Pain Management Injection Therapies for Low Back Pain

Appendixes

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Appendix A. Search Strategies

Database: Ovid MEDLINE(R) without Revisions

1 Low Back Pain/ or Spinal Stenosis/ or Radiculopathy/ or ("low back pain" or "spinal adj3 stenosis" or "radiculopathy").mp.
2 spine/ or coccyx/ or intervertebral disk/ or lumbar vertebrae/ or sacrum/ or spinal canal/ or exp back/ or facet joint/ or zygapophysial joint/ or sacroiliac.mp.
3 Chronic Pain/ or (chronic adj3 pain).mp.
4 2 and 3
5 1 or 4
6 Patient Selection/
7 exp Treatment Outcome/
8 Prognosis/ or (prognosis or prognostic).mp.
9 (patient$ adj5 select$).mp.
10 (select$ adj5 method$).mp.
11 or/6-10
12 exp Injections, Spinal/ or exp Injections, Intra-Articular/
13 ((spine$ or spinal$ or epidural or facet or sacroiliac or "medial branch") adj5 (block or injection$)).mp.
14 12 or 13
15 5 and 14
16 5 and 11
17 16 and inject*.mp.
18 11 and 14
19 18 and "low back pain".mp.
20 15 or 17 or 19
21 20 and (random* or control* or cohort).mp.
22 limit 21 to yr="2008 - 2014"

Database: EBM Reviews - Cochrane Central Register of Controlled Trials

1 Low Back Pain/ or Spinal Stenosis/ or Radiculopathy/ or ("low back pain" or "spinal adj3 stenosis" or "radiculopathy").mp.
2 spine/ or coccyx/ or intervertebral disk/ or lumbar vertebrae/ or sacrum/ or spinal canal/ or exp back/ or facet joint/ or zygapophysial joint/ or sacroiliac.mp.
3 Chronic Pain/ or (chronic adj3 pain).mp.
4 2 and 3
5 1 or 4
6 Patient Selection/
7 exp Treatment Outcome/
8 Prognosis/ or (prognosis or prognostic).mp.
9 (patient$ adj5 select$).mp.
10 (select$ adj5 method$).mp.
11 or/6-10
12 exp Injections, Spinal/ or exp Injections, Intra-Articular/
13 ((spine$ or spinal$ or epidural or facet or sacroiliac or "medial branch") adj5 (block or injection$)).mp.

Appendix A. Search Strategies

14 12 or 13
15 5 and 14
16 5 and 11
17 16 and inject*.mp.
18 11 and 14
19 18 and "low back pain".mp.
20 15 or 17 or 19 (1306)
21 limit 20 to yr="2008 - 2014"

Database: EBM Reviews - Cochrane Database of Systematic Reviews
1 low back pain.ti.
2 1 and (epidural or facet or sacroiliac or "medial branch" or injection).mp.

Appendix B. PICOTS

PICOT	Include	Exclude
Population and Conditions of Interest	• For all KQs: Adults with subacute (4 to 12 weeks) or chronic (>12 weeks) symptoms of the following: o For epidural corticosteroid injections-Nonradicular low back pain, low back pain with radiculopathy, or spinal stenosis o For facet joint corticosteroid injection and medial branch block- Nonradicular low back pain o For sacroiliac joint corticosteroid injection-Nonradicular back pain in the sacroiliac region	• Persons younger than 18 years of age
Interventions	• All KQs: Epidural corticosteroid injection, facet joint corticosteroid injection, medial branch block, sacroiliac joint corticosteroid joint injection	• Intraspinal injections involving anti-tumor necrosis factor agents, radiofrequency denervation, intradiscal electrothermal therapy, chemonucleolysis, and intradiscal methylene blue or ozone
Comparators	• For KQ 2: Studies that evaluate the effects of patient characteristics (e.g., age, sex, duration of pain, pain level, expectations of treatment benefits, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, or other treatment received) or findings with interventional diagnostic techniques (e.g., discography, selective nerve root block, facet joint block, medial branch block, sacroiliac joint block), imaging studies, and/or other clinical criteria. • For KQs 1, 3, and 4: Saline epidural, epidural with local anesthetic, nonepidural injection, no injection, surgery, or nonsurgical therapies.	• Uncontrolled or pre-post studies
Outcomes	• For KQs 1 2, 3: Pain, function, quality of life, opioid use, subsequent surgery, health care utilization • For KQ 4: Harms, including bleeding, infection, neurological events, and systemic complications, such as weight gain, diabetes, osteoporosis, and other endocrinological effects	
Timing	• For all KQs: Outcomes measured 1 week or later after the injection; durability of treatment response will be assessed	
Setting	• For all KQs: No restrictions	
Study Design	• For KQs 1-3: randomized trials • For KQ 4: randomized trials or controlled cohort studies	

KQ=key question; PICOT=populations; interventions, comparators, outcomes, timing, setting.

Appendix C. Included Studies

Please refer to this section as a reference list for Appendixes E and F.

Ackerman WE, 3rd, Ahmad M. The efficacy of lumbar epidural steroid injections in patients with lumbar disc herniations. Anesth Analg. 2007 May;104(5):1217-22, tables of contents. PMID: 17456677.

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Beliveau P. A comparison between epidural anaesthesia with and without corticosteroid in the treatment of sciatica. Rheumatol Phys Med. 1971 Feb;11(1):40-3. PMID: 5551095.

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Appendix C. Included Studies

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Appendix C. Included Studies

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Appendix C. Included Studies

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Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Ackerman, 2007	RCT	U.S. Number of centers and clinic setting not reported	Radicular pain in S1 dermatomal distribution; L5-S1 disk herniation confirmed by MRI; electromyographic evidence of S1 nerve root involvement; pain intensity >7; duration not specified	Pregnancy; allergies to steroids; steroid use within 3 weeks prior to study; bleeding history; infection; use of anticoagulants; allergies to study medications	Approached: 487 Eligible: 285 Randomized: 90 (30 vs. 30 vs. 30) Analyzed: 90 at 24 weeks	A: Transforaminal epidural injection with 40 mg triamcinolone (1 ml) and saline (4 ml), with fluoroscopic guidance (n=30) B: Interlaminar epidural injection with 40 mg triamcinolone (1 ml) and saline (4 ml), with fluoroscopic guidance (n=30) C: Caudal epidural injection with 40 mg triamcinolone (1 ml) and saline (19 ml), with fluoroscopic guidance (n=30)
Ahadian, 2011	RCT	U.S. Two centers	≥18 years of age; distal radicular pain ≥6 months in duration; previously benefitted from transforaminal epidural steroid injection with betamethasone 6 to 12 mg with recurrence of pain; VAS score ≥50 out of 100	Pregnancy; infection; coagulopathy; uncontrolled diabetes or hypertension; allergy to iodinated contrast medium; interventional therapies for pain in last 90 days	Approached: 449 Eligible: 98 Randomized: 98 (32 vs. 33. vs. 33) Analyzed: 98 at 12 weeks	A: Transforaminal epidural injection with 12 mg dexamethasone (3 ml), with fluoroscopic guidance (n=32) B: Transforaminal epidural injection with 8 mg dexamethasone (2 ml), with fluoroscopic guidance (n=33) C: Transforaminal epidural injection with 4 mg dexamethasone (1 ml), with fluoroscopic guidance (n=33)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Ackerman, 2007	A vs. B vs. C: Age (mean): 34 vs. 39 vs. 36 years Male: 67% vs. 70% vs. 63% Duration of symptoms (days): 35 vs. 33 vs. 38 Baseline pain (0 to 10): 8.6 vs. 8.8 vs. 8.9 Baseline ODI (0-70): 30 vs. 33 vs. 37	A vs. B vs. C: Treatments prior to intervention: Not specified Treatments following intervention: Tizanidine and celecoxib; otherwise not specified Other patient characteristics: Not reported	Number and frequency of injections: 3 injections performed at 2 week intervals Number of levels: Transforaminal vs. interlaminar vs. caudal Provider experience: Not reported	Fluoroscopic guidance with contrast verification	Head-to-head comparison of different approaches for epidural injections
Ahadian, 2011	A vs. B vs. C: Age (median): 58 vs. 57 vs. 60 years Male: 53% vs. 70% vs. 88% Duration of symptoms >2 years: 91% vs. 88% vs. 91% Baseline pain (0 to 100): 73 vs. 71 vs. 68 Baseline ODI (0 to 50): 23 vs. 24 vs. 24	A vs. B vs. C: Treatments prior to intervention: Previous response to transforaminal epidural injection with betamethasone Treatment following intervention: Not specified L3-L4 disc abnormality: 25% vs. 45% vs. 36% L4-L5 disc abnormality: 31% vs. 39% vs. 27% Central stenosis: 28% vs. 39% vs. 39% Post laminectomy syndrome: 9.4% vs. 15% vs. 3.0%	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification in epidural space	Transforaminal epidural injection with different doses of corticosteroid

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Ackerman, 2007	A vs B vs C: <u>Pain</u> Complete pain relief (complete, partial, or no pain relief): 30% (9/30) vs. 10% (3/30) vs. 3% (1/30) at 24 weeks: A vs. B, RR 3.0 (95% CI 0.90 to 10.07); A vs. C, RR 9.0 (95% CI 1.21 to 66.71); B vs. C, RR 3.0 (95% CI 0.33 to 27.23) Complete or partial pain relief: 83% (25/30) vs. 60% (18/30) vs. 57% (17/30) at 24 weeks: A vs B, RR 1.39 (95% CI 1.0 to 1.9); A vs. C, RR 1.47 (95% CI 1.03 to 2.10; B vs. C, RR 1.06 (95% CI 0.69 to 1.62) Pain (mean, 0-10): 2.4 vs. 5.7 vs. 6.1 at 2 weeks after last injection ($p<0.05$ for A vs. B or C) <u>Function</u> ODI (mean, 0-70): 14 vs. 13 vs. 14 at 2 weeks after last injection ($p>0.05$) <u>Other outcomes</u> Beck Depression Inventory (mean, 0-63): 12 vs. 11 vs. 13 at 2 weeks after last injection ($p>0.05$)
Ahadian, 2011	A vs. B vs. C: <u>Pain</u> Pain (mean, 0-100 VAS, estimated from graph): 73 vs. 71 vs. 68 at baseline; 42 vs. 38 vs. 41 at 4 weeks; 51 vs. 37 vs. 50 at 8 weeks; 52 vs. 45 vs. 54 at 12 weeks ($p>0.05$ for between group differences at all time points) <u>Function</u> ODI (mean, 0-100 VAS, estimated from graph): 23 vs. 24 vs. 24 at baseline; 18 vs. 17 vs. 18 at 4 weeks; 20 vs. 17 vs. 19 at 8 weeks; 21 vs. 19 vs. 20 at 12 weeks, ($p>0.05$ for between group differences at all time points) <u>Global improvement</u> Global impression of change <=3 (7 point scale): No difference between groups, data not reported Global satisfaction scale >=2 (5 point scale): No difference between groups, data not reported

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Ackerman, 2007	24 weeks	A vs. B vs. C: 0% (0/90)	Appears complete	A vs. B vs. C: No infection, headache, intravascular injection, reaction to contrast material, steroid, or subarachnoid injection in any patient	Not reported	Fair
Ahadian, 2011	12 weeks	A vs. B vs. C: 0% (0/98)	Appears complete	A vs. B vs. C: Paresthesia: 6% (6/98) overall No serious adverse events	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Arden, 2005 Price, 2005	RCT	UK Multicenter Specialty clinics	18 to 70 years of age; back pain with unilateral radicular symptoms, extending below the knee, with signs including reduced SLR and a positive sciatic nerve stretch test; duration 4 weeks to 18 months; normal laboratory results; lumbar spine X-ray to exclude other causes of radicular pain including infection and malignancy	Previous back surgery; bleeding disorder or anticoagulation; bilateral symptoms; previous epidural injection; current litigation relating to sciatica; significant psychological disorder	Approached: Not reported Eligible: Not reported Randomized: 228 (120 vs. 108) Analyzed: 228 (120 vs. 108) at 12 months, including 25 (14 vs. 11) with missing data	A: Interlaminar epidural injection with 80 mg triamcinolone acetonide plus 0.125% bupivacaine (10 ml) (n=120) B: Soft tissue injection into interspinous ligament of normal saline (2 ml) (n=108)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Arden, 2005 Price, 2005	A vs. B: Age (mean): 43 vs. 44 years Male: 52% vs. 54% Duration of symptoms: Mean not reported (4 weeks to 18 months by inclusion criteria); 38% vs. 35% acute (4 weeks to 4 months) Baseline leg pain (0-100 VAS): 52 vs. 56 Baseline back pain (0-100 VAS): 40 vs. 44 Baseline ODI (0-100): 44 vs. 45	A vs. B: Treatments prior to intervention: Physiotherapy package with education and exercise regimens Treatments following intervention: Not specified HAD depression: 7 vs. 4 Off work with sciatica: 34% vs. 32% Decreased sensation: 78% vs. 63% Absence/decreased ankle reflexes: 32% vs. 32% Decreased power: 42% vs. 43%	Number and frequency of injections: Mean not reported, up to three injections at 3 week intervals if ODI improved less than 75% from baseline Number of levels: Not reported Provider experience: "Operators were all very experienced"	None reported	Soft tissue injection with saline

