, et al. Lumbar strengthening in chronic low back pain patients. Physiologic and psychological benefits. Spine (Phila Pa 1976). 1993 Feb;18(2):232-8. PMID: 8185727.

202. Rittweger J, Just K, Kautzsch K, et al. Treatment of chronic lower back pain with lumbar extension and whole-body vibration exercise: a randomized controlled trial. Spine (Phila Pa 1976). 2002 Sep 1;27(17):1829-34. PMID: 12221343.

203. Roche G, Ponthieux A, Parot-Shinkel E, et al. Comparison of a functional restoration program with active individual physical therapy for patients with chronic low back pain: a randomized controlled trial. Archives of Physical Medicine & Rehabilitation. 2007 Oct;88(10):1229-35. PMID: 17908562.

204. Sherman KJ, Cherkin DC, Erro J, et al. Comparing yoga, exercise, and a self-care book for chronic low back pain: a randomized, controlled trial. Annals of Internal Medicine. 2005 Dec 20;143(12):849-56. PMID: 16365466.

205. Sjogren T, Nissinen KJ, Jarvenpaa SK, et al. Effects of a workplace physical exercise intervention on the intensity of headache and neck and shoulder symptoms and upper extremity muscular strength of office workers: a cluster randomized controlled cross-over trial. Pain. 2005 Jul;116(1-2):119-28. PMID: 15927388.

206. Smeets RJ, Vlaeyen JW, Hidding A, et al. Active rehabilitation for chronic low back pain: cognitive-behavioral, physical, or both? First direct post-treatment results from a randomized controlled trial [ISRCTN22714229]. BMC Musculoskeletal Disorders. 2006;7:5. PMID: 16426449.

207. Tekur P, Singphow C, Nagendra HR, et al. Effect of short-term intensive yoga program on pain, functional disability and spinal flexibility in chronic low back pain: a randomized control study. Journal of Alternative & Complementary Medicine. 2008 Jul;14(6):637-44. PMID: 18673078.

208. Tritilanunt T, Wajanavisit W. The efficacy of an aerobic exercise and health education program for treatment of chronic low back pain. Journal of the Medical Association of Thailand. 2001 Oct;84 Suppl 2:S528-33. PMID: 11853276.

209. Turner JA, Clancy S, McQuade KJ, et al. Effectiveness of behavioral therapy for chronic low back pain: a component analysis. J Consult Clin Psychol. 1990 Oct;58(5):573-9. PMID: 2147702.

210. Williams KA, Petronis J, Smith D, et al. Effect of Iyengar yoga therapy for chronic low back pain. Pain. 2005 May;115(1-2):107-17. PMID: 15836974.

211. Yelland MJ, Glasziou PP, Bogduk N, et al. Prolotherapy injections, saline injections, and exercises for chronic low-back pain: a randomized trial. Spine (Phila Pa 1976). 2004 Jan 1;29(1):9-16; discussion PMID: 14699269.

212. Yozbatiran N, Yildirim Y, Parlak B. Effects of fitness and aquafitness exercises on physical fitness in patients with chronic low back pain. The Pain Clinic. 2004;16(1):35-42. PMID: No PMID.

213. Niemisto L, Rissanen P, Sarna S, et al. Cost-effectiveness of combined manipulation, stabilizing exercises, and physician consultation compared to physician consultation alone for chronic low back pain: a prospective randomized trial with 2-year follow-up. Spine (Phila Pa 1976). 2005 May 15;30(10):1109-15. PMID: 15897822.

214. Alaranta H, Rytokoski U, Rissanen A, et al. Intensive physical and psychosocial training program for patients with chronic low back pain. A controlled clinical trial. Spine (Phila Pa 1976). 1994 Jun 15;19(12):1339-49. PMID: 8066514.

215. Bendix AF, Bendix T, Ostenfeld S, et al. Active treatment programs for patients with chronic low back pain: a prospective, randomized, observer-blinded study. European Spine Journal. 1995;4(3):148-52. PMID: 7552649.

216. Bendix AF, Bendix T, Vaegter K, et al. Multidisciplinary intensive treatment for chronic low back pain: a randomized, prospective study. Cleve Clin J Med. 1996 Jan-Feb;63(1):62-9. PMID: 8590519.

217. Bendix T, Bendix A, Labriola M, et al. Functional restoration versus outpatient physical training in chronic low back pain: a randomized comparative study. Spine (Phila Pa 1976). 2000 Oct 1;25(19):2494-500. PMID: 11013502.

218. Harkapaa K, Jarvikoski A, Mellin G, et al. A controlled study on the outcome of inpatient and outpatient treatment of low back pain. Part I. Pain, disability, compliance, and reported treatment benefits three months after treatment. Scand J Rehabil Med. 1989;21(2):81-9. PMID: 2526364.

219. Hurri H. The Swedish back school in chronic low back pain. Part I. Benefits. Scand J Rehabil Med. 1989;21(1):33-40. PMID: 2523558.

220. Jousset N, Fanello S, Bontoux L, et al. Effects of functional restoration versus 3 hours per week physical therapy: a randomized controlled study. Spine (Phila Pa 1976). 2004 Mar 1;29(5):487-93; discussion 94. PMID: 15129059.

221. White AW. Low back pain in men receiving workmen's compensation. Can Med Assoc J. 1966 Jul 9;95(2):50-6. PMID: 4222996.

222. Albaladejo C, Kovacs FM, Royuela A, et al. The efficacy of a short education program and a short physiotherapy program for treating low back pain in primary care: a cluster randomized trial. Spine. 2010 Mar 1;35(5):483-96. PMID: 20147875.

223. Albert HB, Manniche C. The efficacy of systematic active conservative treatment for patients with severe sciatica: a single-blind, randomized, clinical, controlled trial. Spine. 2012 Apr 1;37(7):531-42. PMID: 21494193.

224. Bronfort G, Maiers MJ, Evans RL, et al. Supervised exercise, spinal manipulation, and home exercise for chronic low back pain: a randomized clinical trial. Spine Journal: Official Journal of the North American Spine Society. 2011 Jul;11(7):585-98. PMID: 21622028.

225. George SZ, Zeppieri G, Jr., Cere AL, et al. A randomized trial of behavioral physical therapy interventions for acute and sub-acute low back pain (NCT00373867). Pain. 2008 Nov 15;140(1):145-57. PMID: 18786762.

226. Hagen EM, Odelien KH, Lie SA, et al. Adding a physical exercise programme to brief intervention for low back pain patients did not increase return to work. Scandinavian Journal of Public Health. 2010 Nov;38(7):731-8. PMID: 20817653.

227. Hartvigsen J, Morso L, Bendix T, et al. Supervised and non-supervised Nordic walking in the treatment of chronic low back pain: a single blind randomized clinical trial. BMC Musculoskeletal Disorders. 2010;11:30. PMID: 20146793.

228. Helmhout PH, Harts CC, Viechtbauer W, et al. Isolated lumbar extensor strengthening versus regular physical therapy in an army working population with nonacute low back pain: a randomized controlled trial. Archives of Physical Medicine & Rehabilitation. 2008 Sep;89(9):1675-85. PMID: 18675396.

229. Henchoz Y, de Goumoens P, So AKL, et al. Functional multidisciplinary rehabilitation versus outpatient physiotherapy for non specific low back pain: randomized controlled trial. Swiss Medical Weekly. 2010;140:w13133. PMID: 21181567.

230. Hofstee DJ, Gijtenbeek JM, Hoogland PH, et al. Westeinde sciatica trial: randomized controlled study of bed rest and physiotherapy for acute sciatica. Journal of Neurosurgery. 2002 Jan;96(1 Suppl):45-9. PMID: 11797655.

231. Hurley DA, Tully MA, Lonsdale C, et al. Supervised walking in comparison with fitness training for chronic back pain in physiotherapy: results of the SWIFT single-blinded randomized controlled trial (ISRCTN17592092). Pain. 2015 Jan;156(1):131-47. PMID: 25599309.

232. Jensen RK, Leboeuf-Yde C, Wedderkopp N, et al. Rest versus exercise as treatment for patients with low back pain and Modic changes. A randomized controlled clinical trial. BMC Medicine. 2012;10:22. PMID: 22376791.

233. Kell RT, Risi AD, Barden JM. The response of persons with chronic nonspecific low back pain to three different volumes of periodized musculoskeletal rehabilitation. Journal of Strength & Conditioning Research. 2011 Apr;25(4):1052-64. PMID: 20647943.

234. Little P, Lewith G, Webley F, et al. Randomised controlled trial of Alexander technique lessons, exercise, and massage (ATEAM) for chronic and recurrent back pain. Br J Sports Med. 2008 Dec;42(12):965-8. PMID: 19096019.

235. Machado LAC, Maher CG, Herbert RD, et al. The effectiveness of the McKenzie method in addition to first-line care for acute low back pain: a randomized controlled trial. BMC Medicine. 2010;8:10. PMID: 20102596.

236. Pengel LHM, Refshauge KM, Maher CG, et al. Physiotherapist-directed exercise, advice, or both for subacute low back pain: a randomized trial.[Summary for patients in Ann Intern Med. 2007 Jun 5;146(11):I56; PMID: 17548406]. Annals of Internal Medicine. 2007 Jun 5;146(11):787-96. PMID: 17548410.

237. Henchoz Y, de Goumoens P, Norberg M, et al. Role of physical exercise in low back pain rehabilitation: a randomized controlled trial of a three-month exercise program in patients who have completed multidisciplinary rehabilitation. Spine. 2010 May 20;35(12):1192-9. PMID: 20098350.

238. Bi X, Zhao J, Zhao L, et al. Pelvic floor muscle exercise for chronic low back pain. Journal of International Medical Research. 2013 Feb;41(1):146-52. PMID: 23569140.

239. Bruce-Low S, Smith D, Burnet S, et al. One lumbar extension training session per week is sufficient for strength gains and reductions in pain in patients with chronic low back pain ergonomics. Ergonomics. 2012;55(4):500-7. PMID: 22397454.

240. Chan CW, Mok NW, Yeung EW. Aerobic exercise training in addition to conventional physiotherapy for chronic low back pain: a randomized controlled trial. Archives of Physical Medicine & Rehabilitation. 2011 Oct;92(10):1681-5. PMID: 21839983.

241. Jackson JK, Shepherd TR, Kell RT. The influence of periodized resistance training on recreationally active males with chronic nonspecific low back pain. Journal of Strength & Conditioning Research. 2011 Jan;25(1):242-51. PMID: 20093971.

242. Kell RT, Asmundson GJG. A comparison of two forms of periodized exercise rehabilitation programs in the management of chronic nonspecific low-back pain. Journal of Strength & Conditioning Research. 2009 Mar;23(2):513-23. PMID: 19209082.

243. Marshall P, Murphy B. Self-report measures best explain changes in disability compared with physical measures after exercise rehabilitation for chronic low back pain. Spine. 2008 Feb 1;33(3):326-38. PMID: 18303467.

244. Masharawi Y, Nadaf N. The effect of non-weight bearing group-exercising on females with non-specific chronic low back pain: a randomized single blind controlled pilot study. Journal of Back & Musculoskeletal Rehabilitation. 2013 Jan 1;26(4):353-9. PMID: 23948819.

245. McDonough SM, Tully MA, Boyd A, et al. Pedometer-driven walking for chronic low back pain: a feasibility randomized controlled trial. Clinical Journal of Pain. 2013 Nov;29(11):972-81. PMID: 23446066.

246. Mohseni-Bandpei MA, Rahmani N, Behtash H, et al. The effect of pelvic floor muscle exercise on women with chronic non-specific low back pain. Journal of Bodywork & Movement Therapies. 2011 Jan;15(1):75-81. PMID: 21147422.

247. Nassif H, Brosset N, Guillaume M, et al. Evaluation of a randomized controlled trial in the management of chronic lower back pain in a French automotive industry: an observational study. Archives of Physical Medicine & Rehabilitation. 2011 Dec;92(12):1927-36.e4. PMID: 22133239.

248. Norris C, Matthews M. The role of an integrated back stability program in patients with chronic low back pain. Complementary Therapies in Clinical Practice. 2008 Nov;14(4):255-63. PMID: 18940712.

249. Rhee HS, Kim YH, Sung PS. A randomized controlled trial to determine the effect of spinal stabilization exercise intervention based on pain level and standing balance differences in patients with low back pain. Medical Science Monitor. 2012 Mar;18(3):CR174-81. PMID: 22367128.

250. Schenkman ML, Jordan S, Akuthota V, et al. Functional movement training for recurrent low back pain: lessons from a pilot randomized controlled trial. Pm & R. 2009 Feb;1(2):137-46. PMID: 19627887.

251. Smith D, Bissell G, Bruce-Low S, et al. The effect of lumbar extension training with and without pelvic stabilization on lumbar strength and low back pain. Journal of Back & Musculoskeletal Rehabilitation. 2011;24(4):241-9. PMID: 22142713.

252. Steele J, Bruce-Low S, Smith D, et al. A randomized controlled trial of limited range of motion lumbar extension exercise in chronic low back pain. Spine. 2013 Jul 1;38(15):1245-52. PMID: 23514876.

