



# Effective Health Care Program

## Noninvasive Treatments for Low Back Pain *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.<sup>1,2</sup> Low back pain can have major adverse impacts on quality of life and function. Low back pain is also costly: total U.S. health care expenditures for low back pain in 1998 were estimated at \$90 billion.<sup>3</sup> Since that time, costs of low back pain care have risen at a rate higher than observed for overall health expenditures.<sup>4</sup> 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.<sup>5</sup>

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

#### Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at [www.effectivehealthcare.ahrq.gov/reports/final.cfm](http://www.effectivehealthcare.ahrq.gov/reports/final.cfm).

disability, and are able to return to work.<sup>6</sup> In those with persistent symptoms, continued improvement is often seen in the subacute phase between 4 and 12 weeks, although at a slower rate than observed at first. In a

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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.<sup>7</sup> 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.<sup>8</sup> Patients with chronic back pain account for the bulk of the burdens and costs of low back pain.<sup>9,10</sup> Predictors of chronicity are primarily related to psychosocial factors, such as presence of psychological comorbidities, maladaptive coping strategies (e.g., fear avoidance [avoiding activities because of fears that they will further damage the back] or catastrophizing [anticipating the worst possible outcomes from low back pain]), presence of nonorganic signs (symptoms without a distinct anatomical or physiological basis),<sup>11</sup> high baseline functional impairment, and low general health status.<sup>7</sup> 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.<sup>12</sup> Spinal imaging abnormalities, such as degenerative disc disease, facet joint arthropathy, and bulging or herniated intervertebral discs, are extremely common in patients with or without low back pain, particularly in older adults, and such findings are poor predictors for the presence or severity of low back pain.<sup>13</sup> 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.<sup>14</sup>

## 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,<sup>15</sup> noninvasive nonpharmacological treatments,<sup>16</sup>

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

## Scope of Review and Key Questions

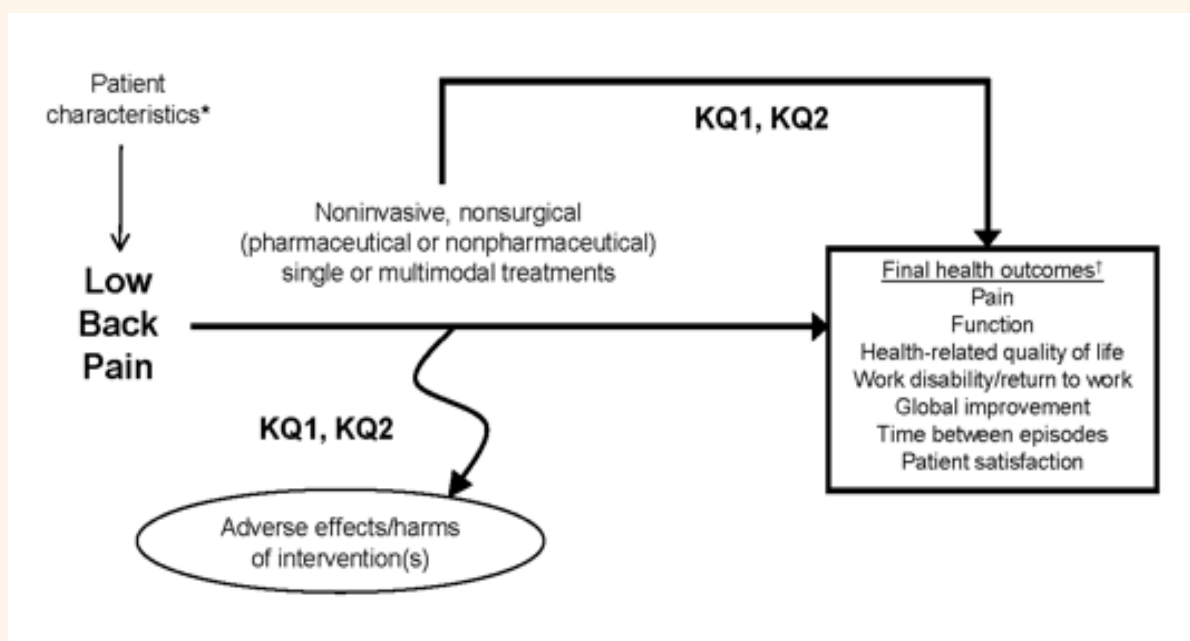
The provisional Key Questions; populations, interventions, comparators, outcomes, timing, settings, and study designs (PICOTS); and analytic framework for this topic (Figure A) were posted on the Agency for Healthcare Research and Quality (AHRQ) Web site for public comment from December 17, 2013, through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