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Arden, 2005 Price, 2005	A vs. B: <u>Pain</u> Leg pain (mean improvement from baseline, 0-100 VAS): 12 vs. 10 at 3 weeks; 15 vs. 15 at 6 weeks; 13 vs. 18 at 12 weeks; 17 vs. 20 at 52 weeks (p>0.05 at all time points) Leg pain improved >50%: 35% (42/120) vs. 26% (28/108) at 3 weeks, RR 1.35 (95% CI 0.90 to 2.02); 47% (56/120) vs. 41% (44/108) at 6 weeks, RR 1.15 (95% CI 0.85 to 1.54); 43% (52/120) vs. 46% (50/108) at 12 weeks, RR 0.94 (95% CI 0.70 to 1.25); 48% (58/120) vs. 44% (48/108) at 52 weeks, RR 1.09 (95% CI 0.82 vs 1.44) Back pain (mean improvement from baseline, 0-100 VAS): 6 vs. 2 at 3 weeks; 6 vs. 8 at 6 weeks; 4 vs. 7 at 12 weeks, 8 vs. 9 at 52 weeks <u>Function</u> ODI (mean improvement from baseline, 0-100): 10 vs. 7 at 3 weeks; 13 vs. 10 at 6 weeks; 12 vs. 12 at 12 weeks;16 vs. 14 at 52 weeks (p>0.05 at all time points) (p>0.05 at all time points) ODI (0-100, estimated from figure): 44 vs. 45 at baseline; 32 vs. 39 at 3 weeks (p=0.05); 31 vs. 35 at 6 weeks (p=0.15); 33 vs. 34 at 12 weeks (p=0.92), 29 vs. 33 at 52 weeks (p=0.55) ODI improved >75%: 12% (15/120) vs. 3.7% (4/108) at 3 weeks, RR 3.38 (95% CI 1.16 to 9.86); 15% (18/120) vs. 13% (14/108) at 6 weeks, RR 1.16 (95% CI 0.61 to 2.21); 16% (19/120) vs 22% (24/108) at 12 weeks, RR 0.71 ((5% CI 0.41 to 1.23); 32% (38/120) vs. 30% (32/108) at 52 weeks, RR 1.07 (95% CI 0.72 to 1.58) SF-36: No statistically significant differences (data not reported) <u>Other outcomes</u> Surgery: 13% (15/120) vs. 13% (14/108) through 52 weeks, RR, 0.96 (95% CI 0.49 to 1.9) Physiotherapy: 26% vs. 23% over 52 weeks Other injections: 13% vs. 11% over 52 weeks HAD anxiety (mean improvement from baseline): 2 vs. 2 at 3 weeks; 2 vs. 2 at 6 weeks; 2 vs. 3 at 12 weeks; 3 vs. 3 at 52 weeks HAD depression (mean improvement from baseline): 1 vs. 1 at 3 weeks; 2 vs. 2 at 6 weeks; 2 vs. 2 at 12 weeks; 2 vs. 2 at 52 weeks Analgesic use (mean change in number consumed in a week, baseline 37 vs. 48): -6 vs. -11 at 3 weeks; -8 vs. -13 at 6 weeks; -9 vs. -16 at 12 weeks; -14 vs. -16 at 52 weeks Days off work with sciatica (median change, baseline 98 vs. 93): -21 vs -21 at 3 weeks; -21 vs. -21 at 6 weeks; -37 vs. -23 at 12 weeks; -65 vs. -33 at 52 weeks

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Arden, 2005 Price, 2005	12 months	A vs. B: 12% (14/120) vs. 10% (11/108)	Appears complete	A vs. B: One post-dural puncture headache Non-specific headache: 3% (4) vs. 4% (4)	UK National Health Service, Health Technology Assessment Programme	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Aronsohn, 2010	RCT	U.S. Number of settings and clinic setting not reported	Chronic lumbar discogenic pain; radiculopathy; MRI or CT scans consistent with diagnosis of contained disc herniation at L3-4, L4-5, or L5S-1; ≥50% preserved disc height; duration not specified	Not Reported	Approached: Not reported Eligible: Not reported Randomized: 50 (24 vs. 26) Analyzed: Unclear	A: Epidural injection (approach not reported) with 40 mg methylprednisolone plus 0.25% bupivacaine (3 ml), with fluoroscopic guidance (n=24) B: Lumbar discectomy using Stryker disc Dekompressor (n=26)
Becker, 2007	RCT	Germany Single center Orthopedic surgery	Unilateral lumbar radicular compression, confirmed by MRI or CT showing herniation of nucleus pulposus or scarring after previous surgery; duration ≥6 weeks; pain intensity moderate to severe	Need for early surgery; additional neurologic illnesses; cervical myopathy; systemic bone or joint illness; previous epidural or epidural perineural injection in the last 3 months; cortisone or opioid use in the last 6 months	Approached: Not reported Eligible: Not reported Randomized: 84 (25 vs. 27 vs. 32) Analyzed: 83 (24 vs. 27 vs. 32) at 24 weeks	A: Perineural epidural injection using oblique interlaminar approach with 10 mg triamcinolone plus unspecified local anesthetic (1 ml), with fluoroscopic guidance (n=24) B: Perineural epidural injection using oblique interlaminar approach with 5 mg triamcinolone plus unspecified local anesthetic (1 ml), with fluoroscopic guidance (n=24) C: Perineural epidural injection using oblique interlaminar approach with autologous conditioned serum (1 ml), with fluoroscopic guidance (n=24)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Aronsohn, 2010	A vs. B: Age (mean): 51 vs. 41 years Male: 56% vs. 64% Duration of symptoms: Not reported Baseline back pain (0-10): 7.1 vs. 7.5 Baseline radicular pain (0-10): 9.3 vs. 9.1 Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not reported Treatments following intervention: Not reported Other patient characteristics: Not reported	Number of injections: Single injection Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance	Percutaneous microdiscectomy
Becker, 2007	A vs. B vs. C: Age (mean): 54 years (reports no difference between groups) Male: Reports no difference between groups, data not provided Duration of symptoms: Reports no difference between groups, data not provided Baseline pain: Not reported Baseline function: Not reported	A vs. B vs. C: Treatments prior to intervention: Pain medication discontinued for 2 weeks prior to first injection Treatments following intervention: No additional medical therapy or physical therapy	Number and frequency of injections: 3 injections at 1 week intervals Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance	Perineural epidural injection with different doses of corticosteroid or autologous conditioned serum

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Aronsohn, 2010	A vs. B: Pain Back pain (0-10 VAS): 7.1 vs. 7.5 at baseline; 6.7 vs. 3.0 at 1 week (p<0.05); 6.5 vs. 1.0 at 6 weeks (p<0.05) Radicular pain (0-10 VAS): 9.3 vs. 9.1 at baseline; 4.8 vs. 8.0 at 1 week (p<0.05); 2.0 vs. 7.1 at 6 weeks (p<0.05)
Becker, 2007	A vs. B vs. C: Pain Pain (mean, 0-100 VAS, estimated from graph): 84 vs. 82 vs. 78 at baseline; 30 vs. 29 vs. 35 at 4 weeks; 30 vs. 27 vs. 17 at 6 weeks; 22 vs. 33 vs. 22 at 22 weeks; mean difference A vs. B: -4.2 (95% CI -19 to 11); A vs. C: 9.3 (95% CI -4.9 to 24); for B vs. C: 14 (95% CI -0.4 to 27) Function ODI (mean, 0-50): 19 vs. 21 vs. 22 at baseline; 11 vs. 12 vs. 14 at 6 weeks; 11 vs. 12 vs. 11 at 10 weeks; 11 vs. 11 vs. 12 at 22 weeks (p>0.05 at all time points)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Aronsohn, 2010	6 weeks	Not reported	Appears complete	A vs. B: Paresthesia: 4.2% (1/24) vs. 13% (3/26) Infection: 0% vs. 3.8% (1/26)	Not reported	Poor
Becker, 2007	22 weeks	Not reported	Appears complete	A vs. B vs. C: Severe headache: 4.0% (1/25) vs. 3.7% (1/27) vs. 3.1% (1/32) "No serious adverse events"	No funding received	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Beliveau, 1971	RCT	UK Single center Rheumatology clinic	Moderate or severe unilateral sciatica thought to be caused by a herniated disk, with or without neurologic signs; duration of symptoms and imaging findings not specified	Not reported	Approached: Not reported Eligible: Not reported Randomized: 48 (24 vs. 24) Analyzed: Unclear at 1 week	A: Caudal epidural injection with 80 mg methylprednisolone (2 ml) + 0.5% procaine (40 ml) (n=24) B: Caudal epidural injection with 0.5% procaine (42 ml) (n=24)
Breivik, 1976	RCT	Norway Single center Neurology and anesthesiology clinic	Incapacitating chronic (several months to several years) low back pain and sciatica unresponsive to non-invasive treatments; radiculography with metrizamide showing arachnoiditis, prolapsed disc, no abnormality, or inconclusive findings	Not reported	Approached: Not reported Eligible: Not reported Randomized: 35 (16 vs. 19) Analyzed: 35	A: Caudal epidural injection with 80 mg methylprednisolone and 0.25% cc bupivacaine (20 ml) (n=16) B: Caudal epidural injection with 0.25% bupivacaine (20 ml) followed by 100 cc saline (n=19)
Buchner, 2000	RCT	Germany Single center Orthopedic clinic	Herniated disk ≥5 mm confirmed by MRI with corresponding clinical symptoms of nerve root compression; positive straight leg raise test at <60 degrees; age <50 years; duration not specified	Previous lumbar surgery; lumbar spinal stenosis by MRI; cauda equina syndrome; acute severe motor paresis	Approached: Not reported Eligible: Not reported Randomized: 36 (17 vs. 19) Analyzed: 36 at 6 months	A: Interlaminar epidural injection with 100 mg methylprednisolone in 0.25% bupivacaine (10 ml) (n=17) B: No epidural injection (n=19)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Beliveau, 1971	A vs. B: Age (mean): 41 years (overall) Male: 75% Duration of symptoms: Not reported Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: Not reported	Not reported	Interlaminar epidural injection with local anesthetic
Breivik, 1976	A vs. B: Age (mean): Not reported, range 30-63 years Male: 50% vs. 47% Duration of symptoms: Not reported Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Prior surgery: 25% vs. 37% Other patient characteristics: Not reported	Number and frequency of injections: Mean 2.6 vs. 2.5 injections; repeated at weekly intervals for up to 3 injections; 5/16 vs. 11/19 patients received other type of injection after no relief from 3 injections Number of levels: Not reported Provider experience: Not reported	Not reported	Caudal epidural local anesthetic injection
Buchner, 2000	A vs. B: Age (mean): 37 vs. 32 years Male: 47% vs. 79% Duration of symptoms (weeks): median 8 vs. 8 Baseline pain (0-100): 84 vs. 81 Hannover Functional Ability Questionnaire: 39% vs. 40%	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Bed rest; analgesics; NSAIDS or tramadol; graded rehabilitation including hydrotherapy, electroanalgesia, spinal mobilization physiotherapy	Number and frequency of injections: 3 injections within 14 days Number of levels: Single level Provider experience: Not reported	Not reported	No injection

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Beliveau, 1971	A vs. B: <u>Pain</u> Improved or completely relieved (clinician rated): 75% (18/24) vs. 67% (16/24), RR 1.13 (95% CI 0.78 to 1.62)
Breivik, 1976	A vs. B: <u>Pain</u> Pain relief "considerable" (defined as diminution of pain and/or paresis to enable return to work or rehabilitation for other work): 65% (9/16) vs. 26% (5/19) RR, 2.14 (95% CI 0.90 to 5.09)
Buchner, 2000	A vs. B: <u>Pain</u> Pain (0-100 VAS): 84 vs. 81 at baseline; 31 vs. 37 at 2 weeks; 33 vs. 38 at 6 weeks; 33 vs. 39 at 6 months (p>0.05 at all time points) <u>Function</u> Hannover Functional Ability Questionnaire: 39% vs. 40% at baseline; 64% vs. 57% at 2 weeks; 62% vs. 58% at 6 weeks; 62% vs. 57% at 6 months (p>0.05 at all time points) <u>Other outcomes</u> Return to work: 88% (15/17) vs. 74% (14/19) at 6 months, RR: 1.20 (95% CI 0.87 to 1.65) Overall results "very good" or "good": 88% (15/17) vs. 74% (14/19), RR 1.20 (95% CI 0.87 to 1.65) at 6 months Surgery: 12% (2/17) vs. 21% (4/19) at 6 months, RR 0.56 (95% CI 0.12 to 2.68)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Beliveau, 1971	1 week	Not reported	Appears complete	A vs. B: Mild headache and dizziness for <30 minutes in 10 patients (not reported by group) Procedure stopped in 2 patients due to theca penetration	Not reported	Poor
Breivik, 1976	Unclear	Not reported	Appears complete (5/16 vs. 11/19 received other injection per protocol after 3 failed primary injections)	Not reported	Upjohn	Poor
Buchner, 2000	6 months	None	Appears complete	Not reported	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Burgher, 2011	RCT	US Single center Pain clinic	≥18 years of age, intervertebral disc herniation with low back and leg pain due to encroachment of disc material on a spinal nerve root as confirmed by CT or MRI; positive nerve root tension sign with unilateral symptoms at a single level of the lumbosacral spine; duration ≤3 months	Pain intensity was less than 3 of 10 or more than 8 of 10 if already taking opioids; recent spinal trauma; cauda equina syndrome; progressive motor deficit; chronic anticoagulation; infectious etiology; workers' compensation claim; history of adverse reaction to study medications; 1 or more corticosteroid injection in the preceding 4 months; pregnant; severe medical disease	Approached: 33 Eligible: Not reported Randomized: 26 (15 vs. 11) Analyzed: 23 (14 vs. 9)	A: Transforaminal epidural injection with 40 or 80 mg triamcinolone (2 ml) plus 2% lidocaine (1 ml), with fluoroscopic guidance (n=15) B: Transforaminal epidural injection with 200 or 400 mcg clonidine (2 ml) plus 2% lidocaine (1 ml), with fluoroscopic guidance (n = 11)
Bush, 1991	RCT	UK Single center Rheumatology clinic	Unilateral sciatica associated with paresthesia; positive straight leg raise, duration >1 month; imaging findings not required	Cauda equina syndrome; nonorganic physical signs; other serious pathology; inadequate contraception in women of child-bearing age	Approached: Not reported Eligible: Not reported Randomized: 28 Analyzed: 23 (12 vs. 11)	A: Caudal epidural injection with 80 mg triamcinolone acetonide in normal saline with 0.5% procaine hydrochloride (total 25 ml) (n=12) B: Caudal epidural injection with saline (25 ml) (n=11)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Burgher, 2011	A vs. B: Age (mean): 50 vs. 44 years Male: 67% vs. 82% Duration of symptoms (weeks): 5.3 vs. 5.0 Baseline pain (0-10 NRS): 7.0 vs. 7.0 Baseline ODI (0-50): 29 vs. 31	A vs. B: Treatments prior to intervention: 67% vs. 91% opioids Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Mean 2.3 vs. 2.0 injections, repeated at 10-14 day intervals Number of levels: 1 Provider experience: Not reported	Fluoroscopic guidance (digital subtraction angiography) with contrast verification	Transforaminal epidural injection with clonidine and local anesthetic
Bush, 1991	A vs. B: Age (mean): 38 vs. 37 years Male: 83% vs. 45% Duration of symptoms: Not reported Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: 2 at 2 week intervals Number of levels: Caudal injection Provider experience: Not reported	None reported	Caudal epidural injection with normal saline