253. Tsauo J-Y, Chen W-H, Liang H-W, et al. The effectiveness of a functional training programme for patients with chronic low back pain--a pilot study. Disability & Rehabilitation. 2009;31(13):1100-6. PMID: 19802926.

254. Bonetti F, Curti S, Mattioli S, et al. Effectiveness of a 'Global Postural Reeducation' program for persistent low back pain: a non-randomized controlled trial. BMC Musculoskeletal Disorders. 2010;11:285. PMID: 21162726.

255. Engbert K, Weber M. The effects of therapeutic climbing in patients with chronic low back pain: a randomized controlled study. Spine. 2011 May 15;36(11):842-9. PMID: 21192296.

256. Gatti R, Faccendini S, Tettamanti A, et al. Efficacy of trunk balance exercises for individuals with chronic low back pain: a randomized clinical trial. Journal of Orthopaedic & Sports Physical Therapy. 2011 Aug;41(8):542-52. PMID: 21654092.

257. George SZ, Wittmer VT, Fillingim RB, et al. Comparison of graded exercise and graded exposure clinical outcomes for patients with chronic low back pain. Journal of Orthopaedic & Sports Physical Therapy. 2010 Nov;40(11):694-704. PMID: 20972340.

258. Javadian Y, Behtash H, Akbari M, et al. The effects of stabilizing exercises on pain and disability of patients with lumbar segmental instability. Journal of Back & Musculoskeletal Rehabilitation. 2012;25(3):149-55. PMID: 22935853.

259. Sertpoyraz F, Eyigor S, Karapolat H, et al. Comparison of isokinetic exercise versus standard exercise training in patients with chronic low back pain: a randomized controlled study. Clinical Rehabilitation. 2009 Mar;23(3):238-47. PMID: 19218298.

260. Hayden JA, van Tulder MW, Tomlinson G. Systematic Review: Strategies for Using Exercise Therapy To Improve Outcomes in Chronic Low Back Pain. Annals of Internal Medicine. 2005;142(9):776-85. PMID: 15867410.

261. Hall AM, Maher CG, Lam P, et al. Tai chi exercise for treatment of pain and disability in people with persistent low back pain: a randomized controlled trial. Arthritis care & research. 2011 Nov;63(11):1576-83. PMID: 22034119.

262. Bystrom MG, Rasmussen-Barr E, Grooten WJA. Motor control exercises reduces pain and disability in chronic and recurrent low back pain: a meta-analysis. Spine. 2013 Mar 15;38(6):E350-8. PMID: 23492976.

263. Franca FR, Burke TN, Hanada ES, et al. Segmental stabilization and muscular strengthening in chronic low back pain: a comparative study. Clinics (Sao Paulo, Brazil). 2010;65(10):1013-7. PMID: 21120303.

264. Rasmussen-Barr E, Ang B, Arvidsson I, et al. Graded exercise for recurrent low-back pain: a randomized, controlled trial with 6-, 12-, and 36-month follow-ups. Spine. 2009 Feb 1;34(3):221-8. PMID: 19179916.

265. Unsgaard-Tondel M, Fladmark AM, Salvesen O, et al. Motor control exercises, sling exercises, and general exercises for patients with chronic low back pain: a randomized controlled trial with 1-year follow-up. Physical Therapy. 2010 Oct;90(10):1426-40. PMID: 20671099.

266. Akbari A, Khorashadizadeh S, Abdi G. The effect of motor control exercise versus general exercise on lumbar local stabilizing muscles thickness: Randomized controlled trial of patients with chronic low back pain. Journal of back and musculoskeletal rehabilitation. 2008;21(2):105-12. PMID: No PMID.

267. Critchley DJ, Ratcliffe J, Noonan S, et al. Effectiveness and cost-effectiveness of three types of physiotherapy used to reduce chronic low back pain disability: a pragmatic randomized trial with economic evaluation. Spine. 2007 Jun 15;32(14):1474-81. PMID: 17572614.

268. Miller ER, Schenk RJ, Karnes JL, et al. A comparison of the McKenzie approach to a specific spine stabilization program for chronic low back pain. Journal of Manual & Manipulative Therapy. 2005;13(2):103-12. PMID: No PMID.

269. Costa LOP, Maher CG, Latimer J, et al. Motor control exercise for chronic low back pain: a randomized placebo-controlled trial. Physical Therapy. 2009 Dec;89(12):1275-86. PMID: 19892856.

270. Shaughnessy M, Caulfield B. A pilot study to investigate the effect of lumbar stabilisation exercise training on functional ability and quality of life in patients with chronic low back pain. International Journal of Rehabilitation Research. 2004 Dec;27(4):297-301. PMID: 15572993.

271. Kumar S, Sharma VP, Shukla R, et al. Comparative efficacy of two multimodal treatments on male and female sub-groups with low back pain (part II). Journal of Back & Musculoskeletal Rehabilitation. 2010;23(1):1-9. PMID: 20231783.

272. O'Sullivan PB, Phyty GD, Twomey LT, et al. Evaluation of specific stabilizing exercise in the treatment of chronic low back pain with radiologic diagnosis of spondylolysis or spondylolisthesis. Spine (Phila Pa 1976). 1997 Dec 15;22(24):2959-67. PMID: 9431633.

273. Kumar S, Negi MPS, Sharma VP, et al. Efficacy of two multimodal treatments on physical strength of occupationally subgrouped male with low back pain. Journal of Back & Musculoskeletal Rehabilitation. 2009;22(3):179-88. PMID: 20023348.

274. Koumantakis GA, Watson PJ, Oldham JA. Trunk muscle stabilization training plus general exercise versus general exercise only: randomized controlled trial of patients with recurrent low back pain. Physical Therapy. 2005 Mar;85(3):209-25. PMID: 15733046.

275. Cairns MC, Foster NE, Wright C. Randomized controlled trial of specific spinal stabilization exercises and conventional physiotherapy for recurrent low back pain. Spine (Phila Pa 1976). 2006 Sep 1;31(19):E670-81. PMID: 16946640.

276. Macedo LG, Latimer J, Maher CG, et al. Effect of motor control exercises versus graded activity in patients with chronic nonspecific low back pain: a randomized controlled trial.[Erratum appears in Phys Ther. 2012 Apr;92(4):631]. Physical Therapy. 2012 Mar;92(3):363-77. PMID: 22135712.

277. Inani SB, Selkar SP. Effect of core stabilization exercises versus conventional exercises on pain and functional status in patients with non-specific low back pain: a randomized clinical trial. Journal of Back & Musculoskeletal Rehabilitation. 2013;26(1):37-43. PMID: 23411647.

278. Wells C, Kolt GS, Marshall P, et al. The effectiveness of pilates exercise in people with chronic low back pain: a systematic review. PLoS ONE [Electronic Resource]. 2014;9(7):e100402. PMID: 24984069.

279. Borges J, Baptista AF, Santana N, et al. Pilates exercises improve low back pain and quality of life in patients with HTLV-1 virus: a randomized crossover clinical trial. J Bodyw Mov Ther. 2014 Jan;18(1):68-74. PMID: 24411152.

280. da Fonseca JL, Magini M, de Freitas TH. Laboratory gait analysis in patients with low back pain before and after a pilates intervention. Journal of Sport Rehabilitation. 2009 May;18(2):269-82. PMID: 19561369.

281. MacIntyre L. The effect of Pilates on patients' chronic low back pain: A pilot study [dissertation]. . 2006PMID: No PMID.

282. Miyamoto GC, Costa LO, Galvanin T, et al. Efficacy of the addition of modified Pilates exercises to a minimal intervention in patients with chronic low back pain: a randomized controlled trial. Physical Therapy. 2013 Mar;93(3):310-20. PMID: 23064732.

283. Quinn K, Barry S, Barry L. Do patients with chronic low back pain benefit from attending Pilates classes after completing conventional physiotherapy treatment? Physiotherapy Practice and Research. 2011;32(1):5-12. PMID: No PMID.

284. Rydeard R. Evaluation of a targeted exercise rehabilitation approach and its effectiveness in the treatment of pain, functional disability and muscle function in a population with longstanding unresolved low back pain [dissertation]. [Dissertation]. Kingston, Canada: Queens University; 2001.

285. Gagnon L. Efficacy of pilates exercises as therapeutic intervention in treating patients with low back pain [dissertation] [dissertation]. Knoxville: University of Tennessee; 2005.

286. Marshall PWM, Kennedy S, Brooks C, et al. Pilates exercise or stationary cycling for chronic nonspecific low back pain: does it matter? a randomized controlled trial with 6-month follow-up. Spine. 2013 Jul 1;38(15):E952-9. PMID: 23615384.

287. Rajpal N, Arora M, Chauhan V The study on efficacy of Pilates and McKenzie exercise in postural low back pain – A rehabilitative protocol. Physiotherapy and Occupational Therapy Journal 2008;1:33-56. PMID: No PMID.

288. Wajswelner H, Metcalf B, Bennell K. Clinical pilates versus general exercise for chronic low back pain: randomized trial. Medicine & Science in Sports & Exercise. 2012 Jul;44(7):1197-205. PMID: 22246216.

289. Quinn F. Influence of Pilates-based mat exercise on chronic lower back pain [dissertation]. . 2005PMID: No PMID.

290. Zeada M. Effects of Pilates on low back pain and urine catecholamine. Ovidius University Annals, Series Physiotherapy Education and Sport. 2011(12):41-7. PMID: No PMID.

291. Weifen W, Muheremu A, Chaohui C, et al. Effectiveness of tai chi practice for non-specific chronic low back pain on retired athletes: A randomized controlled study. Journal of musculoskeletal pain. 2013;21(1):37-45. PMID: No PMID.

292. Cox H, Tilbrook H, Aplin J, et al. A randomised controlled trial of yoga for the treatment of chronic low back pain: results of a pilot study. Complementary Therapies in Clinical Practice. 2010 Nov;16(4):187-93. PMID: 20920800.

293. Pushpika Attanayake AM, Somarathna KIWK, Vyas GH, et al. Clinical evaluation of selected Yogic procedures in individuals with low back pain. Ayu. 2010 Apr;31(2):245-50. PMID: 22131719.

294. Saper RB, Sherman KJ, Cullum-Dugan D, et al. Yoga for chronic low back pain in a predominantly minority population: a pilot randomized controlled trial. Alternative Therapies in Health & Medicine. 2009 Nov-Dec;15(6):18-27. PMID: 19943573.

295. Sherman KJ, Cherkin DC, Wellman RD, et al. A randomized trial comparing yoga, stretching, and a self-care book for chronic low back pain. Archives of Internal Medicine. 2011 Dec 12;171(22):2019-26. PMID: 22025101.

296. Tilbrook HE, Cox H, Hewitt CE, et al. Yoga for chronic low back pain: a randomized trial. Annals of Internal Medicine. 2011 Nov 1;155(9):569-78. PMID: 22041945.

297. Williams K, Abildso C, Steinberg L, et al. Evaluation of the effectiveness and efficacy of Iyengar yoga therapy on chronic low back pain. Spine. 2009 Sep 1;34(19):2066-76. PMID: 19701112.

298. Nambi GS, Inbasekaran D, Khuman R, et al. Changes in pain intensity and health related quality of life with Iyengar yoga in nonspecific chronic low back pain: A randomized controlled study. International Journal of Yoga. 2014 Jan;7(1):48-53. PMID: 25035607.

299. Saper RB, Boah AR, Keosaian J, et al. Comparing Once- versus Twice-Weekly Yoga Classes for Chronic Low Back Pain in Predominantly Low Income Minorities: A Randomized Dosing Trial. Evidence-Based Complementary & Alternative Medicine: eCAM. 2013;2013:658030. PMID: 23878604.

300. Tekur P, Nagarathna R, Chametcha S, et al. A comprehensive yoga programs improves pain, anxiety and depression in chronic low back pain patients more than exercise: an RCT. Complementary Therapies in Medicine. 2012 Jun;20(3):107-18. PMID: 22500659.

301. Tekur P, Chametcha S, Hongasandra RN, et al. Effect of yoga on quality of life of clbp patients: A randomized control study. International journal of yoga. 2010;3(1):10-7. PMID: 20948896.

302. Cramer H, Lauche R, Haller H, et al. A systematic review and meta-analysis of yoga for low back pain. Clinical Journal of Pain. 2013 May;29(5):450-60. PMID: 23246998.

303. Hoffman BM, Papas RK, Chatkoff DK, et al. Meta-analysis of psychological interventions for chronic low back pain. Health Psychology. 2007 Jan;26(1):1-9. PMID: 17209691.

304. Ostelo RW, van Tulder MW, Vlaeyen JW, et al. Behavioural treatment for chronic low-back pain. Cochrane Database of Systematic Reviews. 2005(1):CD002014. PMID: 15674889.

305. Henschke N, Ostelo WJGR, van Tulder MW, et al. Behavioural treatment for chronic low-back pain. Cochrane Database of Systematic Reviews. 2011(2)PMID: No PMID.

306. Lamb SE, Hansen Z, Lall R, et al. Group cognitive behavioural treatment for low-back pain in primary care: a randomised controlled trial and cost-effectiveness analysis. Lancet. 2010 Mar 13;375(9718):916-23. PMID: 20189241.

