

APPENDIX A
Spinal Injections

Introduction

Spinal injections are of clinical interest in low back pain because medication is directly delivered to the anatomic location that has been identified as the likely source of pain. Depending upon the type of injection, some injections may bring about long-lasting relief while others may only provide temporary relief. Several spinal injections are used in practice today. They can be classified as either intraspinal injections or injections outside the spine. Intraspinal injections are further categorized into either intraspinal steroid injections or chemonucleolysis. These include:

Intraspinal injections

- Intraspinal steroid injections
 - Epidural steroid injection
 - Facet joint steroid injection
 - Sacroiliac joint steroid injection
 - Intradiscal steroid injection

- Nerve blocks
 - Medial branch blocks
 - Sympathetic nerve blocks
 - Selective nerve root blocks

- Chemonucleolysis

Injections outside the spine

- Botulinum toxin injections
- Local injections
- Prolotherapy

Intraspinal injections

Intraspinal steroid injections

Epidural steroid injections (ESIs) deliver the steroid into the epidural space, the space between the dura and the spine. The injection typically includes both a long-lasting steroid and a local anesthetic. ESIs may be delivered in three different ways. The transforaminal approach delivers the needle to the neural foramen, the space through which nerve roots exit the spinal canal to form the peripheral nerves. Interlaminar (or translaminar) injections deliver steroid directly into the epidural space. Finally, caudal injections approach the epidural space by going through the sacral opening.

Additional types of steroid injections have other anatomic targets. Facet joint steroid injections deliver corticosteroids into the facet joints, joints that are located between and behind adjacent vertebrae. Sacroiliac joint steroid injections are corticosteroid injections into or around the sacroiliac joint, the joint that connects the sacrum to the pelvis. Intradiscal steroid injections involve injecting a corticosteroid into an intervertebral disc to treat discogenic pain.

Nerve blocks

Nerve block injections include an anesthetic and may also include a corticosteroid. These injections are intended to target specific areas thought to be the source of pain, temporarily blocking pain signals. Most commonly, these injections target the medial branch nerves, which emanate from the facet joints and in turn carry pain signals from these joints. Nerve-blocking injections may also target the sympathetic nervous system, which control some of the body's involuntary functions.

Finally, nerve blocks may target selective nerve roots. These injections are intended primarily to diagnose the source of pain, not to treat it.

Chemonucleolysis

Chemonucleolysis uses a proteolytic enzyme, usually chymopapain, to dissolve the inner part of a herniated disc, in an effort to resolve radicular pain.

Injections outside the spine

Injections that take place outside of the spine target the muscles or the soft tissues of the back. Botulinum toxin (Botox) injections are injected into the muscles of the back to control muscle spasms. Local injections utilize a local anesthetic, injected into the muscles or soft tissues of the back. These are used to treat inflammation in small areas of the back.

Prolotherapy is a procedure in which a chemical irritant is injected into the soft tissues of the back. This promotes an inflammatory response, which is thought to lead to a natural healing that will strengthen the injured soft tissue and thus, reduce back pain. Also known as sclerotherapy, it is used to treat sciatica and degenerative disc disease.

Each type of injection procedure may last between 15 and 30 minutes. The patient lies on an X-ray table and the skin in the lower back area is cleaned and numbed with a local anesthetic. Spinal injections are best done under fluoroscopic (live X-ray) guidance. Once the needle is in the proper position, a contrast dye is injected to confirm the position of the needle. Following confirmation, the steroid/anesthetic solution is injected.

Risks associated with these procedures include misplacement of the needle (either advancing the needle too deeply or placing it in the wrong position). The outcomes of incorrect needle position include nerve damage, infection, bleeding, and headaches. Risks associated with the medications include elevated blood sugars, arthritis, stomach ulcers, and weight gain. Chemonucleolysis may also cause anaphylactic reactions in some patients.

One risk specifically associated with epidural steroid injections is wet tap, in which the needle penetrates the spinal sac and enters the cerebrospinal fluid. This causes the fluid to leak, resulting in severe headaches. Other rare complications associated with epidural steroid injections include epidural hematoma and abscess.

Professional Organization and Agency Recommendations

American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010)

http://journals.lww.com/anesthesiology/Fulltext/2010/04000/Practice_Guidelines_for_Chronic_Pain_Management.13.aspx

Intra-articular facet joint injections may be used for symptomatic relief of facet-mediated pain. Sacroiliac joint injections may be considered for symptomatic relief of sacroiliac joint pain. Medial branch blocks may be used for treatment of facet-mediated pain. Epidural steroid injections with or without local anesthetics may be used as part of a multimodal treatment regimen in select patients with radiculopathy.

The American Pain Society (APS, 2009)

http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies_Surgery_and.14.aspx

In patients with persistent nonradicular low back pain, facet joint corticosteroid injection and intradiscal corticosteroid injection are not recommended because randomized trials consistently found them to be no more effective than sham therapies. In patients with persistent radiculopathy due to a herniated lumbar disc, it is recommended that clinicians discuss the risks and benefits of epidural steroid injection as a treatment option. It is also recommended that any shared decision-making regarding epidural steroid injection include a specific discussion about inconsistent evidence showing moderate short-term benefits and the lack of long-term benefits. There is little evidence to sufficiently assess the benefits and harms of epidural steroid injection for spinal stenosis.

American Society of Interventional Pain Physicians (AIPP, 2009)

<http://www.painphysicianjournal.com/2009/july/2009;12;699-802.pdf>

Based on the quality of evidence, the use of therapeutic lumbar facet joint nerve blocks for both short-term and long-term relief is strongly recommended. For those with either lumbar spinal pain with disc herniation and radiculitis, or discogenic pain without disc herniation, or radiculitis, the use of epidural steroid injections is strongly recommended. For those with disc herniation and radiculitis, lumbar interlaminar epidural injections are strongly recommended for short-term relief, although this recommendation may change when higher quality evidence becomes available. Interlaminar epidural injections are not highly recommended for long-term relief. For those with spinal stenosis and discogenic pain without disc herniation and radiculitis, the use of lumbar intralaminar epidural injection is not highly recommended. For managing chronic low back and lower extremity pain, the use of transforaminal epidural injections is strongly recommended.

American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Section on Disorders of the Spine and Peripheral Nerves (AANS/CNS, 2005)

http://www.spinesection.org/fusion_guidelines.php

The use of facet epidural injections or lumbar epidural injections is not recommended for long-term treatment of low back pain. The use of lumbar epidural injections is recommended, however, as a treatment option that provides temporary, symptomatic relief in selected patients with low back pain.

Recent Technology Assessments

Canadian Agency for Drugs and Technologies in Health (CADTH, 2007)

http://www.cadth.ca/media/pdf/I3003_tr_Facet_Joint_Injections_e.pdf. Facet joint injections should be used as an adjunct to other forms of conservative treatment, such as physical exercise, rather than as a stand-alone treatment.

The Cochrane Collaboration (2009)

<http://www2.cochrane.org/reviews/en/ab001824.html>

There is not enough evidence to recommend the use of injection therapy for sub-acute and chronic low back pain.

Institute for Clinical Systems improvement (2004)

http://www.icsi.org/technology_assessment_reports_-_active/ta_fluoroscopically_guided_transforaminal_epidural_steroid_injections_for_lumbar_radicular_pain.html

When performed by an experienced physician, fluoroscopically-guided epidural steroid injections are generally safe. There is limited information, however, to comment on the short- or long-term efficacy of epidural steroid injections.

Coverage Policies

Centers for Medicare and Medicaid Services (CMS): Medicare currently does not have a National Coverage Determination (NCD) for spinal injections.

Representative local coverage determinations for epidural and transforaminal epidural injections indicate that both types of injections may only be used in the presence of radiculopathy. Therapeutic facet joint/nerve block injections may be considered for coverage provided that:

- Injections do not exceed a frequency parameter of more than once every two (2) months for a specific region (cervical/thoracic, lumbosacral);
- Initial pain relief of greater than or equal to (\geq) 80%-90% with the ability to perform previously painful maneuvers and persistent pain relief for a minimum of six (6) weeks of \geq 50% with the continued ability to perform previously painful maneuvers; and

- Appropriate consideration is given to the adverse effects (e.g., adrenal suppression of corticosteroid injections).

Aetna: Aetna considers any of the following injections or procedures medically necessary for the treatment of back pain; provided, however, that only one invasive modality or procedure will be considered medically necessary at a time.

- Epidural steroid injections are considered medically necessary when:
 1. Intraspinal tumor or other space-occupying lesion has been ruled out as a cause of pain; and
 2. The patient has failed to improve after two or more weeks using conservative measures; and
 3. Epidural steroid injections beyond the first set of three injections are provided as part of a comprehensive pain management program.
- Selective nerve root blocks are considered medically necessary in the treatment of persons with radiculopathy when non-invasive measures have failed and when any of the following conditions are met:
 1. Radicular pain is due to post-surgical or post-traumatic scarring; or
 2. Radicular pain when a surgically correctable lesion cannot be identified; or
 3. Radicular pain in persons with surgically correctable lesions but who are not surgical candidates.

Humana: Humana members may be eligible for epidural steroid injections for back and neck pain when all of the following criteria are met:

1. Failure to improve after six weeks of conservative therapy; and
2. Pain is radicular in nature; and
3. With low back pain, radicular pain radiates below the knee.

Members may be eligible for lumbar facet joint injections or medical branch nerve blocks when all of the following criteria are met:

1. Absence of radiculopathy; and
2. Since initial diagnosis, back pain is not responsive to conservative therapy; and
3. There are no more than three levels of facet joint injections per side, per region; and
4. Pain is aggravated by rotation, extension, or lateral bending of the spine and is not associated with neurological deficits.

UnitedHealthCare: Facet joint injections are unproven for the treatment of chronic spinal pain while epidural steroid injections are proven for treatment of sub-acute sciatica or low back radicular pain caused by disc herniation or degenerative changes in the vertebrae. Epidural steroid injections have a role in short-term management of low back pain when the symptoms of nerve root irritation and/or low back pain are due to disc extrusions and/or contained herniations and pain has been unresponsive to conservative treatment.

Ongoing Research (from www.clinicaltrials.gov)

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
Franklin Pierce University University of Colorado, Denver, NCT00786981/Epidural Steroid Injection Versus Epidural Steroid Injection and Manual Physical Therapy and Exercise in the Management of Lumbar Spinal Stenosis; a Randomized Clinical Trial	RCT	Change in disability as measured by the Modified Oswestry Disability Index	<ul style="list-style-type: none"> • 50 Years to 90 Years • N=80 	Epidural steroid injection plus physical therapy vs. Epidural steroid injection	May 2011
Coastal Orthopedics & Sports Medicine Vertos Medical, Inc., NCT00995371/Study of Epidural Steroid Injection (ESI) Versus Minimally Invasive Lumbar Decompression (MILD®) in Patients With Symptomatic Lumbar Central Canal Stenosis	RCT	Changes in back pain (as by Visual Analog Scale); Changes in quality of life on SF-12; change in function as measured by the Oswestry Disability Index and Zürich Claudication Questionnaire	<ul style="list-style-type: none"> • 18 Years and older • N=40 	MILD® (Minimally Invasive Lumbar Decompression) vs. Epidural Steroid Injection	June 2011
Pain Management Center of Paducah, NCT01053273/A Randomized, Equivalence Trial of Percutaneous Lumbar Adhesiolysis and Caudal Epidural Steroid Injections	RCT	Numeric rating scale (NRS), Oswestry Disability Index (ODI), duration of significant pain relief, opioid intake, and return to work	<ul style="list-style-type: none"> • 18 Years and older • N=120 	Caudal Epidural Injection vs. percutaneous adhesiolysis	January 2014

APPENDIX B
Radiofrequency Denervation and Intradiscal Electrothermal Therapy

Introduction

Radiofrequency denervation

Radiofrequency denervation (also known as radiofrequency neurotomy) is a type of injection procedure that uses heat to cauterize the affected nerve(s) thought to be associated with back pain. This procedure attempts to interrupt pain signals from these nerves, thereby reducing pain perception by the brain.

On the day of the procedure, patients are advised to avoid engaging in any strenuous activities. Patients may continue to take their normal medications except for blood-thinning medications. The patient lies face down on an X-ray table. The skin over the lower back is cleaned and numbed. The physician uses fluoroscopy to help advance the placement of the needle into the desired location. A small amount of current is passed through the needle to ensure that it is next to the target nerve; this may briefly cause facet joint or sacroiliac pain. The nerves are then numbed to minimize facet or sacroiliac joint pain while the lesion is being created. The process is repeated for up to 1-5 additional nerves. The entire procedure can last between 30 and 90 minutes and is performed in an outpatient setting. Patients are usually able to resume their normal activities in a short period. Risks associated with this procedure include pain or discomfort around the injection site, worsened facet or sacroiliac joint pain, permanent nerve pain, infection, and bleeding.

Intradiscal electrothermal therapy (IDET)

IDET involves the insertion of a probe into the disc(s) thought to be the source of pain and application of heat through a catheter in the disc. It is not known how IDET reduces pain. Proposed mechanisms of action include thermal destruction of nerve endings in the posterior disc wall; thickening of the collagen, which changes its form, thus destroying the painful nerves near the disc; stimulation of new collagen formation; and destruction of inflammatory or pain mediators within the disc tissue.

Using X-ray guidance, an electrothermal catheter is inserted through a needle and guided into the proper position. The temperature of the catheter is slowly increased to 90° Celsius (195° Fahrenheit). The heat shrinks and repairs the tears in the disc wall. The catheter is removed and the disc is then injected with small amounts of antibiotic and anesthetic to reduce the risk of infection and diminish discomfort, respectively. The procedure is performed on an outpatient basis. Several discs may be treated during a single session. The most common complaint is mild irritation at the needle insertion site after the local anesthetic has worn off. Other risks associated with the procedure include bleeding, infection, and nerve damage.

Professional Organization and Agency Recommendations

Radiofrequency Denervation

American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010)

http://journals.lww.com/anesthesiology/Fulltext/2010/04000/Practice_Guidelines_for_Chronic_Pain_Management.13.aspx

Radiofrequency ablation of the medial branch nerves to the facet joint should be performed for low back pain when previous therapeutic injections have provided temporary relief. Radiofrequency ablation of the dorsal root ganglion should not be routinely used in the treatment of lumbar radicular pain.

The American Pain Society (APS, 2009)

http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx

There is insufficient evidence to adequately evaluate the benefits of radiofrequency denervation for patients with persistent nonradicular low back pain. The evidence supporting the use of radiofrequency denervation for low back pain is limited.

Though radiofrequency denervation appears to be safe, there appears to be a trend towards increased pain immediately after the procedure as compared to sham denervation.

American Society of Interventional Pain Physicians (AIPP, 2009)

<http://www.painphysicianjournal.com/2009/july/2009;12;699-802.pdf>

The level of evidence for lumbar radiofrequency neurotomy is limited. Despite the limited evidence for radiofrequency neurotomy, the procedure is strongly recommended for the management of low back pain.

Intradiscal Electrothermal Therapy

American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010)

http://journals.lww.com/anesthesiology/Fulltext/2010/04000/Practice_Guidelines_for_Chronic_Pain_Management.13.aspx

IDET may be considered for young active patients with early single-level degenerative disc disease and well-maintained disc height.

The American Pain Society (APS, 2009)

http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx

There is insufficient evidence to evaluate adequately, the benefits of IDET for patients with persistent nonradicular low back pain.

American Society of Interventional Pain Physicians (AIPP, 2009)

<http://www.painphysicianjournal.com/2009/july/2009;12;699-802.pdf>

The level of evidence for IDET is limited. Based on this level of evidence, the procedure is not recommended for treatment of low back pain.

Recent Technology Assessments

Radiofrequency denervation

National Institute for Health and Clinical Excellence (NICE, 2009)

<http://www.nice.org.uk/nicemedia/live/11115/31119/31119.pdf>

The current evidence on the safety and efficacy of the procedure for low back pain does not appear to be adequate to support its use without special arrangements for consent, audit, or research.

The Cochrane Collaboration (2003)

<http://www2.cochrane.org/reviews/en/ab004058.html>

Radiofrequency denervation may not relieve pain originating from the lumbar discs. The evidence on the effects for low-back joint pain is conflicting and there is some evidence to suggest that it does not relieve pain for the lower back.

Intradiscal electrothermal therapy

National Institute for Health and Clinical Excellence (NICE, 2009)

<http://guidance.nice.org.uk/IPG319>

This procedure should only be used with special arrangements for clinical governance, as the current evidence on safety and efficacy for low back pain is inconsistent.

California Technology Assessment Form (CTAF, 2003)

<http://www.ctaf.org/content/assessment/detail/551>

IDET with either the radionics RF system or the Oratec IDET system does not meet CTAF criteria 1-5.

Coverage Policies

Radiofrequency Denervation

Centers for Medicare and Medicaid Services (CMS): Medicare currently does not have a National Coverage Determination (NCD) for radiofrequency denervation. An identified local coverage determination for paravertebral facet joint denervation indicates that this procedure is appropriate following the results of previous diagnostic and therapeutic paravertebral facet joint blockade. This procedure may be considered, provided that:

1. Injections do not exceed a frequency parameter of more than once every two (2) months for a specific region (cervical/thoracic, lumbosacral);
2. Initial pain relief of greater than or equal to (\geq) 80%-90% with the ability to perform previously painful maneuvers and persistent pain relief for a minimum of six (6) weeks of \geq 50% with the continued ability to perform previously painful maneuvers; and
3. Appropriate consideration is given to the adverse effects (e.g., adrenal suppression of corticosteroid injections).

Aetna: Radiofrequency facet denervation is considered medically necessary for treatment of members with back pain with or without sciatica in the outpatient setting when all of the following criteria are met:

1. The member has experienced severe pain-limiting activities of daily living for at least 6 months; and
2. Member has not had prior spinal fusion surgery; and
3. Neuroradiologic studies have failed to confirm disc herniation; and
4. There is no significant narrowing of the vertebral canal or presence of spinal instability requiring surgery; and
5. The member has tried and failed conservative treatment options; and
6. A trial of facet joint injections has been successful in relieving pain.

Anthem: Radiofrequency neurolysis of lumbosacral facet pain is considered medically necessary when all of the following conditions are met:

1. No prior spinal fusion surgery has been performed; and
2. The pain is not radicular in nature; and
3. Low back pain evidenced by the absence of nerve root compression is documented in the patient medical record; and
4. Pain has been resistant to 3 months of conservative treatment and it is documented in the medical record; and
5. A diagnostic, temporary block with local anesthetic of the facet nerve or injection under fluoroscopic guidance into the facet joint resulted in at least 50% reduction in pain; and
6. A minimum of 6 months has elapsed since prior RF treatment.

CIGNA: Radiofrequency ablation of chronic spinal pain is covered when all of the following criteria are met:

1. Severe pain that is unresponsive to at least 6 months of conservative medical treatment; and
2. The pain is of face joint origin and medial branch block/injection of the fact joint with local anesthetic results in either the elimination of marked decrease in the intensity of pain; and
3. Clinical findings do not suggest any other obvious source of the pain.

Humana: Members may be eligible for facet denervation for the following indications:

1. Severe neck or back pain; and
2. Must be at least 3 months since the initial diagnosis of neck or back pain that has not responded to conservative therapy; and
3. A diagnostic, temporary facet joint injection(s) that has been performed and has provided significant pain reduction; and
4. No more than three levels of facet joints per side, per region may be treated during a session.

UnitedHealthCare: Radiofrequency ablation is proven for the treatment of chronic thoracic and low back pain when confirmed by medial branch block injection with subsequent improvement. However, it is unproven in the treatment of all other sources of spinal or orthopedic pain for negative response to medial blocks and specific causes of spinal pain (e.g. disc herniation).

Intradiscal Electrothermal Therapy

Centers for Medicare and Medicaid Services (CMS):

Effective September 29, 2008, CMS determined that thermal intradiscal procedures (TIPs) are not reasonable and necessary for the treatment of low back pain. This includes intradiscal thermal annuloplasty (IDTA), percutaneous intradiscal radiofrequency thermocoagulation (PIRFT), radiofrequency annuloplasty (RA), intradiscal biacuplasty (IDB), percutaneous (or plasma) disc decompression (PDD) or coblation, or targeted disc decompression (TDD).

[http://www.cms.gov/mcd/viewncd.asp?ncd_id=150.11&ncd_version=1&basket=ncd:150.11:1:Thermal+Intradiscal+Procedures+\(TIPs\)](http://www.cms.gov/mcd/viewncd.asp?ncd_id=150.11&ncd_version=1&basket=ncd:150.11:1:Thermal+Intradiscal+Procedures+(TIPs)).

Aetna: Aetna considers thermal intradiscal procedures (TIPs) experimental and investigational for the relief of discogenic pain or other indications.

Anthem: Intradiscal annuloplasty procedures (including IDET, PIRFT, and IDB) are considered investigational and therefore not medically necessary.

CIGNA: CIGNA does not cover intradiscal electrothermal annuloplasty (e.g., IDET) because it is considered experimental, investigational, or unproven.

UnitedHealthCare: United Health Care considers IDET and PIRFT for the treatment of low back pain caused by a herniated intervertebral disc to be unproven.

Ongoing Research (from www.clinicaltrials.gov)

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
The Cleveland Clinic, NCT00750191/Placebo-Controlled Trial of Transdiscal Radiofrequency Annuloplasty	RCT	Effectiveness at 1 year	<ul style="list-style-type: none"> • 18 Years and older • N=8 	Transdiscal Radiofrequency Annuloplasty vs. Placebo	September 2010
Maastricht University Medical Center ZOL Hospital Genk Belgium Sint Jozef Hospital Bornem en Willebroek Belgium, NCT00991237/PRF Treatment for Patients With Chronic Lumbosacral Radicular Pain Compared to Conventional Medical Management	Comparative Cohort	Pain reduction at 2 months post-treatment	<ul style="list-style-type: none"> • 18 Years and older • N=29 	Pulsed Radiofrequency Denervation vs. Historical Control	March 2014

APPENDIX C
Interspinous Spacer Devices

Introduction

Interspinous spacer devices are implanted between two spinous processes. They hold the spine in a slight flexion position, in an effort to allow for decompression of the spinal cord or nerve roots. Consequently, they may limit spinal extension. However, the implants do not restrict rotation or lateral bending. Interspinous spacer devices are used in the treatment of spinal stenosis. This procedure serves as an alternative to spinal fusion and laminectomy.

The implantation of interspinous spacer devices is performed in an outpatient setting and is performed under local anesthesia. The patient may lay face down or on his or her side while the area is cleaned. A small incision is made in the back and an opening is created in the ligaments at the rear of the spine. Under fluoroscopic guidance, the surgeon uses a sizing distractor to create a space between the spinous processes. If the patient is conscious, he or she may be asked to bend his or her back to help create more space between the processes. After the implantation, the incision is closed and a bandage is applied. Strenuous activity should be avoided or limited for up to 6 weeks post-procedure. Physical therapy may be required in some cases. Some potential complications include incorrect positioning of implant, spinous process fracture, implant dislodgement, allergic reaction, and implant mechanical failure.

The X-STOP® Interspinous Process Decompression System is currently the only interspinous spacer system that has been approved by the U.S. Food and Drug Administration (FDA). The labeled indication for the device is for patients ages 50 and older or patients who are experiencing neurogenic intermittent claudication secondary to a confirmed diagnosis of lumbar spinal stenosis. The device has been approved for implantation at one or two lumbar levels. Contraindications to X-STOP include titanium or titanium alloy allergies, significant instability of the lumbar spine, cauda equina syndrome, and osteoporosis.

Professional Organization and Agency Recommendations

The American Pain Society (APS, 2009)

http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies_Surgery_and.14.aspx

Use of an interspinous spacer device is more effective compared to nonsurgical therapy for spinal stenosis. However, the results are only applicable to patients with either 1- or 2-level stenosis. Data on long-term follow-up are lacking.

North American Spine Society (NASS, 2007)

http://www.spine.org/Documents/NASSCG_Stenosis.pdf

At two-year follow-up, use of an interspinous spacer device in patients with mild-to-moderate symptoms of lumbar spinal stenosis was more effective than medical/interventional treatment. However, this is based upon only one high quality randomized controlled trial and until more evidence is published, no recommendation can be made.

National Institute for Health and Clinical Excellence (NICE, 2006)

<http://www.nice.org.uk/nicemedia/live/11162/31350/31350.pdf>

Based on current evidence, there appear to be no major safety concerns associated with the implantation of interspinous spacer devices for those with lumbar spinal stenosis. However, the evidence on efficacy is limited and based only on short- to mid-term outcomes.

Recent Technology Assessments

California Technology Assessment Form (CTAF, 2006)

<http://www.ctaf.org/content/assessment/detail/528>

The use of the X-STOP interspinous process distractor device meets CTAF criteria 1-5 for safety, effectiveness, and improvement in health outcomes when used in the following patient population:

1. Age > 50 years old;
2. Moderate impairment of physical function, symptomatic lumbar spinal stenosis at no more than 2 levels;
3. Failed ≥ 6 months of non-operative, conservative care;
4. No evidence of radiculopathy; and
5. Image evidence of spinal stenosis.

Coverage Policies

Centers for Medicare and Medicaid Services (CMS): Medicare currently does not have a National Coverage Determination (NCD) for interspinous spacer devices. However, in August 2006, CMS approved a pass-through payment for X-STOP procedures, allowing for additional device payments when the X-STOP Interspinous

Process Decompression procedure is performed in a hospital outpatient setting. Representative local coverage determinations indicate that interspinous process decompression is medically reasonable and necessary for those who meet all of the following criteria:

1. Aged 50 or older suffering from (intermittent neurogenic claudication) secondary to a confirmed diagnosis of lumbar spinal stenosis;
2. Those with moderately impaired physical function who experience relief in flexion from their symptoms of leg/buttock/groin pain, with or without back pain; and
3. Patients who have undergone at least 6 months of non operative treatment

Aetna: Aetna considers interspinous distraction devices experimental and investigational.

Anthem: Anthem does not cover implanted devices that are used for the treatment of spinal stenosis, as they are considered investigational and not medically necessary.

Blue Cross Blue Shield Massachusetts (BCBS): BCBS covers the use of X-STOP Interspinous Process Decompression system for its Medicare HMO Blue and Medicare PPO Blue members only.

CIGNA: CIGNA does not cover interspinous spacer devices because they are considered experimental, investigational, or unproven.

Humana: Members are not eligible for the implantation of interspinous decompression spacers, as the technology is considered experimental.