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Burgher, 2011	A vs. B: <u>Pain</u> Pain, difference between groups compared with baseline (0-10 NRS): at 2 weeks, 0.11 (95% CI -1.79 to 2.01); at 4 weeks, 1.54 (95% CI -0.52 to 3.60) <u>Function</u> Roland Morris Disability Questionnaire, difference between groups compared with baseline: at 2 weeks, 2.96 (95% CI -1.04 to 6.96); at 4 weeks, 5.67 (95% CI 1.22 to 10.1) ODI, difference between groups compared with baseline: at 2 weeks, 5.86 (95% CI -0.57 to 12.3); at 4 weeks, 7.04 (95% CI 0.83 to 13.2) Multidimensional Pain Inventory, difference between groups compared with baseline: at 2 weeks, -4.83 (95% CI -0.57 to 12.3); at 4 weeks, -0.35 (95% CI -6.96 to 6.26) <u>Global Assessment</u> Patient Global Impression of Change <=2 (much improved) at 4 weeks: 50% vs. 67% (p=0.669) <u>Other outcomes</u> Surgery: 6.7% (1/15) vs. 27% (3/11) at 6 months, 0.24 (95% CI) 0.30 to 2.05
Bush, 1991	A vs. B: <u>Pain</u> Pain (0-100 VAS): at 4 weeks 16 vs. 45 (p not reported); at 1 year 14 vs. 30 (p>0.05) <u>Function</u> Function/lifestyle (6-18 scale): at 4 weeks 16 vs. 14 (p not reported); at 1 year 17 vs. 16 (p>0.05) <u>Other outcomes</u> Surgery: 8.3% (1/12) vs.18% (2/11), RR 0.39 (95% CI 0.04 to 3.80)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Burgher, 2011	4 weeks for pain, function, and global impression of change; 6 months for surgery	A vs. B: 6.7% (1/15) vs. 18% (2/11)	Appears complete	A vs. B: Discomfort at injection site: 27% (4/15) vs. 18% (2/11) Worsening of symptoms: 13% (2/15) vs. 36% (4/11) Lightheadedness: 7% (1/15) vs. 45% (5/11) Drowsiness: 20% (3/20) vs. 18% (2/11) Dry mouth: 20% (3/20) vs. 18% (2/11) Weakness: 7% (1/15) vs. 36% (4/11) Constipation: 7% (1/15) vs. 18% (2/11) Nausea: 13% (2/15) vs. 9% (1/11) 1 group B patient withdrew due to side effects (nausea, lightheadedness)	National Institutes of Health	Fair
Bush, 1991	1 year	A vs. B: 18% (5/28)	Appears complete	A vs. B: Irregular menses: 8% (1/12) vs. 0%	ER Squibb & Sons and the Boots Company PLC	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Buttermann, 2004	RCT	USA Single center Surgery clinic	18 to 70 years of age; lumbar disc herniation >25% of cross-sectional area of the spinal canal on MRI or CT; failure to respond to 6 weeks of noninvasive treatments; duration not specified	Cauda equina syndrome; pars defect at the level of the herniation; far-lateral disc herniation; multilevel symptomatic disc herniation; recurrent disc herniation	Approached: 169 Eligible: Not reported Randomized: 100 (50 vs. 50) Analyzed: 71 (23 vs. 48) at 2-3 years (on-treatment analysis)	A: Interlaminar epidural injection with 10 to 15 mg betamethasone, with fluoroscopic guidance in 76% of patients (n=50) B: Discectomy (technique not specified) (n=50)
Candido, 2013	RCT	US Single center Pain management center	>18 years of age, unilateral lumbosacral radiculopathic pain, MRI findings of degenerative lumbar disc disease including protruding or bulging discs, desiccated discs, or herniated discs with preservation of at least 50% of disc height	Required injections for multi-level disease; a history of previous spinal surgery; lumbar epidural steroid injection(s) in the past year; allergies to study medications, using systemic corticosteroids or chronic opioid use	Approached: Not reported Eligible:137 Randomized:106 (53 vs. 53) Analyzed: 100 (50 vs. 50)	A. Lateral parasagittal interlaminar epidural injection with 120 mg methylprednisolone acetate (2 ml) plus lidocaine 1% (1 ml), with fluoroscopic guidance B. Midline interlaminar epidural injection with 120 mg methylprednisolone acetate (2 ml) plus lidocaine 1% (1 ml), with fluoroscopic guidance

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Buttermann, 2004	A vs. B: Age (mean): 41 vs. 40 years Male: Not reported Duration of symptoms (months): 3.3 vs. 3.8 Baseline back pain (0-10): 5.4 vs. 5.2 Baseline leg pain (0-10): 7.4 vs. 7.0 Baseline ODI (0-100): 47 vs. 48	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient Characteristics: Smokers: 30% vs. 36% Size of disc herniation: 42% vs. 43% Motor deficit: 82% vs. 88%	Number and frequency of injections: Mean not reported, patients could receive 1-3 at one week intervals based on response Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance in 76% of patients undergoing epidural injection	Epidural steroid injection vs. discectomies vs. crossover
Candido, 2013	A vs. B: Age (mean): 49 v. 49 years Male: 48% vs. 40% (p=0.5) Duration of symptoms: 14 vs. 14 months Baseline pain at rest (mean, 0-10 NRS): 4.9 vs. 5.1 Baseline pain during movement (mean, 0-10 NRS): 7.6 vs. 7.2 Baseline function (mean ODI, 0 to 100): 44.9% vs. 40.6% (p=NS)	A vs. B: Treatments prior to intervention: Pain medications: 54% vs. 64%; Opioid use: 28% vs. 36%; NSAIDS: 54% vs. 62% (p>0.05) Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of intervention: mean number of injections 1.82 vs. 1.88 (p>0.05) Number of levels: Appears to be single Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space	Head-to-head comparison of alternative epidural steroid injection methods

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Buttermann, 2004	A vs. B: Pain Back pain (mean, 0-10 VAS, estimated from graph): 5.4 vs. 5.2 at baseline, 3.0 vs. 2.0 at 1-3 months; 2.6 vs. 1.7 at 4-6 months; 2.3 vs. 1.8 at 7-12 months; 2.4 vs. 1.9 at 1-2 years; 1.8 vs. 2.4 at 2-3 years (p>0.05 at all time points) Leg pain (mean, 0-10 VAS, estimated from graph): 7.4 vs. 7.0 at baseline; 4.1 vs. 1.4 at 1-3 months; 2.7 vs. 1.2 at 4-6 months; 1.8 vs. 1.1 at 7-12 months; 1.7 vs. 1.2 at 1-2 years; 0.8 vs. 1.5 at 2- 3 years (p>0.05 at all time points) Function ODI (0-100): 47 vs. 48 at baseline; 34 vs. 22 at 1-3 months; 15 vs. 16 at 4-6 months; 14 vs. 14 at 7-12 months; 11 vs. 14 at 1-2 years; 8 vs. 16 at 2-3 years (p>0.05 at all time points except 1-3 months) Motor deficit (estimated from graph): 82% (41/50) vs. 88% (44/50) at baseline, RR, 0.93 (95% CI 0.79 to 1.10); 72% (36/50) vs. 38% (19/50) at 1-3 months, RR 1.89 (95% CI 1.28 to 2.81); 30% (8/27) vs. 20% (10/50) at 4-6 months, RR 1.48 (95% CI 0.66 to 3.31); 20% (5/25) vs. 12% (6/50) at 7-12 months, RR 1.67 (95%CI 0.56 to 4.93); 12% (3/24) vs. 8.0% (4/50) at 1-2 years, RR 1.56 (95% CI 0.38 to 6.43); 8.7% (2/23) vs. 4.0% (2/50) at 2-3 years, RR 2.17 (95% CI 0.33 to 14.5) Other outcomes Medication use "much less" (5 category scale, much less to much more): 16% (8/50) vs. 24% (12/50) at 1-3 months, RR 0.43 (95 % CI 0.23 to 0.78); 57% (13/23) vs. 32% (15/47) at 2-3 years, RR 1.77 (95 % CI 1.02 to 3.07)
Candido, 2013	A vs. B Pain Pain, Numeric Rating Scale at rest (NRS, 11-point scale, estimated from graph): at baseline, 4.9 vs. 5.1; at 14 days, 2.8 vs. 3; at 28 days, 2.7 vs. 3; at 60 days, 2.6 vs. 3.2; at 120 days, 2.6 vs. 3; at 180 days, 2 vs. 3.2; at 365 days, 2 vs. 3.2 (p>0.05) Pain, Numeric Rating Scale during movement (NRS, 11-point scale, estimated from graph): at baseline, 7.6 vs. 7.2; at 14 days, 3.3 vs. 4.5; at 28 days, 3.3 vs. 4.5; at 60 days, 3.7 vs. 5; at 120 days, 3.7 vs. 4.7; at 180 days, 3.7 vs. 5; at 365 days, 4 vs. 5 (p>0.05) Function ODI (scores 0-50 multiplied by 2 and presented as a percentage from 0-100%, estimated from graph): at baseline: 44.9% vs. 40.6% (p=NS); at 14 days, 25% vs. 28%; at 28 days, 23% vs. 27%; at 60 days, 22% vs. 25%; at 120 days, 24% vs. 27%; at 180 days, 21% vs. 31%; at 365 days, 20% vs. 33% (p>0.05) Other Outcomes Patient Satisfaction (5-point scale, where 1 = complete dissatisfaction and 5 = complete satisfaction, estimated from GRA ph): at 1 day, 3.9 vs. 3.6; at 14 days, 4.1 vs. 2.9; at 28 days, 3.7 vs. 3.4; at 60 days, 3.7 vs. 3. 4; at 120 days, 3.5 vs. 3.3; at 180 days, 4 vs. 3.2; at 365 days, 4.1 vs. 3.2 (p-values not reported, but states "better satisfaction" in group A on days 7, 14, 180, and 365.)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Buttermann, 2004	2-3 years	A vs. B: 3% (3/100) at 3 years	46% (23/50) of patients in epidural injection group crossed over to discectomy at 2-3 years	A vs. B: Epidural injection (n=50): 2 incidental dural puncture, 3 recurrent disc herniation Discectomy (n=77, including crossovers): 2 incidental durotomies, 1 seroma	None	Poor
Candido, 2013	12 months	A vs. B 3 vs. 3	Appears complete	Discomfort and pain at the injection site: 22% vs. 30% (p>0.05) Headache, nonpositional, not related to dural puncture: 22% vs. 12% (p>0.05) Nausea: 6% vs. 14% (p>0.05)	Department of Anesthesiology, Advocate Illinois Masonic Medical Center, Chicago, IL	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Candido, 2008	RCT	US Single center Clinical setting unclear	Low back pain; unilateral lumbosacral radiculopathy	Previous spinal surgery; epidural steroid injections in the past year; allergy to study drugs; concurrent systemic steroids; opioid use; pregnancy	Approached: Not reported Eligible: Not reported Randomized: 60 (30 vs. 30) Analyzed: 57 (29 vs. 28) at 6 months	A: Posterolateral interlaminar epidural injection with 80 mg methylprednisolone plus lidocaine 1% (1 ml), with fluoroscopic guidance B: Transforaminal epidural injection with 80 mg methylprednisolone plus lidocaine 1% (1 ml), with fluoroscopic guidance

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Candido, 2008	A vs. B: Age (mean): 52 vs. 52 years Male: 57% vs. 40% Duration of symptoms <3 months: 24% vs. 7.1% Baseline pain (0-10 VAS): 6.8 vs. 6.3 Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of intervention: Appears to be single Number of levels: Appears to be single Provider experience: Attending physicians supervising fellows	Fluoroscopy with contrast verification in epidural space	Head-to-head comparison of alternative epidural steroid injection methods