307. Lamb SE, Mistry D, Lall R, et al. Group cognitive behavioural interventions for low back pain in primary care: extended follow-up of the Back Skills Training Trial (ISRCTN54717854). Pain. 2012 Feb;153(2):494-501. PMID: 22226729.

308. Morone NE, Greco CM, Weiner DK. Mindfulness meditation for the treatment of chronic low back pain in older adults: a randomized controlled pilot study. Pain. 2008 Feb;134(3):310-9. PMID: 17544212.

309. Morone NE, Rollman BL, Moore CG, et al. A mind-body program for older adults with chronic low back pain: results of a pilot study. Pain Medicine. 2009 Nov;10(8):1395-407. PMID: 20021599.

310. Siemonsma PC, Stuive I, Roorda LD, et al. Cognitive treatment of illness perceptions in patients with chronic low back pain: a randomized controlled trial. Physical Therapy. 2013 Apr;93(4):435-48. PMID: 23162040.

311. Vong SK, Cheing GL, Chan F, et al. Motivational enhancement therapy in addition to physical therapy improves motivational factors and treatment outcomes in people with low back pain: a randomized controlled trial. Archives of Physical Medicine & Rehabilitation. 2011 Feb;92(2):176-83. PMID: 21272712.

312. Stuckey SJ, Jacobs A, Goldfarb J. EMG biofeedback training, relaxation training, and placebo for the relief of chronic back pain. Perceptual & Motor Skills. 1986 Dec;63(3):1023-36. PMID: 2949196.

313. Turner JA. Comparison of group progressive-relaxation training and cognitive-behavioral group therapy for chronic low back pain. J Consult Clin Psychol. 1982 Oct;50(5):757-65. PMID: 6216275.

314. Turner JA, Jensen MP. Efficacy of cognitive therapy for chronic low back pain. Pain. 1993 Feb;52(2):169-77. PMID: 8455964.

315. Newton-John TR, Spence SH, Schotte D. Cognitive-behavioural therapy versus EMG biofeedback in the treatment of chronic low back pain. Behav Res Ther. 1995 Jul;33(6):691-7. PMID: 7654161.

316. Nouwen A. EMG biofeedback used to reduce standing levels of paraspinal muscle tension in chronic low back pain. Pain. 1983 Dec;17(4):353-60. PMID: 6229707.

317. Bush C, Ditto B, Feuerstein M. A controlled evaluation of paraspinal EMG biofeedback in the treatment of chronic low back pain. Health Psychology. 1985;4(4):307-21. PMID: 2932330.

318. Linton SJ, Bradley LA, Jensen I, et al. The secondary prevention of low back pain: a controlled study with follow-up. Pain. 1989 Feb;36(2):197-207. PMID: 2521930.

319. Turner JA, Clancy S. Comparison of operant behavioral and cognitive-behavioral group treatment for chronic low back pain. J Consult Clin Psychol. 1988 Apr;56(2):261-6. PMID: 2967314.

320. Linton SJ, Boersma K, Jansson M, et al. A randomized controlled trial of exposure in vivo for patients with spinal pain reporting fear of work-related activities. European Journal of Pain. 2008 Aug;12(6):722-30. PMID: 18155934.

321. Poole H, Glenn S, Murphy P. A randomised controlled study of reflexology for the management of chronic low back pain. European Journal of Pain. 2007 Nov;11(8):878-87. PMID: 17459741.

322. Von Korff M, Balderson BH, Saunders K, et al. A trial of an activating intervention for chronic back pain in primary care and physical therapy settings. Pain. 2005 Feb;113(3):323-30. PMID: 15661440.

323. Donaldson S, Romney D, Donaldson M, et al. Randomized study of the application of single motor unit biofeedback training to chronic low back pain. Journal of Occupational Rehabilitation. 1994 Mar;4(1):23-37. PMID: 24234261.

324. McCauley JD, Thelen MH, Frank RG, et al. Hypnosis compared to relaxation in the outpatient management of chronic low back pain. Archives of Physical Medicine & Rehabilitation. 1983 Nov;64(11):548-52. PMID: 6227304.

325. van der Roer N, van Tulder M, Barendse J, et al. Intensive group training protocol versus guideline physiotherapy for patients with chronic low back pain: a randomised controlled trial. European Spine Journal. 2008 Sep;17(9):1193-200. PMID: 18663487.

326. Friedrich M, Gittler G, Halberstadt Y, et al. Combined exercise and motivation program: effect on the compliance and level of disability of patients with chronic low back pain: a randomized controlled trial. Archives of Physical Medicine & Rehabilitation. 1998 May;79(5):475-87. PMID: 9596385.

327. Nicholas MK, Wilson PH, Goyen J. Operant-behavioural and cognitive-behavioural treatment for chronic low back pain. Behav Res Ther. 1991;29(3):225-38. PMID: 1831972.

328. Nicholas MK, Wilson PH, Goyen J. Comparison of cognitive-behavioral group treatment and an alternative non-psychological treatment for chronic low back pain. Pain. 1992 Mar;48(3):339-47. PMID: 1534400.

329. Strong J. Incorporating cognitive-behavioral therapy with occupational therapy: A comparative study with patients with low back pain. Journal of Occupational Rehabilitation. 1998;8(1):61-71. PMID: No PMID.

330. Altmaier EM, Lehmann TR, Russell DW, et al. The effectiveness of psychological interventions for the rehabilitation of low back pain: a randomized controlled trial evaluation. Pain. 1992 Jun;49(3):329-35. PMID: 1408299.

331. Schweikert B, Jacobi E, Seitz R, et al. Effectiveness and cost-effectiveness of adding a cognitive behavioral treatment to the rehabilitation of chronic low back pain. Journal of Rheumatology. 2006 Dec;33(12):2519-26. PMID: 17143986.

332. Johnson RE, Jones GT, Wiles NJ, et al. Active exercise, education, and cognitive behavioral therapy for persistent disabling low back pain: a randomized controlled trial. Spine. 2007 Jul 1;32(15):1578-85. PMID: 17621203.

333. Kole-Snijders AM, Vlaeyen JW, Goossens ME, et al. Chronic low-back pain: what does cognitive coping skills training add to operant behavioral treatment? Results of a randomized clinical trial. J Consult Clin Psychol. 1999 Dec;67(6):931-44. PMID: 10596514.

334. van den Hout JHC, Vlaeyen JWS, Heuts PHTG, et al. Secondary Prevention of Work-Related Disability in Nonspecific Low Back Pain: Does Problem-Solving Therapy Help? A Randomized Clinical Trial. Clinical Journal of Pain March/April. 2003;19(2):87-96. PMID: 12616178.

335. Rose MJ, Reilly JP, Pennie B, et al. Chronic low back pain rehabilitation programs: a study of the optimum duration of treatment and a comparison of group and individual therapy. Spine (Phila Pa 1976). 1997 Oct 1;22(19):2246-51; discussion 52-3. PMID: 9346145.

336. Leeuw M, Goossens MEJB, van Breukelen GJP, et al. Exposure in vivo versus operant graded activity in chronic low back pain patients: results of a randomized controlled trial. Pain. 2008 Aug 15;138(1):192-207. PMID: 18242858.

337. Guzman J, Esmail R, Karjalainen K, et al. Multidisciplinary bio-psycho-social rehabilitation for chronic low back pain. Cochrane Database of Systematic Reviews. 2002(1):CD000963. PMID: 11869581.

338. Guzman J, Esmail R, Karjalainen KA, et al. Multidisciplinary rehabilitation for chronic low-back pain: systematic review. BMJ. 2001;322PMID: 11420271.

339. Karjalainen KA, Malmivaara A, van Tulder MW, et al. Multidisciplinary biopsychosocial rehabilitation for subacute low-back pain among working age adults. Cochrane Database of Systematic Reviews. 2009(4)PMID: No PMID.

340. Tveito TH, Hysing M, Eriksen HR. Low back pain interventions at the workplace: a systematic literature review. Occup Med (Lond). 2004 Jan;54(1):3-13. PMID: 14963248.

341. Kamper SJ, Apeldoorn AT, Chiarotto A, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. Cochrane Database of Systematic Reviews. 2014;9:CD000963. PMID: 25180773.

342. Eisenberg DM, Buring JE, Hrbek AL, et al. A model of integrative care for low-back pain. Journal of Alternative & Complementary Medicine. 2012 Apr;18(4):354-62. PMID: 22455544.

343. Gatchel RJ, Polatin PB, Noe C, et al. Treatment- and cost-effectiveness of early intervention for acute low-back pain patients: a one-year prospective study. Journal of Occupational Rehabilitation. 2003 Mar;13(1):1-9. PMID: 12611026.

344. Skouen JS, Grasdal AL, Haldorsen EM, et al. Relative cost-effectiveness of extensive and light multidisciplinary treatment programs versus treatment as usual for patients with chronic low back pain on long-term sick leave: randomized controlled study. Spine (Phila Pa 1976). 2002 May 1;27(9):901-9; discussion 9-10. PMID: 11979157.

345. Morone G, Paolucci T, Alcuri MR, et al. Quality of life improved by multidisciplinary back school program in patients with chronic non-specific low back pain: a single blind randomized controlled trial. European journal of physical & rehabilitation medicine. 2011 Dec;47(4):533-41. PMID: 21508915.

346. Tavafian SS, Jamshidi AR, Montazeri A. A randomized study of back school in women with chronic low back pain: quality of life at three, six, and twelve months follow-up. Spine. 2008 Jul 1;33(15):1617-21. PMID: 18580739.

347. Kool J, Bachmann S, Oesch P, et al. Function-centered rehabilitation increases work days in patients with nonacute nonspecific low back pain: 1-year results from a randomized controlled trial. Archives of Physical Medicine & Rehabilitation. 2007 Sep;88(9):1089-94. PMID: 17826451.

348. Kaapa EH, Frantsi K, Sarna S, et al. Multidisciplinary group rehabilitation versus individual physiotherapy for chronic nonspecific low back pain: a randomized trial. Spine (Phila Pa 1976). 2006 Feb 15;31(4):371-6. PMID: 16481945.

349. Smeets RJ, Severens JL, Beelen S, et al. More is not always better: cost-effectiveness analysis of combined, single behavioral and single physical rehabilitation programs for chronic low back pain. European Journal of Pain. 2009 Jan;13(1):71-81. PMID: 18434221.

350. Smeets RJEM, Vlaeyen JWS, Hidding A, et al. Chronic low back pain: physical training, graded activity with problem solving training, or both? The one-year post-treatment results of a randomized controlled trial.[Reprint in Ned Tijdschr Geneeskd. 2009 Mar 21;153(12):543-9; PMID: 19368107]. Pain; 2008. p. 263-76.

351. Mangels M, Schwarz S, Worringen U, et al. Evaluation of a behavioral-medical inpatient rehabilitation treatment including booster sessions: a randomized controlled study. Clinical Journal of Pain. 2009 Jun;25(5):356-64. PMID: 19454868.

352. Lambeek LC, van Mechelen W, Knol DL, et al. Randomised controlled trial of integrated care to reduce disability from chronic low back pain in working and private life. BMJ. 2010;340:c1035. PMID: 20234040.

353. Cherkin DC, Sherman KJ, Deyo RA, et al. A review of the evidence for the effectiveness, safety, and cost of acupuncture, massage therapy, and spinal manipulation for back pain. Annals of Internal Medicine. 2003 Jun 3;138(11):898-906. PMID: 12779300.

354. Furlan AD, van Tulder MW, Cherkin DC, et al. Acupuncture and dry-needling for low back pain. Cochrane Database of Systematic Reviews. 2005(1):CD001351. PMID: 15674876.

355. Manheimer E, White A, Berman B, et al. Meta-analysis: acupuncture for low back pain. Ann Intern Med. 2005 April 19, 2005;142(8):651-63. PMID: 15838072.

356. Lee J-H, Choi T-Y, Lee MS, et al. Acupuncture for acute low back pain: a systematic review. Clinical Journal of Pain. 2013 Feb;29(2):172-85. PMID: 23269281.

357. Lam M, Galvin R, Curry P. Effectiveness of acupuncture for nonspecific chronic low back pain: a systematic review and meta-analysis. Spine. 2013 Nov 15;38(24):2124-38. PMID: 24026151.

358. Gao H, Wei C. Extrapoint acupuncture treatement of 36 cases of acute lumbar sprain [in Chinese]. J Gansu Coll Trad Cin Med. 2006;2006(23):49-50. PMID: No PMID.

359. Jin M, Chen J. Acupuncture treatment for 40 cases of acute lumbar sprain [in Chinese]. J Gansu Coll Trad Chin Med. 2008;2006(23):49-50. PMID: No PMID.

360. Lan J. Analysis of application of acupuncture analgesia in acute lumbar sprain [in Chinese]. J Community Med. 2009(7):68-9. PMID: No PMID.

361. Wu Y-c, Zhang B-m, Wang C-m, et al. [Observation on short-term and long-term therapeutic effects of electroacupuncture at Houxi (SI 3) on acute lumbar sprain]. Zhongguo Zhen Jiu. 2007 Jan;27(1):3-5. PMID: 17378192.

362. Zheng Z. Observations on the therapeutic effects of treating 90 cases of acute lumbar sprain by acupunctuing Xing Jian (LR2) [in Chinese]. J Community Med. 2005;1(7):68-9. PMID: No PMID.