Ongoing Research (from www.clinicaltrials.gov)

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
Norwegian University of Science and Technology, NCT00546949/Treatment of Lumbar Spinal Stenosis; Comparison of Two Different Surgical Methods; Mini-invasive Decompression to X-STOP	RCT	Zürich Claudication Questionnaire	<ul style="list-style-type: none"> • 50 Years to 85 Years • N=180 	Minimal invasive decompression vs. Interspinous device	December 2010
VertiFlex, Incorporated, NCT00692276/ Investigating Superior™ In Spinal Stenosis [ISS]	RCT	Effectiveness will be determined based on Zürich Claudication Questionnaire	<ul style="list-style-type: none"> • 45 Years and older • N=400 	Superion™ Interspinous Spacer vs. X-STOP® IPD® Device	June 2011
Synthes Spine, NCT00697827/ A Study of the In-Space Device for Treatment of Moderate Spinal Stenosis	RCT	Zürich Claudication Questionnaire	<ul style="list-style-type: none"> • 50 Years and older • N=500 	In-Space vs. X-STOP®	December 2011

APPENDIX D
Discectomy

Introduction

Lumbar discectomy is a surgical procedure to remove part of a bulging or herniated disc in an attempt to alleviate pressure on the surrounding nerve roots. Open discectomy involves making a small incision in the skin over the spine, removing some of the ligament and bone to access the disc, and removing some of the disc material.

Open discectomy is performed under general anesthesia and typically requires a one-day hospital stay. The patient lies face down or is in a kneeling position. The surgeon makes an incision in the skin over the affected area of the spine. The muscle is removed from the bone. Retractors are used to hold the muscle and skin away from the surgical site so that the surgeon may have clear access to the problem disc. In some cases, ligaments and bone must be removed in order to have better access to the disc without damaging the nerve. Once the surgeon can visualize the lamina, disc, and other surrounding structures, he or she will remove the section of the disc that is protruding from the disc wall. No material is used to replace the removed disc. The incision is then closed and the patient is taken to a recovery room. After the procedure, patients should avoid strenuous activity and heavy lifting for some time. Sedentary work may be resumed within 1-2 weeks.

In addition to the open procedure, there are also minimally-invasive approaches to discectomy. Microdiscectomy is a form of discectomy where only the ruptured portion of the disc is removed. To perform this procedure, the surgeon utilizes a surgical microscope. Alternatively, the surgeon may use an endoscope to help guide the surgical approach (percutaneous discectomy). With microdiscectomy, the surgeon makes a very small incision in the lower back over the problem disc. A small portion of the vertebra is removed. An X-ray is used to help guide the surgeon to the right disc. Once the bony material has been removed, the surgeon locates the area near the pinched nerve root. With the aid of a microscope or endoscope, the ruptured portion of the disc is removed as well as any disc fragments that have broken off in the process.

Discectomy is generally a safe procedure but it is associated with some risks. These risks include infection, bleeding, injury to surrounding blood vessels or nerves, leaking cerebrospinal fluid, and injury to the dura mater, the outer layer of the spinal cord. An open discectomy may require an overnight hospital stay, while microdiscectomy and percutaneous discectomy are typically performed on an outpatient basis.

Professional Organization and Agency Recommendations

The American Pain Society (APS, 2009)

http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies_Surgery_and.14.aspx

For those with persistent and disabling radiculopathy due to a herniated lumbar disc, standard open discectomy and microdiscectomy are associated with moderate short-term (6-12 weeks) benefits compared to nonsurgical therapy. However, differences in outcomes in some trials are diminished or are nonexistent after 1-2 years.

National Institute for Health and Clinical Excellence (NICE, 2005-2006)

<http://www.nice.org.uk/nicemedia/live/11179/31406/31406.pdf>

Current evidence suggests there are no major safety concerns. There is however, limited evidence on the efficacy based on uncontrolled case series. Evidence from small randomized controlled trials show conflicting results.

Recent Technology Assessments

California Technology Assessment Form (CTAF, 2008)

Laser discectomy is not recommended for the treatment of symptomatic lumbar disc prolapse, as it does not meet CTAF criteria 2-5 for safety, efficacy, and improvement in health outcomes.

Coverage policies

Centers for Medicare and Medicaid Services (CMS): Medicare does not have a National Coverage Determination (NCD) or any representative local coverage determinations for discectomy or microdiscectomy.

Aetna: Percutaneous lumbar discectomy is considered medically necessary when all the following conditions are met:

1. Member is otherwise a candidate for open laminectomy; and
2. Has failed 6 months of conservative treatment; and
3. Diagnostic studies show that the nuclear bulge of the disc is contained within the annulus; and
4. Member has not had previous surgery or chemonucleolysis of the disc being treated; and
5. Members must have clinical symptoms that are consistent with the level of disc involvement.

CIGNA: CIGNA does not cover automated percutaneous lumbar discectomy, laser discectomy (percutaneous or laparoscopic), laser-assisted disc decompression (LADD), or laser disc decompression as they are considered to be experimental, investigational, or unproven.

Humana: Member may be eligible for lumbar discectomy for the following indications:

1. Rapidly progressive neurologic signs/symptoms of lumbar spine compression confirmed by imaging studies; or
2. Spinal fractures confirmed by imaging studies; or
3. Herniated disc, confirmed by imaging studies, radicular neck, or back pain that has persisted despite conservative treatment.

UnitedHealthCare: United Health Care considers both percutaneous disc decompression, automated percutaneous lumbar discectomy (APLD) and percutaneous laser disc decompression (PLDD) unproven for the treatment of low back pain cause by a herniated intervertebral disc.

Ongoing Research (from www.clinicaltrials.gov)

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
University of Manitoba, NCT00927056/Evaluation of Minimally Invasive Microdiscectomy Versus Conventional Open Microdiscectomy For Lumbar Herniated Disc	RCT	Physical activity monitor	<ul style="list-style-type: none"> • 18 Years to 90 Years • N=50 	Minimally Invasive Microdiscectomy vs. Conventional Open Microdiscectomy	TBD
Norwegian University of Science and Technology, NCT00546949/Treatment of Lumbar Spinal Stenosis; Comparison of Two Different Surgical Methods; Mini-invasive Decompression to X-stop	RCT	Zürich Claudication Questionnaire	<ul style="list-style-type: none"> • 50 Years to 85 Years • N=180 	Minimal invasive decompression vs. X-stop	December 2010
Medtronic Spine LLC, NCT00905359/Neurogenic Intermittent Claudication Evaluation Study	RCT	Zürich Claudication Questionnaire	<ul style="list-style-type: none"> • 21 Years and older • N=280 	Aperius™ PercLID™ System and Standalone Decompressive Surgery vs. Standalone Decompressive Surgery	October 2015
Coastal Orthopedics & Sports Medicine Vertos Medical, Inc., NCT00995371/Study of Epidural Steroid Injection (ESI) Versus Minimally Invasive Lumbar Decompression (MILD®) in Patients With Symptomatic Lumbar Central Canal Stenosis	RCT	10-point visual analog scale and pain medication requirements, Oswestry Disability, Zürich Claudication Questionnaire, Work Production Index, Quality of Life Physical Component Score (PCS) on SF-12	<ul style="list-style-type: none"> • 18 Years and older • N=40 	MILD® (Minimally Invasive Lumbar Decompression) vs. Epidural Steroid Injection	June 2011

APPENDIX E
Laminectomy & Spinal Fusion

Introduction

A lumbar laminectomy (also known as open decompression) is a surgical procedure used to alleviate pain that is caused by neural impingement resulting from spinal stenosis. The surgery involves the removal of the lamina bone, a thin bony layer that covers and protects both the spinal canal and spinal cord. Surgeons may also remove bone spurs from the facet joints during laminectomy; this also helps to remove pressure from the spinal nerves.

Laminectomies are usually performed under general anesthesia. First, an incision is made over the lower back. The surgeon uses a retractor to spread the muscles and fatty tissues of the spine apart to expose the lamina. After the laminectomy, the patient is moved to a recovery room for observation. Hospital stays may range from one to 3 days. Activities such as lifting and bending should be avoided for a few weeks after the laminectomy.

In addition to a laminectomy, a spinal fusion may be performed in order to achieve adequate decompression of the nerve root. The spine is stabilized by fusing two or more vertebrae together, using metal rods, bone grafts, or screws. There are a number of potential reasons to fuse vertebrae. These include treatment of a fractured vertebra; correction of spinal deformities; elimination of pain from painful motion; and treatment of spinal instability. Spinal fusions are classified as either simple (1 or 2 disc levels or a single surgical approach) or complex (more than 2 disc levels or a combined anterior and posterior approach). Fusion may or may not use instrumentation such as screws, plates, or cages. Instrumentation is generally used as an internal splint to hold the vertebrae together while the bone grafts heal. Bone or bone substitutes are used to help fuse the vertebrae together. The bone may be taken from another bone in the patient (autograft) or from a bone bank (allograft).

During the operation, the surgeon removes the lamina to help relieve the pressure on the nerve. The surgeon then removes any additional bone that may impinge upon the affected nerve. Bone grafts are then added to the spine; these will eventually fuse with the spine to form a solid bone. Instrumentation may be added to provide additional stability while the grafts heal. There is generally more discomfort experienced after fusion surgery compared to other procedures and recovery takes much longer. Patients usually stay in the hospital for at least 3-4 days post-procedure. Substantial bone healing takes some time to achieve and the healing process varies from person to person. The indication of bone healing, as evidenced by an X-ray, is not attempted until approximately 6 weeks post-procedure. During this time, the patient's activity must be limited. The surgeon may recommend a post-operative rehabilitation program.

Risks associated with laminectomy and spinal fusion are rare but include nerve root damage, bowel or bladder incontinence, cerebrospinal fluid leakage, bleeding, and infection. Other complications, common to all types of major surgery, may include blood clots, myocardial infarction, pulmonary embolism, and pneumonia.

Professional Organization and Agency Recommendations

Laminectomy

American Pain Society (APS, 2009)

http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx

For patients with persistent and disabling leg pain due to spinal stenosis, either with or without degenerative spondylolisthesis, decompressive laminectomy is associated with moderate benefits, compared to nonsurgical therapy through 1 to 2 years. However, effects appear to diminish with long-term follow-up.

North American Spine Society (NASS, 2007)

http://www.spine.org/Documents/NASSCG_Stenosis.pdf

At long-term follow-up (8-10 years) compared to medical/interventional treatment, surgical decompression treatment of spinal stenosis is consistently supported. In patients with severe symptoms of lumbar spinal stenosis, decompressive surgery alone is effective about 80% of the time while medical/interventional treatment alone is effective about 33% of the time. In patients with severe symptoms of lumbar spinal stenosis, surgery is more effective than medical/interventional treatment.

Spinal Fusion

National Institute for Health and Clinical Excellence (NICE, 2009)

<http://www.nice.org.uk/nicemedia/live/12138/46410/46410.pdf>

The current evidence on the safety and efficacy of lateral interbody fusion is inadequate in both quantity and quality. Therefore, this procedure should only be performed under special arrangements.

North American Spine Society (NASS, 2007)

http://www.spine.org/Documents/NASSCG_Stenosis.pdf

For patients with spinal stenosis and spondylolisthesis, decompression with fusion results in better surgical outcomes than for patients who undergo decompression alone. For patients with lumbar spinal stenosis without spondylolisthesis or instability, there is no evidence to support the addition of fusion.

American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Section on Disorders of the Spine and Peripheral Nerves (AANS/CNS, 2005)

http://www.spinesection.org/fusion_guidelines.php

- Lumbar fusion is not recommended following disc excision in patients with a herniated lumbar disc causing radiculopathy. However, spinal fusion is recommended as a potential supplemental procedure in patients with a herniated disc in whom there is evidence of preoperative lumbar spinal

deformity or instability. It is also recommended as a potential surgical adjunct in patients with chronic axial low back pain associated with radiculopathy due to a herniated disc.

- Posterolateral fusion (PLF) is recommended for patients with spinal stenosis and associated degenerative spondylolisthesis who require decompression. Pedicle screw fixation added to lumbar PLF should be considered as a treatment option for those with spinal stenosis and spondylolisthesis in which there is preoperative evidence of spinal instability.

Recent Technology Assessments

Laminectomy

There are no recent technology assessments of laminectomy for low back pain.

Spinal Fusion

Agency for Healthcare Research and Quality (AHRQ, 2006)

<http://www.cms.gov/determinationprocess/downloads/id41ta.pdf>

The amount of evidence on lumbar spinal fusion does not demonstrate either short- or long-term benefits when compared with non-surgical treatment, especially for patients over 65 years of age, or for those with degenerative disc disease.

Agency for Healthcare Research and Quality (AHRQ, 2001)

<http://www.ahrq.gov/clinic/epcsums/stenosum.htm>

Evidence from two RCTs seems to suggest that instrumentation in addition to fusion does not improve surgical outcomes among patients with spondylolisthesis.

Evidence from one study suggests that surgical outcomes from fusion are better in comparison to those among patients who undergo decompressive surgery alone.

Coverage Policies

Laminectomy

Centers for Medicare and Medicaid Services (CMS): Medicare does not have a National Coverage Determination (NCD) or current local coverage determinations for laminectomy.

Aetna: Lumbar laminectomy is considered medically necessary for individuals with a herniated disc when all of the following criteria are met:

1. The member's daily living activities are limited by persistent pain radiating from the back down to the lower extremity;
2. Physical findings of nerve root tension are present;
3. Demonstrated presence of neurological abnormalities;

4. Imaging studies which indicate and correspond to clinical findings of specific affected nerve root;
5. Members have failed at least 6 weeks of conservative therapy; and
6. All other sources of pain have been ruled out.

Spinal Fusion

Centers for Medicare and Medicaid Services (CMS): Medicare currently does not have a National Coverage Determination (NCD) for spinal fusion surgery. A meeting of the Medicare Evidence Development and Coverage Advisory Committee (MedCAC) meeting was held in November 2006 to discuss this topic. The results of the voting demonstrate a need for better evidence to conclude that lumbar spinal fusion leads to better health outcomes for patients with low back pain due to degenerative disc disease.

Aetna: Lumbar fusion is considered medically necessary for the following (but not necessarily limited to): spinal fracture, spondylolisthesis with segmental instability, and spinal stenosis with unremitting pain, all as confirmed by imaging studies.

CIGNA: CIGNA covers lumbar fusion with or without spinal instrumentation for multiple adjacent spinal segment levels for a number of conditions including progressive neurological impairment, spinal deformity, and neural compression after spinal fracture. CIGNA covers lumbar fusion with or without spinal instrumentation for up to two adjacent spinal segment levels for either:

1. Chronic low back pain when both pain and disability has failed to respond to at least six consecutive months of conservative treatment; or
2. Degenerative disc disease has been demonstrated on appropriate imaging studies.

CIGNA also covers lumbar fusion as treatment for spinal instability with persistent pain and disability. CIGNA does not cover anterior interbody fusion, extreme lateral interbody fusion, or axial interbody fusion, as they are considered experimental.

Humana: Members are eligible under the plan for lumbar fusion surgery for any of the following (but not limited to) spinal stenosis associated with spondylolisthesis, spinal fracture with instability or neural compression, or failure of three months of conservative treatment.

United Health Care: United Health Care covers spinal fusion, with the addition of instrumentation, imaging, and discectomy (when performed). United Health Care however considers the following spinal fusion techniques to be unproven: laparoscopic anterior lumbar interbody fusion (LALIF), minimally-invasive transforaminal lumbar interbody fusion (MITLIF) and axial lumbar interbody fusion via a presacral approach (AxiaLIF).

Ongoing Research (from www.clinicaltrials.gov)

Trial Sponsor/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
Exactech, NCT00254852/Evaluation of Radiographic and Patient Outcomes Following Lumbar Spine Fusion Using Demineralized Bone Matrix (DBM) Mixed With Autograft	RCT	Radiographic evidence of fusion on x-rays	<ul style="list-style-type: none"> • 21 Years and older • N = 94 	Posterior Lateral Fusion (PLF), Anterior Lumbar Interbody Fusion (ALIF), Transforaminal lumbar interbody fusion (TLIF), Posterior lumbar interbody fusion (PLIF), Extreme lateral interbody fusion (XLIF) supplemented with Optecure vs. PLF, ALIF, TLIF, PLIF, XLIF non-supplemented	January 2010
Jyväskylä Central Hospital Tampere University Hospital University of Tampere, NCT00834015/Spinal Fusion Study	RCT	Pain disability quality of life	<ul style="list-style-type: none"> • 20 Years and older • N = 100 	Lumbar spinal fusion patients and postoperative exercise therapy vs. Lumbar spinal fusion patients without postoperative exercise therapy	December 2012
Interventional Spine, Inc., NCT00878579/Percutaneous Dynamic Stabilization (PDS) System Versus Fusion for Treating Degenerative Disc Disease	RCT	Improvement in Oswestry Disability Index (ODI)	<ul style="list-style-type: none"> • 18 Years to 70 Years • N = 292 	Percutaneous Dynamic Stabilization System vs. TLIF with Autograft and Pedicle Screws	TBD

APPENDIX F
*Systematic Reviews on Conservative Treatment of Low Back Pain to
Support American College of Physicians/American Pain Society Joint
Guideline Statements*

Nonpharmacologic Therapies for Acute and Chronic Low Back Pain: A Review of the Evidence for an American Pain Society/American College of Physicians Clinical Practice Guideline

Roger Chou, MD, and Laurie Hoyt Huffman, MS

Background: Many nonpharmacologic therapies are available for treatment of low back pain.

Purpose: To assess benefits and harms of acupuncture, back schools, psychological therapies, exercise therapy, functional restoration, interdisciplinary therapy, massage, physical therapies (interferential therapy, low-level laser therapy, lumbar supports, short-wave diathermy, superficial heat, traction, transcutaneous electrical nerve stimulation, and ultrasonography), spinal manipulation, and yoga for acute or chronic low back pain (with or without leg pain).

Data Sources: English-language studies were identified through searches of MEDLINE (through November 2006) and the Cochrane Database of Systematic Reviews (2006, Issue 4). These electronic searches were supplemented by hand searching of reference lists and additional citations suggested by experts.

Study Selection: Systematic reviews and randomized trials of 1 or more of the preceding therapies for acute or chronic low back pain (with or without leg pain) that reported pain outcomes, back-specific function, general health status, work disability, or patient satisfaction.

Data Extraction: We abstracted information about study design, population characteristics, interventions, outcomes, and adverse events. To grade methodological quality, we used the Oxman criteria for systematic reviews and the Cochrane Back Review Group criteria for individual trials.

Data Synthesis: We found good evidence that cognitive-behavioral therapy, exercise, spinal manipulation, and interdisciplinary rehabil-

itation are all moderately effective for chronic or subacute (>4 weeks' duration) low back pain. Benefits over placebo, sham therapy, or no treatment averaged 10 to 20 points on a 100-point visual analogue pain scale, 2 to 4 points on the Roland-Morris Disability Questionnaire, or a standardized mean difference of 0.5 to 0.8. We found fair evidence that acupuncture, massage, yoga (Viniyoga), and functional restoration are also effective for chronic low back pain. For acute low back pain (<4 weeks' duration), the only nonpharmacologic therapies with evidence of efficacy are superficial heat (good evidence for moderate benefits) and spinal manipulation (fair evidence for small to moderate benefits). Although serious harms seemed to be rare, data on harms were poorly reported. No trials addressed optimal sequencing of therapies, and methods for tailoring therapy to individual patients are still in early stages of development. Evidence is insufficient to evaluate the efficacy of therapies for sciatica.

Limitations: Our primary source of data was systematic reviews. We included non-English-language trials only if they were included in English-language systematic reviews.

Conclusions: Therapies with good evidence of moderate efficacy for chronic or subacute low back pain are cognitive-behavioral therapy, exercise, spinal manipulation, and interdisciplinary rehabilitation. For acute low back pain, the only therapy with good evidence of efficacy is superficial heat.

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For author affiliations, see end of text.

www.annals.org

Many nonpharmacologic therapies are available for treatment of low back pain. In 1 study of primary care clinicians, 65% reported recommending massage therapy; 55% recommended therapeutic ultrasonography; and 22% recommended, prescribed, or performed spinal manipulation (1). In another study, 38% of patients with spine disorders were referred to a physical therapist for exercise therapy, physical therapies, or other interventions (2). Other noninvasive interventions are also available, including psychological therapies, back schools, yoga, and interdisciplinary therapy.

Clinicians managing low back pain vary substantially in the noninvasive therapies they recommend (3). Although earlier reviews found little evidence demonstrating efficacy of most noninvasive therapies for low back pain (4–6), many more randomized trials are now available. This article summarizes current evidence on noninvasive therapies for low back pain in adults. It is part of a larger evidence review commissioned by the American Pain Society and the American College of Physicians to guide rec-

ommendations for management of low back pain (7). Pharmacologic therapies are reviewed in a separate article in this issue (8).

METHODS

Data Sources and Searches

An expert panel convened by the American Pain Society and American College of Physicians determined which

See also:

Print

Related articles 478, 505
Summary for Patients I-45

Web-Only

Appendix Tables
CME quiz
Conversion of graphics into slides
Audio summary

nonpharmacologic therapies would be included in this review. **Appendix Table 1** (available at www.annals.org) shows the 17 therapies chosen by the panel and how we defined and grouped them. Several therapies that have not been studied in the United States or are not widely available (such as acupressure, neuroreflexotherapy, spa therapy, and percutaneous electrical nerve stimulation) are reviewed in the complete evidence review (7). Therapies solely involving advice or back education are also reviewed separately, as are surgical and interventional pain procedures.

We searched MEDLINE (1966 through November 2006) and the Cochrane Database of Systematic Reviews (2006, Issue 4) for relevant systematic reviews, combining terms for low back pain with a search strategy for identifying systematic reviews. When higher-quality systematic reviews were not available for a particular intervention, we conducted additional searches for primary studies (combining terms for low back pain with the therapy of interest) on MEDLINE, the Cochrane Central Register of Controlled Trials, and PEDro. Full details of the search strategies are available in the complete evidence report (7). Electronic searches were supplemented by reference lists and additional citations suggested by experts. We did not include trials published only as conference abstracts.

Evidence Selection

We included all randomized, controlled trials meeting all of the following criteria: 1) reported in English, or in a non-English language but included in an English-language systematic review; 2) evaluated nonpregnant adults (>18 years of age) with low back pain (alone or with leg pain) of any duration; 3) evaluated a target therapy; and 4) reported at least 1 of the following outcomes: back-specific function, generic health status, pain, work disability, or patient satisfaction (9, 10).

We excluded trials of low back pain associated with acute major trauma, cancer, infection, the cauda equina syndrome, fibromyalgia, and osteoporosis or vertebral compression fracture.

Because of the large number of studies on therapies for low back pain, our primary source for trials was systematic reviews. When multiple systematic reviews were available for a target therapy, we excluded outdated systematic reviews, which we defined as systematic reviews with a published update or those published before 2000. When a higher-quality systematic review was not available for a particular therapy, we included all relevant randomized, controlled trials. We also supplemented systematic reviews with data from recent, large (>250 patients) trials.

Data Extraction and Quality Assessment

For each included systematic review, we abstracted information on search methods; inclusion criteria; methods for rating study quality; characteristics of included studies; methods for synthesizing data; and results, including the number and quality of trials for each comparison and outcome in patients with acute (<4 weeks' duration) low back

pain, chronic/subacute (>4 weeks' duration) low back pain, and back pain with sciatica. If specific data on duration of trials were not provided, we relied on the categorization (acute or chronic/subacute) assigned by the systematic review. For each trial not included in a systematic review, we abstracted information on study design, participant characteristics, interventions, and results.

We considered mean improvements of 5 to 10 points on a 100-point visual analogue pain scale (or equivalent) to be small or slight; 10 to 20 points, moderate; and more than 20 points, large or substantial. For back-specific functional status, we classified mean improvements of 2 to 5 points on the Roland-Morris Disability Questionnaire (RDQ; scale, 0 to 24) and 10 to 20 points on the Oswestry Disability Index (ODI; scale, 0 to 100) as moderate (11). We considered standardized mean differences of 0.2 to 0.5 to be small or slight; 0.5 to 0.8, moderate; and greater than 0.8, large (12). Some evidence suggests that our classification of mean improvements and standardized mean differences for pain and functional status are roughly concordant in patients with low back pain (13–18). Because few trials reported the proportion of patients meeting specific thresholds (such as >30% reduction in pain score) for target outcomes, it was usually not possible to report numbers needed to treat for benefit. When those were reported, we considered a relative risk of 1.25 to 2.00 for the proportion of patients reporting greater than 30% pain relief to indicate a moderate benefit.

Two reviewers independently rated the quality of each included trial. Discrepancies were resolved through joint review and a consensus process. We assessed internal validity (quality) of systematic reviews by using the Oxman criteria (**Appendix Table 2**, available at www.annals.org) (19, 20). According to this system, systematic reviews receiving a score of 4 or less (on a scale of 1 to 7) have potential major flaws and are more likely to produce positive conclusions about effectiveness of interventions (20, 21). We classified such systematic reviews as “lower quality”; those receiving scores of 5 or more were graded as “higher quality.”

We did not abstract results of individual trials if they were included in a higher-quality systematic review. Instead, we relied on results and quality ratings for the trials as reported by the systematic reviews. We considered trials receiving more than half of the maximum possible quality score to be “higher quality” for any quality rating system used (22, 23).

We assessed internal validity of randomized clinical trials not included in a higher-quality systematic review by using the criteria of the Cochrane Back Review Group (**Appendix Table 3**, available at www.annals.org) (24). When blinding was not feasible, we removed blinding of providers (for studies of acupuncture, spinal manipulation, and massage) or blinding of patients and providers (for studies of back schools, exercise, psychological interventions, interdisciplinary rehabilitation, and functional resto-

ration) as a quality criterion; thus, the maximum score was 10 or 9, respectively. We considered trials receiving more than half of the total possible score to be “higher quality” and those receiving less than or equal to half to be “lower quality” (22, 23).

Data Synthesis

We assessed overall strength of evidence for a body of evidence by using methods adapted from the U.S. Preventive Services Task Force (25). To assign an overall strength of evidence (good, fair, or poor), we considered the number, quality and size of studies; consistency of results among studies; and directness of evidence. Minimum criteria for fair and good quality ratings are shown in **Appendix Table 4** (available at www.annals.org).

Consistent results from many higher-quality studies across a broad range of populations support a high degree of certainty that the results of the studies are true (the entire body of evidence would be considered good quality). For a fair-quality body of evidence, results could be due to true effects or to biases operating across some or all of the studies. For a poor-quality body of evidence, any conclusion is uncertain.

To evaluate consistency, we classified conclusions of trials and systematic reviews as positive (the therapy is beneficial), negative (the therapy is harmful or not beneficial), or uncertain (the estimates are imprecise, the evidence unclear, or the results inconsistent) (20). We defined “inconsistency” as greater than 25% of trials reaching discordant conclusions (positive vs. negative), 2 or more higher-quality systematic reviews reaching discordant conclusions, or unexplained heterogeneity (for pooled data).

Role of the Funding Source

The funding source had no role in the design, conduct, or reporting of this review or in the decision to publish the manuscript.