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Candido, 2008	A vs. B: <u>Pain</u> Pain intensity (mean, 0-100 VAS): 63 vs. 63 at baseline; 41 vs. 49 at 2 weeks (p=0.31); 52 vs. 53 at 1 month (p=0.94); 47 vs. 43 at 3 months (p=0.68); 41 vs. 47 at 6 months (p=0.46)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Candido, 2008	6 months	None reported	2 in transforaminal injection group and 1 in parasagittal interlaminar group did not receive treatment and were excluded	A vs. B: 1 parasagittal interlaminar group had paresthesia requiring procedure to be aborted (excluded from analysis)	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Carette, 1997	RCT	Canada Two centers Type of clinic not reported	>18 years of age; sciatica for >4 weeks and <1 year with constant or intermittent pain in one or both legs radiating below knee; nerve root irritation based on positive straight leg raise and/or motor, sensory, or reflex deficits, with CT evidence of herniated disk corresponding to clinical findings; ODI >20	Cauda equina syndrome; CT findings of nerve root compression from causes other than herniated disk; epidural steroid injection in the preceding year; prior low back surgery; pregnant; known blood-coagulation disorder or allergy to local anesthetics	Approached: Not reported Eligible: Not reported Randomized: 158 (78 vs. 80) Analyzed: 156 (77 vs. 79) at 3 months	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) plus isotonic saline (8 ml) (n=78) B: Interlaminar epidural injection with isotonic saline (1 ml) (n=80)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Carette, 1997	A vs. B: Age (mean): 39 vs. 41 years Male: 72% vs. 59% Duration of symptoms (weeks): 12.9 vs. 13.0 Baseline pain (0 to 100): 66 vs. 62 Baseline ODI (0 to 100): 50 vs. 50	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Acetaminophen, otherwise not specified Other patient characteristics: Disability compensation: 24% vs. 21% First episode of sciatica: 76% vs. 76% L4-L5: 49% vs. 51% L5-S1: 45% vs. 48%	Number and frequency of injections: Mean 2.1 injections, repeated injections permitted at 3 and 6 weeks for failure to improve Number of levels: Single level Provider experience: Not reported	None reported	Interlaminar epidural injection with saline

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Carette, 1997	A vs. B: *(differences are difference in change from baseline; ANCOVA results adjusted for male sex and living partner performed but reported as similar to unadjusted and not presented)* <u>Pain</u> Pain (0-100 VAS): 66 vs. 62 at baseline;45 vs. 49 at 3 weeks, difference -8.6 (95% CI -18 to 0.3); 39 vs. 40 at 3 months, difference -4.0 (95% CI -15 to 7.2) McGill Present Pain Intensity (0-5): 2.6 vs. 2.8 at baseline; 2.2 vs. 2.4 at 3 weeks, difference 0.0 (95% CI -0.4 to 0.4); 1.9 vs. 1.9 at 3 months, difference 0.2 (95% CI -0.3 to 0.7) McGill Pain-rating Index (0-77): 28 vs. 26 at baseline; 20 vs. 22 at 3 weeks; difference -3.4 (95% CI -8.1 to 1.3), 18 vs. 18 at 3 months, difference -1.2 (95% CI -7.2 to 4.9) <u>Function</u> ODI (0-100): 50 vs. 50 at baseline, 42 vs. 44 at 3 weeks, difference -2.5 (95% CI -7.1 to 2.2); 32 vs. 35 at 3 months, difference -1.9 (95% CI -9.3 to 5.4) ODI <=20: 20% (15/77) vs. 16% (13/80) at 3 weeks, RR 1.20 (95% CI 0.61 to 2.35); 38% (29/77) vs. 42% (33/79) at 3 months, RR 0.90 (95% CI 0.61 to 1.33) Marked or very marked improvement: 33% (25/76) vs. 30% (23/78) at 3 weeks, RR 1.12 (95% CI 0.70 to 1.78); 55% (41/74) vs. 56% (43/77) at 3 months, RR 0.99 (95% CI 0.75 to 1.32) Sickness Impact Profile, Overall (0 to 100): 22 vs. 21 at baseline; 16 vs. 18 at 3 weeks; difference -2.5 (95% CI -5.1 to 0.1); 12 vs. 13 at 3 months, difference -1.2 (95% CI -5.2 to 2.8) (no differences on physical or psychosocial dimensions subscales) Restricted activity in previous 2 weeks (number of days): 9.9 vs. 9.7 at baseline; 8.9 vs. 7.9 at 3 weeks; difference 0.8 (95% CI -0.6 to 2.2); 5.9 vs. 5.4 at 3 months; difference 0.3 (95% CI -1.8 to 2.5) <u>Other outcomes</u> Underwent surgery: 26% (n=77) vs. 25% (n=79) at 12 months (p=0.90, log-rank test) Returned to work within 3 months: 33% (14/43) vs. 44% (18/41), RR 0.74 (95% CI 0.43 to 1.29) Lack of efficacy withdrawal: 15% (12/78) vs. 25% (20/80) at 3 months, RR 0.62 (95% CI 0.32 to 1.17)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Carette, 1997	3 months	A vs. B: 1.3% (1/78) vs. 1.2% (1/80)	Appears complete	A vs. B: Dural puncture: 1.3% (1/78) vs. 1.2% (1/80) Transient headache: 27% (21/78) vs. 20% (16/80) (p=0.30)	Medical Research Council of Canada and the Canadian Arthritis Society	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Cocelli, 2009	RCT	Turkey Single center Clinic setting unclear	20-55 years of age; acute discal radiculopathy <3 months duration not responding to conservative management; radiologic disc bulge corresponding to symptoms; ODI score >20	Bilateral symptoms; neurological deficits; prior lumbar disc surgery; severe medical comorbidities; urinary retention; allergy to study drugs	Approached: Not reported Eligible: Not reported Randomized: 70 (40 vs. 30) Analyzed: 70 at 6 months	A: Interlaminar epidural injection with 10 mg betamethasone diproprionate and 4 mg betamethasone sodium phosphate plus 0.125% bupivacaine (total 20 ml) (n=40) B: Interlaminar epidural injection with 80 mg triamcinolone acetonide plus 0.125% bupivacaine (total 20 ml) (n=40)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Cocelli, 2009	A vs. B: Age (mean): 49 vs. 50 years Male: 25% vs. 40% Duration of symptoms (weeks): 3 vs. 3 Baseline pain (0-10 VAS): 9.5 vs. 9.3 Baseline ODI (0-100): 51 vs. 62	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Amitriptyline 10 mg starting on day of injection to 50 mg/day for 6 months and postural exercise program L3-L4: 20% vs. 20% L4-L5: 55% vs. 60% L5-S1: 20% vs. 20%	Not reported	None reported	Head-to-head comparison of alternative corticosteroids

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Cocelli, 2009	A vs. B: <u>Pain</u> Pain (0-10 VAS): 9.5 vs. 9.3 at baseline, 5.7 vs. 1.1 at 2 weeks; 0.8 vs. 0.0 at 6 weeks; 0.0 vs. 0.0 at 3 months; 0.0 vs. 0.0 at 6 months <u>Function</u> ODI (0-100): 51 vs. 62 at baseline, 36 vs. 32 at 2 weeks; 25 vs. 23 at 6 weeks; 22 vs. 22 at 3 months; 19 vs. 20 at 6 months

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Cocelli, 2009	6 months	Reports none	Appears complete	A vs. B: "No side effects related to this treatment in any of the patients"	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Cohen, 2012	RCT	US and Germany Multicenter Pain clinics	18 to 70 years of age; lumbosacral radiculopathy for 4 weeks to 6 months; leg pain as or more severe than back pain; failure of conservative therapy; MRI evidence of pathologic disc condition correlating with symptoms	Coagulopathy; systemic infection; unstable medical or psychiatric condition; previous spinal surgery; previous epidural steroid injection; allergy to contrast dye	Approached: 164 Eligible: 96 Randomized: 84 (28 vs. 26 vs. 30) Analyzed: 84 at 1 month (primary analysis)	A. Transforaminal epidural injection with 60 mg methylprednisolone acetate in 2 ml sterile water and 0.5% bupivacaine (0.5 ml), with fluoroscopic guidance (n=28) B. Transforaminal epidural injection with 4 mg etanercept in 2 ml sterile water and 0.5% bupivacaine (0.5 ml), with fluoroscopic guidance (n=26) C. Transforaminal epidural injection with 2 ml sterile water and 0.5% bupivacaine (0.5 ml) , with fluoroscopic guidance (n=30)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Cohen, 2012	A vs. B vs. C: Age (mean): 43 vs. 41 vs. 41 years Male: 79% vs. 69% vs. 63% Duration of symptoms (months): 2.61 vs. 2.67 vs. 2.82 Baseline leg pain (0-10): 5.71 vs. 6.62 vs. 6.31 Baseline back pain (0-10): 5.30 vs. 6.08 vs. 4.75 Baseline ODI (0-100): 42.93 vs. 41.12 vs. 40.87	A vs. B vs. C: Treatments prior to intervention: Not reported Treatments following intervention: Analgesic medications Other patient characteristics: Disability/worker's compensation/medical board: 4 % vs. 12% vs. 10% Baseline opioid therapy: 39% vs. 39% vs. 47% L4-5: 29% vs. 35% vs. 27% L5-S1: 43% vs. 50% vs. 47%	Number and frequency of injections: 86% vs. 88% vs. 93% received 2 injections (2nd injection two weeks after first) Number of levels: 1-2 levels, dose divided for multiple levels Provider experience: Board-certified pain medicine physician or attending or pain-management fellow at teaching hospital	Fluoroscopic guidance with contrast verification of nerve root and epidural space	Transforaminal epidural injection with etanercept and local anesthetic Transforaminal epidural injection with saline and local anesthetic

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Cohen, 2012	A vs. B vs. C: *(difference ANCOVA adjusted for study site, sex, duration of pain, opioid use, baseline outcome score)* <u>Pain</u> Leg Pain (0-10 NRS): 5.71 vs. 6.62 vs. 6.31 at baseline; 2.54 vs. 3.56 vs. 3.78 at 1 month, difference -1.26 (95% CI -2.79 to 0.27) for A vs. C, -1.01 (95% CI -2.60 to 0.58) for A vs. B Back pain (0-10 NRS): 5.30 vs. 6.08 vs. 4.75 at baseline, 3.49 vs. 4.41 vs. 4.01 at 1 month, difference -0.52 (95% CI -1.85 to 0.81) for A vs. C, -0.92 (95% CI -2.28 to 0.44) for A vs. B <u>Function</u> ODI (0-100): 42.9 vs. 41.1 vs. 40.9 at baseline, 24.1 vs. 40.3 vs. 30.0 at 1 month, difference -5.87 (95% CI -15.6 to 3.85) for A vs. C, -16.2 (95% CI -26.0 to -6.27) for A vs. B <u>Global Assessment</u> Global Perceived Effect positive (pain improved and patient satisfied): at 1 month: 82% (23/28) vs. 58% (15/26) vs. 57% (17/30) (p=0.14); A vs. B adjusted OR 3.16 (95% CI 0.88 to 11.3), A vs. C adjusted OR 3.12 (95% CI 0.91 to 10.8), B vs. C adjusted OR 0.99 (95% CI 0.33 to 2.94); 65% vs. 50% vs. 48% at 3 months, 63% vs. 45% vs. 48% at 6 months Success (>=50% decrease in leg pain and positive Global Perceived Effect): at 1 month 75% (21/28) vs. 42% (11/26) vs. 50% (15/30), A vs. C adjusted OR 3.63 (95% CI 1.10 to 12.0), A vs. B adjusted OR 2.62 (95% CI 0.82 to 8.37), B vs. C adjusted OR 0.72 (95% CI 0.24 to 2.16); at 3 months 50% (14/28) vs. 42% (11/26) vs. 43% (13/30); at 6 months 29% (8/28) vs. 38% (10/26) vs. 40% (12/30), A vs. B RR 0.74 (95% CI 0.35 to 1.59), A vs. C RR 0.71 (95% CI 0.34 to 1.48), B vs. C RR 0.96 (95 % CI 0.50 to 1.85) <u>Other outcomes</u> Surgery: at 12 months 21% (6/28) vs. 23% (6/26) vs. 17% (5/30); A vs. B RR 0.93 (95% CI 0.34 to 2.52), A vs. C RR 1.29 (95% CI 0.44 to 3.74), B vs. C RR 1.38 (95% CI 0.48 to 4.01) Remained on active duty: at 12 months 100% (15/15) vs. 93% (13/14) vs. 90% (17/19); A vs. B: RR 1.04 (95% CI 0.61 to 1.77); A vs. C: RR 1.06 (95% CI 0.64 to 1.74); B vs. C: RR 1.06 (95% CI 0.64 to 1.74) Analgesic use decreased >=20%: 63% (17/28) vs. 36% (9/30) vs. 50% (14/30) at 1 month (p=0.24), A vs. B adjusted OR 3.0 (95% CI 0.83 to 10.8), A vs. C adjusted OR 1.67 (95% CI 0.48 to 5.77), B vs. C adjusted OR 0.56 (95% CI 0.16 to 1.89); 92% (11/12) vs. 65% (7/11) vs. 75% (9/12) at 6 months, A vs. B RR 1.44 (95% CI 0.89 to 2.32), A vs. C RR 1.22 (95% CI 0.85 to 1.76), B vs. C RR 0.84 (95% CI 0.49 to 1.47)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Cohen, 2012	6 months; surgery and remained on active duty assessed through 1 year	None	Appears complete	A vs. B. vs. C: Worsening pain: 4% (1/28) vs. 19% (5/26) vs. 20% (6/30) New neurological symptom: 0% (1/28) vs. 4% (1/26) vs. 3% (1/30) Nonlocal infection: 0% (0/28) vs. 4% (1/26) vs. 10% (3/30) Nonlocal rash: 4% (1/28) vs. 0% vs. 0%	John P. Murtha Neuroscience and Pain Institute, International Spinal Intervention Society, the Center for Rehabilitation Sciences Research	Good