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

**Key Question 2. What are the comparative benefits and harms of different nonpharmacological noninvasive therapies for acute or chronic nonradicular low back pain, radicular low back pain, or spinal stenosis? Includes but is not limited to multidisciplinary rehabilitation, exercise (various types), physical modalities**

**(ultrasound, transcutaneous electrical nerve stimulation, electrical muscle stimulation, interferential therapy, heat [various forms], and ice), traction tables/devices, back supports/bracing, spinal manipulation, various psychological therapies, acupuncture, massage therapy (various types), yoga, magnets, and low-level lasers.**

**Figure A. Analytic framework**



\*Patient characteristics include clinical, demographic, and psychosocial risk factors associated with low back pain outcomes.

†Intermediate outcomes (e.g., inflammation) are typically not measured.

KQ = Key Question.

## Methods

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

## Literature Search and Selection

A research librarian conducted searches in Ovid MEDLINE®, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews through August 2014. We restricted search start dates to January 2008 because searches in a prior American Pain Society/American College of Physicians (APS/ACP) review were conducted through October 2008; the APS/ACP review was used to identify studies published prior to 2008.<sup>20</sup> For interventions not addressed in the APS/

ACP review, we searched the same databases without a search date start restriction. We also hand searched the reference lists of relevant studies and searched for unpublished studies in ClinicalTrials.gov. Scientific information packets were solicited from drug and device manufacturers, and a notice published in the Federal Register invited interested parties to submit relevant published and unpublished studies. We conducted an update search in April 2015 using the same search strategy as in the original search.

We developed criteria for inclusion and exclusion of studies based on the Key Questions and PICOTS. Abstracts were reviewed by two investigators, and all citations deemed potentially appropriate for inclusion by at least one of the reviewers were retrieved. Two investigators then independently reviewed all full-text articles for final inclusion. Discrepancies were resolved by discussion and consensus.

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

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

**Outcomes of interest.** We evaluated effects of interventions on reduction or elimination of low back

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

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

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

## Data Extraction

For systematic reviews we abstracted the following data: inclusion criteria, search strategy, databases searched, search dates, the number of included studies, study characteristics of included studies (e.g., sample sizes, interventions, duration of treatment, duration of followup, comparison, and results), methods of quality assessment, quality ratings for included studies, methods for synthesis, and results. For primary studies not included in systematic reviews, we abstracted the following data: study

design, year, setting, country, sample size, eligibility criteria, population and clinical characteristics, intervention characteristics, and results. Information relevant for assessing applicability was also abstracted, including the characteristics of the population, interventions, and care settings; the use of run-in or washout periods; and the number of patients enrolled relative to the number assessed for eligibility. All study data were verified for accuracy and completeness by a second team member.

## Risk-of-Bias Assessment of Individual Studies

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

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

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

## Data Synthesis

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

In addition, we reported meta-analysis from systematic reviews that reported pooled estimates from studies that were judged to be homogeneous enough to provide a meaningful combined estimate and used appropriate pooling methods (e.g., random-effects model in the presence of statistical heterogeneity). When statistical heterogeneity was present, we examined the type of inconsistency present and evaluated subgroup and sensitivity analyses based on study characteristics, intervention factors, and patient factors. We did not conduct updated meta-analysis with new studies. Rather, we qualitatively examined whether results of new studies were consistent with pooled or qualitative findings from prior systematic reviews. When we included more than one systematic review for a particular intervention and comparison, we evaluated the consistency of results among reviews.