363. Su J-t, Zhou Q-h, Li R, et al. [Immediate analgesic effect of wrist-ankle acupuncture for acute lumbago: a randomized controlled trial]. Zhongguo Zhenjiu. 2010 Aug;30(8):617-22. PMID: 20942274.

364. Liu J, Li N. Clinical observation of a combination of acupuncture and drug administration for non-specific acute lumbar sprain. J Acupunct Tuina Sci. 2010;8(1):47-9. PMID: No PMID.

365. Chen Y. Clinical observation of electroacupuncture at SI3 in addition to drug therapy in acute lumbar sprain [in Chinese]. J Community Med. 2010(8):39. PMID: No PMID.

366. Kennedy S, Baxter GD, Kerr DP, et al. Acupuncture for acute non-specific low back pain: a pilot randomised non-penetrating sham controlled trial. Complementary Therapies in Medicine. 2008 Jun;16(3):139-46. PMID: 18534326.

367. Araki S, Kawamura O, Mataka T. Randomized controlled trial comparing the effect of manual acupuncture with sham acupuncture for acute low back pain [in Japanese]. J Japan Soc Acupunct Moxibustion. 2001;2001(51):382. PMID: No PMID.

368. Wu D, Guo X. Is the sham acupuncture group a real sham control group? Comments on "Vas J et al. Acupuncture in patients with acute low back pain: a multicentre randomised controlled clinical trial [PAIN 2012;153(9):1883-9]". Pain. 2013 Nov;154(11):2575-6. PMID: 23962589.

369. Kittang G, Melvaer T, Baerheim A. [Acupuncture contra antiphlogistics in acute lumbago]. Tidsskrift for Den Norske Laegeforening. 2001 Apr 20;121(10):1207-10. PMID: 11402745.

370. Cherkin DC, Sherman KJ, Avins AL, et al. A randomized trial comparing acupuncture, simulated acupuncture, and usual care for chronic low back pain. Archives of Internal Medicine. 2009 May 11;169(9):858-66. PMID: 19433697.

371. Haake M, Muller H-H, Schade-Brittinger C, et al. German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups.[Erratum appears in Arch Intern Med. 2007 Oct 22;167(19):2072]. Archives of Internal Medicine. 2007 Sep 24;167(17):1892-8. PMID: 17893311.

372. Inoue M, Hojo T, Nakajima M, et al. Comparison of the effectiveness of acupuncture treatment and local anaesthetic injection for low back pain: a randomised controlled clinical trial. Acupuncture in Medicine. 2009 Dec;27(4):174-7. PMID: 19942724.

373. Itoh K, Itoh S, Katsumi Y, et al. A pilot study on using acupuncture and transcutaneous electrical nerve stimulation to treat chronic non-specific low back pain. Complementary Therapies in Clinical Practice. 2009 Feb;15(1):22-5. PMID: 19161950.

374. Shankar N, Thakur M, Tandon OP, et al. Autonomic status and pain profile in patients of chronic low back pain and following electro acupuncture therapy: a randomized control trial. Indian Journal of Physiology & Pharmacology. 2011 Jan-Mar;55(1):25-36. PMID: 22315807.

375. Yun M, Shao Y, Zhang Y, et al. Hegu acupuncture for chronic low-back pain: a randomized controlled trial. Journal of Alternative & Complementary Medicine. 2012 Feb;18(2):130-6. PMID: 22339101.

376. Witt CM, Manheimer E, Hammerschlag R, et al. How well do randomized trials inform decision making: systematic review using comparative effectiveness research measures on acupuncture for back pain. PLoS ONE [Electronic Resource]. 2012;7(2):e32399. PMID: 22389699.

377. Kerr DP, Walsh DM, Baxter D. Acupuncture in the management of chronic low back pain: a blinded randomized controlled trial. Clinical Journal of Pain. 2003 Nov-Dec;19(6):364-70. PMID: 14600536.

378. Thomas KJ, MacPherson H, Thorpe L, et al. Randomized controlled trial of a short course of traditional acupuncture compared with usual care for persistent non-specific low back pain. Journal of the Acupuncture Association of Chartered Physiotherapists. Issue. 2007;3:47-56. PMID: No PMID.

379. Carlsson CP, Sjolund BH. Acupuncture for chronic low back pain: a randomized placebo-controlled study with long-term follow-up. Clinical Journal of Pain. 2001 Dec;17(4):296-305. PMID: 11783809.

380. Itoh K, Katsumi Y, Hirota S, et al. Effects of trigger point acupuncture on chronic low back pain in elderly patients--a sham-controlled randomised trial. Acupuncture in Medicine. 2006 Mar;24(1):5-12. PMID: 16618043.

381. Hasegawa TM, Baptista AS, de Souza MC, et al. Acupuncture for acute non-specific low back pain: a randomised, controlled, double-blind, placebo trial. Acupuncture in Medicine. 2014 Apr;32(2):109-15. PMID: 24316509.

382. Vas J, Aranda JM, Modesto M, et al. Acupuncture in patients with acute low back pain: a multicentre randomised controlled clinical trial. Pain. 2012 Sep;153(9):1883-9. PMID: 22770838.

383. Cho Y-J, Song Y-K, Cha Y-Y, et al. Acupuncture for chronic low back pain: a multicenter, randomized, patient-assessor blind, sham-controlled clinical trial. Spine. 2013 Apr 1;38(7):549-57. PMID: 23026870.

384. Yun M, Xiong N, Guo M, et al. Acupuncture at the back-pain-acupoints for chronic low back pain of Peacekeepers in Lebanon: A randomized controlled trial. Journal of musculoskeletal pain. 2012;20(2):107-15. PMID: No PMID.

385. Weiss J, Quante S, Xue F, et al. Effectiveness and acceptance of acupuncture in patients with chronic low back pain: results of a prospective, randomized, controlled trial. Journal of Alternative & Complementary Medicine. 2013 Dec;19(12):935-41. PMID: 23738680.

386. Sator-Katzenschlager SM, Scharbert G, Kozek-Langenecker SA, et al. The short- and long-term benefit in chronic low back pain through adjuvant electrical versus manual auricular acupuncture. Anesthesia & Analgesia. 2004 May;98(5):1359-64, table of contents. PMID: 15105215.

387. Itoh K, Katsumi Y, Kitakoji H. Trigger point acupuncture treatment of chronic low back pain in elderly patients--a blinded RCT. Acupuncture in Medicine. 2004 Dec;22(4):170-7. PMID: 15628774.

388. Inoue M, Kitakoji H, Ishizaki N, et al. Relief of low back pain immediately after acupuncture treatment--a randomised, placebo controlled trial. Acupuncture in Medicine. 2006 Sep;24(3):103-8. PMID: 17013356.

389. Brinkhaus B, Witt CM, Jena S, et al. Acupuncture in patients with chronic low back pain: a randomized controlled trial. Archives of Internal Medicine. 2006 Feb 27;166(4):450-7. PMID: 16505266.

390. Leibing E, Leonhardt U, Koster G, et al. Acupuncture treatment of chronic low-back pain -- a randomized, blinded, placebo-controlled trial with 9-month follow-up. Pain. 2002 Mar;96(1-2):189-96. PMID: 11932074.

391. Coan RM, Wong G, Ku SL, et al. The acupuncture treatment of low back pain: a randomized controlled study. American Journal of Chinese Medicine. 1980 Spring-Summer;8(1-2):181-9. PMID: 6446852.

392. Zaringhalam J, Manaheji H, Rastqar A, et al. Reduction of chronic non-specific low back pain: a randomised controlled clinical trial on acupuncture and baclofen. Chinesische Medizin. 2010;5:15. PMID: 20416100.

393. Giles LG, Muller R. Chronic spinal pain: a randomized clinical trial comparing medication, acupuncture, and spinal manipulation. Spine (Phila Pa 1976). 2003 Jul 15;28(14):1490-502; discussion 502-3. PMID: 12865832.

394. Muller R, Giles LG. Long-term follow-up of a randomized clinical trial assessing the efficacy of medication, acupuncture, and spinal manipulation for chronic mechanical spinal pain syndromes. Journal of Manipulative & Physiological Therapeutics. 2005 Jan;28(1):3-11. PMID: 15726029.

395. Cherkin DC, Eisenberg D, Sherman KJ, et al. Randomized trial comparing traditional Chinese medical acupuncture, therapeutic massage, and self-care education for chronic low back pain. Archives of Internal Medicine. 2001 Apr 23;161(8):1081-8. PMID: 11322842.

396. Furlan AD, Brosseau L, Imamura M, et al. Massage for low-back pain: a systematic review within the framework of the Cochrane Collaboration Back Review Group. Spine (Phila Pa 1976). 2002 Sep 1;27(17):1896-910. PMID: 12221356.

397. Furlan AD, Imamura M, Dryden T, et al. Massage for low-back pain. Cochrane Database of Systematic Reviews. 2010(6)PMID: No PMID.

398. Cherkin DC, Sherman KJ, Kahn J, et al. A comparison of the effects of 2 types of massage and usual care on chronic low back pain: a randomized, controlled trial.[Summary for patients in Ann Intern Med. 2011 Jul 5;155(1):I28; PMID: 21727286]. Annals of Internal Medicine. 2011 Jul 5;155(1):1-9. PMID: 21727288.

399. Kong LJ, Fang M, Zhan HS, et al. Chinese massage combined with herbal ointment for athletes with nonspecific low back pain: a randomized controlled trial. Evidence-Based Complementary & Alternative Medicine: eCAM. 2012;2012:695726. PMID: 23258996.

400. Sritoomma N, Moyle W, Cooke M, et al. The effectiveness of Swedish massage with aromatic ginger oil in treating chronic low back pain in older adults: a randomized controlled trial. Complementary Therapies in Medicine. 2014 Feb;22(1):26-33. PMID: 24559813.

401. Romanowski M, Romanowska J, Grzeskowiak M. A comparison of the effects of deep tissue massage and therapeutic massage on chronic low back pain. Studies in Health Technology & Informatics. 2012;176:411-4. PMID: 22744541.

402. Preyde M. Effectiveness of massage therapy for subacute low-back pain: a randomized controlled trial. CMAJ. 2000 Jun 27;162(13):1815-20. PMID: 10906914.

403. Farasyn A, Meeusen R, Nijs J. A pilot randomized placebo-controlled trial of roptrotherapy in patients with subacute non-specific low back pain. Journal of back and musculoskeletal rehabilitation. 2006;19(4):111-7. PMID: No PMID.

404. Mackawan S, Eungpinichpong W, Pantumethakul R, et al. Effets of traditional Thai massage versus joint mobilization on substance P and pain perception in patients with non-specific low back pain. Journal of Bodywork and Movement Therapies. 2007;11(1):9-16. PMID: No PMID.

405. Hernandez-Reif M, Field T, Krasnegor J, et al. Lower back pain is reduced and range of motion increased after massage therapy. Int J Neurosci. 2001;106(3-4):131-45. PMID: 11264915.

406. Field T, Hernandez-Reif M, Diego M, et al. Lower back pain and sleep disturbance are reduced following massage therapy. Journal of bodywork and movement therapies. 2007;11(2):141-5. PMID: No PMID.

407. Hsieh LL, Kuo CH, Lee LH, et al. Treatment of low back pain by acupressure and physical therapy: randomised controlled trial. BMJ. 2006 Mar 25;332(7543):696-700. PMID: 16488895.

408. Hsieh LL, Kuo CH, Yen MF, et al. A randomized controlled clinical trial for low back pain treated by acupressure and physical therapy. Prev Med. 2004 Jul;39(1):168-76. PMID: 15207999.

409. Franke A, Gebauer S, Franke K, et al. [Acupuncture massage vs Swedish massage and individual exercise vs group exercise in low back pain sufferers--a randomized controlled clinical trial in a 2 x 2 factorial design]. Forsch Komplementarmed Klass Naturheilkd. 2000 Dec;7(6):286-93. PMID: 11155022.

410. Geisser ME, Wiggert EA, Haig AJ, et al. A randomized, controlled trial of manual therapy and specific adjuvant exercise for chronic low back pain. Clinical Journal of Pain. 2005 Nov-Dec;21(6):463-70. PMID: 16215330.

411. Yip YB, Tse SH. The effectiveness of relaxation acupoint stimulation and acupressure with aromatic lavender essential oil for non-specific low back pain in Hong Kong: a randomised controlled trial. Complementary Therapies in Medicine. 2004 Mar;12(1):28-37. PMID: 15130569.

412. Chatchawan U, Thinkhamrop B, Kharmwan S, et al. Effectiveness of traditional Thai massage versus Swedish massage among patients with back pain associated with myofascial trigger points. Journal of Bodywork and Movement Therapies. 2005;9(4):298-309. PMID: No PMID.

413. Assendelft WJ, Morton SC, Yu EI, et al. Spinal manipulative therapy for low back pain. A meta-analysis of effectiveness relative to other therapies. Annals of Internal Medicine. 2003 Jun 3;138(11):871-81. PMID: 12779297.

414. Assendelft WJJ, Morton SC, Yu EI, et al. Spinal manipulative therapy for low-back pain Cochrane Database of Systematic Reviews. 2004(1)PMID: 14973958.