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Cohen, 2012b	RCT	USA Multicenter Pain clinics	Age >18 years; signs and symptoms of lumbosacral radiculopathy; leg pain as great as or greater than back pain; agreement to receive injection regardless of MRI findings	Previous back surgery; duration of pain >4 years; treated with epidural steroid injection within the past 2 years; serious neurologic deficit; serious psychiatric disease	Approached: 323 Eligible: Unclear Randomized: 132 (67 vs. 65) Analyzed: 132	A: Transforaminal epidural injection with 60 mg methylprednisolone, 0.25% bupivacaine (1 ml), and saline (0.5 ml) (total 3 ml) or interlaminar epidural injection with 60 mg methylprednisolone, 0.25% bupivacaine (1 ml), and saline (1.5 ml) (total 4 ml), with fluoroscopic guidance; treatment and level based on MRI findings (n=67) B: Injection as above, based on history and physical examination findings (n=65)
Cuckler, 1985	RCT	USA >1 center Type of clinics not reported	Acute unilateral sciatica and well defined, discrete neurological findings or neurogenic claudication; failed to improved with at least two weeks of non-invasive therapy; duration of symptoms not specified; imaging findings not required	Lumbar surgery for similar symptoms or any lumbar surgery within 6 months	Approached: Not reported Eligible: Not reported Randomized: 73 (42 vs. 31) Analyzed: 73 at 20-22 months	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) and 1% procaine (5 ml) (n=42) B: Interlaminar epidural injection with saline (2 ml) and 1% procaine (5 ml) (n=31)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Cohen, 2012b	A vs. B: Age (mean): 51 vs. 53 Male: 42% vs. 45% Duration of symptoms (years): 1.5 vs. 1.6 Baseline leg pain (0-10 NRS): 6.6 vs. 6.7 Baseline back pain (0-10 NRS): 6.1 vs. 6.1 Baseline ODI (0-100): 44 vs. 45	A vs. B: Treatments prior to intervention: Not specified Treatments following interventions: Not specified Opioid use: 37% vs. 31%	Number and frequency of injections: Could undergo second injection after 1 month, 66% vs. 77% underwent two injections Number of levels: Appears single; 61% vs. 77% received transforaminal and 31% vs. 23% interlaminar injections Provider experience: Not reported	Fluoroscopic guidance with contrast verification in epidural space	Epidural steroid injection based on MRI findings vs. without MRI
Cuckler, 1985	A vs. B: Age (years): 49 vs. 50 Male: 48% vs. 55% Duration of symptoms (months): 17.3 vs. 13.8 Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Previous surgery: 2% (1/42) vs. 7% (2/31) Herniated disc: 52% vs. 45% Spinal stenosis: 48% vs. 55%	Number of injections: 43% (18/42) vs. 58% (18/31) received second injection with corticosteroid and local anesthetic after 24 hours due to no relief after initial injection Number of levels: Single level Provider experience: Not reported	None reported	Epidural injection with local anesthetic

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Cohen, 2012b	A vs. B: <u>Pain</u> Leg pain (0-10 NRS): 6.6 vs. 6.7 at baseline, 3.6 vs. 4.4 at 1 month (p=0.12), 2.7 vs. 3.0 at 3 months (p=0.77) Back pain (0-10 NRS): 6.1 vs. 6.1 at baseline, 4.0 vs. 4.6 at 1 m (p=0.21), 3.2 vs. 3.5 at 3 m (p=0.81) <u>Function</u> ODI (0-100): 44 vs. 45 at baseline, 35 vs. 35 at 1 month (p=0.98), 30 vs. 31 at 3 months (p=0.79) Medication reduction: 48% (26/67) vs. 27% (14/65) at 1 month (p=0.02); 57% (17/67) vs. 56% (14/65) at 3 months (p=0.96) <u>Global assessment</u> Global Perceived Effect positive: 69% (42/67) vs. 55% (36/65) at 1 month (p=0.12), 53% (26/67) vs. 40% (24/65) at 3 months (p=0.17) Overall success (>=2 point decrease in leg pain plus positive Global Perceived Effect): 41% (24/67) vs. 35% (23/65) at 3 months (p=0.54) No statistically significant effect of age, sex, type of injection, duration of pain, opioid use, baseline ODI, or baseline pain on likelihood of success
Cuckler, 1985	A vs. B: <u>Pain</u> Pain improved >=75%: 26% (11/42) vs. 13% (4/31) at mean 20 months, RR 2.40 (95% CI 0.93 to 6.58) Pain improved >=75%, herniated disc patients: 26% (6/23) vs. 15% (2/13) at mean 20 months, RR 1.94 (95% CI 0.56 to 7.66) <u>Other outcomes</u> Surgery: 38% (16/42) vs. 29% (9/31) at mean 20 months, RR 1.50 (95% CI 0.86 to 2.81) Surgery (herniated disk): 43% (10/23) vs. 23% (3/13) at mean 20 months, RR 2.56 (95% CI 1.12 to 7.35)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Cohen, 2012b	3 months	A vs. B: 1.5% (2/132) lost to followup (states 5 patients who did not undergo epidural injections excluded from analysis, but 132 of 132 randomized patients presented in results)	Appears complete	A vs. B: 3 patients had worsening of pain, 1 had unstable angina, and 1 had arrhythmia following epidural steroid injection (group not specified)	John P. Murtha Neuroscience and Pain Institute, International Spinal Intervention Society, the Center for Rehabilitation Sciences Research	Fair
Cuckler, 1985	13 to 30 months (mean 20.2 vs. 21.5 months)	None	Appears complete	Not reported	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Dashfield, 2005	RCT	UK Single center Pain clinic	>18 years of age; sciatica accompanied by neurosensory and motor deficits, with or without back pain; duration 6 to 18 months; imaging findings not required	Previous spinal surgery; coagulopathy; progressive motor neuron disorders; peripheral vascular disease; epidural corticosteroid injection within three months	Approached: Not reported Eligible: Not reported Randomized: 60 (30 vs. 30) Analyzed: 52 (29 vs. 23) at 6 months	A: Caudal epidural injection with triamcinolone 40 mg plus 1% lidocaine (10 ml), with fluoroscopic guidance (n=33) B: Epidural injection with 40 mg triamcinolone plus 1% lidocaine (10 ml) and saline (50 to 150 ml), via sacral approach with spinal endoscopic guidance (n=27)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Dashfield, 2005	A vs. B: Age (mean): 48 vs. 45 years Male: 51% vs. 37% Duration of symptoms (months): 9.4 vs. 10.1 Baseline pain (0 -10): 6.6 vs. 7.2 Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number of injections: Single injection Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification in epidural space for caudal epidural injection, Spinal endoscopic guidance	Epidural injection with steroid, with spinal endoscopic guidance

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Dashfield, 2005	A vs. B: <u>Pain</u> Pain (mean, 0-10): 6.6 vs. 7.2 at baseline; 5.7 vs. 6.7 at 6 weeks; 5.4 vs. 6.4 at 3 months; 5.2 vs. 6.0 at 6 months Short-form McGill Pain Questionnaire, sensory subscale (scale not reported): 14.8 vs. 15.5 at baseline; 13.9 vs. 16.0 at 6 weeks; 13.1 vs. 16.4 at 3 months; 12.5 vs. 16.0 at 6 months Short-form McGill Pain Questionnaire affective subscale (scale not reported): 4.2 vs. 5.9 at baseline; 4.7 vs. 4.9 at 6 weeks; 4.6 vs. 6.6 at 3 months; 4.2 vs. 5.9 at 6 months Present Pain Intensity (0-10): 2.8 vs. 3.5 at baseline; 2.3 vs. 2.6 at 6 weeks; 2.1 vs. 3.1 at 3 months; 2.0 vs. 2.5 at 6 months <u>Other outcomes</u> HAD-anxiety (0-21): 10.9 vs. 103 at baseline; 9.3 vs.10.0 at 6 weeks; 8.4 vs. 9.6 at 3 months; 7.8 vs. 8.7 at 6 months HAD-depression (0-21): 8.4 vs. 9.0 at baseline; 8.2 vs. 8.0 at 6 weeks; 7.7 vs. 8.0 at 3 months; 7.0 vs. 7.9 at 6 months

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Dashfield, 2005	6 months	A vs. B: 12% (4/33) vs. 15% (4/27) at 6 months	3 patients randomized to epiduroscopy crossed over to caudal injection and analyzed as treated	A vs. B: Post-procedural back discomfort: More frequent in spinal endoscopy group	Defense Secondary Care Agency	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Datta, 2011	RCT	India Single center Pain clinic	20-70 years of age; BMI 18-30 kg/m2; recurrent episodes of sciatica >4 weeks but <1 year with failure of ≥6 weeks conservative therapy; CT evidence of herniated disc at level correlating with symptoms and clinical findings; RDQ score >20	Requiring surgery, structural spinal deformities; symptoms from causes other than herniated disc; spinal injection in last year; prior low back surgery, chemonucleolysis or nucleotomy; pregnant; allergy to corticosteroids; use of tricyclic antidepressants or lithium	Approached: Not reported Eligible: Not reported Randomized: 207 (50 vs. 52 vs. 50 vs. 55) Analyzed: 163 (39 vs. 40 vs. 42 vs. 42) at 12 weeks	A: Caudal epidural injection with 80 mg methylprednisolone plus 0.125% bupivacaine (10-15 ml) (n=50) B: Caudal epidural injection with 80 mg triamcinolone plus 0.125% bupivacaine (10-15 ml) (n=52) C: Caudal epidural injection with 15 mg dexamethasone plus 0.125% bupivacaine (10-15 ml) (n=50) D: Caudal epidural injection with 0.125% bupivacaine (10-15 ml) (n=55)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Datta, 2011	A vs. B vs. C vs. D: Age (mean): 40 vs. 39 vs. 42 vs. 43 years Male: 92% vs. 94% vs. 90% vs. 91% Duration of leg pain (weeks): 16 vs. 17 vs. 16 vs. 16 Baseline pain (0-10 VAS): 7.5 vs. 7.4 vs. 7.3 vs. 7.2 Baseline RDQ (0-24): 21 vs. 22 vs. 21 vs. 22	A vs. B vs. C vs. D: Treatments prior to intervention: 51 vs. 49 vs. 47 vs. 48 diclofenac tablets/week Treatments following intervention: Analgesics other than diclofenac prohibited; no injections during followup Single disc: 82% vs. 86% vs. 88% vs. 86% Two or more discs: 18% vs. 14% vs. 12% vs. 14% L3-L4: 82% vs. 73% vs. 81% vs. 73% L4-L5: 78% vs. 75% vs. 80% vs. 64% L5-S1: 12% vs. 13% vs. 10% vs. 16%	Number and frequency of injections: Up to 3 injections over 1 year Number of levels: Caudal Provider experience: Not reported	None reported	Head-to-head comparison of various corticosteroids and epidural injection with local anesthetic

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Datta, 2011	A vs. B vs. C vs. D: <u>Pain</u> Pain (0-10 VAS): 7.4 vs. 7.4 vs. 7.3 vs. 7.2 at baseline; 6.3 vs. 6.3 vs. 6.4 vs. 6.8 at 3 weeks; 4.9 vs. 4.8 vs. 5.2 vs. 6.2 at 12 weeks Complete pain relief (complete, incomplete but satisfactory, unsatisfactory): at 12 weeks: A vs. B: 43% (17/39) vs. (18/42), RR 1.45 (95% CI 0.86 to 2.60) A vs. C: 43% (17/39) vs. 38% (15/40), RR 1.16 (95% CI 0.68 to 1.99) A vs. D: 43% (17/39) vs. 26% (11/42), RR 1.66 (95% CI 0.89 to 3.10) <u>Function</u> RDQ improved >5 points (percent improvement, 0-24): at 3 weeks, 41% (16/39) vs. 40% (17/42) vs. 35% (14/40) vs. 38% (16/42): A vs. B: (16/39) vs. 40% (17/42), RR 1.66 (95% CI 0.60 to 1.71) A vs. C: 41% (16/39) vs. 35% (14/40), RR 1.17 (95% CI 0.67 to 2.06) A vs. D: (16/39) vs. 38% (16/42), RR 1.17 (95% CI 0.63 to 1.84) at 12 weeks: 69% (27/39) vs. 71% (30/42) vs. 62% (25/40) vs. 24% (10/42): A vs. B: 69% (27/39) vs. 71% (30/42), RR 0.97 (95% CI 0.73 to 1.29) A vs. C: 69% (27/39) vs. 62% (25/40), RR 1.11 (95% CI 0.81 to 1.52) A vs. D: 69% (27/39) vs. 24% (10/42): RR, 2.91(95% CI 1.63 to 5.19) <u>Other outcomes</u> Use of diclofenac (tablets/day): 3.8 vs. 3.3 vs. 4.0 vs. 4.8 at 3 weeks; 18 vs. 17 vs. 18 vs. 26 at 12 weeks Use of physiotherapy: 25% (9/39) vs. 17% (7/42) vs. 30% (12/40) vs 45% (19/42) at 6 weeks; 15% (6/39) vs. 12% (5/42) vs. 25% (10/40) vs. 38% (16/42) from 6 weeks to 3 months Sensory deficits: 13% (5/39) vs. 21% (9/42) vs. 28% (11/40) vs. 48% (20/42) at 3 months Underwent surgery: 6.0% (3/50) vs. 7.7% (4/52) vs. 6.0% (3/50) vs. 16% (9/55) at 3 months