RESULTS

Size of Literature Reviewed

We reviewed 1292 abstracts identified by searches for systematic reviews of low back pain. Of these, 96 seemed potentially relevant and were retrieved. A total of 40 systematic reviews (26–70) met inclusion criteria (see **Appendix Table 5** for quality ratings and **Appendix Table 6** for characteristics and results of the systematic reviews that evaluated efficacy; both are available at www.annals.org). We excluded 59 systematic reviews (71–129), most frequently because they met our criteria for outdated reviews or did not report results for patients with low back pain (**Appendix Table 7**, available at www.annals.org). Five recent, large (>200 patients) trials of acupuncture (130–132) and spinal manipulation or exercise (133, 134) supplemented the systematic reviews.

We found no systematic reviews of interferential therapy, low-level laser therapy, shortwave diathermy, ultra-

sonography, or yoga for low back pain. We identified 532 citations from 5 searches for randomized trials of these interventions. Three trials of interferential therapy (135–137), 7 trials of low-level laser therapy (138–144), 3 trials of shortwave diathermy (145–147), 3 trials of ultrasonography (148–150), and 3 trials of yoga (151–153) met inclusion criteria.

Spinal Manipulation, Massage, and Acupuncture

Spinal Manipulation

Sixty-nine unique trials on efficacy of spinal manipulation were included in 12 systematic reviews (15, 55–63, 68–71). Four other systematic reviews focused on harms associated with spinal manipulation (21, 64–67).

For acute low back pain, a higher-quality Cochrane review found spinal manipulation to be slightly to moderately superior to sham manipulation for short-term pain relief in a meta-regression analysis (weighted mean difference, –10 points on a 100-point visual analogue scale [95% CI, –17 to –2 points]) (15, 55). However, this estimate is mainly based on a lower-quality trial of patients with acute or subacute sacroiliac pain (154). Short-term effects on the RDQ (2 trials, 1 higher-quality) were moderate but did not reach statistical significance (weighted mean difference, –2.8 points [CI, –5.6 to 0.1 points]). Differences between spinal manipulation and therapies judged ineffective or harmful (traction, bed rest, home care, topical gel, no treatment, diathermy, and minimal massage) did not reach clinical significance for pain (weighted mean difference, –4 points [CI, –8 to –1 points]) and reached clinical but not statistical significance on the RDQ (weighted mean difference, –2.1 points [CI, –4.4 to 0.2 points]). There were no clear differences between spinal manipulation and usual care or analgesics (3 trials), physical therapy or exercises (5 trials), and back schools (2 trials).

For chronic low back pain, the Cochrane review found spinal manipulation moderately superior to sham manipulation (3 trials) and therapies thought to be ineffective or harmful (5 trials). Against sham manipulation, differences in short- and long-term pain averaged 10 and 19 points on a 100-point visual analogue scale, and differences for short-term function averaged 3.3 points on the RDQ. There were no differences between manipulation and general practitioner care or analgesics (6 trials), physical therapy or exercises (4 trials), and back school (3 trials). Evidence was insufficient to conclude that effectiveness of spinal manipulation varies depending on the presence or absence of radiating pain or the profession or training of the manipulator.

Five higher-quality systematic reviews reached conclusions generally consistent with those of the Cochrane review (58, 60, 61, 69, 70). Two recent, large trials (133, 134) not included in the systematic reviews also reported consistent results (**Appendix Table 8**, available at www.annals.org [130, 132–134, 155]). For low back pain of

unspecified duration, 1 higher-quality trial (681 patients) found no differences in pain, functional status, or other outcomes between patients randomly assigned to chiropractic versus medical management (133). The other trial (1334 patients) found spinal manipulation to be slightly superior to usual care for pain and disability (about 5 points on 100-point scales) after 3 months in patients with subacute or chronic low back pain, although effects were not as pronounced after 12 months, and differences on the RDQ did not reach clinical significance (about 1 point) (134). Manipulation and exercise did not significantly differ, and the addition of manipulation to exercise therapy was no better than exercise alone.

Two lower-quality systematic reviews found spinal manipulation superior to some other effective interventions (57, 68). However, these conclusions were based on sparse data (1 to 3 trials, often lower-quality and often with small sample sizes).

Five systematic reviews consistently found that serious adverse events after spinal manipulation (such as worsening lumbar disc herniation or the cauda equina syndrome) were very rare (64–67, 69). One systematic review found no serious complications reported in more than 70 controlled clinical trials (65). Including data from observational studies, the risk for a serious adverse event was estimated as less than 1 per 1 million patient visits (66, 67).

One higher-quality randomized trial evaluated a decision tool for identifying patients more likely to benefit from spinal manipulation (156). It found that patients who met at least 4 of 5 predefined criteria had a higher likelihood of greater than 50% improvement in ODI scores when randomly assigned to spinal manipulation (odds ratio [OR], 60.8 [CI, 5.2 to 704.7]) compared with those who had negative findings according to the rule who were randomly assigned to manipulation (OR, 2.4 [CI, 0.83 to 6.9]) and those with positive findings according to the rule who were randomly assigned to exercise (OR, 1.0 [CI, 0.28 to 3.6]). However, no studies have examined how applying the decision tool versus not using the tool affects clinical outcomes, and the decision tool may not be practical for many primary care settings because it requires the clinician to perform and interpret potentially unfamiliar physical examination maneuvers and administer a specific questionnaire. A more pragmatic version of the decision tool has not been prospectively validated (157).

Massage

Eight unique trials of massage were included in 2 systematic reviews (26, 27, 69). For acute low back pain, evidence is insufficient to determine efficacy of massage (1 lower-quality trial evaluating a minimal massage intervention [158]). One higher-quality trial found combined treatment with massage, exercise, and education to be superior to exercise and education alone for subacute or chronic low back pain 1 month after treatment (159).

For chronic low back pain, a higher-quality Cochrane review found no clear differences between massage and manipulation at the end of a course of treatment (3 lower-quality trials) (26, 27). Superficial massage was inferior to transcutaneous electrical nerve stimulation (TENS) for relieving pain in 1 higher-quality trial (160). Single trials found massage similar in effectiveness to corsets and exercise and moderately superior to relaxation therapy, acupuncture, sham laser, and self-care education (26, 27). Nearly all trials assessed outcomes only during or shortly after (within 1 month) a course of treatment. However, 1 higher-quality trial found that beneficial effects of massage compared with acupuncture and self-care education persisted for 1 year (161). Results of a second systematic review are consistent with the Cochrane review (69).

Only 1 trial (rated higher-quality) directly compared different massage techniques. It found acupuncture massage superior to classical (Swedish) massage (162). Massage seemed more effective in trials that used a trained massage therapist with many years of experience or a licensed massage therapist (26, 27). Evidence was insufficient to determine effects of the number or duration of massage sessions on efficacy. Several trials with negative results evaluated superficial massage techniques, brief treatment sessions (10 to 15 minutes), or few sessions (<5).

Acupuncture

Fifty-one unique trials on efficacy of acupuncture were included in 3 systematic reviews (16–18, 69). All of the systematic reviews identified substantial methodological shortcomings in most trials. About one third of the trials were conducted in Asia. A fourth systematic review focused on adverse events associated with acupuncture and included observational studies (163).

For acute low back pain, 2 higher-quality systematic reviews found sparse, inconclusive evidence from 4 small trials on efficacy of acupuncture versus sham acupuncture or other interventions (16–18).

For chronic low back pain, both systematic reviews found acupuncture moderately more effective than no treatment or sham treatments for short-term (<6 weeks' [16] or <3 months' [17, 18] duration) pain relief. Acupuncture was also associated with moderate short-term improvements in functional status compared with no treatment (standardized mean differences, 0.62 [CI, 0.30 to 0.95] [16], and 0.63 [CI, 0.19 to 1.08] [17, 18]), but not compared with sham therapies. A recent, higher-quality trial not included in the systematic reviews found no differences between acupuncture and sham acupuncture for pain or function (**Appendix Table 8**, available at www.annals.org) (130).

Evidence of longer-term benefits from acupuncture is mixed. Acupuncture was moderately superior for long-term (>6 weeks' duration) pain relief compared with sham TENS in 2 trials and compared with no additional treat-

ment in 5 trials, although there were no significant differences compared with sham acupuncture (16). One higher-quality trial found no differences in pain 1 year after acupuncture therapy compared with provision of a self-care education book (161). A higher-quality trial not included in the systematic reviews found clinically insignificant differences (<5 points on 100-point scales) between acupuncture and no acupuncture for pain and function after 6 months (**Appendix Table 8**, available at www.annals.org) (132). Another recent, higher-quality trial found acupuncture slightly superior to usual care on Short Form-36 pain scores after 24 months (weighted mean difference, 8 points [CI, 0.7 to 15.3 points]) and for recent use of medications for low back pain (60% vs. 41%), although ODI scores and other outcomes did not differ (131).

Efficacy does not clearly differ between acupuncture and massage, analgesic medication, or TENS (each evaluated in 1 to 4 trials) (16–18). Although 2 trials found acupuncture inferior to spinal manipulation for short-term pain relief, both were rated lower-quality (16). The addition of acupuncture to a variety of noninvasive interventions significantly improved pain and function through 3 to 12 months in 4 higher-quality trials (17, 18).

Few higher-quality trials directly compared different acupuncture techniques. One trial found deep-stimulation acupuncture to be superior to superficial stimulation for immediate outcomes (164). Another found no difference between manual acupuncture and electroacupuncture (165).

Only 14 of 35 trials of acupuncture reported any complications or side effects (17, 18). Minor complications occurred in 5% (13 of 245) of patients receiving acupuncture. A systematic review of acupuncture for various conditions (data from >250 000 treatments) found wide variation in rates of adverse events, ranging from 1% to 45% for needle pain and 0.03% to 38% for bleeding (163). Feelings of faintness and syncope occurred after 0% to 0.3% of treatments. Serious adverse events were rare. Pneumothorax was reported in 2 patients, and there were no cases of infections.

Exercise Therapy, Yoga, and Back Schools

Exercise Therapy

Seventy-nine unique trials of exercise therapy were included in 6 systematic reviews (34–40).

For acute low back pain, a higher-quality Cochrane review found exercise therapy superior to usual care or no treatment in 2 of 9 trials (35, 36). Among trials that could be pooled, exercise therapy and no exercise did not differ for pain relief or functional outcomes. There were also no differences between exercise therapy and other noninvasive treatments for acute low back pain or between exercise therapy and placebo or usual care for subacute low back pain.

For chronic low back pain (43 trials), the Cochrane review found exercise slightly to moderately superior to no

treatment for pain relief at earliest follow-up (weighted mean difference, 10 points on a 100-point scale [CI, 1.31 to 19.09 points]), although not for functional outcomes (35, 36). Results were similar at later follow-up. Exercise therapy was associated with statistically significant but small effects on pain (weighted mean difference, 5.93 points [CI, 2.21 to 9.65 points]) and function (weighted mean difference, 2.37 points [CI, 0.74 to 4.0 points]) compared with other noninvasive interventions.

Three systematic reviews were less comprehensive than the Cochrane review but reached consistent conclusions (34, 38, 40). A fourth, higher-quality systematic review focusing on work outcomes (14 trials) found that exercise slightly reduced sick leave during the first year (standardized mean difference, -0.24 [CI, -0.36 to -0.11]) and decreased the proportion of patients who had not returned to work at 1 year (relative risk, 0.73 [CI, 0.56 to 0.95]), although no benefit was observed in the severely disabled subgroup (>90 days of sick leave) or in patients receiving disability payments (37).

Results of a large (1334 patients), recently published trial are consistent with those of the systematic reviews (**Appendix Table 8**, available at www.annals.org) (134). It found exercise therapy to be marginally superior to usual care for pain and disability in patients with low back pain for more than 28 days, but no differences were seen between exercise therapy and manipulation.

The authors of the Cochrane review also conducted a meta-regression analysis and found that exercise therapy using individualized regimens, supervision, stretching, and strengthening was associated with the best outcomes (36). They estimated that exercise therapy incorporating all of these features would improve pain scores by 18.1 points (95% credible interval, 11.1 to 25.0 points) compared with no treatment and would improve function by 5.5 points (95% credible interval, 0.5 to 10.5 points). However, no trials of such an intervention have been conducted. The Cochrane review also found addition of exercise to other noninvasive therapies to be associated with small improvements in pain (about 5 points on a 100-point scale) and function (about 2 points on a 100-point scale). One recent, higher-quality systematic review found no clear differences between the McKenzie method and other exercise regimens (39).

Yoga

We identified no systematic reviews of yoga for low back pain. From 27 citations, 3 trials (all in patients with chronic low back pain) met inclusion criteria (**Appendix Table 9**, available at www.annals.org) (151–153). One higher-quality trial (101 patients) found 6 weeks of Viniyoga (a therapeutically oriented style) to be slightly superior to conventional exercise (mean difference in RDQ scores, -1.8 [CI, -3.5 to -0.1]) and moderately superior to a self-care education book (mean difference in RDQ

scores, -3.4 [CI, -5.1 to -1.6]) in terms of RDQ scores at 12 weeks, but only superior to the self-care book at 26 weeks (mean difference in RDQ scores, -3.6 [CI, -5.4 to -1.8]) (152). Effects on symptom bothersomeness scores were similar at 12 weeks for all 3 interventions, although yoga was substantially superior to the self-care book at 26 weeks (mean difference, -2.2 on a 0 to 10 scale [CI, -3.2 to -1.2]). Yoga was also associated with decreased medication use at week 26 (21% of patients) compared with exercise (50%) and the self-care book (59%), although the rate of back pain–related health care provider visits did not differ.

Two lower-quality, smaller trials (60 and 22 patients) evaluated Iyengar yoga, a commonly practiced style of Hatha yoga that frequently uses physical props (151, 153). Results were inconclusive. Although 1 trial found Iyengar yoga more effective than exercise instruction for reducing disability through 3 months after treatment, effects on pain were small and were statistically significant only when adjusted for baseline differences (153). The other, smaller trial found no significant differences between Iyengar yoga and standard exercise (151).

Back Schools

Thirty-one unique trials of back schools were included in 3 systematic reviews (28–31). For acute or subacute low back pain, a higher-quality Cochrane review (19 trials) included 1 lower-quality trial (166) that found back schools superior to sham diathermy for short-term recovery and return to work, but not for pain or long-term recurrences (29, 30).

For chronic low back pain, the Cochrane review found inconsistent evidence on efficacy of back schools versus placebo or wait-list controls (8 trials), although most studies found no benefits (29, 30). Results were generally better in trials of back schools conducted in an occupational setting and for more intensive programs based on the original Swedish back school, although benefits were small. Conclusions of 2 other systematic reviews of back schools are consistent with those of the Cochrane review (28, 31).

Psychological Therapies, Interdisciplinary Rehabilitation, and Functional Restoration

Psychological Therapies

Thirty-five unique trials of psychological therapies for chronic low back pain were included in 2 systematic reviews (32, 33). One of the systematic reviews included trials of psychological therapies as part of interdisciplinary therapy (32).

A higher-quality Cochrane review (33) included 4 trials (1 higher-quality [167]) that found cognitive-behavioral therapy to be moderately superior to a wait-list control for short-term pain intensity (standardized mean difference, 0.59 [CI, 0.10 to 1.09]), but not for functional status (standardized mean difference, 0.31 [CI, -0.20 to 0.82]). It also included 2 lower-quality trials that found progres-

sive relaxation to be associated with large effects on short-term pain (standardized mean difference, 1.16 [CI, 0.47 to 1.85]) and behavioral outcomes (standardized mean difference, 1.31 [CI, 0.61 to 2.01]). Results in the electromyography biofeedback group compared with those in the wait-list control group were mixed. Although 3 trials found biofeedback superior for pain intensity (standardized mean difference, 0.84 [CI, 0.32 to 1.35]), a fourth trial found no differences. There were no differences between patients receiving operant treatment and wait-list control participants. Conclusions of another higher-quality systematic review (22 trials) are consistent with those of the Cochrane review (32).

No differences were seen between psychological therapies and other active therapies (such as exercise or usual care) for most outcomes, although 1 systematic review found small to moderate effects on short-term (standardized mean difference, 0.36 [CI, 0.06 to 0.65]; 3 trials) and long-term (standardized mean difference, 0.53 [CI, 0.19 to 0.86]; 4 trials) disability (32).

Psychological therapies did not improve outcomes when added to a variety of other noninvasive therapies (6 lower-quality trials), although diversity in both psychological and nonpsychological therapies limits interpretability of this finding (33).

Interdisciplinary Rehabilitation and Functional Restoration

Twenty-eight unique trials were included in 4 systematic reviews of interdisciplinary rehabilitation (43–47) or functional restoration (41, 42). For subacute low back pain, a higher-quality Cochrane review found interdisciplinary rehabilitation with a workplace visit more effective than usual care for subacute low back pain, but only 2 lower-quality trials were included (45, 46).

For chronic low back pain, a second higher-quality Cochrane review included 3 trials (1 higher-quality) that found intensive (>100 hours), daily interdisciplinary rehabilitation to be moderately superior to noninterdisciplinary rehabilitation or usual care for short- and long-term functional status (standardized mean differences, -0.40 to -0.90 at 3 to 4 months and -0.56 to -1.07 at 60 months) (43, 44). Interdisciplinary rehabilitation was also moderately superior for pain outcomes at 3 to 4 months in 2 trials (standardized mean differences, -0.56 and -0.74 , respectively), although long-term (60 months) results were inconsistent (standardized mean differences, -0.51 and 0.00 , respectively) (168, 169). Evidence was also inconsistent regarding effects on return to work and sick leave. In contrast to more intensive interventions, less intensive interdisciplinary rehabilitation was no better than noninterdisciplinary rehabilitation or usual care (5 trials, 2 higher-quality) (43, 44). A smaller (5 trials) systematic review reported results consistent with those of the Cochrane review (47).

Functional restoration often involves a multidisci-

plinary component (41, 42). For acute low back pain, a higher-quality Cochrane review found functional restoration no better than usual care, normal activities, or standard exercise therapy in 3 trials (2 higher-quality) (41, 42). For chronic low back pain, the Cochrane review found functional restoration with a cognitive-behavioral component more effective than usual care, normal activities, or standard exercise therapy for reducing time lost from work, but little evidence that functional restoration without a cognitive-behavioral component is effective.

Physical Therapies

Interferential Therapy

We identified no systematic reviews of interferential therapy for low back pain. From 8 citations, 3 trials met inclusion criteria (**Appendix Table 9**, available at www.annals.org) (135–137). In 2 trials (1 higher-quality [136]), there were no clear differences between interferential therapy and either spinal manipulation or traction for subacute or chronic back pain (137). A third, lower-quality trial found interferential therapy superior to a self-care book for improvements in RDQ scores in patients with subacute low back pain, but it reported large baseline differences (135). Median RDQ scores after 3 months were identical in the 2 groups.

Low-Level Laser Therapy

We identified no systematic reviews of low-level laser therapy for low back pain. From 218 citations, 7 trials met inclusion criteria (**Appendix Table 9**) (138–144). The trials were generally small (20 to 120 patients) and evaluated heterogeneous outcome measures and different types of lasers at varying doses. In addition, language or publication bias is possible because low-level laser therapy is more commonly used in Russia and Asia.

For chronic low back pain or back pain of unspecified duration, 4 trials (138, 141, 143, 144) (3 higher-quality) found laser therapy superior to sham for pain or functional status up to 1 year after treatment, but another higher-quality trial (140) found no differences between laser and sham in patients also receiving exercise. One lower-quality trial found laser, exercise, and the combination of laser plus exercise similar for pain and back-specific functional status (139).

One trial reported 1 transient adverse event in both the laser and sham laser groups (138). In a systematic review of low-level laser therapy for various musculoskeletal conditions, 6 of 11 trials evaluating higher doses reported no adverse events (95).

Lumbar Supports

Six trials of lumbar supports for treatment of low back pain were included in a higher-quality Cochrane review (48, 49). For low back pain of unspecified duration, the Cochrane review found insufficient evidence from 1 small (30 patients), lower-quality trial (170) to assess efficacy of a

lumbar support compared with no lumbar support. For chronic or subacute low back pain, 1 higher-quality trial found lumbar support to be superior to superficial massage for RDQ scores, but not for ODI scores or pain relief (171, 172). There were no differences between lumbar support and spinal manipulation or transcutaneous muscular stimulation. Evidence from 3 lower-quality trials was insufficient to determine efficacy of lumbar supports compared with other interventions (48, 49).

Shortwave Diathermy

We identified no systematic reviews of shortwave diathermy for low back pain. From 14 citations, 3 lower-quality trials met inclusion criteria (**Appendix Table 9**, available at www.annals.org) (145–147). For acute low back pain, 1 small (24 patients) trial found shortwave diathermy to be inferior to spinal manipulation for pain relief after 2 weeks, but no details about the diathermy intervention were provided (146). For chronic low back pain (145) or low back pain lasting more than 1 week (147), 2 trials found no differences between shortwave diathermy versus sham diathermy or spinal manipulation (145) or shortwave diathermy versus sham diathermy, extension exercises, or traction (147).

Superficial Heat

Nine trials of superficial heat or cold were included in a higher-quality Cochrane review (50). For acute low back pain, the Cochrane review found consistent evidence from 3 higher-quality trials that heat wrap therapy or a heated blanket is moderately superior to placebo or a nonheated blanket for short-term pain relief and back-specific functional status. A higher-quality trial (173) also found heat wrap therapy to be moderately superior to oral acetaminophen or ibuprofen for short-term (3 to 4 days' duration) pain relief (differences of 0.66 and 0.93 on a 6-point scale, respectively) and RDQ scores (differences of about 2 points). For acute low back pain, another higher-quality trial (174) found heat wrap therapy superior to an educational booklet, but not exercise, for early pain relief, although benefits were no longer present after 1 week. Adverse events in trials of superficial heat were minor and mainly consisted of mild skin irritation (50).

Traction

Twenty-four unique trials of traction were included in 3 systematic reviews (51–53, 70). For low back pain of varying duration (with or without sciatica) a higher-quality Cochrane review included 2 higher-quality trials (175–177) that found traction no more effective than placebo, sham, or no treatment for any reported outcome (51, 52). For sciatica of mixed duration, autotraction was more effective than placebo, sham, or no treatment in 2 lower-quality trials (178, 179), but continuous or intermittent traction was not effective (8 trials, 1 higher-quality [180]). There was no clear evidence that various types of traction are

more effective than other interventions (51, 52). Two other systematic reviews found no evidence traction is effective (70) or insufficient evidence to draw reliable conclusions (53).

Adverse events associated with traction include aggravation of neurologic signs and symptoms and subsequent surgery, but these were inconsistently and poorly reported (harms were not mentioned in 16 of 24 trials) (51, 52).

TENS

Eleven unique trials of TENS were included in a higher-quality Cochrane review of TENS (54) and 5 systematic reviews of other interventions (15, 16, 26, 27, 50–52, 55). For chronic low back pain, the Cochrane review included 1 lower-quality trial that found TENS superior to placebo, but a larger, higher-quality trial (181) found no differences between TENS and sham TENS for any measured outcome (54). A systematic review of acupuncture for low back pain also found no difference in short- or long-term pain relief between TENS and acupuncture in 4 trials (16). One higher-quality trial found TENS superior to superficial massage (160). Evidence from single, lower-quality trials is insufficient to accurately judge efficacy of TENS versus other interventions for chronic low back pain or for acute low back pain. For subacute low back pain, 1 higher-quality trial found TENS moderately inferior to spinal manipulation for subacute low back pain (171, 172).

The Cochrane review found that one third of patients randomly assigned to either active or sham TENS had minor skin irritation, with 1 patient (in the sham group) discontinuing therapy because of severe dermatitis (54).

Ultrasonography

We identified no systematic reviews of ultrasonography for low back pain. From 265 potentially relevant citations, 3 lower-quality trials met inclusion criteria (**Appendix Table 9**, available at www.annals.org) (148–150). For chronic low back pain (148) or low back pain of unspecified duration (150), 2 small (10 and 36 patients, respectively) trials reported inconsistent results for ultrasonography versus sham ultrasonography, with the larger trial reporting no differences. For acute sciatica, a nonrandomized trial (73 patients) found ultrasonography superior to sham ultrasonography or analgesics for pain relief, with patients in all groups also prescribed bed rest (149).

DISCUSSION

This review synthesizes evidence from systematic reviews and randomized, controlled trials of 17 nonpharmacologic therapies for low back pain. Nearly all therapies were evaluated in patients with nonspecific low back pain or in mixed populations of patients with and without sciatica. Main results are summarized in **Appendix Table 10** (acute low back pain), **Appendix Table 11** (chronic or subacute low back pain), and **Appendix Table 12** (back

pain with sciatica) (all appendix tables are available at www.annals.org).

We found good evidence that psychological interventions (cognitive-behavioral therapy and progressive relaxation), exercise, interdisciplinary rehabilitation, functional restoration, and spinal manipulation are effective for chronic or subacute (>4 weeks' duration) low back pain. Compared with placebo or sham therapies, these interventions were associated with moderate effects, with differences for pain relief in the range of 10 to 20 points on a 100-point visual analogue pain scale, 2 to 4 points on the RDQ, or a standardized mean difference of 0.5 to 0.8. The exception was exercise therapy, which was associated with small to moderate (10 points on a 100-point visual analogue pain scale) effects on pain. We found fair evidence that acupuncture is more effective than sham acupuncture, and fair evidence that massage is similar in efficacy to other noninvasive interventions for chronic low back pain. We found little evidence of clinically meaningful, consistent differences between most interventions found effective. One exception was intensive interdisciplinary rehabilitation, which was moderately more effective than noninterdisciplinary rehabilitation for improving pain and function. We also found fair evidence that Vinyoga is slightly superior to traditional exercises for functional status and use of analgesic medications.

For acute low back pain (<4 weeks' duration), the only nonpharmacologic therapies with evidence of efficacy are superficial heat (good evidence for moderate benefits) and spinal manipulation (fair evidence for small to moderate benefits). Other noninvasive therapies (back schools, interferential therapy, low-level laser therapy, lumbar supports, TENS, traction, and ultrasonography) have not been shown to be effective for either chronic or subacute or acute low back pain.

We found only rare reports of serious adverse events for all of the noninvasive therapies evaluated in this review. However, assessment and reporting of harms were generally suboptimal. For example, less than half of the trials of acupuncture reported adverse events (17). Better reporting of harms is needed for more balanced assessments of interventions (182).