415. Avery S, O'Driscoll M-L. Randomised Controlled Trials on the Efficacy Of Spinal Manipulation Therapy in The Treatment of Low Back Pain. Physical Therapy Reviews. 2004;9(3):146-52. PMID: 15179309.

416. Bronfort G, Haas M, Evans RL, et al. Efficacy of spinal manipulation and mobilization for low back pain and neck pain: a systematic review and best evidence synthesis. Spine Journal: Official Journal of the North American Spine Society. 2004 May-Jun;4(3):335-56. PMID: 15125860.

417. Brown A, Angus A, Chen S, et al. Costs and outcomes of chiropractic treatment for low back pain. Ottowa, Canada: July 2005 2005.

418. Ernst E, Canter PH. Chiropractic Spinal Manipulation Treatment for Back Pain? A Systematic Review of Randomised Clinical Trials. Physical Therapy Reviews. 2003;8(2):85. PMID: 11029157.

419. Ferreira ML, Ferreira PH, Latimer J, et al. Does spinal manipulative therapy help people with chronic low back pain? Australian Journal of Physiotherapy. 2002;48(4):277-84. PMID: 12443522.

420. Ferreira ML, Ferreira PH, Latimer J, et al. Efficacy of spinal manipulative therapy for low back pain of less than three months' duration. Journal of Manipulative & Physiological Therapeutics. 2003 Nov-Dec;26(9):593-601. PMID: 14673408.

421. Gay RE, Bronfort G, Evans RL. Distraction manipulation of the lumbar spine: a review of the literature. Journal of Manipulative & Physiological Therapeutics. 2005 May;28(4):266-73. PMID: 15883580.

422. Licciardone JC, Brimhall AK, King LN. Osteopathic manipulative treatment for low back pain: a systematic review and meta-analysis of randomized controlled trials. BMC Musculoskeletal Disorders. 2005;6:43. PMID: 16080794.

423. Vroomen PC, de Krom MC, Slofstra PD, et al. Conservative treatment of sciatica: a systematic review. J Spinal Disord. 2000 Dec;13(6):463-9. PMID: 11132976.

424. Woodhead T, Clough A. A systematic review of the evidence for manipulation in the treatment of low back pain. Journal of Orthopaedic Medicine. 2005;27:99-120. PMID: No PMID.

425. Rubinstein SM, Terwee CB, Assendelft WJJ, et al. Spinal manipulative therapy for acute low-back pain. Cochrane Database of Systematic Reviews. 2012;9:CD008880. PMID: 22972127.

426. Rubinstein SM, van Middelkoop M, Assendelft WJ, et al. Spinal manipulative therapy for chronic low-back pain. Cochrane Database of Systematic Reviews. 2011(2):CD008112. PMID: 21328304.

427. Brennan GP, Fritz JM, Hunter SJ, et al. Identifying subgroups of patients with acute/subacute "nonspecific" low back pain: results of a randomized clinical trial. Spine (Phila Pa 1976). 2006 Mar 15;31(6):623-31. PMID: 16540864.

428. Childs JD, Fritz JM, Flynn TW, et al. A clinical prediction rule to identify patients with low back pain most likely to benefit from spinal manipulation: a validation study. Annals of Internal Medicine. 2004 Dec 21;141(12):920-8. PMID: 15611489.

429. Cleland JA, Fritz JM, Kulig K, et al. Comparison of the effectiveness of three manual physical therapy techniques in a subgroup of patients with low back pain who satisfy a clinical prediction rule: a randomized clinical trial. Spine. 2009 Dec 1;34(25):2720-9. PMID: 19940729.

430. Hallegraeff JM, de Greef M, Winters JC, et al. Manipulative therapy and clinical prediction criteria in treatment of acute nonspecific low back pain.[Erratum appears in Percept Mot Skills. 2009 Jun;108(3):981 Note: Hallegraeff, H J M [corrected to Hallegraeff, J M]]. Perceptual & Motor Skills. 2009 Feb;108(1):196-208. PMID: 19425461.

431. Hancock MJ, Maher CG, Latimer J, et al. Assessment of diclofenac or spinal manipulative therapy, or both, in addition to recommended first-line treatment for acute low back pain: a randomised controlled trial. Lancet. 2007 Nov 10;370(9599):1638-43. PMID: 17993364.

432. Hoiriis KT, Pfleger B, McDuffie FC, et al. A randomized clinical trial comparing chiropractic adjustments to muscle relaxants for subacute low back pain. Journal of Manipulative & Physiological Therapeutics. 2004 Jul-Aug;27(6):388-98. PMID: 15319761.

433. Juni P, Battaglia M, Nuesch E, et al. A randomised controlled trial of spinal manipulative therapy in acute low back pain. Annals of the Rheumatic Diseases. 2009 Sep;68(9):1420-7. PMID: 18775942.

434. Sutlive TG, Mabry LM, Easterling EJ, et al. Comparison of short-term response to two spinal manipulation techniques for patients with low back pain in a military beneficiary population. Military Medicine. 2009 Jul;174(7):750-6. PMID: 19685848.

435. Cramer GD, Humphreys CR, Hondras MA, et al. The Hmax/Mmax ratio as an outcome measure for acute low back pain. Journal of Manipulative & Physiological Therapeutics. 1993 Jan;16(1):7-13. PMID: 8423429.

436. Farrell JP, Twomey LT. Acute low back pain. Comparison of two conservative treatment approaches. Med J Aust. 1982 Feb 20;1(4):160-4. PMID: 6210835.

437. Hadler NM, Curtis P, Gillings DB, et al. A benefit of spinal manipulation as adjunctive therapy for acute low-back pain: a stratified controlled trial. Spine (Phila Pa 1976). 1987 Sep;12(7):702-6. PMID: 2961085.

438. Rasmussen G. Manipulation in treatment of low back pain: a randomized clinical trial. Man Med. 1979;1:8-10. PMID: No PMID.

439. Seferlis T, Nemeth G, Carlsson AM, et al. Conservative treatment in patients sick-listed for acute low-back pain: a prospective randomised study with 12 months' follow-up. European Spine Journal. 1998;7(6):461-70. PMID: 9883955.

440. Bergquist-Ullman M, Larsson U. Acute low back pain in industry. A controlled prospective study with special reference to therapy and confounding factors. Acta Orthop Scand. 1977(170):1-117. PMID: 146394.

441. Cherkin DC, Deyo RA, Battie M, et al. A comparison of physical therapy, chiropractic manipulation, and provision of an educational booklet for the treatment of patients with low back pain. New England Journal of Medicine. 1998 Oct 8;339(15):1021-9. PMID: 9761803.

442. Hoehler FK, Tobis JS, Buerger AA. Spinal manipulation for low back pain. JAMA. 1981 May 8;245(18):1835-8. PMID: 6453240.

443. MacDonald RS, Bell CM. An open controlled assessment of osteopathic manipulation in nonspecific low-back pain. Spine (Phila Pa 1976). 1990 May;15(5):364-70. PMID: 2141951.

444. Postacchini F, Facchini M, Palieri P. Efficacy of various forms of conservative treatment in low back pain. A comparative study. Neuro-Orthopedics. 1988;6(1):28-35. PMID: No PMID.

445. Skargren EI, Oberg BE, Carlsson PG, et al. Cost and effectiveness analysis of chiropractic and physiotherapy treatment for low back and neck pain. Six-month follow-up. Spine (Phila Pa 1976). 1997 Sep 15;22(18):2167-77. PMID: 9322328.

446. Chown M, Whittamore L, Rush M, et al. A prospective study of patients with chronic back pain randomised to group exercise, physiotherapy or osteopathy. Physiotherapy. 2008;94(1):21-8. PMID: No PMID.

447. Ghroubi S, Elleuch H, Baklouti S, et al. [Chronic low back pain and vertebral manipulation]. Annales de Readaptation et de Medecine Physique. 2007 Oct;50(7):570-6. PMID: 17382426.

448. Gudavalli MR, Cambron JA, McGregor M, et al. A randomized clinical trial and subgroup analysis to compare flexion-distraction with active exercise for chronic low back pain. European Spine Journal. 2006 Jul;15(7):1070-82. PMID: 16341712.

449. Hondras MA, Long CR, Cao Y, et al. A randomized controlled trial comparing 2 types of spinal manipulation and minimal conservative medical care for adults 55 years and older with subacute or chronic low back pain. Journal of Manipulative & Physiological Therapeutics. 2009 Jun;32(5):330-43. PMID: 19539115.

450. Hsieh CY, Adams AH, Tobis J, et al. Effectiveness of four conservative treatments for subacute low back pain: a randomized clinical trial. Spine (Phila Pa 1976). 2002 Jun 1;27(11):1142-8. PMID: 12045509.

451. Hurwitz EL, Morgenstern H, Harber P, et al. A randomized trial of medical care with and without physical therapy and chiropractic care with and without physical modalities for patients with low back pain: 6-month follow-up outcomes from the UCLA low back pain study. Spine (Phila Pa 1976). 2002 Oct 15;27(20):2193-204. PMID: 12394892.

452. Licciardone JC, Stoll ST, Fulda KG, et al. Osteopathic manipulative treatment for chronic low back pain: a randomized controlled trial. Spine (Phila Pa 1976). 2003 Jul 1;28(13):1355-62. PMID: 12838090.

453. Mohseni-Bandpei MA, Critchley J, Staunton T, et al. A prospective randomised controlled trial of spinal manipulation and ultrasound in the treatment of chronic low back pain. Physiotherapy. 2006;92(1):34-42. PMID: No PMID.

454. Paatelma M, Kilpikoski S, Simonen R, et al. Orthopaedic manual therapy, McKenzie method or advice only for low back pain in working adults: a randomized controlled trial with one year follow-up. Journal of Rehabilitation Medicine. 2008 Nov;40(10):858-63. PMID: 19242624.

455. Rasmussen J, Laetgaard J, Lindecrona A-L, et al. Manipulation does not add to the effect of extension exercises in chronic low-back pain (LBP). A randomized, controlled, double blind study. Joint, Bone, Spine: Revue du Rhumatisme. 2008 Dec;75(6):708-13. PMID: 19028434.

456. Rasmussen-Barr E, Nilsson-Wikmar L, Arvidsson I. Stabilizing training compared with manual treatment in sub-acute and chronic low-back pain. Man Ther. 2003 Nov;8(4):233-41. PMID: 14559046.

457. Skillgate E, Vingard E, Alfredsson L. Naprapathic manual therapy or evidence-based care for back and neck pain: a randomized, controlled trial. Clinical Journal of Pain. 2007 Jun;23(5):431-9. PMID: 17515742.

458. Wilkey A, Gregory M, Byfield D, et al. A comparison between chiropractic management and pain clinic management for chronic low-back pain in a national health service outpatient clinic. Journal of Alternative & Complementary Medicine. 2008 Jun;14(5):465-73. PMID: 18564952.

459. Zaproudina N, Hietikko T, Hanninen OOP, et al. Effectiveness of traditional bone setting in treating chronic low back pain: a randomised pilot trial. Complementary Therapies in Medicine. 2009 Jan;17(1):23-8. PMID: 19114225.

460. Bronfort G, Goldsmith CH, Nelson CF, et al. Trunk exercise combined with spinal manipulative or NSAID therapy for chronic low back pain: a randomized, observer-blinded clinical trial. Journal of Manipulative & Physiological Therapeutics. 1996 Nov-Dec;19(9):570-82. PMID: 8976475.

461. Hemmila HM, Keinanen-Kiukaanniemi SM, Levoska S, et al. Long-term effectiveness of bone-setting, light exercise therapy, and physiotherapy for prolonged back pain: a randomized controlled trial. Journal of Manipulative & Physiological Therapeutics. 2002 Feb;25(2):99-104. PMID: 11896377.

462. Koes BW, Bouter LM, van Mameren H, et al. Randomised clinical trial of manipulative therapy and physiotherapy for persistent back and neck complaints: results of one year follow up. BMJ. 1992 Mar 7;304(6827):601-5. PMID: 1532760.

463. Gibson T, Grahame R, Harkness J, et al. Controlled comparison of short-wave diathermy treatment with osteopathic treatment in non-specific low back pain. Lancet. 1985 Jun 1;1(8440):1258-61. PMID: 2860453.

464. Balthazard P, de Goumoens P, Rivier G, et al. Manual therapy followed by specific active exercises versus a placebo followed by specific active exercises on the improvement of functional disability in patients with chronic non specific low back pain: a randomized controlled trial. BMC Musculoskeletal Disorders. 2012;13:162. PMID: 22925609.

465. Bicalho E, Setti JAP, Macagnan J, et al. Immediate effects of a high-velocity spine manipulation in paraspinal muscles activity of nonspecific chronic low-back pain subjects. Manual Therapy. 2010 Oct;15(5):469-75. PMID: 20447857.

466. Cecchi F, Molino-Lova R, Chiti M, et al. Spinal manipulation compared with back school and with individually delivered physiotherapy for the treatment of chronic low back pain: a randomized trial with one-year follow-up. Clinical Rehabilitation. 2010 Jan;24(1):26-36. PMID: 20053720.