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Datta, 2011	3 months	A vs. B vs. C vs. D: 22% (11/50) vs. 23% (12/52) vs. 16% (8/50) vs. 24% (13/55) lost to followup or had laminectomy and excluded at 3 months	Appears complete	A vs. B vs. C vs. D: Local pain >24 h: 21% (8/39) vs. 17% (7/42) vs. 10% (4/40) vs. 7.1% (3/42) Headache: 38% (15/39) vs. 38% (16/42) vs. 22% (9/40) vs. 31% (31/42) Tinnitus: 2.6% (1/39) vs. 9.5% (4/42) vs. 2.5% (1/40) vs. 7.1% (3/42) Nausea: 15% (6/39) vs. 17% (7/42) vs. 20% (8/40) vs. 17% (7/42) Weight gain: 0% (0/39) vs. 2.4% (1/42) vs. 0% (0/40) vs. 0% (0/42)	Not reported	Poor

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Dilke, 1973	RCT	UK Single center Rheumatology clinic	Unilateral sciatica with painful limitation of sciatic or femoral nerve stretch; sciatic scoliosis, appropriate neurologic deficit; duration not specified; imaging findings not required	Diagnostic uncertainty; bilateral manifestations; prior lumbar spine surgery; medical conditions affecting rehabilitation; doubt about the technical success of an injection	Approached: Not reported Eligible: Not reported Randomized: 100 Analyzed: 82 at 3 months	A: Interlaminar epidural injection with 80 mg methylprednisolone in saline (10 ml) B: Interspinous ligament injection with saline (1 ml)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Dilke, 1973	A vs. B: Age (mean): 39 vs. 42 years Male: 53% vs. 58% Duration of symptoms >4 weeks: 90% vs. 90% Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Mefenamic acid; diazepam; bed rest; graded rehabilitation with hydrotherapy; postural exercise; and spinal mobilizing exercise Other patient characteristics: Not reported	Number and frequency of injections: Mean not reported, second injection permitted after 1 week if no improvement Number of levels: Single level Provider experience: Not reported	None reported	Soft tissue injection with saline

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Dilke, 1973	A vs. B: <u>Pain</u> Pain clearly relieved during admission (clearly relieved, clearly not relieved, or intermediate): 31% (16/51) vs. 8% (4/43), RR 3.37 (95% CI 1.21 to 9.33) Pain assessment "none" (none, not severe, severe): 36% (16/44) vs. 21% (8/38) at 3 months, RR 1.72 (95% CI 0.83 to 3.58) Pain assessment "none" or "not severe": 91% (40/44) vs. 74% (28/38) at 3 months, RR 1.23 (95 % CI 0.10 to 1.52) <u>Other outcomes</u> Full bed rest (days): 8.25 vs. 8.61 (p>0.05) Time to institution of spinal mobility exercises (days): 18.4 vs. 20.4 (NS) Time in hospital (days): 25.2 vs. 28.0 (p>0.05) Not resumed work at 3 months: 8.3% (3/36) vs. 40% (14/35), RR 0.21 (95 % CI 0.07 to 0.66) Analgesic consumption "none" (none, less than daily, daily) at 3 months: 50% (19/38) vs. 38% (11/29), RR 1.32 ((95 % CI 0.75 to 2.32) Underwent surgery at 3 months: 14% (7/51) vs. 21% (10/48), RR 0.66 (95% CI 0.27 to 1.59) Underwent second injection at 3 months: 31% (16/51) vs. 48% (23/48), RR 0.65 (95% CI 0.40 to 1.08) Underwent other conservative treatment at 3 months: 18% (9/51) vs. 29% (14/48), RR 0.61 (95% CI 0.29 to 1.27)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Dilke, 1973	3 months	A vs. B: 18% (18/100) at 3 months	Appears complete	"There were no complications attributable to the injections"	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Gerstzen, 2010	RCT	USA Multicenter Clinical setting not described	18 to 75 years of age; BMI <40; radicular pain score >50 on 0 to 100 VA; epidural corticosteroid injection within 3 weeks to 6 months; normal neurological function; imaging evidence of focal lumbar disc protrusion correlating with clinical symptoms; disc height >50% of normal adjacent discs	Extruded or sequestered disc herniation; sciatica from more than one disc level; axial pain more severe than radicular pain; cauda equina syndrome; progressive neurological deficit; radiological evidence of spondylolisthesis or moderate or severe stenosis at level to be treated; history of previous spinal surgery at or adjacent to level to be treated; spinal fracture; tumor; infection; suspected or planned pregnancy; cardiac pacemaker or defibrillator; spinal cord stimulator; allergy to contrast media or study drugs; severe medical comorbidities; Workman's Compensation or ongoing litigation	Approached: Not reported Eligible: Not reported Randomized: 90 (44 vs. 46) Analyzed: 85 (40 vs. 45) at 2 years, including 12 with missing data	A: Transforaminal epidural injection with corticosteroid, medication type (methylprednisolone acetate, betamethasone, methylprednisolone, triamcinolone acetonide) and dose left to discretion of clinician, with fluoroscopic guidance (n=44) B: Plasma disc decompression procedure with Coblation DLR or DLG Spine Wand surgical device, with fluoroscopic guidance (n=46)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Gerstzen, 2010	A vs. B: Age (mean): 42 vs. 46 years Male: 52% vs. 47% Duration of symptoms (months): median 24 vs. 12 Baseline leg pain (0-100 VAS): 75 vs. 72 Baseline back pain (0-100 VAS): 53 vs. 44 Baseline ODI (0-100): 43 vs. 42	A vs. B: Treatments prior to intervention: Opioid 55% vs. 47% Treatments following intervention: Not specified Other patient characteristics: Full or part-time employment: 65% vs. 62%	Number and frequency of injections: Up to 2 injections 3 weeks apart;75% (30/40) underwent 2 epidural injections Number of levels: Single Provider experience: Not reported	Fluoroscopic guidance	Plasma disc decompression

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Gerstzen, 2010	A vs. B: <u>Pain</u> Leg pain (mean change, 0-100 VAS): at 6 weeks -21 vs. -42 (p=0.002), at 3 months -23 vs. -46 (p=0.0001), at 6 months -21 vs. -47 (p=0.0008) Leg pain improved >=25 points: at 6 months 21% (8/39) vs. 49% (21/43), RR 0.42 (95% CI 0.21 to 0.83); at 1 year 18% (7/39) vs. 44% (19/43), RR 0.42 (95% CI 0.21 to 0.84); at 2 years 21% (8/39) vs. 42% (18/43), RR 0.49 (95% CI 0.24 to 1.0) Back pain (mean change, 0-100 VAS): at 6 weeks 1 vs. -18 (p=0.0005), at 3 months 7 vs. -17 (p=0.0001); at 6 months -0.4 vs. -21 at 6 months (p=0.002) Back pain improved >=12 points: at 6 months 22% (8/36) vs. 49% (19/39), RR 0.46 (95% CI 0.23 to 0.91); at 1 year 11% (4/36) vs. 39% (15/39), RR 0.26 (95 % CI 0.11 to 0.79); at 2 years 17% (6/36) vs. 39% (15/39), RR 0.43 (95% CI 0.19 to 1.0) <u>Function</u> ODI (mean change, 0-100): at 6 weeks -5 vs. -13 at 6 weeks (p=0.002); at 3 months -2 vs. -11 (p=0.002); at 6 months -4 vs. -14 (p=0.002) ODI improved >=13 points: at 6 months15% (6/40) vs. 32% (14/44), RR 0.47 (95% CI 0.20 to 1.10); at 1 year 10% (4/40) vs. 25% (11/44), RR 0.40 (95 % CI 0.14 to 1.16); at 2 years 10% (4/40) vs. 30% (13/44), RR 0.34 (95 % CI 0.12 to 0.95) SF-36 improved >=5 points: at 6 months 21% (8/39) vs. 37% (16/43), RR 0.55 (95% CI 0.27 to 1.14); at 1 year 13% (5/39) vs. 33% (14/43), RR 0.39 (95% CI 0.16 to 0.99); at 2 years 13% (5/39) vs. 33% (14/43), RR 0.39 (95% CI 0.16 to 0.99) <u>Other outcomes</u> Patient satisfaction "extremely satisfied": 15% vs. 38% Did not undergo secondary procedure: 17% vs. 52%, adjusted HR 2.0 (p=0.025) Surgery (not including plasma disc decompression): through 2 years: 5% (2/40) vs.11% (5/45), RR 0.45 (95% CI 0.09 to 2.19)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Gerstzen, 2010	2 years	A vs. B: 15% (6/40) vs. 13% (6/45) at 2 years; 5 post-randomization exclusions	13 patients in group B received epidural injection, 20 patients in group A received plasma disc decompression	A vs. B: Procedure related adverse events: 18% (7/40) vs. 11% (5/45), RR 1.58 (95% CI 0.54 to 4.57) Injection site pain: 5.0% (2/40) vs. 4.4% (2/45), RR 1.12 (95% CI 0.17 to 7.62) Increased radicular pain: 2.5% (1/40) vs. 11% (5/45), RR 0.22 (95% CI 0.03 to 1.85) Increased weakness: 2.5% (1/40) vs. 0% (0/45), RR 3.37 (95% CI 0.14 to 80) Increased back pain: 2.5% (1/40) vs. 8.9% (4/45), RR 0.28 (95% CI 0.03 to 2.36) Lightheadedness: 0% (0/40) vs. 2.2% (1/45), RR 0.37 (95% CI 0.02 to 8.93) Muscle tightness of spasms: 5.0% (2/40) vs. 2.2% (1/45), RR 2.25 (95% CI 0.21 to 24)	ArthoCare Corp	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Ghahreman, 2010 See also Ghahreman, 2011	RCT	Australia Two centers Neurosurgery clinic	Pain radiating into lower limb with lancinating, burning, stabbing, or electric quality; limitation of straight-leg-raise <30° or < 45° with history of lancinating pain & disc herniation; duration not specified; required imaging correlation	Foraminal stenosis; severe motor deficit; history of substance abuse; previous surgery at affected level; conditions that contraindicated spinal injection (e.g., pregnancy, recent infection, or spinal deformity)	Approached: Not reported Eligible: Not reported Randomized: 150 (28 vs. 37 vs. 27 vs. 28 vs. 30) Analyzed: 150 at 12 months, including 22 with missing data (1 vs. 7 vs. 8 vs. 2 vs. 4)	A: Transforaminal injection with 40 mg/ml triamcinolone (1.75 ml) plus 0.5% bupivacaine (0.75 ml), with fluoroscopic guidance (n=28) B: Transforaminal injection of 0.5% bupivacaine (2 ml), with fluoroscopic guidance (n=27) C: Transforaminal injection of normal saline (2 ml), with fluoroscopic guidance (n=37) D: Intramuscular injection of 40 mg/ml triamcinolone (1.75 ml), with fluoroscopic guidance (n=28) E. Intramuscular injection of normal saline (2 ml), with fluoroscopic guidance (n=30)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Ghahreman, 2010 See also Ghahreman, 2011	A vs. B vs. C vs. D vs. E: Age (median): 49 vs. 44 vs. 43 vs. 49 vs. 46 years Male: 61% vs. 51% vs. 63% vs. 54% vs. 70% Duration of symptoms: Mean not reported, range 2 to 560 weeks Baseline leg pain (median, 0-10): 7 vs. 7 vs. 7 vs. 7 vs. 8 Baseline Roland Morris score (median, 0-24): 17 vs. 17 vs. 19 vs. 17 vs. 15	A vs. B vs. C vs. D vs. E: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not specified	Number and frequency of injections: Single injection Number of levels: Appears single Provider experience: Not reported	Fluoroscopic guidance with contrast verification of nerve root for transforaminal injections	Transforaminal injection of normal saline Transforaminal injection of local anesthetic Intramuscular injection of corticosteroid Intramuscular injection of normal saline