We assessed the strength of evidence (i.e., evidence in prior reviews as well as new evidence) for each Key Question and outcome using the approach described in the AHRQ Methods Guide<sup>19</sup> based on the overall quality of each body of evidence.

## Results

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

Most trials were conducted in patients with nonradicular low back pain or mixed populations with primarily nonradicular low back pain. Some

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

## Key Question 1. Pharmacological Therapies

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

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

too inconsistent to determine effects of opioids versus NSAIDs (Table D).

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

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

## Key Question 2. Nonpharmacological Noninvasive Therapies

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

For chronic low back pain, a number of nonpharmacological therapies appear to be effective for improving pain or function (Table G). These include exercise, yoga, and tai chi; various psychological therapies; multidisciplinary rehabilitation; acupuncture; spinal manipulation (vs. an inert treatment); and low-level laser therapy. Effects were small to moderate in magnitude. Other physical modalities were not associated with beneficial effects, or evidence was insufficient to estimate effects. Based on head-to-head comparisons, multidisciplinary rehabilitation was associated with small to moderate beneficial effects on pain and function versus standard physical therapy, and spinal

manipulation and massage were associated with small beneficial effects versus other active interventions (Table H). There was no strong evidence of differences in effectiveness among different exercise, massage, spinal manipulation, or acupuncture techniques, or among different types of psychological therapies.

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

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

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

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

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

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

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

\*Although some RCTs found long-acting opioids to be associated with greater pain relief than short-acting opioids, patients randomized to long-acting opioids also received higher doses of opioids.

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

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

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

\*Although some RCTs found long-acting opioids to be associated with greater pain relief than short-acting opioids, patients randomized to long-acting opioids also received higher doses of opioids.

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

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

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

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

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

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

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

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

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
Exercise vs. usual care	Small	1 SR (19 RCTs) + 1 SR	Moderate	Small	1 SR (17 RCTs) + 1 SR	Moderate
Motor control exercises vs. minimal intervention	Moderate (short to long term)	1 SR (2 RCTs)	Low	Small (short to long term)	1 SR (3 RCTs)	Low
Tai chi vs. wait list or no tai chi	Moderate	2 RCTs	Low	Small	1 RCT	Low
Yoga vs. usual care	Moderate	1 RCT	Low	Moderate	1 RCT	Low
Yoga vs. education	Small (short term) and no effect (long term)	5 RCTs (short term) + 4 RCTs (long term)	Low	Small (short term) and no effect (long term)	5 RCTs (short term) + 4 RCTs (long term)	Low
Progressive relaxation vs. wait-list control	Moderate	1 SR (3 RCTs)	Low	Moderate	1 SR (3 RCTs)	Low