467. de Oliveira RF, Liebano RE, Costa LdCM, et al. Immediate effects of region-specific and non-region-specific spinal manipulative therapy in patients with chronic low back pain: a randomized controlled trial. Physical Therapy. 2013 Jun;93(6):748-56. PMID: 23431209.

468. Goertz CM, Long CR, Hondras MA, et al. Adding chiropractic manipulative therapy to standard medical care for patients with acute low back pain: results of a pragmatic randomized comparative effectiveness study. Spine. 2013 Apr 15;38(8):627-34. PMID: 23060056.

469. Haas M, Vavrek D, Peterson D, et al. Dose-response and efficacy of spinal manipulation for care of chronic low back pain: a randomized controlled trial. Spine Journal: Official Journal of the North American Spine Society. 2014 Jul 1;14(7):1106-16. PMID: 24139233.

470. Petersen T, Larsen K, Nordsteen J, et al. The McKenzie method compared with manipulation when used adjunctive to information and advice in low back pain patients presenting with centralization or peripheralization: a randomized controlled trial. Spine. 2011 Nov 15;36(24):1999-2010. PMID: 21358492.

471. Senna MK, Machaly SA. Does maintained spinal manipulation therapy for chronic nonspecific low back pain result in better long-term outcome? Spine. 2011 Aug 15;36(18):1427-37. PMID: 21245790.

472. von Heymann WJ, Schloemer P, Timm J, et al. Spinal high-velocity low amplitude manipulation in acute nonspecific low back pain: a double-blinded randomized controlled trial in comparison with diclofenac and placebo. Spine. 2013 Apr 1;38(7):540-8. PMID: 23026869.

473. Bronfort G, Evans RL, Maiers M, et al. Spinal manipulation, epidural injections, and self-care for sciatica: a pilot study for a randomized clinical trial. Journal of Manipulative & Physiological Therapeutics. 2004 Oct;27(8):503-8. PMID: 15510093.

474. Burton AK, Tillotson KM, Cleary J. Single-blind randomised controlled trial of chemonucleolysis and manipulation in the treatment of symptomatic lumbar disc herniation. European Spine Journal. 2000 Jun;9(3):202-7. PMID: 10905437.

475. Santilli V, Beghi E, Finucci S. Chiropractic manipulation in the treatment of acute back pain and sciatica with disc protrusion: a randomized double-blind clinical trial of active and simulated spinal manipulations. Spine Journal: Official Journal of the North American Spine Society. 2006 Mar-Apr;6(2):131-7. PMID: 16517383.

476. Waagen GN, Haldeman S, Cook G, et al. Short term trial of chiropractic adjustments for the relief of chronic low back pain. Manual Med. 1986(2):63-7. PMID: No PMID.

477. Glover JR, Morris JG, Khosla T. Back pain: a randomized clinical trial of rotational manipulation of the trunk. Br J Ind Med. 1974 Jan;31(1):59-64. PMID: 4274488.

478. Pope MH, Phillips RB, Haugh LD, et al. A prospective randomized three-week trial of spinal manipulation, transcutaneous muscle stimulation, massage and corset in the treatment of subacute low back pain. Spine (Phila Pa 1976). 1994 Nov 15;19(22):2571-7. PMID: 7855683.

479. Evans DP, Burke MS, Lloyd KN, et al. Lumbar spinal manipulation on trial. Part I--clinical assessment. Rheumatol Rehabil. 1978 Feb;17(1):46-53. PMID: 153574.

480. Ansari NN, Ebadi S, Talebian S, et al. A randomized, single blind placebo controlled clinical trial on the effect of continuous ultrasound on low back pain. Electromyography & Clinical Neurophysiology. 2006 Nov;46(6):329-36. PMID: 17147074.

481. Nwuga VC. Ultrasound in treatment of back pain resulting from prolapsed intervertebral disc. Archives of Physical Medicine & Rehabilitation. 1983 Feb;64(2):88-9. PMID: 6218793.

482. Roman MP. A clinical evaluation of ultrasound by use of a placebo technic. Phys Ther Rev. 1960 Sep;40:649-52. PMID: 13742988.

483. Ebadi S, Henschke N, Nakhostin Ansari N, et al. Therapeutic ultrasound for chronic low-back pain. Cochrane Database of Systematic Reviews. 2014;3:CD009169. PMID: 24627326.

484. Durmuş D, Akyol Y, Cengiz K, et al. Effects of therapeutic ultrasound on pain, disability, walking performance, quality of life, and depression in patients with chronic low back pain: A randomized, placebo controlled trial. Turkish Journal of Rheumatology. 2010;25(2):82-7. PMID: No PMID.

485. Durmus D, Durmaz Y, Canturk F. Effects of therapeutic ultrasound and electrical stimulation program on pain, trunk muscle strength, disability, walking performance, quality of life, and depression in patients with low back pain: a randomized-controlled trial. Rheumatology International. 2010 May;30(7):901-10. PMID: 19644691.

486. Durmus D, Alayli G, Goktepe AS, et al. Is phonophoresis effective in the treatment of chronic low back pain? A single-blind randomized controlled trial. Rheumatology International. 2013 Jul;33(7):1737-44. PMID: 23283539.

487. Ebadi S, Ansari NN, Naghdi S, et al. The effect of continuous ultrasound on chronic non-specific low back pain: a single blind placebo-controlled randomized trial. BMC Musculoskeletal Disorders. 2012;13:192. PMID: 23031570.

488. Grubisic F, Grazio S, Jajic Z, et al. [Therapeutic ultrasound in chronic low back pain treatment]. Reumatizam. 2006;53(1):18-21. PMID: 17580544.

489. Licciardone JC, Minotti DE, Gatchel RJ, et al. Osteopathic manual treatment and ultrasound therapy for chronic low back pain: a randomized controlled trial. Annals of Family Medicine. 2013 Mar-Apr;11(2):122-9. PMID: 23508598.

490. Unlu Z, Tasci S, Tarhan S, et al. Comparison of 3 physical therapy modalities for acute pain in lumbar disc herniation measured by clinical evaluation and magnetic resonance imaging. Journal of Manipulative & Physiological Therapeutics. 2008 Mar;31(3):191-8. PMID: 18394495.

491. Khadilkar A, Milne A, Brosseau L, et al. Transcutaneous electrical nerve stimulation (TENS) for chronic low-back pain Cochrane Database of Systematic Reviews. 2005(3):Art. No.: CD003008. PMID: 16034883.

492. Deyo RA, Walsh NE, Martin DC, et al. A controlled trial of transcutaneous electrical nerve stimulation (TENS) and exercise for chronic low back pain. New England Journal of Medicine. 1990 List 4/20/05;322:1627-34. PMID: 2140432.

493. Cheing GL, Hui-Chan CW. Transcutaneous electrical nerve stimulation: nonparallel antinociceptive effects on chronic clinical pain and acute experimental pain. Archives of Physical Medicine & Rehabilitation. 1999;80(3):305-12. PMID: 10084439.

494. Furlan AD, Brosseau L, Imamura M, et al. Massage for low-back pain Cochrane Database of Systematic Reviews. 2002 (2):Art. No.: CD001929. PMID: 12076429.

495. French S, Cameron M, Walker B, et al. Superficial heat or cold for low back pain. Cochrane Database of Systematic Reviews. 2006(1):Art. No.: CD004750. PMID: No PMID.

496. van Middelkoop M, Rubinstein SM, Kuijpers T, et al. A systematic review on the effectiveness of physical and rehabilitation interventions for chronic non-specific low back pain. European Spine Journal; 2011. p. 19-39.

497. Ghoname EA, Craig WF, White PF, et al. Percutaneous electrical nerve stimulation for low back pain: a randomized crossover study. JAMA. 1999 Mar 3;281(9):818-23. PMID: 10071003.

498. Jarzem PF, Harvey EJ, Arcaro N, et al. Transcutaneous electrical nerve stimulation [TENS] for chronic low back pain. Journal of musculoskeletal pain. 2005;13(2):3-9. PMID: No PMID.

499. Jarzem PF, Harvey EJ, Arcaro N, et al. Transcutaneous electrical nerve stimulation [TENS] for short-term treatment of low back pain - Randomized double blind crossover study of sham versus conventional TENS. Journal of musculoskeletal pain. 2005;13(2):11-7. PMID: No PMID.

500. Topuz O, Ozfidan E, Ozgen M, et al. Efficacy of transcutaneous electrical nerve stimulation and percutaneous neuromodulation therapy in chronic low back pain. Journal of Back and Musculoskeletal Rehabilitation. 2004;17(3-4):127-33. PMID: No PMID.

501. Buchmuller A, Navez M, Milletre-Bernardin M, et al. Value of TENS for relief of chronic low back pain with or without radicular pain. European Journal of Pain. 2012 May;16(5):656-65. PMID: 22337531.

502. Shimoji K, Takahashi N, Nishio Y, et al. Pain relief by transcutaneous electric nerve stimulation with bidirectional modulated sine waves in patients with chronic back pain: a randomized, double-blind, sham-controlled study. Neuromodulation. 2007 Jan;10(1):42-51. PMID: 22151811.

503. Facci LM, Nowotny JP, Tormem F, et al. Effects of transcutaneous electrical nerve stimulation (TENS) and interferential currents (IFC) in patients with nonspecific chronic low back pain: randomized clinical trial. Sao Paulo Medical Journal = Revista Paulista de Medicina. 2011;129(4):206-16. PMID: 21971895.

504. Tsukayama H, Yamashita H, Amagai H, et al. Randomised controlled trial comparing the effectiveness of electroacupuncture and TENS for low back pain: a preliminary study for a pragmatic trial. Acupuncture in Medicine. 2002 20(4):175-80. PMID: 12512791.

505. Melzack R, Jeans ME, Stratford JG, et al. Ice massage and transcutaneous electrical stimulation: comparison of treatment for low-back pain. Pain. 1980 Oct;9(2):209-17. PMID: 6450393.

506. Sherry E, Kitchener P, Smart R. A prospective randomized controlled study of VAX-D and TENS for the treatment of chronic low back pain. Neurol Res. 2001;23(7):780-4. PMID: 11680522.

507. Melzack R, Vetere P, Finch M. Transcutaneous electrical nerve stimulation for low back pain. A comparison of TENS and massage for pain and range of motion. Phys Ther. 1983;63:489-93. PMID: 6220415.

508. Durmus D, Akyol Y, Alayli G, et al. Effects of electrical stimulation program on trunk muscle strength, functional capacity, quality of life, and depression in the patients with low back pain: a randomized controlled trial. Rheumatology International. 2009 Jun;29(8):947-54. PMID: 19099308.

509. Glaser JA, Baltz MA, Nietert PJ, et al. Electrical muscle stimulation as an adjunct to exercise therapy in the treatment of nonacute low back pain: a randomized trial. Journal of Pain. 2001 Oct;2(5):295-300. PMID: 14622808.

510. Moore SR, Shurman J. Combined neuromuscular electrical stimulation and transcutaneous electrical nerve stimulation for treatment of chronic back pain: a double-blind, repeated measures comparison. Archives of Physical Medicine & Rehabilitation. 1997 Jan;78(1):55-60. PMID: 9014958.

511. Ghoname EA, White PF, Ahmed HE, et al. Percutaneous electrical nerve stimulation: an alternative to TENS in the management of sciatica. Pain. 1999 Nov;83(2):193-9. PMID: 10534590.

512. Weiner DK, Rudy TE, Glick RM, et al. Efficacy of percutaneous electrical nerve stimulation for the treatment of chronic low back pain in older adults. J Am Geriatr Soc. 2003 May;51(5):599-608. PMID: 12752833.

513. Yokoyama M, Sun X, Oku S, et al. Comparison of percutaneous electrical nerve stimulation with transcutaneous electrical nerve stimulation for long-term pain relief in patients with chronic low back pain. Anesthesia & Analgesia. 2004 Jun;98(6):1552-6, table of contents. PMID: 15155304.

514. Perez-Palomares S, Olivan-Blazquez B, Magallon-Botaya R, et al. Percutaneous electrical nerve stimulation versus dry needling: effectiveness in the treatment of chronic low back pain. Journal of musculoskeletal pain. 2010;18(1):23-30. PMID: No PMID.

515. Hamza MA, Ghoname EA, White PF, et al. Effect of the duration of electrical stimulation on the analgesic response in patients with low back pain. Anesthesiology. 1999 Dec;91(6):1622-7. PMID: 10598602.

516. Hurley DA, McDonough SM, Dempster M, et al. A randomized clinical trial of manipulative therapy and interferential therapy for acute low back pain. Spine (Phila Pa 1976). 2004 Oct 15;29(20):2207-16. PMID: 15480130.

517. Hurley DA, Minder PM, McDonough SM, et al. Interferential therapy electrode placement technique in acute low back pain: a preliminary investigation. Archives of Physical Medicine & Rehabilitation. 2001 Apr;82(4):485-93. PMID: 11295009.

518. Werners R, Pynsent PB, Bulstrode CJ. Randomized trial comparing interferential therapy with motorized lumbar traction and massage in the management of low back pain in a primary care setting. Spine (Phila Pa 1976). 1999 Aug 1;24(15):1579-84. PMID: 10457578.

519. Lara-Palomo IC, Aguilar-Ferrandiz ME, Mataran-Penarrocha GA, et al. Short-term effects of interferential current electro-massage in adults with chronic non-specific low back pain: a randomized controlled trial. Clinical Rehabilitation. 2013 May;27(5):439-49. PMID: 23035006.