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Ghahreman, 2010 See also Ghahreman, 2011	A vs. B vs. C vs. D vs. E: <u>Pain</u> Pain (mean, 0-10): at baseline 7.0 vs. 7.4 vs. 6.6 vs. 7.6 vs. 7.0; at 1 month 4.1 vs. 6.7 vs. 5.5 vs. 5.9 vs. 6.0, difference -2.9 vs. -0.7 vs. -1.1 vs. -1.7 vs. -1.0, A vs. C (p=0.07); A vs. B, D, or E (p<0.05); for other comparisons: (p>0.05) Achieved >=50% pain relief: at 1 month 54% (15/28) vs. 7.4% (2/27) vs.19% (7/37) vs. 21% (6/28) vs. 13% (4/30): A vs. B: RR, 7.23 (95% CI 1.82 to 28.67; A vs. C: RR, 2.83 (95% CI 1.33 to 6.00; A vs. D: RR, 2.50 (95% CI 1.14 to 5.50; A vs. E, RR 4.02 (95% CI 1.52 to 10.66): (p>0.05); B vs. C, RR 0.39 95% CI 0.89 to 1.73; B vs. D, RR 0.35 (95% CI 0.08 to 1.57); B vs. E, RR 0.56 (95% CI 0.11 to 2.80): C vs. D, RR 0.88 (95% CI 0.33 to 2.34); C vs. E, RR 1.42 (95% CI 0.46 to 4.39); D vs. E, RR 1.61 (95% CI 0.51 to 5.10); no interaction between duration of symptoms, presence of sensory changes or neurologic signs, location [central or paracentral versus foraminal] or level affected, type of herniation (broad-based bulge, focal protrusion, extrusion, sequestration), dimensions of herniation (thickness, cross-section area of herniation or vertebral canal, ratio area of herniation and spinal canal), or presence of degenerative changes; low grade nerve root compression 75% (30/40) and high grade 26% (8/31), p for difference in estimates <0.0005 <u>Function</u> Patient-specified Functional Outcome Scale (median, 0-12): at 1 month 8 vs. 6 vs. 6 vs. 10 vs. 10 (p>0.05) <u>Other outcomes</u> Underwent surgery at 12 months: 36% (10/28) vs. 26% (7/27) vs. 26% (7/27) vs. 21% (6/28) vs. 30% (9/30): A vs. B, RR 1.38 (95% CI 0.61 to 3.09); A vs. C, RR 1.38 (95% CI 0.61 to 3.09); A vs. D, RR 1.67 95% CI 0.70 to 3.10; A vs. E, RR 1.19 (95% CI 0.57 to 2.49); B vs. C, RR 1.00 (95% CI 0.39 to 2.54); B vs. D, RR 0.96 (95% CI 0.36 to 2.53); B vs. E, RR 0.69 (95% CI 0.29 to 1.62); C vs. D, RR 0.96 (95% CI 0.36 to 2.53); C vs. E, RR 0.69 (95% CI 0.29 to 1.62); D vs. E, RR 0.71 (95% CI 0.29 to 1.75) Underwent rescue transforaminal injection with steroid at 12 months: 14% (4/28) vs.67% (18/27) vs. 61% (23/38) vs. 64% (18/28) vs.73% (22/30): A vs. B, RR 0.21 (95% CI 0.83 to 0.55); A vs. C, RR 0.24 (95% CI 0.09 to 3.09); A vs. D, RR 0.22 95% CI 0.09 to 0.57; A vs. E, RR 0.19 (95% CI 0.07 to 0.50); B vs. C, RR 1.10 (95% CI 0.76 to 1.60); B vs. D, RR 1.04 (95% CI 0.71 to 1.52); B vs. E, RR 0.91 (95% CI 0.65 to 1.28); C vs. D, RR 0.94 (95% CI 0.65 to1.37); C vs. E, RR 0.83 (95% CI 0.59 to 1.62); D vs. E, RR 0.83 (95% CI 0.59 to 1.12) No differences in health care utilization No effect of chronicity on response to treatment

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Ghahreman, 2010 See also Ghahreman, 2011	12 months	A vs. B vs. C vs. D vs. E: 3.6% (1/28) vs. 26% (7/27) vs. 22% (8/37) vs. 7.1% (2/28) vs. 13% (14/30) at 12 months	Appears complete	"No complications occurred that could be attributed to the treatment" 1 case of bladder incontinence after transforaminal injection of local anesthetic	Not reported	Good

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Ghai, 2014	RCT	India Single center Pain clinic	18 to 65 years, with chronic (>3 months) low back pain and unilateral lumbosacral radicular pain, not responding to medications and physical therapies, pain score >=50 on a 0 to 100 VAS at baseline were eligible; MRI was performed for correlation with symptoms	Clinically significant or unstable medical or psychiatric illness, previous surgery on the lumbar spine, facet joint arthropathy, spinal canal stenosis, unstable neurological deficits, or cauda equine syndrome. prior lumbar epidural steroid injection, corticosteroids or anesthetics allergy, taking anticoagulants or bleeding diathesis, taking systemic corticosteroids, pregnant or lactating women	Approached: 124 Eligible: Not reported Randomized: 62 (32 vs. 30) Analyzed: 62 (32 vs. 30)	A. Parasagittal epidural injection with 80 mg methylprednisolone (2 ml) plus normal saline) 2 ml B. Transforaminal epidural injection with 80 methylprednisolone (2 ml) plus normal saline (2 ml), with fluoroscopic guidance
Ghai, 2013	RCT	India Single center Pain clinic	Low back pain with unilateral lumbosacral radicular pain for at least 3 months (MRI performed in all patients)	Somatic referred pain	Approached: 40 Eligible: Not reported Randomized: 37 (19 vs. 18) Analyzed: 37 at 6 months	A: Parasagittal interlaminar injection with 80 mg methylprednisolone (2 ml) plus normal saline (2 ml), with fluoroscopic guidance B: Midline interlaminar injection with 80 mg methylprednisolone (2 ml) plus normal saline (2 ml), with fluoroscopic guidance

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Ghai, 2014	A vs. B: Age (mean): 43 vs. 46 years Male: 53% vs. 63% Duration of symptoms (months); 25 vs. 30 Baseline pain (0-100 VAS): 73 vs. 74 Modified ODI (0 to 100): 31 vs. 29	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: 58 vs. 60 injections (p = 0.72), mean 1.84 vs. 1.92 procedures per year Number of levels: Appears to be single Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space	Head-to-head comparison of alternative epidural steroid injection methods
Ghai, 2013	A vs. B: Age (mean): 41 vs. 42 years Male: 68% vs. 50% Duration of symptoms (months); 13 vs. 14 Baseline pain (0-100 VAS): 69 vs. 71 Modified ODI (0 to 100): 42 vs. 49	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Mean 1.53 vs. 2.28 over 6 months (up to 3 injections at least 15 days apart if pain relief <50%) Number of levels: Not reported, levels could differ on subsequent injections Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space	Head-to-head comparison of alternative epidural steroid injection methods

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Ghai, 2014	A vs. B: <u>Pain</u> Pain score (mean, VAS 0-100, estimated from graph): at baseline, 73 vs. 73 (p=0.56); at 15 days, 38 vs. 45 (p=0.63); at 1 month, 36 vs. 39 (p=0.61); at 2 months, 36 vs. 36 (p=0.59); at 3 months, 35 vs. 35 (p=0.64); at 6 months, 34 vs. 34 (p=0.56); at 9 months, 33 vs. 33 (p=0.23); at 12 months, 33 vs. 31 (p=0.79) <u>≥</u>50% pain relief from baseline using VAS: at 15 days, 65.6% vs. 50% (p=0.3); at 1 month, 72% vs. 63% (p=0.59); at 2 months, 69% vs. 73% (p=0.78); at 3 months, 78% vs. 77% (p=1.0); at 6 months, 75% vs. 77% (p=1.0); at 9 months, 78% vs. 73% (p=0.77); at 12 months, 69% vs. 77% (p=0.57) <u>Function</u> Modified ODI (estimated from graph): at baseline, 32 vs. 29 (p=0.18); at 15 days, 21 vs. 20 (p=0.29); at 1 month, 19 vs. 18 (p=0.38); at 2 months, 19 vs. 17 (0.38); at 3 months, 20 vs. 18 (p=0.60); at 6 months, 19 vs. 17 (p=0.36); at 9 months, 18 vs. 17 (p=0.52); at 12 months, 18 vs. 17 (p=0.45) <u>Other outcomes</u>: Patient satisfaction: Patient Global Impression of Change Scale (7-point scale where 1-3 = improved, 4 = no change, 5-7 = worse since study start): % improved at 3 months, 78% (25/32) vs/ 77% (23/30); at 6 months, 75% (24/32) vs. 80% (24/30); at 9 months, 78% (25/32) vs. 77% (23/30); at 12 months, 78% (25/32) vs. 80% (24/30) (p>0.05 for all)
Ghai, 2013	A vs. B: <u>Pain</u> Pain score (mean, VAS 0-100, estimated from graph): at baseline, 69 vs. 71; at 15 days, 29 vs. 49; at 1 month, 28 vs. 50; at 3 months, 30 vs. 48; at 6 months, 31 vs. 51, (p<0.05 at all time points) 50% pain relief: at 15 days 79%(15/19) vs. 39% (7/18) RR, 2.03 (95 % CI 1.09 to 3.78); at 1 month 79% (15/19) vs. 39% (7/18) RR 2.03 (95 % CI 1.09 to 3.78); at 3 months 79% (15/19) vs. 39% (7/18) RR, 2.03 (95 % CI 1.09 to 3.78); at 6 months 68% (13/19) vs.17% (3/18), RR 4.1 (95% CI 1.4 to 12) <u>Function</u> ODI (mean, 0-100, estimated from graph): at baseline, 42 vs. 49; at 15 days, 27 vs. 40; at 1 month, 27 vs. 41; at 3 months, 30 vs. 42; at 6 months, 30 vs. 43, (p<0.05 at all time points)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Ghai, 2014	12 months, but 3 month followup is primary outcome	None reported	Appears complete	No patient reported any swelling, redness, or persisting pain at the injection site.	None	Good
Ghai, 2013	6 months	None reported	Appears complete	None reported	None	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Gharibo, 2011	RCT	US Single center Pain clinic	Low back pain radiating to one lower extremity for >1 month and <1 year, due to disc disease; failed analgesic and nonpharmacologic therapy; imaging correlation on CT or MRI; unable to tolerate physical therapy; no benefit from physical therapy	Lumbar spine surgery or epidural steroid injections within 6 months; multilevel degenerative spine disease; unstable spine; spondylolisthesis > grade 1; spondylolysis, cauda equina syndrome; arachnoiditis, progressive neurologic deficit; central spinal canal stenosis; active cancer diagnosis; history of substance abuse; current psychiatric co-morbidity; pregnant; contrast, steroid, or local anesthetic allergy; ongoing medical legal or workman's compensation	Approached: 80 Eligible: 46 Randomized: 42 (21 vs. 21) Analyzed: 38 (20 vs. 18) at 10-16 days (including 3 missing data)	A: Transforaminal epidural injection with 40 mg triamcinolone diacetate (1 ml) plus 0.25% bupivacaine (1 ml) at two levels, with fluoroscopic guidance B: Interlaminar epidural injection with 80 mg triamcinolone diacetate (2 ml) plus 0.25% bupivacaine (2 ml), with fluoroscopic guidance

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Gharibo, 2011	A vs. B: Age (mean): 48 vs. 51 years Male: 55% vs. 72% Duration of symptoms: Not reported Baseline pain (0-10): 6.4 vs. 7.0 Baseline ODI (0-50): 38 vs. 38	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: 1/20 vs. 3/18 underwent two procedures Number of levels: Two levels (transforaminal) vs. single level (interlaminar) Provider experience: Single provider with over 10 years experience	Fluoroscopy with contrast verification in epidural space	Head-to-head comparison of alternative epidural steroid injection methods

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Gharibo, 2011	A vs. B: <u>Pain</u> Pain (mean, 0-10 NRS): 6.4 vs. 7.0 at baseline, 1.7 vs. 3.9 at 10-16 days (p<0.05) <u>Function</u> ODI (mean, 0-50): 38 vs. 38 at baseline, 22 vs. 13 at 10-16 days (p<0.05) <u>Other outcomes</u> Depression (scale not reported): 4.1 vs. 4.4 at baseline, 1.7 vs. 2.2 at 10-16 days (p<0.05) Walking distance (blocks): 8.9 vs. 8.1 at baseline, 11.8 vs. 10.6 at 10-16 days (p<0.05 base on 1-sided test)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Gharibo, 2011	10-16 days	A vs. B: 4.8% (1/21) vs. 10% (2/21) at 10-16 days	2 crossovers in interlaminar injection group after 2 failed injections; one patient excluded for receiving epidural steroid injection outside of protocol	Not reported	None	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Habib, 2013	RCT	Israel Single center Hospital	Patients >18 years, low back pain due to radiculopathy of at least one month's duration that did not respond to physical therapy or nonsteroidal anti-inflammatory drugs (if not contraindicated); imaging findings not required	Having had an epidural corticosteroid, systemic, intra-articular, and/or intramuscular injection; nasal spray, eye drops, or inhalation of steroid compounds during the previous three months; evidence of acute illness (inflammatory or noninflammatory); inflammatory back pain; uncontrolled hypertension; uncontrolled diabetes; anticoagulant treatment; bleeding tendency; allergy to corticosteroids; and/or pregnancy	Approached: Not reported Eligible: 50 Randomized: 42 (21 vs. 21) Analyzed: 35 at 4 w	A: Epidural injection with 80 mg methylprednisolone acetate, approach and other details not provided (n=21) B: Epidural injection with 40 mg methylprednisolone acetate, approach and other details not provided (n=21)
Helliwell, 1985	RCT	UK Single center Rheumatology clinic	Low back pain for >2 months with pain in the sciatic or femoral nerve distribution accompanied by dural tension signs or a neurological deficit consistent with lumbar root compression; radiograph of lumbar spine before randomization	Diagnostic uncertainty; pregnant; prior lumbar spine surgery or the development of progressive neurologic impairment	Approached: Not reported Eligible: Not reported Randomized: 39 (20 vs. 19) Analyzed: 39 at 3 months	A: Interlaminar epidural injection with 80 mg methylprednisolone in saline (10 ml) (n=20) B: Interspinous ligament injection with saline (5 ml) (n=19)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Habib, 2013	A vs. B: Age (mean): 53 vs. 51 Male: 62% vs. 76% Duration of back pain: 2.9 vs. 3.4 years Baseline VAS (0-100): 80 vs. 78	A vs. B: Treatments prior to intervention: Previous back surgery 1 vs 0; Previous epidural injection 4 vs. 2 Treatments following intervention: Not specified Other patient characteristics: Serum cortisol level at baseline 11.1 vs. 13.6 ng/mL	Number and frequency of injections: 1 Number of levels: 1-2 Provider experience: Experienced anesthesiologist	Not reported	Epidural injection with different doses of corticosteroid
Helliwell, 1985	A vs. B: Age (mean): 45 vs. 47 years Male: 25% vs. 20% Duration of symptoms (months): 8.5 vs. 13 Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single Number of levels: Single Provider experience: Not reported	Not reported	Soft tissue injection with saline