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EMG biofeedback vs. wait list or placebo	Moderate	1 SR (3 RCTs)	Low	No effect	1 SR (3 RCTs)	Low
Operant therapy vs. wait-list control	Small	1 SR (3 RCTs)	Low	No effect	1 SR (2 RCTs)	Low
Cognitive-behavioral therapy vs. wait-list control	Moderate	1 SR (5 RCTs)	Low	No effect	1 SR (4 RCTs)	Low
Multidisciplinary rehabilitation vs. no multidisciplinary rehabilitation	Moderate	1 SR (3 RCTs)	Low	Small	1 SR (3 RCTs)	Low
Multidisciplinary rehabilitation vs. usual care	Moderate (short term), small (long term), favors rehabilitation	1 SR (9 RCTs) (short term) + 1 SR (7 RCTs) (long term)	Moderate	Small (short and long term)	1 SR (9 RCTs) (short term) + 1 SR (7 RCTs) (long term)	Moderate
Acupuncture vs. sham acupuncture	Moderate	1 SR (4 RCTs) + 4 RCTs	Low	No effect	1 SR (4 RCTs) + 4 RCTs	Low
Acupuncture vs. no acupuncture	Moderate	1 SR (4 RCTs)	Moderate	Moderate	1 SR (3 RCTs)	Moderate
Spinal manipulation vs. sham manipulation	No effect	1 SR (3 RCTs) + 1 RCT	Low	Unable to estimate	1 RCT	--
Spinal manipulation vs. inert treatment	Small	7 RCTs	Low	--	--	--
Massage vs. usual care	No effect	1 RCT	Low	Unable to estimate	2 RCTs	Insufficient
Ultrasound vs. sham ultrasound	No effect	1 SR (3 RCTs)	Low	Unable to estimate	5 RCTs	Insufficient
Ultrasound vs. no ultrasound	No effect	1 SR (2 RCTs)	Low	No effect	1 SR (2 RCTs)	Low
TENS vs. sham TENS	No effect	1 SR (4 RCTs)	Low	No effect	1 SR (2 RCTs)	Low
PENS vs. sham PENS	Unable to estimate	2 RCTs	Insufficient	Unable to estimate	2 RCTs	Insufficient
Electrical muscle stimulation vs. sham, no stimulation, or usual care	No evidence	--	--	No evidence	--	--
Low-level laser therapy vs. sham laser	Small	3 RCTs	Low	Small	3 RCTs	Low
Lumbar supports vs. no lumbar supports	Unable to estimate	2 RCTs	Insufficient	Unable to estimate	2 RCTs	Insufficient
Traction vs. placebo, sham, or no traction	Unable to estimate	1 SR (13 RCTs)	Insufficient	Unable to estimate	1 SR (13 RCTs)	Insufficient
Kinesio taping® vs. sham taping	No effect	2 RCTs	Low	No effects	2 RCTs	Low

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

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

Intervention	Pain: Magnitude of Effect	Pain: Evidence	Pain: SOE	Function: Magnitude of Effect	Function: Evidence	Function: SOE
MCE vs. general exercise (short term)	Small, favors MCE for short term	1 SR (6 RCTs)	Low	Small, favors MCE	1 SR (6 RCTs)	Low
MCE vs. general exercise (intermediate term)	Small, favors MCE for intermediate term	1 SR (3 RCTs)	Low	--	--	--
MCE vs. general exercise (long term)	Small, favors MCE for long term	1 SR (4 RCTs)	Low	Small, favors MCE	1 SR (3 RCTs)	Low

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MCE vs. multimodal physical therapy (intermediate term)	Moderate, favors MCE	1 SR (4 RCTs)	Low	Moderate, favors MCE	1 SR (3 RCTs)	Low
MCE + exercise vs. exercise alone	No clear difference	2 RCTs	Low	--	--	--
Pilates vs. usual care + physical activity	No effect to small effect, favors Pilates	7 RCTs	Low	No clear difference	7 RCTs	Low
Pilates vs. other exercise	No clear difference	3 RCTs	Low	No clear difference	3 RCTs	Low
Tai chi vs. other exercise	Moderate, favors tai chi	1 RCT	Low	--	--	--
Yoga vs. exercise	Small, favors yoga	1 SR (5 RCTs)	Low	--	--	--
Psychological therapies vs. exercise or physical therapy	No clear difference	1 SR (6 RCTs)	Low	--	--	--
Psychological therapies vs. psychological therapies	No clear difference	10 RCTs	Moderate	No clear difference	10 RCTs	Moderate
Multidisciplinary rehabilitation vs. physical therapy (short term)	Small, favors multidisciplinary rehabilitation	1 SR (12 RCTs)	Moderate	Small, favors multidisciplinary rehabilitation	1 SR (13 RCTs)	Moderate
Multidisciplinary rehabilitation vs. physical therapy (long term)	Moderate, favors multidisciplinary rehabilitation	1 SR (9 RCTs)	Moderate	Moderate, favors multidisciplinary rehabilitation	1 SR (10 RCTs)	Moderate
Spinal manipulation vs. other active interventions (exercise, usual care, medications, massage)	No clear difference	1 SR (6 RCTs)	Moderate	No clear difference	1 SR (6 RCTs)	Moderate
Acupuncture vs. medications	Small, favors acupuncture	1 SR (3 RCTs)	Low	Small, favors acupuncture	1 SR (3 RCTs)	Low