520. French SD, Cameron M, Walker BF, et al. Superficial heat or cold for low back pain. Cochrane Database of Systematic Reviews. 2011(2)PMID: 16437495.

521. Mayer JM, Ralph L, Look M, et al. Treating acute low back pain with continuous low-level heat wrap therapy and/or exercise: a randomized controlled trial. Spine Journal: Official Journal of the North American Spine Society. 2005 Jul-Aug;5(4):395-403. PMID: 15996609.

522. Nadler SF, Steiner DJ, Erasala GN, et al. Continuous low-level heatwrap therapy for treating acute nonspecific low back pain. Archives of Physical Medicine & Rehabilitation. 2003a Mar;84(3):329-34. PMID: 12638099.

523. Nadler SF, Steiner DJ, Petty SR, et al. Overnight use of continuous low-level heatwrap therapy for relief of low back pain. Archives of Physical Medicine & Rehabilitation. 2003b Mar;84(3):335-42. PMID: 12638100.

524. Nuhr M, Hoerauf K, Bertalanffy A, et al. Active warming during emergency transport relieves acute low back pain. Spine (Phila Pa 1976). 2004 Jul 15;29(14):1499-503. PMID: 15247569.

525. Landen BR. Heat or cold for the relief of low back pain? Physical Therapy. 1967 Dec;47(12):1126-8. PMID: 4229712.

526. Roberts D, Walls C, Carlile J, et al. Relief of chronic low back pain: heat versus cold. 2nd edition ed: Baltimore: Urban & Schwarzenberg, 1992; 1992.

527. St. John Dixon A, Owen-Smith BD, Harrison RA. Cold-sensitive, non-specific low back pain: a comparative trial of treatment. Clinical Trials Journal. 1972;4:16-21. PMID: No PMID.

528. van Tulder M, Furlan A, Bombardier C, et al. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. Spine (Phila Pa 1976). 2003 Jun 15;28(12):1290-9. PMID: 12811274.

529. Kettenmann B, Wille C, Lurie-Luke E, et al. Impact of continuous low level heatwrap therapy in acute low back pain patients: subjective and objective measurements. Clinical Journal of Pain. 2007 Oct;23(8):663-8. PMID: 17885344.

530. Tao XG, Bernacki EJ. A randomized clinical trial of continuous low-level heat therapy for acute muscular low back pain in the workplace. Journal of Occupational & Environmental Medicine. 2005 Dec;47(12):1298-306. PMID: 16340712.

531. Basford JR, Sheffield CG, Harmsen WS. Laser therapy: a randomized, controlled trial of the effects of low-intensity Nd:YAG laser irradiation on musculoskeletal back pain. Archives of Physical Medicine & Rehabilitation. 1999 Jun;80(6):647-52. PMID: 10378490.

532. Klein RG, Eek BC. Low-energy laser treatment and exercise for chronic low back pain: double-blind controlled trial. Archives of Physical Medicine & Rehabilitation. 1990 Jan;71(1):34-7. PMID: 2136991.

533. Soriano F, Rios R. Gallium Arsenide laser treatment of chronic low back pain: a prospective, randomized and double blind study. Laser Therapy. 1998;10:175-80. PMID: No PMID.

534. Toya S, Motegi M, Inomata K, et al. Report on a computer-randomized double blind clinical trial to determine the effectiveness of the GaAlAs (830 nm) diode laser for pain attenuation in selected pain groups. Laser Therapy. 1994;6:143-. PMID: No PMID.

535. Gur A, Karakoc M, Cevik R, et al. Efficacy of low power laser therapy and exercise on pain and functions in chronic low back pain. Lasers Surg Med. 2003;32(3):233-8. PMID: 12605431.

536. Longo L, Tamburini A, Monti A, et al. Treatment with 904 nm and 10 600 nm laser of acute lumbago: double blind control. . Laser Clinical Research. 1988;3:16-20. PMID: No PMID.

537. Monticone M, Barbarino A, Testi C, et al. Symptomatic efficacy of stabilizing treatment versus laser therapy for sub-acute low back pain with positive tests for sacroiliac dysfunction: A randomised clinical controlled trial with 1 year follow-up. Europa Medicophysica. 2004;40(4):263-8. PMID: 16175148.

538. Yousefi-Nooraie R, Schonstein E, Heidari K, et al. Low level laser therapy for nonspecific low-back pain. Cochrane Database of Systematic Reviews. 2011(2)PMID: No PMID.

539. Djavid GE, Mehrdad R, Ghasemi M, et al. In chronic low back pain, low level laser therapy combined with exercise is more beneficial than exercise alone in the long term: a randomised trial.[Erratum appears in Aust J Physiother. 2007;53(4):216]. Australian Journal of Physiotherapy. 2007;53(3):155-60. PMID: 17725472.

540. Konstantinovic LM, Kanjuh ZM, Milovanovic AN, et al. Acute low back pain with radiculopathy: a double-blind, randomized, placebo-controlled study. Photomedicine and Laser Surgery. 2010 Aug;28(4):553-60. PMID: 20001318.

541. Ay S, Dogan SK, Evcik D. Is low-level laser therapy effective in acute or chronic low back pain?.[Erratum appears in Clin Rheumatol. 2010 Aug;29(8):911]. Clinical Rheumatology. 2010 Aug;29(8):905-10. PMID: 20414695.

542. Jovicic M, Konstantinovic L, Lazovic M, et al. Clinical and functional evaluation of patients with acute low back pain and radiculopathy treated with different energy doses of low level laser therapy. Vojnosanitetski Pregled. 2012 Aug;69(8):656-62. PMID: 22924260.

543. Gallagher EJ, Liebman M, Bijur PE. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. Annals of Emergency Medicine. 2001 Dec;38(6):633-8. PMID: 11719741.

544. Sweetman BJ, Heinrich I, Anderson JAD. A randomized controlled trial of exercises, short wave diathermy, and traction for low back pain, with evidence of diagnosis-related response to treatment. Journal of Orthopaedic Rheumatology. 1993;6(4):159-66. PMID: No PMID.

545. Ahmed MS, Shakoor MA, Khan AA. Evaluation of the effects of shortwave diathermy in patients with chronic low back pain. Bangladesh Medical Research Council Bulletin. 2009 Apr;35(1):18-20. PMID: 19637541.

546. Shakoor MA, Rahman MS, Moyeenuzzaman M. Effects of deep heat therapy on the patients with chronic low back pain. Mymensingh Medical Journal: MMJ. 2008 Jul;17(2 Suppl):S32-8. PMID: 18946448.

547. Coxhead CE, Inskip H, Meade TW, et al. Multi-centre trial of physiotherapy in the management of sciatic symptoms. Lancet. 1981;1(8229):1065-8. PMID: 6112444.

548. Hsieh CY, Phillips RB, Adams AH, et al. Functional outcomes of low back pain: Comparison of four treatment groups in a randomized controlled trial. Journal of Manipulative & Physiological Therapeutics. 1992;15(1):4-9. PMID: 1531488.

549. Million R, Nilsen K, Jayson M, et al. Evaluation of low back pain and assessment of lumbar corsets with and without back supports. Ann Rheum Dis. 1981;40(5):449-54. PMID: 6458250.

550. Penrose KW, Chook K, Stump JL. Acute and chronic effects of pneumatic lumbar suppor on muscular strength, flexibility, and functional impairment index. Sports Training Med Rehab. 1991;2:121-9. PMID: No PMID.

551. Valle-Jones J, Walsh H, O'Hara J, et al. Controlled trial of a back support ('Lumbotrain') in patients with non-specific low back pain. Curr Med Res Opin. 1992;12(9):604-13. PMID: 1533832.

552. van Duijvenbode I, Jellema P, van Poppel M, et al. Lumbar supports for prevention and treatment of low back pain. Cochrane Database of Systematic Reviews. 2011(2)PMID: No PMID.

553. Dalichau S, Scheele K. [Auswirkungen elastischer lumbalstutzgurte auf den effect eines muskeltrainingsprogrammes fur patienten mit chronischen ruckenschmerzen]. Z Orthop. 2000;138:8-16. PMID: 10730357.

554. Gibson JNA, Ahmed M. The effectiveness of flexible an dridig supports in patients with lumbar backache. Journal of Orthopaedic Medicine. 2002;24:86-9. PMID: No PMID.

555. Calmels P, Queneau P, Hamonet C, et al. Effectiveness of a lumbar belt in subacute low back pain: an open, multicentric, and randomized clinical study. Spine. 2009 Feb 1;34(3):215-20. PMID: 19179915.

556. Sato N, Sekiguchi M, Kikuchi S, et al. Effects of long-term corset wearing on chronic low back pain. Fukushima Journal of Medical Science. 2012;58(1):60-5. PMID: 22790893.

557. Oleske DM, Lavender SA, Andersson GBJ, et al. Are back supports plus education more effective than education alone in promoting recovery from low back pain?: Results from a randomized clinical trial. Spine. 2007 Sep 1;32(19):2050-7. PMID: 17762804.

558. Clarke JA, van Tulder MW, Blomberg SEI, et al. Traction for low-back pain with or without sciatica. Cochrane Database of Systematic Reviews. 2007(2):CD003010. PMID: 17443521.

559. Wegner I, Widyahening IS, van Tulder MW, et al. Traction for low-back pain with or without sciatica. Cochrane Database of Systematic Reviews. 2013;8:CD003010. PMID: 23959683.

560. Konrad K, Tatrai T, Hunka A, et al. Controlled trial of balneotherapy in treatment of low back pain. Annals of the Rheumatic Diseases. 1992 Jun;51(6):820-2. PMID: 1535495.

561. Mathews W, Morkel M, Mathews J. Manipulation and traction for lumbago and sciatica: Physiotherapeutic techniques used in two controlled trials. Physiother Pract. 1988;4(4):201-6. PMID: No PMID.

562. Diab AA, Moustafa IM. Lumbar lordosis rehabilitation for pain and lumbar segmental motion in chronic mechanical low back pain: a randomized trial. Journal of Manipulative & Physiological Therapeutics. 2012 May;35(4):246-53. PMID: 22632584.

563. Diab AAM, Moustafa IM. The efficacy of lumbar extension traction for sagittal alignment in mechanical low back pain: a randomized trial. Journal of Back & Musculoskeletal Rehabilitation. 2013 Jan 1;26(2):213-20. PMID: 23640324.

564. Moustafa IM, Diab AA. Extension traction treatment for patients with discogenic lumbosacral radiculopathy: a randomized controlled trial. Clinical Rehabilitation. 2013 Jan;27(1):51-62. PMID: 22684211.

565. Prasad KSM, Gregson BA, Hargreaves G, et al. Inversion therapy in patients with pure single level lumbar discogenic disease: a pilot randomized trial. Disability & Rehabilitation. 2012;34(17):1473-80. PMID: 22263648.

566. Beurskens AJP, de Vet HCP, Koke AJPT, et al. Efficacy of traction for nonspecific low back pain: 12-week and 6-month results of a randomized clinical trial. Spine. 1997;22(23):2756-62. PMID: 9431610.

567. van der Heijden G, Beurskens A, Dirx M, et al. Efficacy of lumbar traction: a randomised clinical trial. Physiotherapy. 1995;81(1):29-35. PMID: No PMID.

568. Letchuman R, Deusinger R. Comparison of sacrospinalis myoelectric activity and pain levels in patients undergoing static and intermittent lumbar traction. Spine. 1993;18(10):1361-5. PMID: 8211369.

569. Tesio L, Merlo A. Autotraction versus passive traction: an open controlled study in lumbar disc herniation. Arch Phys Med Rehabil. 1993;74(8):871-6. PMID: 8347073.

570. Castro-Sanchez AM, Lara-Palomo IC, Mataran-Penarrocha GA, et al. Kinesio Taping reduces disability and pain slightly in chronic non-specific low back pain: a randomised trial.[Erratum appears in J Physiother. 2012;58(3):143]. Journal of Physiotherapy. 2012;58(2):89-95. PMID: 22613238.

571. Chen S-M, Alexander R, Lo SK, et al. Effects of Functional Fascial Taping on pain and function in patients with non-specific low back pain: a pilot randomized controlled trial. Clinical Rehabilitation. 2012 Oct;26(10):924-33. PMID: 22492922.

572. Kachanathu SJ, Alenazi AM, Seif HE, et al. Comparison between Kinesio Taping and a Traditional Physical Therapy Program in Treatment of Nonspecific Low Back Pain. J Phys Ther Sci. 2014 Aug;26(8):1185-8. PMID: 25202177.

573. Paoloni M, Bernetti A, Fratocchi G, et al. Kinesio Taping applied to lumbar muscles influences clinical and electromyographic characteristics in chronic low back pain patients. European journal of physical & rehabilitation medicine. 2011 Jun;47(2):237-44. PMID: 21430611.

574. Silva Parreira PdC, Costa LC, Takahashi R, et al. Kinesio Taping to generate skin convolutions is not better than sham taping for people with chronic non-speci fi c low back pain: a randomised trial. Journal of Physiotherapy. 2014 Jun;60(2):90-6. PMID: 24952836.