Our evidence synthesis has several potential limitations. First, because of the large number of published trials, our primary source of data was systematic reviews. The reliability of systematic reviews depends on how well they are conducted. We therefore focused on findings from higher-quality systematic reviews, which are less likely than lower-quality systematic reviews to report positive findings (20, 21). In addition, when multiple recent systematic reviews were available for an intervention, we found overall conclusions to be generally consistent. Second, we only included randomized, controlled trials for assessments of efficacy. Although well-conducted randomized, controlled trials are less susceptible to bias than other study designs, nearly all trials were conducted in ideal settings and se-

lected populations, usually with short-term follow-up. “Effectiveness” trials in less highly selected populations could provide additional information on benefits in real-world practice. Third, language bias could affect our results because we included non-English-language trials only if already included in English-language systematic reviews. However, systematic reviews of acupuncture included Asian-language trials (16, 17), and systematic reviews of other interventions with no language restrictions identified few non-English-language studies (55, 183). Fourth, reliable assessments for potential publication bias were not possible for most of the interventions included in this review because of small numbers of trials (184). For the interventions evaluated in the most trials, assessments of potential publication bias varied. Funnel plot asymmetry was present in trials of exercise therapy (36), was not present in trials of spinal manipulation (15) or behavioral therapy (32), and could not be reliably interpreted for trials of acupuncture (16). Finally, we did not include cost-effectiveness analyses. Although many noninvasive interventions for chronic low back pain appear to have similar effects on clinical outcomes, other factors, such as cost or convenience, may vary widely. However, systematic reviews of economic analyses of low back pain interventions have found few full cost-effectiveness analyses and important methodological deficiencies in the available cost studies (185–188).

We also identified several research gaps that limited our ability to reach more definitive conclusions about optimal use of the interventions included in this review. We found no trials on optimal sequencing of interventions, and only limited evidence on methods to guide selection of therapy for individual patients. Although initial studies are promising, decision tools and other methods for individualizing and selecting optimal therapy are still in fairly early stages of development (156). More research on methods for selecting optimal therapy that are practical for use by primary care clinicians is urgently needed. We also found few trials assessing efficacy of adding one noninvasive intervention to another. Although several trials found acupuncture plus another therapy to be more effective than the other therapy alone, other trials found little or no additional benefit from adding exercise therapy (36), behavioral interventions (33), or spinal manipulation (134) to other therapies. Finally, few trials specifically evaluated patients with sciatica (Appendix Table 12, available at www.annals.org) or spinal stenosis. One systematic review of interventions for sciatica identified only 8 trials of therapies included in this review (70). Most trials included in our review enrolled mixed populations of patients with or without sciatica, or did not enroll patients with sciatica. It remains unclear whether optimal nonpharmacologic treatments for sciatica or spinal stenosis differ from those for nonspecific low back pain, although in the case of spinal manipulation, presence or absence of radiating pain did not appear to affect conclusions (55).

In summary, evidence of effective nonpharmacologic therapies for acute low back pain is quite limited. This is not surprising, as the natural history of acute low back pain is for substantial early improvement in most patients (125). On the other hand, several noninvasive therapies seem to be similarly effective for chronic low back pain. Although evidence on effectiveness of therapies specifically for subacute low back pain is sparse (125), many trials enrolled mixed populations of patients with subacute and chronic low back pain. Factors to consider when choosing among noninvasive therapies are patient preferences, cost, convenience, and availability of skilled providers for specific therapies. Clinicians should avoid interventions not proven effective, as many therapies have at least fair evidence of moderate benefits.

From the Oregon Evidence-based Practice Center and Oregon Health & Science University, Portland, Oregon.

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Requests for Single Reprints: Roger Chou, MD, Oregon Evidence-based Practice Center, 3181 SW Sam Jackson Park Road, Mailcode BICC, Portland, OR 97239; e-mail, chour@ohsu.edu.

Current author addresses are available at www.annals.org.

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Current Author Addresses: Dr. Chou and Ms. Huffman: Oregon Evidence-based Practice Center, 3181 SW Sam Jackson Park Road, Mailcode BICC, Portland, OR 97239.

Appendix Table 1. Included Interventions

Intervention	Definition
Spinal manipulation	Manual therapy in which loads are applied to the spine using short- or long-lever methods. High-velocity thrusts are applied to a spinal joint beyond its restricted range of movement. Spinal mobilization, or low-velocity, passive movements within or at the limit of joint range, is often used in conjunction with spinal manipulation.
Massage	Soft tissue manipulation using the hands or a mechanical device through a variety of specific methods.
Acupuncture	An intervention consisting of the insertion of needles at specific acupuncture points.
Exercise therapy	A supervised exercise program or formal home exercise regimen, ranging from programs aimed at general physical fitness or aerobic exercise to programs aimed at muscle strengthening, flexibility, or stretching.
Yoga	An intervention distinguished from traditional exercise therapy by the use of specific body positions, breathing techniques, and emphasis on mental focus. Many styles of yoga are practiced, each emphasizing different postures and techniques.
Back schools	An intervention consisting of an education and a skills program, including exercise therapy, in which all lessons are given to groups of patients and supervised by a paramedical therapist or medical specialist. The original Swedish back school was introduced by Zachrisson Forsell in 1969.
Psychological therapies	Includes biofeedback (the use of auditory and visual signals reflecting muscle tension or activity to inhibit or reduce the muscle activity), progressive relaxation (a technique that involves the deliberate tensing and relaxation of muscles to facilitate the recognition and release of muscle tension), and standard cognitive-behavioral and operant therapy.
Interdisciplinary therapy (also called <i>multidisciplinary therapy</i>)	An intervention that combines and coordinates physical, vocational, and behavioral components and is provided by multiple health care professionals with different clinical backgrounds. The intensity and content of interdisciplinary therapy varies widely.
Functional restoration (also called <i>physical conditioning, work hardening, or work conditioning</i>)	An intervention that involves simulated or actual work tests in a supervised environment in order to enhance job performance skills and improve strength, endurance, flexibility, and cardiovascular fitness in injured workers.
Physical therapies	
Interferential therapy	The superficial application of a medium-frequency alternating current modulated to produce low frequencies up to 150 Hz.
Low-level laser therapy	The superficial application of lasers at wavelengths of 632–904 nm. Optimal treatment parameters (wavelength, dosage, dose intensity) are uncertain.
Lumbar supports	A back brace or orthotic device worn to passively support the back.
Shortwave diathermy	Therapeutic elevation of the temperature of deep tissues by application of shortwave electromagnetic radiation with a frequency range of 10–100 MHz.
Superficial heat	The superficial application of heat to the lumbar area.
Traction	An intervention involving drawing or pulling to stretch the lumbar spine. A variety of methods are used and usually involve a harness around the lower rib cage and around the iliac crest, with the pulling action performed by using free weights and a pulley, motorized equipment, inversion techniques, or an overhead harness.
Transcutaneous electrical nerve stimulation	Use of a small battery-operated device to provide continuous electrical impulses via surface electrodes, with the goal of relieving symptoms by modifying pain perception.
Ultrasonography	The therapeutic application of high-frequency sound waves up to 3 MHz.

Appendix Table 2. Quality Rating System for Systematic Reviews

Criteria for Assessing Scientific Quality of Research Reviews*

1. Were the search methods reported?
Were the search methods used to find evidence (original research) on the primary questions stated?
"Yes" if the review states the databases used, date of most recent searches, and some mention of search terms.
2. Was the search comprehensive?
Was the search for evidence reasonably comprehensive?
"Yes" if the review searches at least 2 databases and looks at other sources (e.g., reference lists, hand searches, queries of experts).
3. Were the inclusion criteria reported?
Were the criteria used for deciding which studies to include in the overview reported?
4. Was selection bias avoided?
Was bias in the selection of studies avoided?
"Yes" if the review reports how many studies were identified by searches, numbers excluded, and appropriate reasons for excluding them (usually because of predefined inclusion/exclusion criteria).
5. Were the validity criteria reported?
Were the criteria used for assessing the validity of the included studies reported?
6. Was validity assessed appropriately?
Was the validity of all the studies referred to in the text assessed by using appropriate criteria (either in selecting studies for inclusion or in analyzing the studies that are cited)?
"Yes" if the review reports validity assessment and did some type of analysis with it (e.g., sensitivity analysis of results according to quality ratings, excluded low-quality studies).
7. Were the methods used to combine studies reported?
Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported?
"Yes" for studies that did qualitative analysis if report mentions that quantitative analysis was not possible and reasons that it could not be done, or if "best evidence" or some other grading of evidence scheme used.
8. Were the findings combined appropriately?
Were the findings of the relevant studies combined appropriately relative to the primary question the overview addresses?
"Yes" if the review performs a test for heterogeneity before pooling or does appropriate subgroup testing, appropriate sensitivity analysis, or other such analysis.
9. Were the conclusions supported by the reported data?
Were the conclusions made by the author(s) supported by the data and/or analysis reported in the overview?
10. What was the overall scientific quality of the overview?
How would you rate the scientific quality of this overview?

Operationalization of Criteria

The purpose of this index is to evaluate the scientific quality (i.e., adherence to scientific principles) of research overviews (review articles) published in the medical literature. It is not intended to measure literary quality, importance, relevance, originality, or other attributes of overviews.

The index is for assessing overviews of primary ("original") research on pragmatic questions regarding causation, diagnosis, prognosis, therapy, or prevention. A research overview is a survey of research. The same principles that apply to epidemiologic surveys apply to overviews: A question must be clearly specified; a target population identified and accessed; appropriate information obtained from that population in an unbiased fashion; and conclusions derived, sometimes with the help of formal statistical analysis, as is done in meta-analyses. The fundamental difference between overviews and epidemiologic studies is the unit of analysis, not the scientific issues that the questions in this index address.

Because most published overviews do not include a methods section, it is difficult to answer some of the questions in the index. Base your answers, as much as possible, on information provided in the overview. If the methods that were used are reported incompletely relative to a specific question, score it as "can't tell," unless there is information in the overview to suggest that the criterion was or was not met.

For question 8, if no attempt has been made to combine findings, and no statement is made regarding the inappropriateness of combining findings, check "No." If a summary (general) estimate is given anywhere in the abstract, the discussion, or the summary section of the paper, and it is not reported how that estimate was derived, mark "No" even if there is a statement regarding the limitations of combining the findings of the studies reviewed. If in doubt, mark "Can't tell."

For an overview to be scored as "Yes" in question 9, data (not just citations) must be reported that support the main conclusions regarding the primary question(s) that the overview addresses.

The score for question 10, the overall scientific quality, should be based on your answers to the first 9 questions. The following guidelines can be used to assist with deriving a summary score: If the "Can't tell" option is used 1 or more times on the preceding questions, a review is likely to have minor flaws at best and it is difficult to rule out major flaws (i.e., a score ≤ 4). If the "No" option is used on question 2, 4, 6, or 8, the review is likely to have major flaws (i.e., a score ≤ 3 , depending on the number and degree of the flaws).

Scoring: Each Question Is Scored as Yes, Partially/Can't Tell, or No

Extensive Flaws		Major Flaws		Minor Flaws		Minimal Flaws	
1	2	3	4	5	6	7	

* Operationalization of the Oxman criteria (19), adapted from reference (20).

Appendix Table 3. Quality Rating System for Randomized, Controlled Trials*

Criteria List for Assessment of Methodologic Quality†	Operationalization of Criteria	Score
A. Was the method of randomization adequate?	A random (unpredictable) assignment sequence. An example of adequate methods is a computer-generated random-number table and use of sealed opaque envelopes. Methods of allocation using date of birth, date of admission, hospital numbers, or alternation should not be regarded as appropriate.	Yes/No/Don't Know
B. Was the treatment allocation concealed?	Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.	Yes/No/Don't Know
C. Were the groups similar at baseline regarding the most important prognostic factors? "Yes", if similar: Age and sex Description of type of pain Intensity, duration, or severity of pain	To receive a "yes," groups have to be similar at baseline regarding demographic factors, duration or severity of symptoms, percentage of patients with neurologic symptoms, and value of main outcome measure(s).	Yes/No/Don't Know
D. Was the patient blinded to the intervention?	The reviewer determines whether enough information about the blinding is given in order to score a "yes." Use the author's statement on blinding, unless there is a differing statement/reason not to (no need for explicit information on blinding).	Yes/No/Don't Know
E. Was the care provider blinded to the intervention?		Yes/No/Don't Know
F. Was the outcome assessor blinded to the intervention?		Yes/No/Don't Know
G. Were co-interventions avoided or similar?	Co-interventions should be avoided in the trial design or similar between the index and control groups.	Yes/No/Don't Know
H. Was adherence acceptable in all groups?	The reviewer determines whether adherence to the interventions is acceptable, based on the reported intensity, duration, number, and frequency of sessions for both the index intervention and control intervention(s).	Yes/No/Don't Know
I. Was the dropout rate described and acceptable? ≤15% dropout rate is acceptable	The number of participants who are included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and dropouts does not exceed 15% and does not lead to substantial bias, a "yes" is scored.	Yes/No/Don't Know
J. Was the timing of the outcome assessment in all groups similar?	Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.	Yes/No/Don't Know
K. Did the analysis include an intention-to-treat analysis? "Yes," if <5% of randomly assigned patients excluded	All randomly assigned patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values), irrespective of nonadherence and co-interventions.	Yes/No/Don't Know

* This list includes only the 11 internal validity criteria that refer to characteristics of the study that might be related to selection bias (criteria A and B), performance bias (criteria D, E, G, and H), attrition bias (criteria I and K), and detection bias (criteria F and J). The internal validity criteria should be used to define methodological quality in the meta-analysis.

† Adapted from methods developed by the Cochrane Back Review Group (24).

Appendix Table 4. Methods for Grading the Overall Strength of Evidence for an Intervention*

Grade	Definition
Good	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (at least 2 consistent, higher-quality trials).
Fair	Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (at least 1 higher-quality trial of sufficient sample size; 2 or more higher-quality trials with some inconsistency; or at least 2 consistent, lower-quality trials, or multiple consistent observational studies with no significant methodological flaws).
Poor	Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality trials, important flaws in trial design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

* Adapted from methods developed by the U.S. Preventive Services Task Force (25). The overall evidence for an intervention was graded on a 3-point scale (good, fair, poor).

Appendix Table 5. Quality Ratings for Included Systematic Reviews of Nonpharmacologic Therapies for Low Back Pain

Intervention	Study, Year (Reference)	Search Methods?	Comprehensive?	Inclusion Criteria?	Bias Avoided?	Validity Criteria?	Validity Assessed?	Methods for Combining Studies?	Appropriately Combined?	Conclusions Supported?	Overall Quality per Oxman Scale (1-7)
Acupuncture	Ernst, 2001 (64)	Yes	Yes	Yes	Can't tell	No	No	No	Can't tell	Can't tell	3
	Furlan et al., 2002 (26, 27)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Back schools	Manheimer et al., 2005 (16)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Yes	6
	Elders et al., 2000 (28)	Yes	Yes	Yes	Yes	No	Yes	Partial	Can't tell	Can't tell	3
	Heymans et al., 2005 (29, 30)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
	Maier-Riehle and Härter, 2001 (31)	Yes	Yes	Yes	Can't tell	No	Partial	Yes	Yes	Yes	4
Psychological interventions	Hoffman et al., 2007 (32)*	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Yes	6
	Ostelo et al., 2005 (33)	Yes	Yes	Yes	Yes	Yes	Partial	Yes	Yes	Yes	6
Exercise	Clare et al., 2004 (34)	Yes	Yes	Yes	Yes	Yes	Partial	Yes	Yes	Yes	6
	Hayden et al., 2005 (35, 36)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
	Kool et al., 2004 (37)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
	Liddle et al., 2004 (38)	Yes	Yes	Yes	Can't tell	Yes	Partial	No	Can't tell	Can't tell	3
	Machado et al., 2006 (39)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Functional restoration	McNeely et al., 2003 (40)	Yes	Yes	Yes	Can't tell	Yes	Partial	No	Yes	Yes	4
	Schonstein et al., 2003 (41, 42)	Yes	Partial	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	6
Interdisciplinary therapy	Guzmán et al., 2002 (43, 44)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	6
	Karjalainen et al., 2001, 2003 (45, 46)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Massage	Tveito et al., 2004 (47)	Partial	Yes	Yes	Yes	Yes	Partial	Yes	Yes	Yes	5
	Furlan et al., 2002 (26, 27)	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Can't tell	6
Lumbar supports	Jellema et al., 2001 (48); Van Tulder et al., 2000 (49)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Superficial heat	French et al., 2006 (50)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Traction	Clarke et al., 2005, 2006 (51, 52)	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	6
	Harte et al., 2003 (53)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Transcutaneous nerve stimulation	Khadilkar et al., 2005 (54)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Spinal manipulation	Assendelft et al., 2003 (15, 55)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
	Avery and O'Driscoll, 2004 (56)	Yes	Yes	Yes	Yes	No	Partial	No	Partial	Partial	2
	Bronfort et al., 2004 (57)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Partial	4
	Brown, 2005 (58)	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	6
	Ernst, 2001 (64)	Yes	Yes	Yes	Yes	No	No	Yes	Can't tell	Can't tell	3
	Ernst and Canter, 2003 (59)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Yes	4

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Appendix Table 5—Continued

Intervention	Study, Year (Reference)	Search Methods?	Comprehensive?	Inclusion Criteria?	Bias Avoided?	Validity Criteria?	Validity Assessed?	Methods for Combining Studies?	Appropriately Combined?	Conclusions Supported?	Overall Quality per Oxman Scale (1–7)
	Ferreira et al., 2002 (60)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Yes	7
	Ferreira et al., 2003 (61)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Yes	5
	Gay et al., 2005 (62)	Yes	Yes	No	Can't tell	No	No	No	Can't tell	Can't tell	2
	Licciardone et al., 2005 (63)	Yes	Yes	Yes	Yes	No	No	Yes	Partial	Can't tell	4
	Meeker and Haldeman, 2002 (65)	Partial	Yes	No	No	No	No	No	Partial	Partial	1
	Oliphant, 2004 (66)	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	No	No	3
	Stevinson and Ernst, 2002 (67)	Yes	Yes	Yes	Can't tell	No	No	No	Can't tell	Can't tell	2
	Woodhead and Clough, 2005 (68)	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Partial	Partial	4
Multiple interventions	Cherkin et al., 2003 (69)†	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	4
	Vroomen et al., 2000 (70)‡	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	5

* 22 trials of behavioral therapy alone or as part of interdisciplinary rehabilitation.

† 20 trials of acupuncture, 3 trials of massage, and 26 trials of spinal manipulation.

‡ 6 trials of traction, 1 trial of exercise, and 2 trials of spinal manipulation.

Appendix Table 6. Systematic Reviews of Efficacy of Nonpharmacologic Therapies for Low Back Pain*

Intervention	Study, Year (Reference)	Type of Systematic Review	Included Trials (Trials Rated Higher-Quality), n (n) [†]	Trials not Included in Any Other Relevant Systematic Review	Duration of Treatment in Included Trials	Sample Sizes in Included Trials, n	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
Acupuncture (51 unique trials in 3 systematic reviews)	Furlan et al., 2002 (26, 27)	Qualitative and quantitative	35 (14)	11	1–20 sessions	17–492 (median, 54)	Acupuncture (32), dry needling (3)	Acupuncture vs. no treatment for chronic LBP: SMD, -0.73 (95% CI, -1.19 to -0.28) for short-term pain (2 RCTs); SMD, -0.63 (CI, -1.08 to -0.19) for short-term function (2 RCTs) Acupuncture vs. sham acupuncture: WMD, -17.79 points (CI, -25.5 to -10.07 points) for short-term pain (6 RCTs); WMD, -5.74 points (CI, -14.7 to 3.25 points) for long-term pain (3 RCTs); no difference for function	7
	Manheimer et al., 2005 (16)	Quantitative	33 (5)	10	1–20 sessions	17–194 (median, 60)	Chinese acupuncture (29), western acupuncture (4), electroacupuncture (14), acupuncture for antenatal LBP (3)	Acupuncture vs. no additional treatment for chronic LBP: SMD, -0.69 (CI, -0.98 to -0.40) for short-term pain (8 RCTs); SMD, -0.74 (CI, -1.47 to -0.02) for long-term pain (5 RCTs); SMD, -0.62 (CI, -0.95 to -0.30) for short-term function (6 RCTs) Acupuncture vs. sham acupuncture: SMD, -0.58 (CI, -0.36 to -0.80) for short-term pain (4 RCTs); SMD, -0.59 (CI, -1.29 to 0.10) for long-term pain (2 RCTs); no difference for function	6
Back schools (31 unique trials in 3 systematic reviews)	Elders et al., 2000 (28)	Qualitative and quantitative	6 trials of back schools (quality not assessed)	3	NR	51–975 (median, 194)	Not described	Back school vs. control: rate difference for return to work rate ranged from -7% to 29% after 21–42 d (4 RCTs), 30% to 37% after 180–200 d, (3 RCTs), -1% to 42% after 360 d (4 RCTs)	3
	Heymans et al., 2004 (29, 30)	Qualitative	19 (6)	8	One 4-h session to twenty-one 85-min sessions	37–975 (median, 106)	Swedish or modified Swedish back school (6), Maastricht (2), others (11)	Conflicting evidence from 8 RCTs on effectiveness of back schools for chronic LBP vs. wait list control or placebo for short-, intermediate-, or long-term pain, functional status and return to work; back school in occupational setting appeared to be more effective	7
	Maier-Riehle and Härter, 2001 (31)	Quantitative	13 (quality not assessed)	9	1–22 h (median, 5 h)	29–299 (median, 76)	Not described	Back school vs. any control: SMD, 0.14 ($P = 0.026$) for pain intensity at <3 mo (9 RCTs); SMD, 0.44 ($P = 0.001$) for recurring back pain through 6 mo (6 RCTs); no significant differences for functional status (7 RCTs) or recurring back pain after 6 mo	4

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Appendix Table 6—Continued

Intervention	Study, Year (Reference)	Type of Systematic Review	Included Trials (Trials Rated Higher-Quality), <i>n</i> (<i>n</i>)*	Trials not Included in Any Other Relevant Systematic Review	Duration of Treatment in Included Trials	Sample Sizes in Included Trials, <i>n</i>	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
Psychological therapies (35 unique trials in 2 systematic reviews)	Hoffman et al., 2007 (32)	Quantitative	22† (6)	14	NR	20–239 (median, 76)	Not described	Any psychological intervention or multidisciplinary intervention vs. wait-list controls: SMD, 0.50 (CI, 0.23–0.77) for pain intensity (7 RCTs); SMD, 0.50 (CI, 0.00–0.83) for health-related quality of life (4 RCTs) Cognitive-behavioral treatment vs. wait-list controls: SMD, 0.62 (CI, 0.25–0.98) for pain intensity (7 RCTs) Self-regulatory treatment vs. wait-list controls: SMD, 0.75 (CI, 0.35–1.15) for pain intensity (4 RCTs)	6
	Ostelo et al., 2005 (33)	Quantitative and qualitative	21 (7)	13	3–12 wk	17–161 (median, 66)	Cognitive-behavioral therapy (14), operant (7), relaxation (11), biofeedback (6)	Progressive relaxation vs. wait-list controls: SMD, 1.16 (CI, 0.47 to 1.85) for pain intensity (2 RCTs) Biofeedback vs. wait-list controls: SMD, 0.84 (CI, 0.32 to 1.35) for pain intensity (3 RCTs) Operant therapy vs. wait-list controls: SMD, 0.29 (CI, –0.14 to 0.72) for pain intensity (2 RCTs) Cognitive-behavioral therapy: SMD, 0.59 (CI, 0.10 to 1.09) for pain intensity (4 RCTs)	6
Exercise (79 unique trials in 7 systematic reviews)	Clare et al., 2004 (34)	Quantitative	5 (3)	1	NR	25–321	All trials evaluated the McKenzie method	McKenzie therapy vs. control (booklet, strength training, spinal mobilization, or massage): WMD, –8.6 points (CI, –13.7 to –3.5 points) on 100-point scale for short-term (<3 mo) pain (3 RCTs); WMD, –5.4 points (CI, –8.4 to –2.4 points) for short-term disability (5 RCTs); no differences for intermediate-term disability	6

Appendix Table 6—Continued

Intervention	Study, Year (Reference)	Type of Systematic Review	Included Trials (Trials Rated Higher-Quality), n (n) [†]	Trials not Included in Any Other Relevant Systematic Review	Duration of Treatment in Included Trials	Sample Sizes in Included Trials, n	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
	Hayden et al., 2005 (35, 36)	Quantitative and qualitative	61 (28)	41	2–150 h	17–473 (median, 75)	McKenzie method (6), extensor (5), flexion (9), isometric (3), aerobics (8), strengthening (16), stretching (12), graded activity (2), other or multiple (17)	Exercise therapy vs. no treatment for acute LBP: WMD, –0.59 points (CI, –12.69 to 11.51 points) on 100-point scale for short-term pain (3 RCTs); no differences for function Exercise therapy vs. no treatment for chronic LBP: WMD, 10.2 points (CI, 1.31 to 19.09 points) for short-term pain (19 RCTs); WMD, 3.00 points (CI, –0.53 to 6.48 points) for short-term function (17 RCTs); results similar at longer-term follow-up	7
	Kool et al., 2004 (37)	Qualitative and quantitative	14 (9)	7	3 wk–12 mo	80–476 (median, 166)	Outpatient exercise therapy (9), inpatient therapy (3), back school (3), interdisciplinary/functional restoration (5)	Exercise vs. usual care: SMD, –0.24 (CI, –0.36 to –0.11) for number of sick days during first year of follow-up (9 RCTs); RR, 0.73 (CI, 0.56 to 0.95) for proportion of patients not returned to work after 1 y (3 RCTs)	7
	Liddle et al., 2004 (38)	Qualitative	16 (8)	4	NR	28–222 (median, 99)	Strength/flexibility (9), multimodal therapy (3), other (4)	Exercise vs. control: 9 of 16 RCTs reported a “positive result” (on any outcome) vs. control (wait-list, advice, or electrotherapy), 7 other RCTs reported “positive result” but no difference compared with control (usually exercise-based); 5 of 7 RCTs reported “positive result” for back-specific function	3