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

## Discussion

### Key Findings and Strength of Evidence

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

New evidence affected conclusions for several classes of medications. The prior review concluded that acetaminophen was effective for acute low back pain, primarily based on indirect evidence from trials of acetaminophen for other conditions and trials of acetaminophen versus other analgesics. However, a recent well-conducted trial—the first placebo-controlled trial in patients with acute low back pain—found acetaminophen to be no more effective than placebo (strength of evidence [SOE]: low).<sup>27</sup> 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).<sup>28-30</sup> However, effects were small (less than 1 point on a 0 to 10 scale), and all trials were funded by the manufacturer of duloxetine and led by the same researcher. For antiseizure medications, new evidence is available on pregabalin for radicular low back pain, but the studies had methodological shortcomings and were too inconsistent to reliably estimate effects (SOE: insufficient).<sup>31,32</sup> The prior review found no studies on the effects of benzodiazepines for radiculopathy. One

recent trial found that benzodiazepines were no more effective than placebo for this condition (SOE: low).<sup>33</sup> The trial also found that for some outcomes, such as return to work, benzodiazepines were associated with worse outcomes than placebo.

Main conclusions regarding the benefits and harms of pharmacological therapies for low back pain were otherwise relatively unchanged from the prior review and are summarized in Tables A–E. One area in which conclusions changed was the effectiveness of tricyclic antidepressants. In our prior review, tricyclic antidepressants were found to be associated with small beneficial effects for chronic low back pain. However, evidence reviewed for this report suggests that tricyclic antidepressants are not effective versus placebo (4 trials; SMD,  $-0.10$ ; 95% confidence interval [CI],  $-0.51$  to  $0.31$ ; I<sup>2</sup> = 32%; SOE: moderate).<sup>34</sup> As noted previously, duloxetine, a serotonin norepinephrine reuptake inhibitor that is not associated with the anticholinergic and cardiac side effects of tricyclics, is now available as a potential alternative antidepressant.

Evidence on the effectiveness of opioids for low back pain remains limited to short-term trials showing modest effects versus placebo on short-term pain and function<sup>35</sup> (SOE: moderate). Findings regarding the increased risk of opioids versus placebo for harms such as constipation, nausea, sedation, and dry mouth are also unchanged. Trials of opioids for low back pain were not designed to assess risk of serious adverse events, such as overdose, abuse or addiction, or accidental injuries, because of their relatively small samples and short duration of followup. In addition, trials of opioids typically excluded patients with risk factors for overdose, abuse, or addiction. However, observational studies of opioids for chronic pain in general (not restricted to low back pain) have shown an association with serious harms that appears to be dose dependent.<sup>36</sup>

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

fracture or infection with corticosteroids, or abuse or addiction with benzodiazepines).

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

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

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

bleeding, or other complications were not reported in trials of acupuncture.

## Findings in Relationship to What Is Already Known

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

Our prior report and other previous systematic reviews<sup>43,44</sup> found that tricyclic antidepressants were associated with small beneficial effects for low back pain. However, the evidence reviewed for this report suggests that they are not effective versus placebo for pain relief (4 trials; SMD,  $-0.10$ ; 95% CI,  $-0.51$  to  $0.31$ ;  $I^2 = 32\%$ ) or function.<sup>34</sup> One potential reason for the discrepancy between this finding and prior reviews is that some of the prior reviews did not conduct a meta-analysis.<sup>44,45</sup> A review<sup>43</sup> that conducted meta-analysis included a study that did not report being randomized and reported the largest effect in favor of antidepressants,<sup>46</sup> did not include relevant studies that were in the more current review,<sup>47-49</sup> and included two relevant studies in the meta-analysis for which data had to be imputed,<sup>50,51</sup> but did not report methods for imputation.