575. Machado LAC, Kamper SJ, Herbert RD, et al. Analgesic effects of treatments for non-specific low back pain: a meta-analysis of placebo-controlled randomized trials. Rheumatology. 2009 May;48(5):520-7. PMID: 19109315.

576. Kuijpers T, van Middelkoop M, Rubinstein SM, et al. A systematic review on the effectiveness of pharmacological interventions for chronic non-specific low-back pain. European Spine Journal. 2011 Jan;20(1):40-50. PMID: 20680369.

577. Martell BA, O'Connor PG, Kerns RD, et al. Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. Annals of Internal Medicine. 2007 Jan 16;146(2):116-27. PMID: 17227935.

578. Chou R, Turner JA, Devine EB, et al. The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention WorkshopEffectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain. Annals of Internal Medicine. 2015;162(4):276-86. PMID: 25581257.

579. Morasco BJ, Duckart JP, Carr TP, et al. Clinical characteristics of veterans prescribed high doses of opioid medications for chronic non-cancer pain. Pain. 2010 Dec;151(3):625-32. PMID: 20801580.

580. Weisner CM, Campbell CI, Ray GT, et al. Trends in prescribed opioid therapy for non-cancer pain for individuals with prior substance use disorders. Pain. 2009 Oct;145(3):287-93. PMID: 19581051.

581. Richards MC, Ford JJ, Slater SL, et al. The effectiveness of physiotherapy functional restoration for post-acute low back pain: a systematic review. Manual Therapy. 2013 Feb;18(1):4-25. PMID: 22796390.

582. Davies RA, Maher CG, Hancock MJ. A systematic review of paracetamol for non-specific low back pain. European Spine Journal. 2008 Nov;17(11):1423-30. PMID: 18797937.

583. Ward N. Tricyclic antidepressants for chronic low-back pain. Mechanisms of ation and predictors of response. Spine (Phila Pa 1976). 1986;11(7):661-5. PMID: 2947334.

584. U.S. Food and Drug Administration. FDA clears Cymbalta to treat chronic musculoskeletal pain [Press Release]. Silver Spring, MD: U.S. Food and Drug Adminstration; 2010. Accessed on March 10th, 2015 2015.

585. Cawston H, Davie A, Paget M-A, et al. Efficacy of duloxetine versus alternative oral therapies: an indirect comparison of randomised clinical trials in chronic low back pain. European Spine Journal. 2013 Sep;22(9):1996-2009. PMID: 23686477.

586. Goertz CM, Pohlman KA, Vining RD, et al. Patient-centered outcomes of high-velocity, low-amplitude spinal manipulation for low back pain: a systematic review. Journal of Electromyography & Kinesiology. 2012 Oct;22(5):670-91. PMID: 22534288.

587. Brosseau L, Wells GA, Poitras S, et al. Ottawa Panel evidence-based clinical practice guidelines on therapeutic massage for low back pain. Journal of Bodywork & Movement Therapies. 2012 Oct;16(4):424-55. PMID: 23036876.

588. Hutchinson AJP, Ball S, Andrews JCH, et al. The effectiveness of acupuncture in treating chronic non-specific low back pain: a systematic review of the literature. Journal of Orthopaedic Surgery. 2012;7:36. PMID: 23111099.

589. Xu M, Yan S, Yin X, et al. Acupuncture for chronic low back pain in long-term follow-up: a meta-analysis of 13 randomized controlled trials. American Journal of Chinese Medicine. 2013;41(1):1-19. PMID: 23336503.

590. Netchanok S, Wendy M, Marie C, et al. The effectiveness of Swedish massage and traditional Thai massage in treating chronic low back pain: a review of the literature. Complementary Therapies in Clinical Practice. 2012 Nov;18(4):227-34. PMID: 23059437.

591. Hidalgo B, Detrembleur C, Hall T, et al. The efficacy of manual therapy and exercise for different stages of non-specific low back pain: an update of systematic reviews. Journal of Manual & Manipulative Therapy. 2014 May;22(2):59-74. PMID: 24976749.

592. Ferreira ML, Smeets RJEM, Kamper SJ, et al. Can we explain heterogeneity among randomized clinical trials of exercise for chronic back pain? A meta-regression analysis of randomized controlled trials. Physical Therapy. 2010 Oct;90(10):1383-403. PMID: 20671101.

593. Waller B, Lambeck J, Daly D. Therapeutic aquatic exercise in the treatment of low back pain: a systematic review. Clinical Rehabilitation. 2009 Jan;23(1):3-14. PMID: 19114433.

594. Yue Y-S, Wang X-D, Xie B, et al. Sling exercise for chronic low back pain: a systematic review and meta-analysis. PLoS ONE [Electronic Resource]. 2014;9(6):e99307. PMID: 24919119.

595. Wang X-Q, Zheng J-J, Yu Z-W, et al. A meta-analysis of core stability exercise versus general exercise for chronic low back pain. PLoS ONE [Electronic Resource]. 2012;7(12):e52082. PMID: 23284879.

596. Laird RA, Kent P, Keating JL. Modifying patterns of movement in people with low back pain -does it help? A systematic review. BMC Musculoskeletal Disorders. 2012;13:169. PMID: 22958597.

597. Ward L, Stebbings S, Cherkin D, et al. Yoga for functional ability, pain and psychosocial outcomes in musculoskeletal conditions: a systematic review and meta-analysis. Musculoskeletal Care. 2013 Dec;11(4):203-17. PMID: 23300142.

598. Holtzman S, Beggs RT. Yoga for chronic low back pain: a meta-analysis of randomized controlled trials. Pain Research & Management. 2013 Sep-Oct;18(5):267-72. PMID: 23894731.

599. van Geen J-W, Edelaar MJA, Janssen M, et al. The long-term effect of multidisciplinary back training: a systematic review. Spine. 2007 Jan 15;32(2):249-55. PMID: 17224822.

600. Bunzli S, Gillham D, Esterman A. Physiotherapy-provided operant conditioning in the management of low back pain disability: A systematic review. Physiotherapy Research International. 2011 Mar;16(1):4-19. PMID: 20310071.

601. Schonstein E, Kenny DT, Keating J, et al. Work conditioning, work hardening and functional restoration for workers with back and neck pain. Cochrane Database of Systematic Reviews. 2003(1):CD001822. PMID: 12535416.

602. Hill JC, Whitehurst DG, Lewis M, et al. Comparison of stratified primary care management for low back pain with current best practice (STarT Back): a randomised controlled trial. Lancet. 2011 Oct 29;378(9802):1560-71. PMID: 21963002.

603. Dubinsky RM, Miyasaki J. Assessment: Efficacy of transcutaneous electric nerve stimulation in the treatment of pain in neurologic disorders (an evidence-based review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2010 January 12, 2010;74(2):173-6. PMID: 20042705.

604. Luijsterburg PAJ, Verhagen AP, Ostelo RWJG, et al. Effectiveness of conservative treatments for the lumbosacral radicular syndrome: a systematic review. European Spine Journal. 2007 Jul;16(7):881-99. PMID: 17415595.

605. Johnson M, Neher JO, St Anna L. Clinical inquiries. How effective--and safe--are systemic steroids for acute low back pain? J Fam Pract. 2011 May;60(5):297-8. PMID: 21544281.

606. Lewis RA, Williams NH, Sutton AJ, et al. Comparative clinical effectiveness of management strategies for sciatica: systematic review and network meta-analyses. Spine Journal: Official Journal of the North American Spine Society. 2013 Oct 4PMID: 24412033.

607. Kalauokalani D, Cherkin DC, Sherman KJ, et al. Lessons from a trial of acupuncture and massage for low back pain: Patient expectations and treatment effects. Spine. 2001;26(13):1418-24. PMID: 11458142.

608. Linde K, Witt CM, Streng A, et al. The impact of patient expectations on outcomes in four randomized controlled trials of acupuncture in patients with chronic pain. Pain. 2007 Apr;128(3):264-71. PMID: 17257756.

609. National Institute for Health and Care Excellence. Low back pain: Early management of persistent non-specific low back pain. 2009. http://www.nice.org.uk/guidance/cg88/chapter/1-guidance. Accessed on March, 10th 2015.

610. Koes BW, Enthoven WT. Do patients with acute low-back pain need paracetamol? Lancet. 2014 Nov 1;384(9954):1556-7. PMID: 25064595.

611. Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. Journal of Pain. 2009 Feb;10(2):113-30. PMID: 19187889.

612. Whitlock EP, Lin JS, Chou R, et al. Using Existing Systematic Reviews in Complex Systematic Reviews. Annals of Internal Medicine. 2008;148(10):776-82. PMID: 18490690.

613. Gagnier JJ, van Tulder M, Berman B, et al. Herbal medicine for low back pain. Cochrane Database of Systematic Reviews. 2006(2):CD004504. PMID: 16625605.

614. Abdel Shaheed C, Maher CG, Williams KA, et al. Interventions available over the counter and advice for acute low back pain: systematic review and meta-analysis. Journal of Pain. 2014 Jan;15(1):2-15. PMID: 24373568.

615. Dupeyron A, Ribinik P, Gelis A, et al. Education in the management of low back pain: literature review and recall of key recommendations for practice. Annals of Physical & Rehabilitation Medicine. 2011 Jul;54(5):319-35. PMID: 21782541.

616. Dahm KT, Brurberg KG, Jamtvedt G, et al. Advice to rest in bed versus advice to stay active for acute low-back pain and sciatica. Cochrane Database of Systematic Reviews. 2010(6):CD007612. PMID: 20556780.

617. Chuter V, Spink M, Searle A, et al. The effectiveness of shoe insoles for the prevention and treatment of low back pain: a systematic review and meta-analysis of randomised controlled trials. BMC Musculoskeletal Disorders. 2014;15:140. PMID: 24775807.

618. Huang C-Y, Choong M-Y, Li T-S. Effectiveness of cupping therapy for low back pain: a systematic review. Acupuncture in Medicine. 2013 Sep;31(3):336-7. PMID: 23886511.

619. Oliveira VC, Ferreira PH, Maher CG, et al. Effectiveness of self-management of low back pain: systematic review with meta-analysis. Arthritis care & research. 2012 Nov;64(11):1739-48. PMID: 22623349.

620. Moore RA, Derry S, Wiffen PJ. Challenges in design and interpretation of chronic pain trials. Br J Anaesth. 2013 Jul;111(1):38-45. PMID: 23794643.

621. van der Windt DA, Dunn KM. Low back pain research--future directions. Best Pract Res Clin Rheumatol. 2013 Oct;27(5):699-708. PMID: 24315150.

622. Henschke N, Kuijpers T, Rubinstein SM, et al. Trends over time in the size and quality of randomised controlled trials of interventions for chronic low-back pain. European Spine Journal. 2012 Mar;21(3):375-81. PMID: 22037844.

623. Pereira LM, Obara K, Dias JM, et al. Comparing the Pilates method with no exercise or lumbar stabilization for pain and functionality in patients with chronic low back pain: systematic review and meta-analysis. Clinical Rehabilitation. 2012 Jan;26(1):10-20. PMID: 21856719.

624. Seco J, Kovacs FM, Urrutia G. The efficacy, safety, effectiveness, and cost-effectiveness of ultrasound and shock wave therapies for low back pain: a systematic review. Spine Journal: Official Journal of the North American Spine Society. 2011 Oct;11(10):966-77. PMID: 21482199.

625. National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). Effectiveness of Oral Prednisone in Improving Physical Functioning and Decreasing Pain in People with Sciatica (ACT FAST). Kaiser Permanente; 2008.

626. Pincus T, McCracken LM. Psychological factors and treatment opportunities in low back pain. Best Practice & Research in Clinical Rheumatology. 2013 Oct;27(5):625-35. PMID: 24315144.

627. Patel S, Friede T, Froud R, et al. Systematic review of randomized controlled trials of clinical prediction rules for physical therapy in low back pain. Spine (Phila Pa 1976). 2013 Apr 20;38(9):762-9. PMID: 23132535.

628. Kent P, Kjaer P. The efficacy of targeted interventions for modifiable psychosocial risk factors of persistent nonspecific low back pain - a systematic review. Manual Therapy. 2012 Oct;17(5):385-401. PMID: 22421188.

629. van der Giessen RN, Speksnijder CM, Helders PJM. The effectiveness of graded activity in patients with non-specific low-back pain: a systematic review. Disability & Rehabilitation. 2012;34(13):1070-6. PMID: 22148906.

630. Balague F, Piguet V, Dudler J. Steroids for LBP - from rationale to inconvenient truth. Swiss Medical Weekly. 2012;142:w13566. PMID: 22495738.

631. Group Health Cooperative. Matching Appropriate Treatments to Consumers' Healthcare Needs, MATCH. 2014.

632. Delitto A. Targeted interventions to Prevent Chronic Low Back Pain in High Risk Patients: A Multi-Site Pragmatic RCT. 2015. http://www.pcori.org/research-results/2015/targeted-interventions-prevent-chronic-low-back-pain-high-risk-patients-multi. Accessed on March, 10th 2015.

633. Foster NE, Hill JC, O'Sullivan P, et al. Stratified models of care. Best Pract Res Clin Rheumatol. 2013 Oct;27(5):649-61. PMID: 24315146.