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Appendix Table 6—Continued

Intervention	Study, Year (Reference)	Type of Systematic Review	Included Trials (Trials Rated Higher-Quality), <i>n</i> (<i>n</i> †)	Trials not Included in Any Other Relevant Systematic Review	Duration of Treatment in Included Trials	Sample Sizes in Included Trials, <i>n</i>	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
	Machado et al., 2006 (39)	Quantitative	11 (6)	3	Not clearly reported	24–321 (median, 75)	All trials evaluated McKenzie method	McKenzie method vs. passive therapy (educational booklets, bed rest, ice packs, and massage) for acute LBP: WMD, –4.16 points (CI, –7.12 to –1.20 points) on 100-point scale for pain (4 RCTs); WMD, –5.22 (CI, –8.28 to –2.16) for disability at 1-wk follow-up; no differences at 4 wk (4 RCTs) McKenzie method vs. advice to stay active for acute LBP: WMD, 3.85 (CI, 0.30 to 7.39) for disability at 12-wk follow-up (2 RCTs) No differences between McKenzie method and other exercise therapy	7
	McNeely et al., 2003 (40)	Qualitative (exercise therapy for spondylolysis and spondylolisthesis)	2 (1)	1	NR	44 and 65	Strengthening (1), flexion/extension (1)	Unable to draw firm conclusions regarding exercise therapy for spondylolysis and spondylolisthesis	4
Functional restoration (18 trials in 1 systematic review)	Schonstein et al., 2003 (41, 42)	Qualitative and quantitative	18 (9)	12 trials not included in systematic reviews of interdisciplinary therapy	1 session to weekly sessions for 1.5 y	45–542 (median, 165)	Cognitive-behavioral component (10), no cognitive-behavioral component (8)	Physical conditioning vs. usual care for time lost from work: WMD, –45 (CI, –88 to –3) for number of sick leave days after 1 y (2 RCTs); OR, 0.80 (CI, 0.58 to 1.09) for proportion of patients off work at 12 mo (3 RCTs) Physical conditioning vs. physical conditioning plus psychological treatment: OR, 0.93 (CI, 0.44 to 1.97) for proportion of patients off work at 6 or 12 mo (2 RCTs)	6
Interdisciplinary therapy (16 unique trials in 3 systematic reviews)	Guzmán et al., 2001, 2002 (43, 44)	Quantitative (chronic LBP)	10 (3)	10	Once-weekly to daily sessions	20–476 (median, 170)	Higher-intensity therapy (4), lower-intensity therapy (4), other (3)	Strong evidence that intensive (>100 h) daily interdisciplinary therapy is more effective than usual care or less intensive therapy for function (3 RCTs) Moderate evidence that less intensive (<30 h) interdisciplinary therapy is no more effective than usual care or nonmultidisciplinary therapy (5 RCTs)	6

Appendix Table 6—Continued

Intervention	Study, Year (Reference)	Type of Systematic Review	Included Trials (Trials Rated Higher-Quality), n (n) [†]	Trials not Included in Any Other Relevant Systematic Review	Duration of Treatment in Included Trials	Sample Sizes in Included Trials, n	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
	Karjalainen et al., 2001 (45), 2003 (46)	Qualitative (subacute LBP)	2 (0)	1	NR	103 and 130	Interdisciplinary therapy not categorized	Moderate evidence that multidisciplinary rehabilitation with a worksite visit or more comprehensive occupational health care intervention is more effective than usual care for return to work, sick leave, and subjective disability (2 RCTs)	7
	Tveito et al., 2004 (47)	Qualitative	5 (0)	4	NR	128–1645 (median, 234)	Interdisciplinary therapy not categorized	Moderate evidence that interdisciplinary therapy has a positive effect on sick leave (4 RCTs); no evidence of a positive effect on pain (1 RCT)	5
Massage (8 unique trials in 2 systematic reviews)	Furlan et al., 2002 (26, 27)	Qualitative	8 (5)	NA	5–9 sessions	24–262 (median, 106)	Massage with hands (6), massage with mechanical device (2)	Massage superior to sham laser in 1 RCT Relative to other therapies, massage superior to relaxation therapy, acupuncture, and self-care education; massage similar to corset and exercises; light massage inferior to manipulation and TENS	6
Lumbar supports (6 trials in 1 systematic review)	Jellema et al., 2001 (48); Van Tulder et al., 2000 (49)	Qualitative	6 trials of treatment (2)	NA	3–8 wk (median, 3.5 wk)	19–334 (median, 190)	Lumbar support with rigid stay (2), pneumatic lumbar support (1), other or not specified (3)	Insufficient evidence to assess efficacy of lumbar support vs. no treatment (1 RCT); lumbar support superior to other interventions in 1 of 4 RCTs	7
Spinal manipulation (69 unique trials in 12 systematic reviews)	Assendelft et al., 2004 (15), 2003 (55)	Quantitative	39 (10)	1	1–24 sessions over 3 wk	21–741 (median, 103)	Rotational manipulation (6), Maitland method (5), thrust (3), sacroiliac method (2), other or not specified (23)	Spinal manipulation vs. sham for acute LBP: WMD, –10 points (CI, –17 to –22 points) on 100-point VAS for short-term pain; WMD, –2.8 points (CI, –5.6 to 0.1 points) for short-term function (RDQ) Spinal manipulation vs. sham for chronic LBP: WMD, –10 points (CI, –17 to –33 points) on 100-point VAS for short-term pain; WMD, –19 points (CI, –35 to –3 points) for long-term pain; WMD, –3.3 points (CI, –6.0 to –0.6 points) for short-term function (RDQ) No differences between spinal manipulation and other therapies judged effective for acute or chronic LBP	7

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Appendix Table 6—Continued

Intervention	Study, Year (Reference)	Type of Systematic Review	Included Trials (Trials Rated Higher-Quality), n (n) [†]	Trials not Included in Any Other Relevant Systematic Review	Duration of Treatment in Included Trials	Sample Sizes in Included Trials, n	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
	Avery and O'Driscoll, 2004 (56)	Qualitative	3 (quality not assessed)	0	NR	155–323	Chiropractic spinal manipulation (2), osteopathic (1)	Insufficient new evidence to assess efficacy of spinal manipulation (updates previous review by Mohseni-Bandpei [114])	2
	Bronfort et al., 2004 (57)	Qualitative	31 (5)	0	1–24 sessions	5202 (mean, 168)	Spinal manipulation (26), mobilization only (5)	Moderate evidence that spinal manipulation is similar to prescriptions of nonsteroidal anti-inflammatory drugs for chronic LBP; limited to moderate evidence that spinal manipulation is superior to some other interventions for acute and chronic LBP	4
	Brown et al., 2005 (58)	Qualitative	14 (6) systematic reviews and 2 (2) RCTs	0	NR	NR	NR	Spinal manipulation is as effective as other noninvasive treatments	6
	Ernst and Canter, 2003 (59)	Qualitative	12 (6)	1	4–12 sessions	12–741 (median, 69)	All trials evaluated chiropractic manipulation	Chiropractic spinal manipulation superior to control treatments in 5 of 12 RCTs; chiropractic manipulation consistently superior to sham manipulation; beneficial effects usually small or moderate; no clear difference between results for acute vs. chronic LBP	4
	Ferreira et al., 2002 (60)	Quantitative	8 (4)	0	4–12 sessions	19–395 (median, 63)	Not specified	Spinal manipulation vs. placebo: WMD, 7 points (CI, 1 to 14 points) on 100-point VAS for short-term pain (2 RCTs) Spinal manipulation vs. NSAIDs: WMD, 14 points (CI, –11 to 40 points) for short-term pain (2 RCTs) and 6 points (CI, 1 to 12 points) on 100-point scale for disability (2 RCTs) No differences between spinal manipulation and other effective therapies	7

Appendix Table 6—Continued

Intervention	Study, Year (Reference)	Type of Systematic Review	Included Trials (Trials Rated Higher-Quality), n (n) [†]	Trials not Included in Any Other Relevant Systematic Review	Duration of Treatment in Included Trials	Sample Sizes in Included Trials, n	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
	Ferreira et al., 2003 (61)	Quantitative	27 (11)	2	1–14 sessions (mean, 6.8)	3817 (mean, 146)	High-velocity thrust (11), high-velocity thrust plus other techniques (8), high-velocity thrust plus low-velocity mobilization (7), compared different types of manipulation (1)	High-velocity-thrust spinal manipulation vs. sham manipulation or no treatment for LBP <3 mo in duration: WMD, 18 points (CI, 13–24 points) on 100-point scale for short-term pain (3 RCTs); WMD, 9 points (CI, 1–17 points) on 100-point scale for short-term disability (3 RCTs) No differences between spinal manipulation and other effective therapies	5
	Gay et al., 2005 (62)	Qualitative	1 (quality not assessed)	1	NR	30	Distraction manipulation (1)	Insufficient evidence to assess efficacy of distraction manipulation	2
	Licciardone et al., 2005 (63)	Quantitative	6 (quality not assessed)	1	4–11 sessions	30–178 (median, 93)	All trials evaluated osteopathic spinal manipulation	Osteopathic spinal manipulation vs. control treatment: SMD, –0.30 (CI, –0.47 to –0.13) for pain reduction (8 comparisons from 6 RCTs)	4
	Woodhead and Clough, 2005 (68)	Qualitative	62 (27)	17	1–14 sessions	12–1633 (median, 95)	Rotational method (8), Maitland method (5), sacroiliac method (3), other or not specified (46)	Limited evidence that spinal manipulation is more effective than placebo for acute LBP; moderate evidence that spinal manipulation is more effective than placebo for chronic or subacute LBP Moderate evidence that spinal manipulation is more effective than some other interventions for acute LBP; strong evidence that spinal manipulation is more effective than some other interventions for chronic LBP	4
Superficial heat (9 trials in 1 systematic review)	French et al., 2006 (50)	Quantitative	9 (5)	NA	Single application—7 days	36–371 (median, 90)	Superficial heat (9), superficial cold (2)	Heat wrap vs. oral placebo or nonheated wrap for acute or subacute LBP (4 RCTs): WMD, 1.06 points (CI, 0.68 to 1.45 points) on a 0–5 scale for pain relief up to day 5 (2 RCTs); WMD, –2.10 points (CI, –3.19 to –1.01 points) for score on RDQ (2 RCTs) Insufficient evidence to assess efficacy of superficial heat vs. superficial cold	7

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Appendix Table 6—Continued

Intervention	Study, Year (Reference)	Type of Systematic Review	Included Trials (Trials Rated Higher-Quality), n (n)†	Trials not Included in Any Other Relevant Systematic Review	Duration of Treatment in Included Trials	Sample Sizes in Included Trials, n	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
Traction (24 unique trials in 3 systematic reviews)	Clarke et al., 2005, 2006 (51, 52)	Qualitative	23 (5)	11	1–8 wk	25–400 (median, 52)	Mechanical or manual traction (13), autotraction (6), Tru-Trac (3), underwater traction (1), other (3)	Strong evidence that continuous traction is not superior to placebo, sham, or no treatment for any outcome at 3 mo or 6 wk in patients with or without sciatica (2 RCTs) Moderate evidence that autotraction is more effective than placebo, sham, or no treatment for pain, global improvement, or work absenteeism in patients with sciatica (2 RCTs); moderate evidence that other forms of traction not more effective than control (8 RCTs)	6
	Harte et al., 2003 (53)	Qualitative	13 (1)	1	1–8 wk	16–334 (median, 62)	Mechanical or manual traction (7), autotraction (2), Tru-Trac (2), other (3)	Traction vs. sham traction: 6 RCTs (1 higher-quality) reported negative results (1 RCT inconclusive)	7
TENS (11 trials in 6 systematic reviews§)	Khadilkar et al., 2005 (54)	Qualitative	2 (1)	2	Single session and 4 wk	30 and 145	TENS given at clinic (1), TENS self-administered at home (1)	TENS vs. placebo (2 RCTs, 1 good-quality): TENS not superior to placebo for any outcomes measured (pain, functional status, range of motion, use of medical services) (1 good-quality RCT); in the other RCT, TENS superior for subjective pain intensity for 60 min after treatment; no longer-term follow-up	7
Multiple interventions	Cherkin et al., 2003 (69)	Qualitative	8 systematic reviews, 9 RCTs (quality not assessed)	0	2–12 wk (RCTs)	24–262 (RCTs)	Acupuncture (20), massage (3), spinal manipulation (26)	Effectiveness of acupuncture unclear; massage effective for subacute and chronic LBP in 3 RCTs; spinal manipulation equivalent to other commonly used therapies	4
	Vroomen et al., 2000 (70)	Quantitative	8 (3) trials of traction, exercise, or spinal manipulation	0	NR	44–322 (median, 77)	Traction (7), exercise (2), spinal manipulation (2)	Traction vs. sham, infrared heat, or corset for sciatica: OR, 1.2 (CI, 0.7 to 2.0) for “treatment success” (4 RCTs) Insufficient evidence to evaluate efficacy of exercise or spinal manipulation for sciatica	5

* LBP = low back pain; NA = not applicable; NR = not reported; NSAID = nonsteroidal anti-inflammatory drug; ODI = Oswestry Disability Index; OR = odds ratio; RCT = randomized, controlled trial; RDQ = Roland-Morris Disability Questionnaire; RR = relative risk; SMD = standardized mean difference; TENS = transcutaneous electrical nerve stimulation; VAS = visual analogue scale; WMD = weighted mean difference.

† Higher-quality trials defined as those receiving >50% of maximum possible quality rating score used by each systematic review.

‡ 22 trials of behavioral therapy alone or as part of interdisciplinary rehabilitation.

§ Including trials of TENS included in systematic reviews of acupuncture (16), massage (26, 27), spinal manipulation (15, 55), superficial heat (50), and traction (52).

Appendix Table 7. Excluded Systematic Reviews*

Intervention	Study, Year (Reference)	Reason for Exclusion
Acupuncture	Ernst and White, 1997 (71)	Outdated
	Ernst and White, 1998 (72)	Outdated
	Ezzo et al., 2000 (73)	Not specific for LBP
	Patel et al., 1989 (74)	Outdated
	Smith et al., 2000 (75)	Not specific for LBP
	Strauss, 1999 (76)	Outdated
	ter Riet et al., 1990 (77)	Outdated
Back schools	van Tulder, 1999 (78)	Not specific for LBP
	Cohen et al., 1994 (79)	Updated Cochrane review available
	Keijsers et al., 1991 (80)	Outdated
	Koes et al., 1994 (81)	Outdated
	Nentwig, 1999 (82)	Outdated
Psychological interventions	van Tulder et al., 2000 (83)	German language
	Morley et al., 1999 (84)	Updated Cochrane review available
Exercise	van Tulder et al., 2001 (85)	Outdated
	Cleland et al., 2002 (86)	Not specific for LBP
	Colle et al., 2002 (87)	Updated Cochrane review available
	Faas, 1996 (88)	Systematic methods not used for synthesizing results
	Hilde and Bo, 1998 (89)	Only evaluated trials identified by an earlier (outdated) systematic review by van Tulder et al. (2000)
	Koes et al., 1991 (90)	Outdated
	Maher et al., 1999 (91)	Outdated
Low-level laser therapy	van Tulder et al., 2000 (92, 93)	Updated Cochrane review available
	Beckerman et al., 1992 (94)	Not specific for LBP
	Bjordal et al., 2003 (95)	Not specific for LBP
	de Bie, 1998 (96)	Not specific for LBP
Lumbar supports	Gam et al., 1993 (97)	Not specific for LBP
	Koes, 1994 (98)	Outdated
Massage Spinal manipulation	van Poppel, 2000 (99)	Does not evaluate clinical outcomes from use of lumbar supports
	Ernst, 1999 (100)	Outdated
	Abenhaim and Bergeron, 1992 (101)	Outdated
	Anderson et al., 1992 (102)	Outdated
	Assendelft et al., 1992 (103)	Outdated
	Assendelft et al., 1995 (104)	Outdated
	Assendelft et al., 1996 (105)	Outdated
	Assendelft et al., 1996 (106)	Outdated
	Brox et al., 1999 (107)	Outdated
	Di Fabio, 1992 (108)	Norwegian language
	Ernst, 2000 (109)	Outdated
	Ernst and Harkness, 2001 (110)	Not specific for LBP
	Ernst et al., 2004 (111)	Not specific for LBP
	Koes et al., 1991 (112)	Cervical manipulation only
	Koes et al., 1996 (113)	Outdated
	Mohseni-Bandpei, 1998 (114)	Outdated
	Ottenbacher and DiFabio, 1985 (115)	Outdated
Shekelle et al., 1992 (116)	Outdated	
TENS	Brosseau et al., 2002 (117)	Updated Cochrane review available
	Flowerdew and Gadsby, 1997 (118)	Outdated
	Gadsby and Flowerdew, 2000 (119)	Updated Cochrane review available
Traction	Milne et al., 2001 (120)	Updated Cochrane review available
	van der Heijden et al., 1995 (121)	Outdated
Ultrasonography Multiple interventions	van der Windt et al., 1999 (122)	No included studies of LBP
	Beckerman et al., 1993 (123) (exercise, low-level laser therapy, spinal manipulation, traction, ultrasonography)	Outdated
	Di Fabio, 1995 (124) (back schools, interdisciplinary rehabilitation)	Not specific for LBP
	Pengel et al., 2002 (125) (exercise, lumbar supports, spinal manipulation, TENS)	Outdated
	Scheer et al., 1995 (126) (back schools, exercise, spinal manipulation)	Limited to trials of subacute (7 wk–6 mo) LBP, all trials included in other systematic reviews
	Scheer et al., 1997 (127) (back schools, behavioral interventions, exercise, lumbar supports)	Outdated
	Turner, 1996 (128) (back schools, behavioral interventions)	Outdated
	van der Weide et al., 1997 (129) (back schools, behavioral interventions, exercise, spinal manipulation)	Outdated
	van Tulder et al., 1997 (5) (back schools, behavioral interventions, exercise, spinal manipulation, TENS, traction)	Outdated

* LBP = low back pain; TENS = transcutaneous electrical nerve stimulation.

Appendix Table 8. Additional, Large Trials of Acupuncture, Exercise, and Spinal Manipulation for Low Back Pain Not Included in Systematic Reviews*

Intervention	Study, Year (Reference)	Patients, <i>n</i> (Duration of Follow-up)	Main Results	Quality
Acupuncture	Brinkhaus et al., 2006 (130)	298 (8 wk [vs. wait-list control] to 52 wk [vs. sham acupuncture])	Acupuncture vs. sham acupuncture vs. wait-list control (8-wk results) Pain intensity (difference from baseline on 0–100 scale): 28.7 vs. 23.6 vs. 6.9 points ($P = 0.26$ for acupuncture vs. sham; $P < 0.001$ for acupuncture vs. wait-list control) Back function (mean score on 0–100 scale): 66.8 vs. 62.9 vs. 57.7 points Pain Disability Index (mean score on 0–100 scale): 18.8 vs. 21.5 vs. 27.1 points SF-36 physical health scale (mean score): 40.5 vs. 36.2 vs. 33.9 points ($P = 0.004$ for acupuncture vs. sham and $P < 0.001$ for acupuncture vs. wait-list control) SF-36 mental health scale: No differences SF-36 pain scale (mean score): 58.8 vs. 50.7 vs. 39.9 points ($P = 0.01$ for acupuncture vs. sham) Depression: No significant differences	8/10†
	Thomas et al., 2005 (155)	241 (24 mo)	Routinely offering acupuncture vs. usual care SF-36 pain score, mean adjusted difference between interventions: 5.6 points at 12 mo ($P = 0.11$), 8.0 points at 24 mo ($P = 0.03$) (favors acupuncture) McGill Present Pain Intensity: No difference at 12 or 24 mo ODI score: No difference at 12 or 24 mo Pain-free in past 12 mo: 18% vs. 8% ($P = 0.06$) Use of low back pain medication in past 4 wk: 60% vs. 41% ($P = 0.03$)	7/10†
	Witt, 2006 (132)	2841 (6 mo)	Acupuncture vs. no acupuncture (difference in change from baseline, positive values favor acupuncture): Back function loss (Hannover Functional Assessment Questionnaire, 0–100 scale): 22.0 points (95% CI, 19.3 to 24.7 points) at 3 mo, 3.7 (CI, 0.7 to 6.7 points) at 6 mo Low Back Pain Rating Scale (0–100): 27.2 points (CI, 20.9 to 24.5 points) at 3 mo, 2.7 points (CI, –0.3 to 5.7 points) at 6 mo SF-36 physical component score: 4.7 points (CI, 4.0 to 5.4 points) at 3 mo, 0.6 point (CI, –0.2 to 1.3 points) at 6 mo SF-36 mental component score: 2.1 points (CI, 1.4 to 2.8 points) at 3 mo, 0.2 point (CI, –0.6 to 1.0 points) at 6 mo	8/10†
Spinal manipulation or exercise therapy	Hurwitz et al., 2002 (133)—UCLA Low Back Pain Study	681 (6 mo)	Chiropractic care vs. medical care (adjusted between-group difference in improvement from baseline) Most severe pain (0–10 scale): –0.25 point (CI, –0.96 to 0.45 point) at 6 mo, –0.64 point (CI, –1.38 to –0.21 points) at 18 mo Average pain (0–10 scale): –0.26 point (CI, –0.81 to 0.29 point) at 6 mo, –0.50 point (CI, –1.09 to 0.08 point) at 18 mo RDQ (0–24 scale): –0.37 point (CI, –1.63 to 0.90 point) at 6 mo, –0.69 point (–2.02 to 0.65 point) at 18 mo	7/9‡
	UK BEAM Trial, 2004 (134)	1334 (12 mo)	Manipulation + exercise vs. manipulation vs. exercise (all results are absolute net benefit relative to usual care at 12 mo) RDQ (0–24 scale): 1.30 points (CI, 0.54 to 2.07 points) vs. 1.01 points (CI, 0.22 to 1.81 points) vs. 0.39 points (CI, –0.41 to 1.19 points) Modified Von Korff pain score (0–100 scale): 6.71 points (CI, 2.47 to 10.95 points) vs. 5.87 points (CI, 1.58 to 10.17 points) vs. 4.90 points (CI, 0.30 to 9.50 points) Modified Von Korff disability score (0–100 scale): 6.71 points (CI, 2.62 to 10.80 points) vs. 5.65 points (CI, 1.57 to 9.72 points) vs. 4.56 points (CI, 0.34 to 8.78 points)	2/9‡

* ODI = Oswestry Disability Index; RDQ = Roland–Morris Disability Questionnaire; SF-36 = Short Form-36; UCLA = University of California, Los Angeles; UK BEAM = United Kingdom Back Pain Exercise and Manipulation.

† Using Cochrane Back Review Group methods, excluding criterion on blinding of care provider, leaving a maximum possible score of 10.

‡ Using Cochrane Back Review Group methods, excluding criteria on blinding of patients and care provider, leaving a maximum possible score of 9.

Appendix Table 9. Trials of Interferential Therapy, Low-Level Laser Therapy, Shortwave Diathermy, Ultrasonography, and Yoga for Low Back Pain*

Intervention	Study, Year (Reference)	Patients, <i>n</i> (Duration of Follow-up)	Main Results	Quality†
Interferential therapy	Hurley et al., 2001 (135)	60 (3 mo)	Interferential therapy applied to painful area + self-care book vs. interferential therapy applied to area of spinal nerve + self-care book vs. self-care book alone (difference in median scores from baseline to 3 mo) McGill Pain Questionnaire Pain Rating Index (0–78): 2.2 vs. –2.5 vs. –9.7 points RDQ score (0–24): –3.5 vs. –8.0 vs. –4.0 points EQ-5D score: no difference RDQ, median score at 3 mo: 2.0 vs. 1.0 vs. 1.0 points	5/11
	Hurley et al., 2004 (136)	240 (12 mo)	Interferential therapy vs. manipulative therapy vs. combination (mean improvement at 12 mo) Pain (0–100 VAS): –26.5 vs. –18.2 vs. –25.7 points (<i>P</i> > 0.05) McGill Pain Questionnaire Pain Rating Index (0–78): –8.3 vs. –6.4 vs. –9.2 points (<i>P</i> > 0.05) RDQ score (0–24): –4.9 vs. –4.7 vs. –6.5 points (<i>P</i> > 0.05) SF-36 score: no differences Recurrent low back pain: 69% vs. 77% vs. 64% (<i>P</i> > 0.05) Absent from work >30 d: 8% vs. 12% vs. 12%	7/11
	Werners et al., 1999 (137)	152 (3 mo)	Interferential therapy vs. traction (mean difference from baseline to 3 mo) Pain score (0–100): –9.8 vs. –14.6 points (<i>P</i> > 0.05) ODI score (0–100): –7.7 vs. –7.4 points	4/11
Low-level laser therapy	Basford et al., 1999 (138)	61 (1 mo after end of treatment)	Nd:YAG laser vs. sham (mean change from baseline) ODI score: –6.3 vs. –2.1 points Maximal pain in the past 24 h (0–100 VAS): –16.1 vs. –2.3 points	8/11
	Gur et al., 2003 (139)	75 (1 mo after treatment)	Laser vs. exercise vs. laser + exercise (mean change from baseline) Pain (0–10 VAS): –4.2 vs. –3.6 vs. –4.4 points (<i>P</i> > 0.05) RDQ score: –9.7 vs. –9.6 vs. –11.5 points (<i>P</i> > 0.05) Modified ODI score: –16.4 vs. –16.9 vs. –17.6 points (<i>P</i> > 0.05)	3/11
	Klein and Eek, 1990 (140)	20 (1 mo after treatment)	GaAs laser + exercise vs. sham + exercise (mean change from baseline) Pain (0–7.5 VAS): –1.3 vs. –1.2 points RDQ score: –1.8 vs. –3.0 points	6/11
	Longo et al., 1988 (141)	120 (1 y after treatment)	904-nm laser vs. 10 600-nm laser vs. sham Complete disappearance of pain 1 mo after treatment: 95% vs. 82.5% vs. 2.5% Relapse 1 y after treatment: 65% vs. 70% vs. 95%	5/11
	Monticone et al., 2004 (142)	22 (up to 12 mo after treatment)	Laser vs. stabilization (exercise, lumbar therapy, and mesotherapy) (mean change from baseline to end of treatment and after 12 mo) Pain at rest (VAS 0–10): 0 vs. –5 points; –1 vs. –6 points Pain with movement (VAS 0–10): –4 vs. –7 points; –2 vs. –8 points	1/11
	Soriano and Rios, 1998 (143)	85 (6 mo after end of treatment)	GaAs laser vs. sham Proportion with >60% pain relief at end of treatment: 71% (27/38) vs. 36% (12/33) (<i>P</i> < 0.007)	6/11
	Toya et al., 1994 (144)	41 (1 d after treatment)	GaAs laser vs. sham Treatment “effective”: 94% (15/16) vs. 48% (12/25)	10/11
Shortwave diathermy	Sweetman et al., 1993 (147)	400 (2 wk)	Shortwave diathermy vs. extension exercises vs. traction vs. sham diathermy Global effect “better” at 2 wk: 39% (39/100) vs. 45% (45/100) vs. 49% (49/100) vs. 37% (37/100) (<i>P</i> > 0.05)	5/11

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Appendix Table 9—Continued

Intervention	Study, Year (Reference)	Patients, <i>n</i> (Duration of Follow-up)	Main Results	Quality
	Gibson et al., 1985 (145)	109 (12 wk)	Shortwave diathermy vs. osteopathic manipulation vs. detuned (sham) diathermy Median daytime pain score (0–100) at 2 wk: 35 vs. 25 vs. 28 points Median daytime pain score (0–100) at 12 wk: 25 vs. 13 vs. 6 points Proportion free of pain at 2 wk: 35% vs. 25% vs. 28% Proportion free of pain at 12 wk: 37% vs. 42% vs. 44% Proportion needing analgesics at 2 wk: 22% vs. 18% vs. 32% Proportion needing analgesics at 12 wk: 7% vs. 18% vs. 22% Proportion unable to work or with modified activities at 2 wk: 31% vs. 13% vs. 38% Proportion unable to work or with modified activities at 12 wk: 7% vs. 5% vs. 19%	4/11
	Rasmussen, 1979 (146)	24 (2 wk)	Shortwave diathermy vs. spinal manipulation Proportion “fully restored” by 14 d: 25% (3/12) vs. 92% (11/12)	3/11
Ultrasonography	Ansari et al., 2006 (148)	15 (3 wk)	Ultrasonography vs. sham ultrasonography for chronic low back pain Functional Rating Index (mean change from baseline, 0–100 scale): –22 vs. –7 (<i>P</i> < 0.05)	2/11
	Nwuga, 1983 (149)	73 (4 wk)	Ultrasonography vs. sham ultrasonography vs. no ultrasonography for acute sciatica (bed rest in all groups) Proportion pain free: 41% (11/27) vs. 12% (3/25) vs. 7% (2/29) (<i>P</i> < 0.001 for ultrasonography vs. sham or no ultrasonography)	3/11
	Roman, 1960 (150)	36 (duration unclear [10 sessions])	Ultrasonography vs. sham ultrasonography for back pain with or without sciatica Proportion “normal”: 22% (4/18) vs. 11% (2/18) Proportion “normal” or “good”: 67% (12/18) vs. 72% (13/18)	1/11
Yoga	Galantino et al., 2004 (151)	22 (6 wk)	Iyengar yoga vs. usual activities ODI score (change from baseline): 3.83 vs. 2.18 Proportion with lower scores on ODI: 46% vs. 40%	3/9
	Sherman et al., 2005 (152)	101 (26 wk)	Viniyoga vs. exercise (mean difference between groups compared to baseline) RDQ score (0–24 scale): –1.8 points (CI, –3.5 to –0.1 points) at 12 wk (<i>P</i> = 0.034) and –1.5 points (CI, –3.2 to 0.2 points) at 26 wk (<i>P</i> = 0.092) Symptom bothersomeness score (0–10 scale): –0.6 points (CI, –1.6 to –0.4 points) at 6 wk (<i>P</i> = 0.22), –1.4 points (CI, –2.5 to –0.2 points) at 26 wk (<i>P</i> = 0.018) Viniyoga vs. self-care book RDQ score: –3.4 points (CI, –5.1 to –1.6 points) at 12 wk (<i>P</i> = 0.0002) and –3.6 points (CI, –5.4 to –1.8 points) at 26 wk (<i>P</i> < 0.001) Symptom bothersomeness score: –1.6 points (CI, –2.6 to –0.5 points) at 6 wk (<i>P</i> = 0.0025) and –2.2 points (CI, –3.2 to –1.2 points) at 26 wk (<i>P</i> < 0.001)	7/9
	Williams et al., 2005 (153)	60 (7 mo)	Iyengar yoga vs. exercise education Present Pain Index, mean change at 7 mo (0–5 scale): –0.5 vs. –0.9 points (<i>P</i> = 0.140) Pain Disability Index, mean change at 7 mo (7–70 scale): –8.5 vs. –10.4 points (<i>P</i> = 0.009) Pain on VAS, mean change at 7 mo (0–10 scale): 1.2 vs. –1.6 points (<i>P</i> = 0.398)	3/9

* EQ-5D = EuroQol-5D; GaAs = gallium arsenide; Nd:YAG = neodymium:yttrium aluminum-garnet; ODI = Oswestry Disability Index; RDQ = Roland–Morris Disability Questionnaire; SF-36 = Short Form-36; VAS = visual analogue scale.