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

Findings regarding the effectiveness of exercise are similar to our prior review and other reviews.<sup>59-61</sup> Our findings are also consistent with reviews that focused on more specific types of exercise, such as aquatic exercise,<sup>62</sup> sling exercise,<sup>63</sup> walking, stability exercises,<sup>64,65</sup> or modifying patterns of movement.<sup>66</sup> Our findings that psychological therapies and

multidisciplinary rehabilitation are both effective are consistent with our prior review and other reviews.<sup>67</sup> 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.<sup>68-70</sup> As in our prior review, we found that for most physical modalities, evidence was too weak to determine effectiveness.

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

## Applicability

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

For nonpharmacological treatments, the applicability of our findings is affected by the variability among trials in the interventions and comparators evaluated. In trials that evaluated “usual care” comparators, the components of usual care were often not well described or standardized, making it difficult to apply findings to clinical practice. Other factors that could impact the applicability of our findings regarding nonpharmacological interventions include differences related to the setting in which the intervention was performed (e.g., United States vs. another country, specialist vs. primary care setting) or to the training or skill of the person performing the intervention.

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

## Implications for Clinical and Policy Decisionmaking

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

as being associated with a more favorable safety profile, which could impact the selection of drugs within the antidepressant class.

The use of opioids for chronic pain has become an area of increasing concern because of uncertain long-term effectiveness and marked increases in the number of accidental overdoses, as well as other harms related to their abuse potential.<sup>36</sup> 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.<sup>77</sup>

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

Our review supports clinical practice guidelines that found insufficient evidence to recommend most physical modalities other than superficial heat. However, these therapies are still commonly used in clinical practice. Among nonpharmacological therapies that were found to be effective, there was insufficient evidence to determine which patients are most likely to benefit from specific therapies. However, a recent trial found that a stratified approach (in which patients are assessed for risk factors for chronicity and higher risk patients receive more intensive cognitive-behavioral-based physical

therapy) is more effective than usual care without a stratified approach, suggesting that psychologically based therapies and multidisciplinary rehabilitation may be the most effective approach in higher risk patients.<sup>78</sup> Other factors that may impact decisions regarding which nonpharmacological therapies to use include cost, availability, and patient preferences. There is some evidence that greater patient expectations of benefit from a particular treatment are associated with greater benefits,<sup>79,80</sup> 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.<sup>81</sup> Therefore, we focused on higher quality reviews. We did not conduct meta-analyses or update meta-analyses included in prior systematic reviews. However, for comparisons without a meta-analysis, we synthesized results qualitatively, using the methods in the AHRQ Methods Guide. For comparisons for which pooled results were available from prior systematic reviews, we evaluated the consistency of results from new trials against the pooled estimates.

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

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

## Limitations of the Evidence Base

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

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

Some limitations of the evidence were particularly relevant for trials of nonpharmacological interventions. Studies of nonpharmacological interventions were typically characterized by marked heterogeneity in the specific intervention techniques evaluated, as well as in the duration and intensity of treatments, which could attenuate treatment benefits if suboptimal treatment techniques or intensity of therapy were evaluated. In addition, a number of nonpharmacological therapies (e.g., psychological therapies, exercise therapy, massage, spinal manipulation) are difficult to blind effectively.

Therefore, observed benefits could be due in part to placebo, attentional, or other nonspecific effects, and results are susceptible to performance and other biases, although it is not possible to reliably quantify the extent of such effects. Finally, trials of nonpharmacological therapies did not report harms well; this could be in part because serious harms are not expected with most of these treatments.

## Research Gaps

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

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

More research is needed to help understand which patients are most likely to benefit from specific therapies.<sup>91-95</sup> Trials are also needed to confirm whether effects of risk-stratified approaches are reproducible in the United States<sup>96,97</sup> and to optimize their implementation.<sup>98</sup> More research is also needed to better understand whether combination therapy with different pharmacological or

nonpharmacological treatments is associated with incremental benefits versus individual components of the combination therapy, and which combinations and sequences of therapy are the most effective.

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

## Conclusions

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

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## Full Report

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