† Using Cochrane Back Review Group methods; maximum score, 11 (for trials of yoga, maximum score, 9, because of exclusion of criteria on blinding of patients and care provider).

Appendix Table 10. Summary of Evidence on Nonpharmacologic Therapies for Acute Low Back Pain

Intervention	Trials (Trials Rated Higher-Quality by ≥ 1 Systematic Review), n (n)	Net Benefit*	Effective vs. Placebo, Sham, Wait List, or No Treatment?	Inconsistency?†	Directness of Evidence?	Overall Quality of Evidence	Comments
Acupuncture	4 (3)	Unable to estimate	Unclear (2 trials)	Some inconsistency	Direct	Poor	
Back schools	1 (0)	Unable to estimate	Unclear (1 trial)	Not applicable	Direct	Poor	
Psychological interventions	0	No evidence	No evidence	No evidence	No evidence	No evidence	
Exercise	13 (7)	Not effective	No (9 trials)	Some inconsistency	Direct	Good	Most trials found no effect
Functional restoration	4 (3)	Not effective	Yes (3 trials)	Some inconsistency	Direct	Fair	Most trials found no effect, but studies were heterogeneous
Interdisciplinary rehabilitation	0	No evidence	No evidence	No evidence	No evidence	No evidence	
Interferential therapy	0	No evidence	No evidence	No evidence	No evidence	No evidence	
Low-level laser therapy	0	No evidence	No evidence	No evidence	No evidence	No evidence	
Lumbar supports	1 (0)	Unable to estimate	No evidence	Not applicable	Direct	Poor	
Massage therapy	1 (0)	Unable to estimate	No evidence	Not applicable	Direct	Poor	
Shortwave diathermy	1 (0)	Unable to estimate	No evidence	Not applicable	Direct	Poor	
Spinal manipulation	11 (2)	Small to moderate	Yes (2 trials)	No	Direct	Fair	
Superficial heat	5 (5)	Moderate	Yes (2 trials)	No	Direct	Good	
Traction	0	No evidence	No evidence	No evidence	No evidence	No evidence	Most trials included patients with back pain of varying duration, with or without sciatica
Transcutaneous electrical nerve stimulation	1 (0)	Unable to estimate	No evidence	Not applicable	Direct	Poor	
Ultrasonography	0	No evidence	No evidence	No evidence	No evidence	No evidence	
Yoga	0	No evidence	No evidence	No evidence	No evidence	No evidence	

* Based on evidence showing medication is more effective than placebo, or evidence showing medication is at least as effective as other medications or interventions thought to be effective, for 1 or more of the following outcomes: pain, functional status, or work status. Compared with placebo, small benefit was defined as 5–10 points on a 100-point visual analogue scale (VAS) for pain (or equivalent), 1–2 points on the Roland–Morris Disability Questionnaire (RDQ), 10–20 points on the Oswestry Disability Index (ODI), or a standardized mean difference (SMD) of 0.2–0.5. Moderate benefit was defined as 10–20 points on a 100-point VAS for pain, 2–5 points on the RDQ, 10–20 points on the ODI, or an SMD of 0.5–0.8. Large benefit was defined as >20 points on a 100-point VAS for pain; >5 points on the RDQ, >20 points on the ODI, or an SMD >0.8.

† Inconsistency was defined as <75% of trials reaching consistent conclusions on efficacy (no effect vs. positive effect was considered inconsistent).

Appendix Table 11. Summary of Evidence on Nonpharmacologic Therapies for Chronic or Subacute Low Back Pain

Intervention	Trials (Trials Rated Higher-Quality by ≥ 1 Systematic Review), n (n)	Net Benefit*	Effective vs. Placebo, Sham, Wait List, or No Treatment?	Inconsistency?†	Directness of Evidence?	Overall Quality of Evidence	Comments
Acupuncture	24 (8)	Moderate	Yes (12 trials)	Some inconsistency (vs. sham acupuncture)	Direct	Fair	Efficacy of acupuncture vs. sham acupuncture inconsistent
Back schools	26 (3)	Small	Yes (13 trials)	Some inconsistency	Direct	Fair	Back schools based on Swedish model seemed most effective
Psychological interventions	35 (11)	Moderate (cognitive-behavioral treatment), substantial (progressive relaxation), unable to estimate (biofeedback), no effect (operant therapy)	Yes (11 trials)	Some inconsistency (for biofeedback)	Direct	Good (cognitive-behavioral and operant therapy), fair (progressive relaxation), poor (biofeedback)	
Exercise	62 (29)	Small to moderate	Yes (24 trials)	No	Direct	Good	
Functional restoration	12 (9)	Moderate	Yes (7 trials)	No	Direct	Fair	
Interdisciplinary rehabilitation	11 (2)	Moderate	Yes (4 trials)	No	Direct	Good	More intense interdisciplinary rehabilitation more effective than less intense interdisciplinary rehabilitation
Interferential therapy	3 (1)	Unable to estimate	No evidence	No	Direct	Poor	
Low-level laser therapy	6 (4)	Unable to estimate	Unclear (5 trials)	Some inconsistency	Direct	Poor	Trials evaluated different types and intensity of laser, with inconsistent findings
Lumbar supports	2 (1)	Unable to estimate	Unclear (1 trial)	Some inconsistency	Direct	Poor	
Massage therapy	4 (3)	Moderate	No evidence	Some inconsistency (vs. spinal manipulation)	Direct	Fair	Some trials evaluated minimal or light massage techniques
Shortwave diathermy	1 (0)	Not effective	No evidence	Not applicable	Direct	Poor	
Spinal manipulation	29 (15)	Moderate	Yes (13 trials)	No	Direct	Good	
Superficial heat	3 (0)	Unable to estimate	Unclear (3 trials)	No	Direct	Poor	3 lower-quality trials
Traction	6 (3)	Not effective (for continuous traction)	No (2 trials)	No	Direct	Fair	
Transcutaneous electrical nerve stimulation	9 (2)	Unable to estimate	Yes (2 trials)	Yes (vs. sham or no treatment)	Direct	Poor	
Ultrasonography	1 (0)	Unable to estimate	Unclear (1 trial)	Not applicable	Direct	Poor	
Yoga	3 (1)	Moderate (for Viniyoga)	No evidence	No	Direct	Fair (for Viniyoga)	Insufficient evidence to judge non-Viniyoga techniques

* Based on evidence showing medication is more effective than placebo, or evidence showing medication is at least as effective as other medications or interventions thought to be effective, for 1 or more of the following outcomes: pain, functional status, or work status. Compared with placebo, small benefit was defined as 5–10 points on a 100-point visual analogue scale (VAS) for pain (or equivalent), 1–2 points on the Roland–Morris Disability Questionnaire (RDQ), 10–20 points on the Oswestry Disability Index (ODI), or a standardized mean difference (SMD) of 0.2–0.5. Moderate benefit was defined as 10–20 points on a 100-point VAS for pain, 2–5 points on the RDQ, 10–20 points on the ODI, or an SMD of 0.5–0.8. Large benefit was defined as >20 points on a 100-point VAS for pain; >5 points on the RDQ, >20 points on the ODI, or an SMD >0.8.

† Inconsistency was defined as <75% of trials reaching consistent conclusions on efficacy (no effect vs. positive effect was considered inconsistent).

Appendix Table 12. Summary of Evidence on Nonpharmacologic Therapies for Radiculopathy or Sciatica

Intervention	Trials (Trials Rated Higher-Quality by ≥ 1 Systematic Review), <i>n</i> (<i>n</i>)	Net Benefit*	Effective vs. Placebo, Sham, Wait List, or No Treatment?	Inconsistency?†	Directness of Evidence?	Overall Quality of Evidence	Comments
Spinal manipulation	3 (0)	Moderate	No evidence	No	Direct	Fair	No clear differences vs. other interventions
Traction	16 (4)	Not effective (continuous or intermittent traction); small to moderate (autotraction)	No for continuous or intermittent traction (8 trials), yes for autotraction (2 trials)	Some inconsistency (for autotraction vs. continuous or intermittent traction)	Direct	Fair	Other trials of traction included patients with back pain of varying duration
Ultrasonography	1 (0)	Unable to estimate	Unclear (1 trial)	Not applicable	Direct	Poor	

* Based on evidence showing medication is more effective than placebo, or evidence showing medication is at least as effective as other medications or interventions thought to be effective, for 1 or more of the following outcomes: pain, functional status, or work status. Compared with placebo, small benefit was defined as 5–10 points on a 100-point visual analogue scale (VAS) for pain (or equivalent), 1–2 points on the Roland–Morris Disability Questionnaire (RDQ), 10–20 points on the Oswestry Disability Index (ODI), or a standardized mean difference (SMD) of 0.2–0.5. Moderate benefit was defined as 10–20 points on a 100-point VAS for pain, 2–5 points on the RDQ, 10–20 points on the ODI, or an SMD of 0.5–0.8. Large benefit was defined as >20 points on a 100-point VAS for pain; >5 points on the RDQ, >20 points on the ODI, or an SMD >0.8.

† Inconsistency was defined as <75% of trials reaching consistent conclusions on efficacy (no effect vs. positive effect was considered inconsistent).

Medications for Acute and Chronic Low Back Pain: A Review of the Evidence for an American Pain Society/American College of Physicians Clinical Practice Guideline

Roger Chou, MD, and Laurie Hoyt Huffman, MS

Background: Medications are the most frequently prescribed therapy for low back pain. A challenge in choosing pharmacologic therapy is that each class of medication is associated with a unique balance of risks and benefits.

Purpose: To assess benefits and harms of acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants, benzodiazepines, antiepileptic drugs, skeletal muscle relaxants, opioid analgesics, tramadol, and systemic corticosteroids for acute or chronic low back pain (with or without leg pain).

Data Sources: English-language studies were identified through searches of MEDLINE (through November 2006) and the Cochrane Database of Systematic Reviews (2006, Issue 4). These electronic searches were supplemented by hand searching reference lists and additional citations suggested by experts.

Study Selection: Systematic reviews and randomized trials of dual therapy or monotherapy with 1 or more of the preceding medications for acute or chronic low back pain that reported pain outcomes, back-specific function, general health status, work disability, or patient satisfaction.

Data Extraction: We abstracted information about study design, population characteristics, interventions, outcomes, and adverse events. To grade methodological quality, we used the Oxman criteria for systematic reviews and the Cochrane Back Review Group criteria for individual trials.

Data Synthesis: We found good evidence that NSAIDs, skeletal muscle relaxants (for acute low back pain), and tricyclic antidepressants

(for chronic low back pain) are effective for pain relief. The magnitude of benefit was moderate (effect size of 0.5 to 0.8, improvement of 10 to 20 points on a 100-point visual analogue pain scale, or relative risk of 1.25 to 2.00 for the proportion of patients experiencing clinically significant pain relief), except in the case of tricyclic antidepressants (for which the benefit was small to moderate). We also found fair evidence that acetaminophen, opioids, tramadol, benzodiazepines, and gabapentin (for radiculopathy) are effective for pain relief. We found good evidence that systemic corticosteroids are ineffective. Adverse events, such as sedation, varied by medication, although reliable data on serious and long-term harms are sparse. Most trials were short term (≤ 4 weeks). Few data address efficacy of dual-medication therapy compared with monotherapy, or beneficial effects on functional outcomes.

Limitations: Our primary source of data was systematic reviews. We included non-English-language trials only if they were included in English-language systematic reviews.

Conclusions: Medications with good evidence of short-term effectiveness for low back pain are NSAIDs, skeletal muscle relaxants (for acute low back pain), and tricyclic antidepressants (for chronic low back pain). Evidence is insufficient to identify one medication as offering a clear overall net advantage because of complex tradeoffs between benefits and harms. Individual patients are likely to differ in how they weigh potential benefits, harms, and costs of various medications.

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For author affiliations, see end of text.

In the United States, low back pain is the fifth most common reason for all physician office visits and the second most common symptomatic reason (1, 2). Medications are the most frequently recommended intervention for low back pain (1, 3). In 1 study, 80% of primary care patients with low back pain were prescribed at least 1 medication at their initial office visit, and more than one third were prescribed 2 or more drugs (4).

The most commonly prescribed medications for low back pain are nonsteroidal anti-inflammatory drugs (NSAIDs), skeletal muscle relaxants, and opioid analgesics (4–7). Benzodiazepines, systemic corticosteroids, antidepressant medications, and antiepileptic drugs are also prescribed (8). Frequently used over-the-counter medications include acetaminophen, aspirin, and certain NSAIDs.

A challenge in choosing pharmacologic therapy for low back pain is that each class of medication is associated with a unique balance of benefits and harms. In addition, benefits and harms may vary for individual drugs within a medication class. Previous reviews found only limited evi-

dence to support use of most medications for low back pain. For example, a systematic review published in 1996 found insufficient evidence to support use of any medication for low back pain other than NSAIDs (good evidence) and skeletal muscle relaxants (fair evidence) (9).

This article reviews current evidence on benefits and harms of medications for acute and chronic low back pain.

See also:

Print

Related articles 478, 492
Summary for Patients I-45

Web-Only

Appendix Tables
CME quiz
Conversion of graphics into slides
Audio summary

It is part of a larger evidence review commissioned by the American Pain Society and the American College of Physicians to guide recommendations for management of low back pain (10).

METHODS

Data Sources and Searches

An expert panel convened by the American Pain Society and the American College of Physicians determined which medications would be included in this review. The panel chose acetaminophen, NSAIDs (nonselective, cyclooxygenase-2 selective, and aspirin), antidepressants, benzodiazepines, antiepileptic drugs, skeletal muscle relaxants, opioid analgesics, tramadol, and systemic corticosteroids.

We searched MEDLINE (1966 through November 2006) and the Cochrane Database of Systematic Reviews (2006, Issue 4) for relevant systematic reviews, combining terms for low back pain with a search strategy for identifying systematic reviews. When higher-quality systematic reviews were not available for a particular medication, we conducted additional searches for primary studies (combining terms for low back pain with the medication of interest) on MEDLINE and the Cochrane Central Register of Controlled Trials. Full details of the search strategies are available in the complete evidence report (10). Electronic searches were supplemented by hand searching of reference lists and additional citations suggested by experts. We did not include trials published only as conference abstracts.

Evidence Selection

We included all randomized, controlled trials that met all of the following criteria: 1) reported in the English language, or in a non-English language but included in an English-language systematic review; 2) evaluated nonpregnant adults (>18 years of age) with low back pain (alone or with leg pain) of any duration; 3) evaluated a target medication, either alone or in addition to another target medication (“dual therapy”); and 4) reported at least 1 of the following outcomes: back-specific function, generic health status, pain, work disability, or patient satisfaction (11, 12).

We excluded trials that compared dual-medication therapy with therapy using a different medication, medication combination, or placebo. We also excluded trials of low back pain associated with acute major trauma, cancer, infection, the cauda equina syndrome, fibromyalgia, and osteoporosis or vertebral compression fracture.

Because of the large number of trials evaluating medications for low back pain, our primary source for trials was systematic reviews. When multiple systematic reviews were available for a target medication, we excluded outdated systematic reviews, which we defined as systematic reviews with a published update, or systematic reviews published before 2000. When a higher-quality systematic review was not available for a particular intervention, we included all relevant randomized, controlled trials.

Data Extraction and Quality Assessment

For each included systematic review, we abstracted information on search methods; inclusion criteria; methods for rating study quality; characteristics of included studies; methods for synthesizing data; and results, including the number and quality of trials for each comparison and outcome in patients with acute (<4 weeks' duration) low back pain, chronic/subacute (>4 weeks' duration) low back pain, and back pain with sciatica. If specific data on duration of trials were not provided, we relied on the categorization (acute or chronic/subacute) assigned by the systematic review. For each trial not included in a systematic review, we abstracted information on study design, participant characteristics, interventions, and results.

We considered mean improvements of 5 to 10 points on a 100-point visual analogue pain scale (or equivalent) to be small or slight; 10 to 20 points, moderate; and more than 20 points, large or substantial. For back-specific functional status, we classified mean improvements of 2 to 5 points on the Roland–Morris Disability Questionnaire (scale, 0 to 24) and 10 to 20 points on the Oswestry Disability Index (scale, 0 to 100) as moderate (13). We also considered standardized mean differences of 0.2 to 0.5 to be small or slight; 0.5 to 0.8, moderate; and greater than 0.8, large (14). Some evidence suggests that our classification of mean improvements and standardized mean differences for pain and functional status are roughly concordant in patients with low back pain (15–20). Because few trials reported the proportion of patients meeting specific thresholds (such as >30% reduction in pain score) for target outcomes, it was usually not possible to report numbers needed to treat for benefit. When those were reported, we considered a relative risk (RR) of 1.25 to 2.00 for the proportion of patients reporting greater than 30% pain relief (or a similar outcome) to indicate a moderate benefit.

Two reviewers independently rated the quality of each included trial. Discrepancies were resolved through joint review and a consensus process. We assessed internal validity (quality) of systematic reviews by using the Oxman criteria (**Appendix Table 1**, available at www.annals.org) (21, 22). According to this system, systematic reviews receiving a score of 4 or less (on a scale of 1 to 7) have potential major flaws and are more likely to produce positive conclusions about effectiveness of interventions (22, 23). We classified such systematic reviews as “lower quality”; those receiving scores of 5 or more were graded as “higher quality.”

We did not abstract results of individual trials if they were included in a higher-quality systematic review. Instead, we relied on results and quality ratings for the trials as reported by the systematic reviews. We considered trials receiving more than half of the maximum possible quality score to be “higher quality” for any quality rating system used (24, 25).

We assessed internal validity of randomized clinical trials not included in a higher-quality systematic review by

using the criteria of the Cochrane Back Review Group (**Appendix Table 2**, available at www.annals.org) (26). We considered trials receiving more than half of the total possible score (≥ 6 of a maximum 11) “higher quality” and those receiving less than half “lower quality” (24, 25).

Data Synthesis

We assessed overall strength of evidence for a body of evidence by using methods adapted from the U.S. Preventive Services Task Force (27). To assign an overall strength of evidence (good, fair, or poor), we considered the number, quality, and size of studies; consistency of results among studies; and directness of evidence. Minimum criteria for fair- and good-quality ratings are shown in **Appendix Table 3** (available at www.annals.org).

Consistent results from many higher-quality studies across a broad range of populations support a high degree of certainty that the results of the studies are true (the entire body of evidence would be considered good quality). For a fair-quality body of evidence, results could be due to true effects or to biases operating across some or all of the studies. For a poor-quality body of evidence, any conclusion is uncertain.

To evaluate consistency, we classified conclusions of trials and systematic reviews as positive (the medication is beneficial), negative (the medication is harmful or not beneficial), or uncertain (the estimates are imprecise, the evidence unclear, or the results inconsistent) (22). We defined “inconsistency” as greater than 25% of trials reaching discordant conclusions (positive vs. negative), 2 or more higher-quality systematic reviews reaching discordant conclusions, or unexplained heterogeneity (for pooled data).

Role of the Funding Source

The funding source had no role in the design, conduct, or reporting of this review or in the decision to publish the manuscript.

RESULTS

Literature Reviewed

We reviewed 1292 abstracts identified by searches for systematic reviews. Of these, 21 appeared potentially relevant and were retrieved. We excluded 7 outdated reviews of NSAIDs (28), antidepressants (29–31), and multiple drugs (9, 32, 33) (**Appendix Table 4**, available at www.annals.org). We also excluded 3 reviews that did not clearly use systematic methods (34–36) and 4 systematic reviews that evaluated target medications but did not report results specifically for patients with low back pain (37–39). We included 7 systematic reviews (**Appendix Table 5**, available at www.annals.org) of NSAIDs (40, 41), antidepressants (42, 43), skeletal muscle relaxants, and benzodiazepines (44–46), or multiple medications (47, 48) (quality ratings shown in **Appendix Table 6**, available at www.annals.org).

We conducted 8 additional searches (1586 citations)

for randomized trials of acetaminophen, celecoxib, aspirin, the serotonin–norepinephrine reuptake inhibitors duloxetine and venlafaxine, antiepileptic drugs, opioids, tramadol, and systemic corticosteroids.

Acetaminophen

Six unique trials of acetaminophen were included in a Cochrane review of NSAIDs (40, 41) and a systematic review of multiple medications for low back pain (47). From 134 potentially relevant citations, we identified 3 other trials of acetaminophen that met inclusion criteria (49–51). The longest trial of acetaminophen for acute or chronic low back pain lasted 4 weeks. We excluded 2 trials that did not evaluate efficacy of acetaminophen specifically for low back pain and 11 trials that compared dual therapy with acetaminophen plus another medication to a different medication, medication combination, or placebo.

For acute low back pain, 1 lower-quality trial included in the Cochrane review found no difference between acetaminophen (3 g/d) and no treatment (52). Four trials (3 of acute low back pain and 1 of mixed-duration back pain) found no clear differences in pain relief between acetaminophen at dosages up to 4 g/d and NSAIDs (40, 41).

For chronic low back pain, 1 higher-quality trial found acetaminophen inferior to diflunisal for patients reporting good or excellent efficacy after 4 weeks (53). Several other higher-quality systematic reviews of patients with osteoarthritis (not limited to the back) consistently found acetaminophen slightly inferior to NSAIDs for pain relief (standardized mean difference, about 0.3) (54–57).

There is insufficient evidence from 5 trials (1 higher-quality [51]) comparing acetaminophen with interventions other than NSAIDs (other medications, physical therapy, superficial heat, a corset, or spinal manipulation) to accurately judge relative efficacy (49–51, 58, 59).

Adverse events associated with acetaminophen for low back pain were poorly reported in the trials. Data on potentially serious harms, such as gastrointestinal bleeding, myocardial infarction, and hepatic adverse events, are particularly sparse.

NSAIDs

A total of 57 unique trials of NSAIDs were included in 3 systematic reviews (40, 41, 47, 48). From 74 potentially relevant citations for aspirin and 85 potentially relevant citations for celecoxib (the only cyclooxygenase-selective NSAID available in the United States), we identified 1 trial of aspirin that met inclusion criteria (60). We excluded 1 trial that did not evaluate aspirin specifically for low back pain (61), 10 trials that evaluated selective NSAIDs not available in the United States, and 3 trials that evaluated celecoxib in postoperative settings.

For acute low back pain, a higher-quality Cochrane review (51 trials) found nonselective NSAIDs superior to placebo for global improvement (6 trials; RR, 1.24 [95% CI, 1.10 to 1.41]) and for not requiring additional analgesics (3 trials; RR, 1.29 [CI, 1.05 to 1.57]) after 1 week of

therapy (40, 41). For chronic low back pain, an NSAID (ibuprofen) was also superior to placebo in 1 higher-quality trial (62). A second, higher-quality systematic review that included fewer ($n = 21$) trials reached conclusions consistent with the Cochrane review (47). For back pain with sciatica, 1 higher-quality systematic review found no difference between NSAIDs and placebo on a combined outcome of effectiveness (3 trials; odds ratio, 0.99 [CI, 0.6 to 1.7]) (48).

The Cochrane review found no evidence from 24 trials that any nonselective NSAID is superior to others for pain relief (40, 41). It also found no clear differences in efficacy between NSAIDs and opioid analgesics or muscle relaxants, although trials were limited by small sample sizes (6 trials, 1 higher-quality; 16 to 44 patients) (40, 41). Use of NSAIDs also was no more effective than nonpharmacologic interventions (spinal manipulation, physical therapy, bed rest).

The Cochrane review found that nonselective NSAIDs were associated with a similar risk for any adverse event compared with placebo (RR, 0.83 [CI, 0.64 to 1.08]) (40, 41). However, the trials were not designed to evaluate risks for less common but serious gastrointestinal and cardiovascular adverse events (63–65). Data on long-term benefits and harms associated with use of NSAIDs for low back pain are particularly sparse. Only 6 of 51 trials included in the Cochrane review were longer than 2 weeks in duration (the longest evaluated 6 weeks of therapy) (40, 41).

We found insufficient evidence from 1 lower-quality trial to accurately judge benefits or harms of aspirin (acetylsalicylic acid) for low back pain (60). Evidence regarding gastrointestinal safety of aspirin is primarily limited to trials of aspirin for prophylaxis of thrombotic events (66, 67).

Antidepressants

Ten unique trials were included in 3 systematic reviews of antidepressants (42, 43, 47). In all of the trials, the duration of therapy ranged from 4 to 8 weeks. From searches for the serotonin–norepinephrine reuptake inhibitors duloxetine or venlafaxine, we identified no relevant trials from 14 citations.

For chronic low back pain, 2 higher-quality systematic reviews (1 qualitative [43] and 1 quantitative [42]) consistently found antidepressants to be more effective than placebo for pain relief. Effects on functional outcomes were inconsistently reported and did not indicate clear benefits. Pooling data for all antidepressants, the quantitative systematic review (9 trials) estimated a standardized mean difference of 0.41 (CI, 0.22 to 0.61) for pain relief. However, effects on pain were not consistent across antidepressants. Tricyclic antidepressants were slightly to moderately more effective than placebo for pain relief in 4 (43) and 6 (42) trials (2 higher-quality) included in the systematic reviews, but paroxetine and trazodone (antidepressants without inhibitory effects on norepinephrine uptake) were no more effective than placebo in 3 trials. Maprotiline, the only

tetracyclic antidepressant evaluated in trials included in the systematic reviews, is not available in the United States. There was insufficient evidence from 1 lower-quality trial (which found no differences) (68) to directly judge relative effectiveness of tricyclic antidepressants versus selective serotonin reuptake inhibitors.

One systematic review found that antidepressants were associated with significantly higher risk for any adverse event compared with placebo (22% vs. 14%), although harms were generally not well reported (42). Drowsiness (7%), dry mouth (9%), dizziness (7%), and constipation (4%) were the most common adverse events. The trials were not designed to assess risks for serious adverse events, such as overdose, increased suicidality, or arrhythmias.

Benzodiazepines

Eight trials of benzodiazepines were included in a higher-quality Cochrane review of skeletal muscle relaxants (45, 46). The trials ranged from 5 to 14 days in duration.

For acute low back pain, 1 higher-quality trial found no differences between diazepam and placebo (69), but another, lower-quality trial found diazepam superior for short-term pain relief and overall improvement (70). For chronic low back pain, pooled results from 2 higher-quality trials (71, 72) found tetrazepam to be associated with a greater likelihood of not experiencing pain relief (RR, 0.71 [CI, 0.54 to 0.93]) or global improvement (RR, 0.63 [CI, 0.42 to 0.97]) after 8 to 14 days. A third, lower-quality, placebo-controlled trial of diazepam for chronic low back pain found no benefit (73).

In head-to-head trials included in the Cochrane review, efficacy did not differ between diazepam and tizanidine (1 higher-quality trial of acute low back pain [74]) or cyclobenzaprine (1 lower-quality trial of chronic low back pain [73]). For acute low back pain, a third, higher-quality trial found diazepam inferior to carisoprodol for muscle spasm, functional status, and global efficacy (global rating of “excellent” or “very good,” 70% vs. 45% of patients) (75). One study that pooled data from 20 trials ($n = 1553$) found no difference between diazepam and cyclobenzaprine for short-term (14 days) global improvement (both were superior to placebo) but was excluded from the Cochrane review because it included patients with back or neck pain (mixed duration) (76).

Central nervous system events, such as somnolence, fatigue, and lightheadedness, were reported more frequently with benzodiazepines than with placebo (45, 46).

Antiepileptic Drugs

We identified no systematic reviews of antiepileptic drugs for low back pain. From 94 citations, we identified 2 trials of gabapentin (77, 78) and 2 trials of topiramate (79, 80) that met inclusion criteria (Appendix Table 7, available at www.annals.org). The trials ranged from 6 to 10 weeks in duration. We identified no other trials of antiepileptic drugs for low back pain.

For low back pain with radiculopathy, 3 small (41 to

80 patients) trials found gabapentin (2 trials [78], 1 higher-quality [77]) and topiramate (1 higher-quality trial [79]) to be associated with small improvements in pain scores compared with placebo (or diphenhydramine as active placebo [79]). One trial reporting functional outcomes found no differences (79). For chronic low back pain with or without radiculopathy, 1 higher-quality trial found topiramate moderately superior to placebo for pain, but only slightly superior for functional status (80).

There was no clear difference between gabapentin and placebo in rates of withdrawal due to adverse events. However, drowsiness (6%), loss of energy (6%), and dizziness (6%) were reported with gabapentin (77). Compared with diphenhydramine (active placebo), topiramate was associated with higher rates of withdrawal due to adverse events (33% vs. 15%), sedation (34% vs. 3%), and diarrhea (30% vs. 10%) in 1 trial (79).

Skeletal Muscle Relaxants

Thirty-six unique trials of skeletal muscle relaxants (drugs approved by the U.S. Food and Drug Administration for treatment of spasticity from upper motor neuron syndromes or spasms from musculoskeletal conditions) were included in 4 systematic reviews (44–48). The duration of therapy in all trials was 2 weeks or less, with the exception of a single 3-week trial.

For acute low back pain, a higher-quality Cochrane review found skeletal muscle relaxants moderately superior to placebo for short-term (2 to 4 days' duration) pain relief (at least a 2-point or 30% improvement on an 11-point pain rating scale) (45, 46). The RRs for not achieving pain relief were 0.80 (CI, 0.71 to 0.89) at 2 to 4 days and 0.67 (CI, 0.13 to 3.44) at 5 to 7 days. There was insufficient evidence to conclude that any specific muscle relaxant is superior to others for benefits or harms (45, 46). However, there is only sparse evidence (2 trials) on efficacy of the antispasticity drugs dantrolene and baclofen for low back pain. Tizanidine, the other skeletal muscle relaxant approved by the Food and Drug Administration for spasticity, was efficacious for acute low back pain in 8 trials. Only 1 trial of patients with chronic low back pain—a lower-quality trial of cyclobenzaprine that did not report pain intensity or global efficacy—evaluated a skeletal muscle relaxant available in the United States (73).

Two other systematic reviews had a smaller scope than the Cochrane review but reached consistent conclusions (44, 47). One of the systematic reviews included 2 additional lower-quality trials of cyclobenzaprine for chronic or subacute low back or neck pain that reported mixed results compared with placebo (44). Another systematic review (48), which focused on interventions for sciatica, found no difference between tizanidine and placebo in 1 higher-quality trial (81).

Skeletal muscle relaxants were associated with a higher total number of adverse events (RR, 1.50 [CI, 1.14 to 1.98]) and central nervous system adverse events (RR, 2.04

[CI, 1.23 to 3.37]) compared with placebo, although most events were self-limited and serious complications were rare (45, 46).

Opioid Analgesics

We identified no systematic reviews of opioids for low back pain. From 600 potentially relevant citations, we identified 9 trials of opioid analgesics that met inclusion criteria (Appendix Table 8, available at www.annals.org) (59, 82–89). Twelve trials were excluded because they evaluated dual therapy with an opioid plus another medication compared with another medication or medication combination, 1 trial because it evaluated single-dose therapy, 2 trials because they did not report efficacy of opioids specifically for low back pain, and 2 trials because they did not evaluate any included outcome.

For chronic low back pain, a single higher-quality trial found that sustained-release oxycodone or sustained-release oxycodone was superior to placebo by an average of 18 points on a 100-point pain scale (87). However, opioids were titrated to stable doses before randomization, so poorer outcomes with placebo could have been due in part to cessation of opioid therapy and to withdrawal. Two lower-quality trials reported no significant differences between propoxyphene and placebo for back pain of mixed duration (83) or codeine and acetaminophen for acute back pain (59).

Two systematic reviews of placebo-controlled trials of opioids for various noncancer pain conditions (most commonly osteoarthritis and neuropathic pain) found opioids to be moderately effective, with a mean decrease in pain intensity with opioids in most trials of at least 30% (38), or a standardized mean difference for pain relief of -0.60 (CI, -0.69 to -0.50) (39). In 1 of the reviews, opioids were also slightly superior for functional outcomes (standardized mean difference, -0.31 [CI, -0.41 to -0.22]) (39). Estimates of benefit were similar for neuropathic and nonneuropathic pain.

There was no evidence from 5 lower-quality trials that sustained-release opioid formulations are superior to immediate-release formulations for low back pain on various outcomes (84–86, 88, 89). In addition, different long-acting opioids did not differ in 2 head-to-head trials (82, 87).

In 1 higher-quality trial, 85% of patients with low back pain randomly assigned to receive opioids reported adverse events, with constipation and sedation as the most frequent symptoms (87). Trials of opioids were not designed to assess risk for abuse or addiction and generally excluded higher-risk patients. In addition with the exception of 2 longer-term (16 weeks and 13 months) studies (82, 88), all trials lasted fewer than 3 weeks.

Tramadol

Three trials of tramadol (90–92) were included in a systematic review of various medications for low back pain (47). From 147 potentially relevant citations, we identified 2 other trials of tramadol that met inclusion criteria (93,

94). We excluded 3 trials that evaluated dual therapy with tramadol plus another drug versus another drug or drug combination (95–97), 1 trial published only as an abstract (98), and 1 small (40 patients) trial cited in an electronic database that we could not locate (99).

For chronic low back pain, tramadol was moderately more effective than placebo for short-term pain and functional status after 4 weeks in 1 higher-quality trial (92). Evidence from 2 trials (1 higher-quality) (90, 91) was insufficient to judge efficacy of tramadol versus the combination of acetaminophen plus codeine or dextropropfen-trometamol (an NSAID not available in the United States). Two other lower-quality trials found no differences in benefits or harms between sustained-release and immediate-release tramadol for chronic low back pain (93, 94). No trial compared tramadol with acetaminophen or opioid monotherapy, or with other NSAIDs. Tramadol was associated with similar rates of withdrawal due to adverse events compared with placebo (92) or the combination of acetaminophen plus codeine (91).

Systemic Corticosteroids

We identified no systematic reviews of systemic corticosteroids for low back pain. From 418 potentially relevant citations, we identified 4 trials that met inclusion criteria (Appendix Table 9, available at www.annals.org) (100–103). We excluded 3 trials that evaluated systemic corticosteroids in operative or postoperative settings and 1 German-language trial.

For acute sciatica or sciatica of unspecified duration, 3 small (33 to 65 patients), higher-quality trials consistently found systemic corticosteroids associated with no clinically significant benefit compared with placebo when given parenterally (single injection) or as a short oral taper (100, 102, 103). For patients with acute low back pain and a negative result on a straight-leg-raise test, a fourth trial found no difference in pain relief through 1 month between a single intramuscular injection of methylprednisolone (160 mg) and placebo (101).

A large (500-mg) intravenous methylprednisolone bolus was associated with 2 cases of transient hyperglycemia and 1 case of facial flushing in 1 trial (100). Another trial found a smaller (160-mg) intramuscular methylprednisolone injection associated with no cases of hyperglycemia requiring medical attention, infection, or gastrointestinal bleeding (101). Adverse events were poorly reported in the other trials.

Dual-Medication Therapy

Five trials comparing dual therapy with a skeletal muscle relaxant plus an analgesic (acetaminophen or an NSAID) versus the analgesic alone were included in a systematic review of skeletal muscle relaxants (45, 46). One other trial evaluated an opioid plus an NSAID versus an NSAID alone (88). We identified no other trials evaluating dual-medication therapy versus monotherapy from any of the other systematic reviews or searches.

A higher-quality Cochrane review of skeletal muscle relaxants (45, 46) found tizanidine combined with acetaminophen or an NSAID to be consistently associated with greater short-term pain relief than acetaminophen or NSAID monotherapy in 3 higher-quality trials. However, 2 lower-quality trials found no benefits from adding orphenadrine to acetaminophen or cyclobenzaprine to an NSAID. Compared with acetaminophen or an NSAID alone, adding a muscle relaxant was associated with a higher risk for adverse events of the central nervous system (4 trials; RR, 2.44 [CI, 1.05 to 5.63]) but a trend toward lower risk for gastrointestinal adverse events (4 trials; RR, 0.54 [CI, 0.26 to 1.14]). Overall risk for adverse events did not significantly differ (4 trials; RR, 1.34 [CI, 0.67 to 2.67]).

For chronic low back pain, 1 small (36 patients) trial found an opioid with naproxen slightly superior to naproxen alone for pain (5 to 10 points on a 100-point scale), anxiety, and depression after 16 weeks, but results are difficult to interpret because doses of naproxen were not clearly specified (88).

DISCUSSION

This review synthesizes evidence from systematic reviews and randomized, controlled trials of medications for treatment of low back pain. Main results are summarized in Appendix Tables 10 (acute low back pain), 11 (chronic or subacute low back pain), and 12 (low back pain with sciatica) (available at www.annals.org).

We found good evidence that NSAIDs, skeletal muscle relaxants (for acute low back pain), and tricyclic antidepressants (for chronic low back pain) are effective for short-term pain relief. Effects were moderate, except in the case of tricyclic antidepressants (small to moderate effects). We found fair evidence that acetaminophen, tramadol, benzodiazepines, and gabapentin (for radiculopathy) are effective for pain relief. Interpreting evidence on efficacy of opioids for low back pain is challenging. Although evidence on opioids versus placebo or nonopioid analgesics specifically for low back pain is sparse and inconclusive, recent systematic reviews of opioids for various chronic pain conditions found consistent evidence of moderate benefits (38, 39). For all medications included in this review, evidence of beneficial effects on functional outcomes is limited. We found good evidence that systemic corticosteroids are ineffective for low back pain with or without sciatica. We could not draw definite conclusions about efficacy of other medications for sciatica or radiculopathy because few trials have specifically evaluated patients with this condition. One systematic review identified only 7 trials evaluating medications for sciatica (48).

Assessing comparative benefits between drug classes was difficult because of a paucity of well-designed, head-to-head trials. Gabapentin, for example, has been evaluated in only 2 small, short-term, placebo-controlled trials, and

no trials directly compared potent opioids with other analgesics. One exception is acetaminophen, which was slightly but consistently inferior for pain relief compared with NSAIDs—although this conclusion assumes that estimates of pain relief from trials of osteoarthritis can be applied to patients with low back pain (54–57).

We also found little evidence of differences in efficacy within medication classes. However, head-to-head trials between drugs in the same class were mostly limited to NSAIDs and skeletal muscle relaxants. Among skeletal muscle relaxants, we found sparse evidence on efficacy of the antispasticity medications baclofen and dantrolene. Among antidepressants, tricyclics are the only class shown to be effective for low back pain, although other drugs with effects on norepinephrine uptake (such as duloxetine and venlafaxine) have not yet been evaluated.

In contrast to limited evidence of clear differences in benefits, we found clinically relevant differences between drug classes in short-term adverse events. For example, skeletal muscle relaxants, benzodiazepines, and tricyclic antidepressants are all associated with more central nervous system events (such as sedation) compared with placebo. Opioids seem to be associated with particularly high rates of short-term adverse events, particularly constipation and sedation. Data on serious (life-threatening or requiring hospitalization) adverse events associated with use of medications for low back pain are sparse. For NSAIDs, this is a critical deficiency because much of the uncertainty regarding their use centers on relative gastrointestinal and cardiovascular safety (63). For opioids and benzodiazepines, reliable evidence on such risks as abuse, addiction, and overdose is not available. Among skeletal muscle relaxants, clinical trials have shown no clear differences in rates of adverse events, but carisoprodol is known to be metabolized to meprobamate (a scheduled drug), dantrolene carries a black box warning for potentially fatal hepatotoxicity, and observational studies have found both tizanidine and chlorzoxazone to be associated with usually reversible and mild hepatotoxicity (104).

Our evidence synthesis has several potential limitations. First, because of the large number of published trials, our primary source of data was systematic reviews. The reliability of systematic reviews depends on how well they are conducted. We therefore focused on results from higher-quality systematic reviews, which are less likely than lower-quality reviews to report positive findings (22, 23). In addition, overall conclusions were generally consistent between multiple higher-quality systematic reviews of a medication. Second, we only included randomized, controlled trials. Although well-conducted randomized, controlled trials are less susceptible to bias than other study designs, nearly all are “efficacy” trials conducted in ideal settings and selected populations, usually with short-term follow-up. “Effectiveness” trials or well-designed observational studies could provide important insight into benefits and harms of medications for low back pain in real-world

practice. Third, high-quality data on harms are sparse. Better assessment and reporting of harms in clinical trials would help provide more balanced assessments of net benefits (105). Fourth, reporting of outcomes was poorly standardized across trials. In particular, the proportion of patients meeting predefined criteria for clinically important differences was rarely reported, making it difficult to assess clinical significance of results. Fifth, language bias could affect our results because we included non-English-language trials only if they were included in English-language systematic reviews. However, only 2 systematic reviews restricted inclusion solely to English-language trials (42, 44). Finally, the systematic reviews included in our evidence synthesis did not assess for potential publication bias. Formal assessments of publication bias would be difficult to interpret because of small numbers of studies and clinical diversity among trials (106).

We also identified several research gaps that limited our ability to reach more definitive conclusions about relative benefits and harms of medications for low back pain. First, no trials formally evaluated different strategies for choosing initial medications. In addition, evidence is sparse on effectiveness of dual-medication therapy relative to monotherapy or sequential treatment, even though patients are frequently prescribed more than 1 medication (4). There is also little evidence on long-term (>4 weeks) use of any medication included in this review, particularly with regard to long-term harms.

In summary, several medications evaluated in this report are effective for short-term relief of acute or chronic low back pain, although each is associated with a unique set of risks and benefits. Individuals are likely to differ in how they prioritize the importance of these various benefits and harms. For mild or moderate pain, a trial of acetaminophen might be a reasonable first option because it may offer a more favorable safety profile than NSAIDs. However, acetaminophen also seems less effective for pain relief. For more severe pain, a small increase in cardiovascular or gastrointestinal risk with NSAIDs in exchange for greater pain relief could be an acceptable tradeoff for some patients, but others may consider even a small increase in these risks unacceptable. For very severe, disabling pain, a trial of opioids in appropriately selected patients (107–109) may be a reasonable option to achieve adequate pain relief and improve function, despite the potential risks for abuse, addiction, and other adverse events. Factors that should be considered when weighing medications for low back pain include the presence of risk factors for complications, concomitant medication use, baseline severity of pain, duration of low back symptoms, and costs. As in other medical decisions, choosing the optimal medication for an individual with low back pain should always involve careful consideration and thorough discussion of potential benefits and risks.

From the Oregon Evidence-based Practice Center and Oregon Health & Science University, Portland, Oregon.

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Requests for Single Reprints: Roger Chou, MD, Oregon Evidence-based Practice Center, 3181 SW Sam Jackson Park Road, Mailcode BICC, Portland, OR 97239; e-mail, chour@ohsu.edu.

Current author addresses are available at www.annals.org.

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Current Author Addresses: Dr. Chou and Ms. Huffman: Oregon Evidence-based Practice Center, 3181 SW Sam Jackson Park Road, Mailcode BICC, Portland, OR 97239.

Appendix Table 1. Quality Rating System for Systematic Reviews

Criteria for Assessing Scientific Quality of Research Reviews*

1. Were the search methods reported?
Were the search methods used to find evidence (original research) on the primary questions stated?
"Yes" if the review states the databases used, date of most recent searches, and some mention of search terms.
2. Was the search comprehensive?
Was the search for evidence reasonably comprehensive?
"Yes" if the review searches at least 2 databases and looks at other sources (e.g., reference lists, hand searches, queries of experts).
3. Were the inclusion criteria reported?
Were the criteria used for deciding which studies to include in the overview reported?
4. Was selection bias avoided?
Was bias in the selection of studies avoided?
"Yes" if the review reports how many studies were identified by searches, numbers excluded, and appropriate reasons for excluding them (usually because of predefined inclusion/exclusion criteria).
5. Were the validity criteria reported?
Were the criteria used for assessing the validity of the included studies reported?
6. Was validity assessed appropriately?
Was the validity of all the studies referred to in the text assessed by using appropriate criteria (either in selecting studies for inclusion or in analyzing the studies that are cited)?
"Yes" if the review reports validity assessment and did some type of analysis with it (e.g., sensitivity analysis of results according to quality ratings, excluded low-quality studies).
7. Were the methods used to combine studies reported?
Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported?
"Yes" for studies that did qualitative analysis if report mentions that quantitative analysis was not possible and reasons that it could not be done, or if "best evidence" or some other grading of evidence scheme used.
8. Were the findings combined appropriately?
Were the findings of the relevant studies combined appropriately relative to the primary question the overview addresses?
"Yes" if the review performs a test for heterogeneity before pooling, does appropriate subgroup testing, appropriate sensitivity analysis, or other such analysis.
9. Were the conclusions supported by the reported data?
Were the conclusions made by the author(s) supported by the data and/or analysis reported in the overview?
10. What was the overall scientific quality of the overview?
How would you rate the scientific quality of this overview?

Operationalization of Criteria

The purpose of this index is to evaluate the scientific quality (i.e., adherence to scientific principles) of research overviews (review articles) published in the medical literature. It is not intended to measure literary quality, importance, relevance, originality, or other attributes of overviews.

The index is for assessing overviews of primary ("original") research on pragmatic questions regarding causation, diagnosis, prognosis, therapy, or prevention. A research overview is a survey of research. The same principles that apply to epidemiologic surveys apply to overviews: A question must be clearly specified; a target population identified and accessed; appropriate information obtained from that population in an unbiased fashion; and conclusions derived, sometimes with the help of formal statistical analysis, as is done in meta-analyses. The fundamental difference between overviews and epidemiologic studies is the unit of analysis, not the scientific issues that the questions in this index address.

Because most published overviews do not include a methods section, it is difficult to answer some of the questions in the index. Base your answers, as much as possible, on information provided in the overview. If the methods that were used are reported incompletely relative to a specific question, score it as "can't tell," unless there is information in the overview to suggest that the criterion was or was not met.

For question 8, if no attempt has been made to combine findings, and no statement is made regarding the inappropriateness of combining findings, check "No." If a summary (general) estimate is given anywhere in the abstract, the discussion, or the summary section of the paper, and it is not reported how that estimate was derived, mark "No" even if there is a statement regarding the limitations of combining the findings of the studies reviewed. If in doubt, mark "Can't tell."

For an overview to be scored as "Yes" in question 9, data (not just citations) must be reported that support the main conclusions regarding the primary question(s) that the overview addresses.

The score for question 10, the overall scientific quality, should be based on your answers to the first 9 questions. The following guidelines can be used to assist with deriving a summary score: If the "Can't tell" option is used 1 or more times on the preceding questions, a review is likely to have minor flaws at best and it is difficult to rule out major flaws (i.e., a score ≤4). If the "No" option is used on question 2, 4, 6, or 8, the review is likely to have major flaws (i.e., a score ≤3, depending on the number and degree of the flaws).

Scoring: Each Question Is Scored as Yes, Partially/Can't Tell, or No

Extensive Flaws	Major Flaws			Minor Flaws		Minimal Flaws
1	2	3	4	5	6	7

* Operationalization of the Oxman criteria (21), adapted from reference 22.

Appendix Table 2. Quality Rating System for Randomized, Controlled Trials*

Criteria List for Assessment of Methodologic Quality†	Operationalization of Criteria	Score
A. Was the method of randomization adequate?	A random (unpredictable) assignment sequence. An example of adequate methods is a computer-generated random-number table and use of sealed opaque envelopes. Methods of allocation using date of birth, date of admission, hospital numbers, or alternation should not be regarded as appropriate.	Yes/No/Don't Know
B. Was the treatment allocation concealed?	Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.	Yes/No/Don't Know
C. Were the groups similar at baseline regarding the most important prognostic factors? "Yes," if similar: Age and sex Description of type of pain Intensity, duration, or severity of pain	To receive a "yes," groups have to be similar at baseline regarding demographic factors, duration or severity of symptoms, percentage of patients with neurologic symptoms, and value of main outcome measure(s).	Yes/No/Don't Know
D. Was the patient blinded to the intervention?	The reviewer determines whether enough information about the blinding is given in order to score a "yes."	Yes/No/Don't Know
E. Was the care provider blinded to the intervention?	Use the author's statement on blinding, unless there is a differing statement/reason not to (no need for explicit information on blinding).	Yes/No/Don't Know
F. Was the outcome assessor blinded to the intervention?		Yes/No/Don't Know
G. Were co-interventions avoided or similar?	Co-interventions should be avoided in the trial design or similar between the index and control groups.	Yes/No/Don't Know
H. Was adherence acceptable in all groups?	The reviewer determines whether adherence to the interventions is acceptable, based on the reported intensity, duration, number, and frequency of sessions for both the index intervention and control intervention(s).	Yes/No/Don't Know
I. Was the dropout rate described and acceptable? ≤15% dropout rate is acceptable.	The number of participants who are included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and dropouts does not exceed 15% and does not lead to substantial bias, a "yes" is scored.	Yes/No/Don't Know
J. Was the timing of the outcome assessment in all groups similar?	Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.	Yes/No/Don't Know
K. Did the analysis include an intention-to-treat analysis? "Yes," if <5% of randomly assigned patients were excluded.	All randomly assigned patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of nonadherence and co-interventions.	Yes/No/Don't Know

* This list includes only the 11 internal validity criteria that refer to characteristics of the study that might be related to selection bias (criteria A and B), performance bias (criteria D, E, G, and H), attrition bias (criteria I and K), and detection bias (criteria F and J). The internal validity criteria should be used to define methodologic quality in the meta-analysis.

† Adapted from methods developed by the Cochrane Back Review Group (26).

Appendix Table 3. Methods for Grading the Overall Strength of the Evidence for an Intervention*

Grade	Definition
Good	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (at least 2 consistent, higher-quality trials).
Fair	Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (at least 1 higher-quality trial of sufficient sample size; 2 or more higher-quality trials with some inconsistency; or at least 2 consistent, lower-quality trials, or multiple consistent observational studies with no significant methodological flaws).
Poor	Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality trials, important flaws in trial design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

* Adapted from methods developed by the U.S. Preventive Services Task Force (27). The overall evidence for an intervention was graded on a 3-point scale (good, fair, poor).

Appendix Table 4. Excluded Systematic Reviews*

Drug	Study, Year (Reference)	Reason for Exclusion
Antidepressants	Fishbain, 2000 (37)	Not specific for LBP
	Goodkin and Gullion, 1989 (29)	Outdated
	Onghena and Van Houdenhove, 1992 (30)	Not specific for LBP
		Outdated
Multiple drugs	Turner and Denny, 1993 (31)	Not specific for LBP
	Deyo, 1996 (9)	Outdated
	van der Weide et al., 1997 (33)	Outdated
	van Tulder et al., 1997 (32)	Outdated
NSAIDs	Koes et al., 1997 (28)	Outdated
Opioids	Bartleson, 2002 (34)	Systematic methods not clearly described
	Brown et al., 1996 (35)	Systematic methods not clearly described
	Furlan et al., 2006 (39)	Not specific for LBP
	Kalso et al., 2004 (38)	Not specific for LBP
Systemic corticosteroids	Rozenberg et al., 1998 (36)	Systematic methods not clearly described

* LBP = low back pain; NSAIDs = nonsteroidal anti-inflammatory drugs.

Appendix Table 5. Systematic Reviews of Medications for Low Back Pain*

Drug	Study, Year (Reference)	Type of Systematic Review	Included Trials (Higher-Quality Trials), n/nt	Trials Not Included in Any Other Relevant Systematic Review, n	Duration of Treatment in Included Trials	Sample Sizes of Included Trials, n	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
Acetaminophen (6 unique trials in 2 systematic reviews)	Schnitzer et al., 2004 (47)	Qualitative (efficacy of multiple medications)	3 (1)	1	7 d–5 wk (median, 4 wk)	30–60 (median, 39)	Acetaminophen, 4 g/d (2), 2 g/d (1)	Does not draw specific conclusions about acetaminophen	4
	van Tulder et al., 2000 (40, 41)	Qualitative	5 (1)	3	7 d–4 wk (median, 2 wk)	30–70 (median, 50)	Acetaminophen, 4 g/d (3), 2 g/d (1), dose not specified (1)	Acetaminophen vs. NSAIDs for acute LBP (3 lower-quality RCTs): no differences in 2 trials; in 3rd trial, 2 of 4 evaluated NSAIDs were superior to acetaminophen Acetaminophen vs. diflunisal for chronic LBP (1 RCT): diflunisal superior for patients reporting no or mild LBP after 2–4 wk and for global assessment of efficacy	7
Antidepressants (10 unique trials in 3 systematic reviews)	Salerno et al., 2002 (42)	Quantitative	9 (5)	2	4–8 wk (median, 6 wk)	16–103 (median, 50)	Nortriptyline (1), imipramine (2), amitriptyline (1), desipramine (1), doxepine (2), maprotiline (1), paroxetine (2), trazodone (1)	Antidepressant vs. placebo for chronic LBP (9 RCTs): SMD, 0.41 (95% CI, –0.61 to 0.22) for pain (9 RCTs); SMD, 0.24 (95% CI, –0.69 to –0.21) for activities of daily living (5 RCTs)	
	Schnitzer et al., 2004 (47)	Qualitative (efficacy of multiple medications)	7 (4)	1	4–8 wk (median, 8 wk)	16–103 (median, 50)	Nortriptyline (1), imipramine (1), amitriptyline (2), maprotiline (1), paroxetine (2), fluoxetine (1), trazodone (1)	Antidepressants vs. placebo for chronic LBP (7 RCTs): antidepressants superior to placebo in 5 of 7 trials	5
	Staiger et al., 2003 (43)	Qualitative	7 (6)	0	4–8 wk (median, 8 wk)	16–103 (median, 50)	Nortriptyline (1), imipramine (2), amitriptyline (1), maprotiline (1), paroxetine (2), trazodone (1)	Tricyclic and tetracyclic antidepressant vs. placebo for chronic LBP (5 RCTs): 3 of 5 trials, including the 2 highest-quality trials, found mild to moderate, significant benefits for pain; insufficient evidence on functional status Paroxetine or trazodone vs. placebo for chronic LBP (3 RCTs): no consistent benefits on pain (SMD range, –0.13 to 0.32 in 3 RCTs)	6

Appendix Table 5—Continued

Drug	Study, Year (Reference)	Type of Systematic Review	Included Trials (Higher-Quality Trials), n/nt	Trials Not Included in Any Other Relevant Systematic Review, n	Duration of Treatment in Included Trials	Sample Sizes in Included Trials, n	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
Benzodiazepines (8 unique trials in 1 systematic review)	van Tulder et al., 2003 (45, 46)	Qualitative and quantitative	8 (5)	8	6–14 d (median, 8 d)	50–152 (median, 73)	Diazepam (6), tetrazepam (2)	Diazepam vs. placebo for acute LBP (1 RCT): diazepam superior for short-term pain and overall improvement Tetrazepam vs. placebo for chronic LBP (3 RCT): RR, 0.71 (CI, 0.54–0.93, 2 RCT) for not achieving pain relief >30% or improvement in pain score >16 points on a 100-point visual analogue scale after 8–14 d (2 RCT) and RR, 0.63 (CI, 0.42–0.97) for no global improvement after 8–14 d (2 RCT) Benzodiazepine vs. skeletal muscle relaxants (3 RCT): no differences in higher-quality trials	7
NSAIDs (57 unique trials in 3 systematic reviews)	Schnitzer et al., 2004 (47)	Qualitative (efficacy of multiple medications)	21 (10)	5	7 d–8 wk (median, 14 d)	30–282 (median, 73)	Naproxen (4), ibuprofen (1), indomethacin (4), diclofenac (3), piroxicam (6), diflunisal (6), others (9)	NSAIDs for acute LBP (14 RCT): NSAIDs superior to placebo in 2 of 3 RCT; 9 of 11 RCT of NSAIDs vs. active control found significant improvements from baseline in NSAID group NSAIDs for chronic LBP (4 RCT): NSAIDs superior to placebo in 1 RCT; 3 of 3 RCT of NSAIDs vs. active control found significant improvements from baseline in NSAID group	5
	van Tulder et al., 2000 (40, 41)	Qualitative and quantitative	51 (15)	34	1–2 d to 6 wk (median, 12 d)	20–459 (median, 72)	Naproxen (4), ibuprofen (6), indomethacin (10), diclofenac (15), piroxicam (7), diflunisal (8), others (18)	NSAID vs. placebo for acute LBP (9 RCT): RR, 1.24 (CI, 1.10–1.41) for global improvement after 1 wk (6 RCT) and RR, 1.29 (CI, 1.05–1.57) for not requiring additional analgesics after 1 wk (3 RCT)	7
	Vroomen et al., 2000 (48)	Quantitative efficacy of medications for sciatica	4 (2)	1	2–4 d to 17 d (median, 10 d)	40–214 (median, 54)	Indomethacin (1), piroxicam (1), others (2)	NSAID vs. placebo for sciatica (3 RCT): OR, 0.99 (CI, 0.6–1.7)	5

Continued on following page

Appendix Table 5. Systematic Reviews of Medications for Low Back Pain*

Drug	Study, Year (Reference)	Type of Systematic Review	Included Trials (Higher-Quality Trials), n/n†	Trials Not Included in Any Other Relevant Systematic Review, n	Duration of Treatment in Included Trials	Sample Sizes in Included Trials, n	Interventions Evaluated (Number of Trials)	Main Conclusions	Overall Quality per Oxman Scale (1–7)
Skeletal muscle relaxants (38 unique trials in 4 systematic reviews)	Browning et al., 2001 (44)	Quantitative (efficacy of cyclobenzaprine for back or neck pain)	14 (5)	11	5–21 d (median, 14 d)	48–1153 (median, 100)	Cyclobenzaprine (14)	Cyclobenzaprine vs. placebo for acute or chronic LBP or neck pain: OR, 4.7 (CI, 2.7–8.1) for global improvement (10 RCTs); SMD, 0.41 (CI, 0.29–0.53) for local pain at 1–4 d (7 RCTs); SMD, 0.54 (CI, 0.34–0.74) for function at 1–4 d (6 RCTs), results for function similar at >9 d	7
	Schnitzer, 2004 (47)	Qualitative (efficacy of multiple medications)	5 (4)	1	5–10 d (median, 7 d)	49–361 (median, 112)	Tizanidine (3), baclofen (1), other (1)	SMR vs. placebo for acute LBP (5 RCTs): SMR superior in 4 of 5 RCTs (no benefit in 1 of 3 RCTs of tizanidine); benefit mostly short-term and early (<7 d)	5
	van Tulder et al., 2003 (45, 46)	Qualitative and quantitative	26 (20)	19	Single dose—21 d (median, 7 d)	20–361 (median, 80)	Cyclobenzaprine (5), carisoprodol (3), chlorzoxazone (1), orphenadrine (4) methocarbamol, tizanidine (8), dantrolene (1), baclofen (1), others (5)	SMR vs. placebo for acute LBP (8 RCTs): RR, 0.80 (CI, 0.71–0.89) for not achieving pain relief >30% or improvement in score >16 points on a 100-point visual analogue scale after 2–4 d (3 RCTs); RR, 0.67 (CI, 0.13–3.44) for pain relief after 5–7 d (2 RCTs); RR, 0.49 (CI, 0.25–0.95) for no global improvement after 2–4 d (4 RCTs); RR, 0.68 (CI, 0.41–1.13) for no global improvement after 5–7 d (4 RCTs)	7
	Vroomen et al., 2000 (48)	Qualitative (efficacy of medications for sciatica)	1 (1)	0	7 d	112	Tizanidine (1)	Tizanidine vs. placebo for sciatica (1 higher-quality RCT): no difference	5

* LBP = low back pain; NSAID = nonsteroidal anti-inflammatory drug; OR = odds ratio; RCT = randomized, controlled trial; RR = relative risk; SMD = standardized mean difference; SMR = skeletal muscle relaxant.

† Higher-quality trials were defined as those receiving >50% of maximum possible quality rating score used by each systematic review.

Appendix Table 6. Quality Ratings of Systematic Reviews of Medications for Low Back Pain*

Drug	Study, Year (Reference)	Search Methods?	Comprehensive?	Inclusion Criteria?	Bias Avoided?	Validity Criteria?	Validity Assessed?	Methods for Combining Studies?	Appropriately Combined?	Conclusions Supported?	Overall Quality per Oxman Scale (1-7)
Antidepressants	Salerno et al., 2002 (42)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Yes	6
	Staiger et al., 2003 (43)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Multiple drugs	Schnitzer et al., 2004 (47)	Yes	Partial	Yes	Yes	Yes	Yes	No	Yes	Partial	5 (4 for acetaminophen)
	Vroomen et al., 2000 (48)	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	5
NSAIDs	van Tulder et al., 2000 (40, 41)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Skeletal muscle relaxants and benzodiazepines	Browning et al., 2001 (44)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
	van Tulder et al., 2003 (45, 46)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7

* NSAIDs = nonsteroidal anti-inflammatory drugs.

Appendix Table 7. Randomized, Controlled Trials of Antiepileptic Drugs for Low Back Pain*

Study, Year (Reference)	Patients, n	Duration of Follow-up, wk	Main Results	Quality Score†
Yildirim et al., 2003 (78)	50 (radiculopathy)	8	Gabapentin, titrated to 3600 mg/d, vs. placebo Back pain at rest (mean change from baseline on 0–3 scale): –1.04 vs. –0.32 ($P < 0.01$)	3/11
McCleane et al., 2001 (77)	80 (radiculopathy)	6	Gabapentin, titrated to 1200 mg/d, vs. placebo Back pain at rest (mean change from baseline on 0–10 VAS): –0.51 ($P > 0.05$) vs. 0.1 ($P > 0.05$) Back pain with movement (mean change from baseline on 0–10 VAS): –0.47 ($P < 0.05$) vs. 0.01 ($P > 0.05$) Leg pain (mean change from baseline on 0–10 VAS): –0.45 ($P < 0.05$) vs. –0.24 ($P > 0.05$)	8/11
Khoromi et al., 2005 (79)	41 (radiculopathy)	6, followed by crossover	Topiramate, titrated to 400 mg/d (average dosage, 208 mg/d), vs. diphenhydramine, titrated to 50 mg/d (average dosage, 40 mg/d) Average pain (mean change from baseline on 0–10 scale): Leg pain, –0.98 vs. –0.24 ($P = 0.06$) Back pain, –1.36 vs. –0.49 ($P = 0.017$) Overall pain, –0.33 vs. 0.49 ($P = 0.02$) Global pain relief moderate or better: 15/29 (54%) vs. 7/29 (24%) ($P = 0.005$) Global pain relief “a lot” or “complete”: 9/29 (31%) vs. 1/29 (3.4%) ODI score: –5 vs. –3 ($P > 0.05$) Beck Depression Inventory score: no difference SF-36 score: no differences for any subscale after correction for multiple comparisons	7/11
Muehlbacher et al., 2006 (80)	96 (chronic low back pain with or without radiculopathy)	10	Topiramate, titrated to 300 mg/d, vs. placebo Pain Rating Index (mean change from baseline on 0–100 scale): –12.9 vs. –1.5 ($P < 0.001$) SF-36 physical functioning subscale score (mean change from baseline on 0–100 scale): 8.7 vs. –0.4 ($P < 0.01$, favors topiramate) SF-36, bodily pain subscale score (0–100): 4.1 vs. 0.9 ($P < 0.01$, favors topiramate) SF-36, other subscale scores: differences in change compared with baseline ranged from 0.6 (role–emotional) to 8.3 (role–physical) points, favoring topiramate for all comparisons at $P < 0.05$	7/11

* ODI = Oswestry Disability Index; SF-36 = Short Form-36; VAS = visual analogue scale.

† Using Cochrane Back Review Group methods; maximum score, 11.

Appendix Table 8. Randomized, Controlled Trials of Opioids for Low Back Pain*

Type of Trial	Study, Year (Reference)	Patients, n	Duration of Follow-up	Main Results	Quality Score†
Opioids vs. placebo or acetaminophen	Barratta et al., 1976 (83)	61	14 d	Propoxyphene vs. placebo Pain on active improvement (mean improvement from baseline): 0.8 vs. 0.4 ($P > 0.05$) Global improvement at least "satisfactory": 22% vs. 14% ($P > 0.05$)	4/11
	Hale et al., 2005 (87)	235	18 d	Long-acting morphine vs. long-acting oxycodone vs. placebo Pain intensity (100-point VAS), mean differences vs. placebo: -18.21 (morphine) vs. -18.55 (oxycodone) ($P = 0.0001$ for each comparison) Global assessment at least "good": 59% vs. 63% vs. 27%	7/11
	Wiesel et al., 1980 (59)	50	14 d	Codeine vs. acetaminophen Mean time before return to work: 10.7 d vs. 13.0 d ($P > 0.05$)	1/11
Sustained-release vs. immediate-release opioid formulations	Gostick et al., 1989 (84)	61	2 wk, followed by crossover	Sustained-release vs. immediate-release dihydrocodeine No differences for pain intensity, rescue drug use, global efficacy, patient preference	5/11
	Hale et al., 1997 (85)	104	5 d	Sustained-release codeine plus acetaminophen vs. immediate-release codeine plus acetaminophen Long-acting codeine superior for pain intensity, but nonequivalent codeine use (200 mg vs. 71 mg)	5/11
	Hale et al., 1999 (86)	57	4-7 d followed by crossover	Sustained-release vs. immediate-release oxycodone No differences for overall pain intensity, mean pain intensity, or rescue drug use	4/11
	Jamison et al., 1998 (88)	36	16 wk	Sustained-release morphine + immediate-release oxycodone (titrated dose) + naproxen vs. immediate-release oxycodone (set dose) + naproxen vs. naproxen alone (mean scores over 16 wk; outcomes for first 4 items expressed on 0-100 scales) Average pain: 54.9 vs. 59.8 vs. 65.5 Anxiety: 11.2 vs. 15.0 vs. 31.6 Depression: 10.8 vs. 16.4 vs. 26.9 Level of activity: 49.3 vs. 49.3 vs. 51.5 Duration of sleep (means): 5.9 h vs. 5.9 h vs. 6.1 h	3/11
	Salzman et al., 1999 (89)	57	10 d	Sustained-release vs. immediate-release oxycodone No differences for pain intensity, time to stable pain control, mean number of dose adjustments	3/11
Long-acting opioid vs. long-acting opioid	Allan et al., 2005 (82)	683	13 mo	Transdermal fentanyl vs. sustained-release oral morphine No differences for pain scores, rescue medication use, quality of life, loss of working days	4/11
	Hale et al., 2005 (87)	235	18 d	Sustained-release morphine vs. sustained-release oxycodone No differences for pain intensity, pain relief, pain interference with activities, global assessment	7/11

* VAS = visual analogue scale.

† Using Cochrane Back Review Group methods; maximum score, 11.

Appendix Table 9. Randomized, Controlled Trials of Systemic Corticosteroids for Low Back Pain with or without Sciatica*

Study, Year (Reference)	Patients, <i>n</i> (Population)	Duration of Follow-up	Main Results	Quality Score†
Finckh et al., 2006 (100)	65 (acute sciatica)	30 d	Methylprednisolone, 500-mg bolus, vs. placebo Leg pain, difference between interventions in VAS pain scores (0–100 scale): 5.7 (favors methylprednisolone) at day 3, (<i>P</i> = 0.04), not significant after 3 d (<i>P</i> = 0.22) Proportion with >20-mm improvement in VAS pain score after 1 d: 48% vs. 28% (<i>P</i> = 0.097)	10/11
Friedman et al., 2006 (101)	88 (no sciatica)	1 mo	Methylprednisolone, 160 mg IM bolus, vs. placebo Pain, mean change from baseline (0–10 scale): –4.1 vs. –4.8 (<i>P</i> > 0.05) after 1 wk, –5.1 vs. –5.8 (<i>P</i> > 0.05) after 1 mo RDQ-18, mean score (0–18): 2.6 vs. 3.4 after 1 wk, 2.6 vs. 3.1 after 1 mo	11/11
Haimovic and Beresford, 1986 (102)	33 (sciatica, duration of symptoms unclear)	1–4 y	Dexamethasone, 1-wk oral taper, vs. placebo Early improvement: 33% (7/21) vs. 33% (4/12) Sustained improvement (1–4 y): 50% (8/16) vs. 64% (7/11)	6/11
Porsman and Friis, 1979 (103)	52 (sciatica, duration of symptoms unclear)	≥9 d	Dexamethasone, 1-wk IM taper vs. placebo "Positive effect": 52% (13/25) vs. 58% (14/24) Subsequent surgery: 32% (8/25) vs. 25% (6/24)	6/11

* IM = intramuscular; RDQ = Roland–Morris Disability Questionnaire; VAS = visual analogue scale.

† Using Cochrane Back Review Group methods; maximum score, 11.

Appendix Table 10. Summary of Evidence on Medications for Acute Low Back Pain*

Drug	Trials (Trials Rated Higher-Quality by ≥ 1 Systematic Review), n (n)†	Net Benefit‡	Effective vs. Placebo?	Inconsistency?§	Directness of Evidence?	Overall Quality of Evidence	Comments
Acetaminophen	3 (0)	Moderate	Unclear (1 lower-quality trial showing no difference)	Some inconsistency (vs. NSAIDs)	Direct	Good	Few data on serious adverse events
Antidepressants	0	No evidence	No evidence	No evidence	No evidence	No evidence	
Antiepileptic drugs	0	No evidence	No evidence	No evidence	No evidence	No evidence	Evaluated only in patients with radicular LBP
Benzodiazepines	5 (3)	Moderate	Unable to determine (2 trials with inconsistent results)	Some inconsistency (vs. placebo and vs. skeletal muscle relaxants)	Direct, with supporting indirect evidence from mixed populations with back and neck pain	Fair	No reliable data on risks of abuse or addiction No differences between diazepam and cyclobenzaprine for short-term global efficacy (both superior to placebo) in 1 large, short-term trial of patients with back or neck pain (mixed duration)
NSAIDs	31 (10)	Moderate	Yes (7 trials)	No	Direct	Good	May cause serious gastrointestinal and cardiovascular adverse events; insufficient evidence to judge benefits and harms of aspirin or celecoxib for LBP
Opioids	1 (1)	Moderate	No evidence	Not applicable	Data available from trials of opioids for other acute pain conditions	Fair	No reliable data on risks of abuse or addiction
Skeletal muscle relaxants	31 (21)	Moderate	Yes (19 trials)	No	Direct	Good	Little evidence on efficacy of antispasticity skeletal muscle relaxants baclofen and dantrolene for LBP
Systemic corticosteroids	1 (1)	Not effective	No (1 trial)	No	Direct	Fair	Mostly evaluated in patients with radicular LBP
Tramadol	1 (1)	Unable to estimate	No evidence	Not applicable	Direct	Poor	The only trial compared tramadol with an NSAID not available in United States

* LBP = low back pain; NSAIDs = nonsteroidal anti-inflammatory drugs.

† Higher-quality trials were defined as those receiving >50% of maximum possible quality rating score used by each systematic review.

‡ Based on evidence showing that medication is more effective than placebo, and/or evidence showing that medication is at least as effective as other medications or interventions thought to be effective, for 1 or more of the following outcomes: pain, functional status, or work status. Compared with placebo, small benefit was defined as 5–10 points on a 100-point visual analogue scale (VAS) for pain (or equivalent), 1–2 points on the Roland–Morris Disability Questionnaire (RDQ), 10–20 points on the Oswestry Disability Index (ODI), or a standardized mean difference (SMD) of 0.2–0.5. Moderate benefit was defined as 10–20 points on a 100-point VAS for pain, 2–5 points on the RDQ, 10–20 points on the ODI, or an SMD of 0.5–0.8. Large benefit was defined as >20 points on a 100-point VAS for pain, >5 points on the RDQ, >20 points on the ODI, or an SMD >0.8.

§ Inconsistency was defined as >25% of trials reaching discordant conclusions on efficacy (no effect vs. positive effect was considered discordant).

Appendix Table 11. Summary of Evidence on Medications for Chronic or Subacute Low Back Pain*

Drug	Trials (Trials Rated Higher-Quality by ≥ 1 Systematic Review), n (n)†	Net Benefit‡	Effective vs. Placebo?	Inconsistency?§	Directness of Evidence?	Overall Quality of Evidence	Comments
Acetaminophen	2 (1)	Moderate	No trials in patients with LBP	No	Data available from trials of acetaminophen for osteoarthritis	Good	Asymptomatic elevations of liver function test results at therapeutic doses
Antidepressants	10 (5)	Small to moderate	Yes (9 trials)	No	Direct	Good	Only tricyclic antidepressants have been shown effective for LBP No evidence on duloxetine or venlafaxine
Antiepileptic drugs	1 (1)	Small to moderate	Yes (1 trial of topiramate)	Not applicable	Direct	Poor	1 small trial evaluated topiramate for back pain with or without radiculopathy
Benzodiazepines	3 (2)	Moderate	Mixed results (3 trials)	Some inconsistency (vs. placebo)	Direct	Fair	No reliable data on risks for abuse or addiction
NSAIDs	6 (3)	Moderate	Yes (1 trial)	No	Direct	Good	May cause serious gastrointestinal and cardiovascular adverse events Insufficient evidence to judge benefits and harms of aspirin or celecoxib for LBP
Opioids	7 (1)	Moderate	Yes (1 trial)	No	Most trials compare different opioids or opioid formulations	Fair	No reliable data on risks of abuse or addiction
Skeletal muscle relaxants	6 (2)	Unable to estimate	Unclear (5 trials)	Not applicable	Most trials evaluated skeletal muscle relaxants not available in United States or mixed populations of patients with back and neck pain	Poor	The 2 higher-quality trials evaluated skeletal muscle relaxants not available in United States
Systemic corticosteroids	0	No evidence	No evidence	No evidence	No evidence	No evidence	Mostly evaluated in patients with radicular LBP
Tramadol	4 (1)	Moderate	Yes (1 trial)	No	Direct	Fair	

* LBP = low back pain; NSAIDs = nonsteroidal anti-inflammatory drugs.

† Higher-quality trials were defined as those receiving $>50\%$ of maximum possible quality rating score used by each systematic review.

‡ Based on evidence showing that medication is more effective than placebo, and/or evidence showing that medication is at least as effective as other medications or interventions thought to be effective, for 1 or more of the following outcomes: pain, functional status, or work status. Compared with placebo, small benefit was defined as 5–10 points on a 100-point visual analogue scale (VAS) for pain (or equivalent), 1–2 points on the Roland–Morris Disability Questionnaire (RDQ), 10–20 points on the Oswestry Disability Index (ODI), or a standardized mean difference (SMD) of 0.2–0.5. Moderate benefit was defined as 10–20 points on a 100-point VAS for pain, 2–5 points on the RDQ, 10–20 points on the ODI, or an SMD of 0.5–0.8. Large benefit was defined as >20 points on a 100-point VAS for pain, >5 points on the RDQ, >20 points on the ODI, or an SMD >0.8 .

§ Inconsistency was defined as $>25\%$ of trials reaching discordant conclusions on efficacy (no effect vs. positive effect was considered discordant).

Appendix Table 12. Summary of Evidence on Medications for Sciatica or Radicular Low Back Pain*

Drug	Trials (Trials Rated Higher-Quality by ≥ 1 Systematic Review), n (n)†	Net Benefit‡	Effective vs. Placebo?	Inconsistency?§	Directness of Evidence?	Overall Quality of Evidence	Comments
Antiepileptic drugs	3 (2)	Small	Yes (2 trials of gabapentin and 1 trial of topiramate)	No	Direct	Fair	No trials of antiepileptic drugs other than gabapentin or topiramate
Nonselective NSAIDs	4 (2)	Not effective	No (3 trials)	No	Direct	Fair	NSAIDs more effective than placebo in mixed populations of patients with low back pain with or without sciatica
Systemic corticosteroids	3 (3)	Not effective	No (3 trials)	No	Direct	Good	

* NSAIDs = nonsteroidal anti-inflammatory drugs.

† Higher-quality trials were defined as those receiving >50% of maximum possible quality rating score used by each systematic review.

‡ Based on evidence showing that medication is more effective than placebo, and/or evidence showing that medication is at least as effective as other medications or interventions thought to be effective, for 1 or more of the following outcomes: pain, functional status, or work status. Compared with placebo, small benefit was defined as 5–10 points on a 100-point visual analogue scale (VAS) for pain (or equivalent), 1–2 points on the Roland–Morris Disability Questionnaire (RDQ), 10–20 points on the Oswestry Disability Index (ODI), or a standardized mean difference (SMD) of 0.2–0.5. Moderate benefit was defined as 10–20 points on a 100-point VAS for pain, 2–5 points on the RDQ, 10–20 points on the ODI, or an SMD of 0.5–0.8. Large benefit was defined as >20 points on a 100-point VAS for pain, >5 points on the RDQ, >20 points on the ODI, or an SMD >0.8.

§ Inconsistency was defined as >25% of trials reaching discordant conclusions on efficacy (no effect vs. positive effect was considered discordant).