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Habib, 2013	A vs. B Pain ≥30% improvement in 0-100 VAS: 62% (13/21) vs. 47% (9/19) at w 1 (p=0.362); 56% (10/18) vs. 35% (7/20) (p=0.210) at w 3, 39% (7/18) vs. 6% (1/17) at w 4 (p=0.049) Other outcomes Serum cortisol levels and number of patients with secondary adrenal insufficiency (serum corticol <18 ng/ml 30 minutes after ACTH stimulation test): 86% (18/21) vs. 53% (10/19) at w 1 (p=0.024), 22% (4/18) vs. 15% (3/20) at w 3 (p=0.87), 17% (3/18) vs. 12% (2/17) at w 4 (p=0.72)
Helliwell, 1985	A vs. B: Pain Pain, mean change from baseline (0-10 VAS, estimated from figure): at 1 month -2.6 vs. -0.7; at 3 months -2.7 vs. -0.3 (p<0.01 at both time points) Other outcomes Analgesic consumption decreased by >=50%: at 3 months 64% (7/11) vs. 40% (4/10), RR 1.6 (95% CI 0.69 to 4.1) Overall outcome "definite improvement" (vs. no improvement): at 3 months 70% 14/20 vs. 26% (5/19) RR, 2.7 (95% CI 1.3 to 6.2)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Habib, 2013	4 weeks	A vs. B: 14% (3/21) vs. 19% (4/21)	Appears complete	Not reported	Departmental funding	Poor
Helliwell, 1985	3 months	Not reported	Appears complete	None reported	Not reported	Poor

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Iversen, 2011	RCT	Norway Multi-center Clinical setting unclear	Unilateral lumbar radiculopathy >12 weeks with leg pain below the knee; leg pain worse than back pain; age 20 to 60 years; MRI or CT performed in all patients	Cauda equina syndrome; severe paresis; severe pain; prior spinal injection or surgery; deformity; pregnancy; breast feeding; warfarin therapy; treatment with non-steroidal anti-inflammatory drugs; body mass index >30; poorly controlled psychiatric conditions with possible secondary gain, or severe comorbidity; severe intraspinal pathology	Approached: 461 Eligible: 133 Enrolled: 116 (37 vs. 39 vs. 40) Analyzed: 116 (37 vs. 39 vs. 40) at 52 weeks (including 4 missing data)	A: Caudal epidural injection with 40 mg triamcinolone in 0.9% saline (29 ml), with ultrasound guidance (n=37) B: Caudal epidural injection with 0.9% saline (30 ml), with ultrasound guidance (n=39) C: Subcutaneous injection superficial to the sacral hiatus and outside spinal canal with 0.9% saline (2 ml), with ultrasound guidance (n=40)
Jeong, 2007	RCT	Korea Single center Radiology clinic	Lumbosacral radiculopathy; imaging (CT or MRI) documentation of nerve root compression with subarticular or paracentral disk herniation or central canal and/or lateral recess stenosis, based on consensus of 3 radiologists; duration of symptoms not specified	Not reported	Approached: Not reported Eligible: Not reported Randomized: 239 (127 vs. 112) Analyzed: 222 (116 vs. 106) at mid-term (>6 m) followup	A: Ganglionic transforaminal epidural injection with 40 mg triamcinolone acetonide (1 ml) plus 0.5% bupivacaine (0.5 cc), with fluoroscopic guidance (n=127) B: Preganglionic transforaminal epidural injection with 40 mg triamcinolone acetonide (1 ml) and 0.5% bupivacaine (0.5 cc), with fluoroscopic guidance (n=112)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Iversen, 2011	A vs. B vs. C: Age (mean): 40 vs. 43 vs. 43 years Male: 54% vs. 62% vs. 60% Duration of leg pain (weeks): 42 vs. 57 vs. 27 Baseline back pain (0-100 VAS): 47 vs. 50 vs. 46 Baseline leg pain (0-100 VAS): 50 vs. 54 vs. 48 Baseline ODI (0-50): 32 vs. 31 vs. 26	A vs. B vs. C: Treatments prior to intervention: Use of morphine: 24% vs. 18% vs. 15% Treatments following intervention: Not reported Other patient characteristics: Physically demanding work: 57% vs. 46% vs. 47% Received sickness benefit: 68% vs. 67% vs. 55% Fear Avoidance Beliefs Questionnaire (FABQ) work: 24 vs. 25 vs. 22 FABQ physical activity: 12 vs. 14 vs. 13	Number and frequency of injections: 2 injections within 2 weeks on all patients unless pain recovered prior to 2nd injection Number of levels: Not reported Provider experience: "Experienced" anesthesiologist	Ultrasound used to identify sacral hiatus	Caudal epidural injection with saline Soft tissue injection with saline
Jeong, 2007	A vs. B: Age (mean): 50 vs. 49 years Male: 40% vs. 48% Spinal stenosis: 18% vs. 20% Herniated disc: 82% vs. 80% Duration of symptoms <6 months: 64% vs. 56% Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: 2-5 years	Fluoroscopic guidance with contrast verification	Head-to-head comparison of alternative transforaminal epidural steroid injection techniques

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Iversen, 2011	A vs. B vs. C: <u>Pain</u> Leg pain: at 6 weeks 3.2 (-9.1 to 16) ; at 12 weeks 2.5 (-9.6 to 15); at 52 weeks 3.1 (-9.6 to 16) Low back pain: at 6 weeks -5.0 (-17 to 6.7); at 12 weeks -7.8 (-19 to 3.8); at 52 weeks -2.0 (-14 to 10) EuroQol: at 6 weeks -0.02 (-0.13 to 0.09); at 12 weeks -0.05 (-0.17 to 0.06); at 52 weeks -0.01 (-0.12 to 0.11) A vs. C: <u>Function</u> ODI: (mean difference, 0-50) A vs B: at 6 weeks; -0.5 (-6.3 to 5.4); at 12 weeks; 1.4 (-4.5 to 7.2); at 52 weeks; -1.9 (-8.0 to 4.3); A vs. C: at 6 weeks; -2.9 (-9.7 to 3.0); at 12 weeks; 4.0 (-1.9 to 9.9); at 52 weeks; 1.9 (-4.2 to 8.0) EuroQol: (mean difference, -0.594 to 1) A vs. B: at 6 weeks; -0.02 (-0.13 to 0.09); at 12 weeks; -0.05 (-0.17 to 0.06); at 52 weeks; -0.01 (-0.12 to 0.11). A vs. C: at 6 weeks; -0.05 (-0.16 to 0.06); at 12 weeks; -0.12 (-0.23 to -0.00); at 52 weeks; -0.05 (-0.17 to 0.06) <u>Other outcomes</u> Morphine use at 6 weeks: 8.1% (3/37) vs. 17% (6/35) vs. 11% (4/37): A vs. B RR 0.47 (95% CI 0.13 to 1.74); A vs. C RR 0.75 (95% CI 0.18 to 3.12); B vs. C RR 1.59 (95 % CI 0.49 to 5.15) Receiving sickness benefit at 52 weeks: 32% (11) vs. 30% (10) vs. 22% (7) (p=0.69) Underwent back surgery: 2.7% (1/37) vs. 15% (6/39) vs. 20% (8/40) (p=0.07): A vs. B, RR 1.72 (95% CI 0.72 to 4.12); A vs. C, RR 1.33 (95% CI 0.61 to 2.88); B vs. C, RR 0.77 (95% CI 0.29 vs. 2.01)
Jeong, 2007	A vs. B: <u>Pain</u> Overall results excellent (4 category scale poor, fair, good, excellent): 47% (56/127) vs. 73% (82/112) at 1 month, RR 0.60 (95% CI 0.48 to 0.75); 34% (39/116) vs. 37% (39/106) at mid-term (> 6 month) follow-up, RR 0.91 (95% CI 0.64 to 1.31) Overall results good or excellent: at 1 month 71% (90/127) vs. 88% (99/112), RR 0.80 (95% CI 0.70 to 0.91); at mid-term follow-up 67% (78/116) vs. 60% (64/106), RR 1.11 (95% CI 0.91 to 1.36) Age, sex, duration of symptoms, cause of radiculopathy were not statistically significant predictors for effectiveness of injection at 1 month or mid-term follow-up

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Iversen, 2011	52 weeks	A vs. B: 0% (0/37) vs. 5.1% (2/39) vs. 5.0% (2/40) at 52 weeks	5 patients did not receive allocated intervention (1 vs. 3 vs. 1), 7 discontinued intervention (2 vs. 4 vs. 1); no crossovers	6 had local pain with injection	North Norway Regional Health Authority and Health Region Nord-Trondelag, Norway	Good
Jeong, 2007	Mean 373 days (range 216-547) post-injection	A vs. B: 7% (17/239) at midterm followup	Appears complete	None reported	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Kang, 2011	RCT	South Korea Single center Pain clinic	Signs and symptoms consistent with nerve root entrapment at neural foramen; radicular leg pain; positive straight leg raise; at least single level disc herniation on MRI correlating with symptoms; age 18 to 60 years; duration not specified	Spinal stenosis; allergic reaction to local anesthetics or corticosteroids; contraindications to epidural steroid injections; epidural steroid injection within 6 months; previous lumbar spine surgery; unstable neurological deficits; cauda equina syndrome	Approached: Not reported Eligible: Not reported Randomized: 160 (40 vs. 40 vs. 40 vs. 40) Analyzed: 160 at 2 weeks	A: Transforaminal epidural injection with 40 mg triamcinolone plus 1% lidocaine (total 3 ml), with fluoroscopic guidance (n=40) B: Transforaminal epidural injection with 20 mg triamcinolone plus 1% lidocaine (total 3 ml), with fluoroscopic guidance (n=40) C: Transforaminal epidural injection with 10 mg triamcinolone plus 1% lidocaine (total 3 ml), with fluoroscopic guidance (n=40) D: Transforaminal epidural injection with 5 mg triamcinolone plus 1% lidocaine (total 3 ml), with fluoroscopic guidance (n=40)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Kang, 2011	A vs. B vs. C vs D: Age (mean): 47 vs. 53 vs. 52 vs. 53 years Male: 40% vs. 42% vs. 38% vs. 35% Duration of symptoms (days): 37 vs. 33 vs. 42 vs. 33 Baseline pain: 7.3 vs. 7.2 vs. 7.0 vs. 7.0 Baseline function: Not reported	A vs. B vs. C vs. D: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: 2 injections 1 weeks apart Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification	Head-to-head comparison of alternative corticosteroid doses

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Kang, 2011	A vs. B vs. C vs. D: <u>Pain</u> Pain (0-10 VAS): at baseline 7.3 vs. 7.2 vs. 7.0 vs. 7.0; at 1 week 3.8 vs. 3.9 vs. 4.3 vs. 5.4; at 2 weeks 3.2 vs. 3.3 vs. 3.4 vs. 3.9, (p>0.05) Pain relief (>=67% improvement in VAS pain): at 1 week 75% (30/40) vs.70% (28/40) vs. 65% (26/40) vs. 45% (18/40): A vs. B, RR 1.07 (95% CI 0.88 to 1.40); A vs. C, RR 1.15 (95% CI 0.86 to 1.54); A vs. D, RR 1.67 (95% CI 1.13 to 2.46); B vs. C RR, 1.08 (95% CI 0.79 to 1.47); B vs. D, RR 1.56 (95% CI 1.04 to 2.32); C vs. D, RR 1.44 (95% CI 0.96 to 2.18) (p<0.05 for A, B, or C vs. D); at 2 weeks 85% (34/40) vs. 80% (32/40) vs. 75% (30/40) vs. 68% (27/40): A vs. B, RR 1.06 (95% CI 0.87 to 1.30); A vs. C, RR 1.13 (95% CI 0.91 to 1.41); A vs. D, RR 1.26 (95% CI 0.98 to 1.62); B vs. C, RR 1.07 (95% CI 0.84 to 1.35); B vs. D, RR 1.19 (95% CI 0.91 to 1.54); C vs. D, RR 1.11 (95% CI 0.84 to 1.49)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Kang, 2011	2 weeks	None reported	Appears complete	Facial flushing (n=2) and itching (n=1); groups not reported	No funding received	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Karppinen, 2001 See also Karpinnen, 2001	RCT	Finland Single center Radiology department	Unilateral back pain radiating dermatomally below knee; duration 3 to 28 weeks; leg pain intensity at least equal to back pain intensity; MRI scans at baseline (findings for inclusion not specified)	Prior back surgery; application for early retirement; clinical depression; anticoagulation treatment; unstable diabetes; epidural injection in past 3 months; pregnant; allergy to study drugs; rare causes of sciatica such as synovial cysts; nondegenerative spondylolisthesis	Approached: 277 Eligible: 171 Randomized: 163 Analyzed: 158 (78 vs. 80) at 12 months	A: Transforaminal (periradicular) injection with 2-3 cc of methylprednisolone 40 mg/cc plus bupivacaine 5 mg/cc, with fluoroscopic guidance (n=78) B: Transforaminal (periradicular) injection with isotonic (0.9%) saline (2-3 cc), with fluoroscopic guidance

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Karppinen, 2001 See also Karpinnen, 2001	A vs. B: Age (mean): 44 vs. 44 years Male: 64% vs. 58% Duration of symptoms (months): 2.4 vs. 2.6 Baseline leg pain (0 to 100 VAS): 71 vs. 75 Baseline back pain (0 to 100 VAS): 53 vs. 60 Baseline ODI (0-100): 43 vs. 44	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Back school instructions by physiotherapist at 2 weeks; pain medication and physiotherapy for persisting sciatic pain; referral to neurosurgeon for severe sciatic pain and disability Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: Experienced radiologist	Fluoroscopic guidance with contrast verification of nerve root site	Transforaminal epidural injection with saline

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Karppinen, 2001 See also Karpinnen, 2001	A vs. B: *(difference ANCOVA adjusted for level of symptomatic disc and days on sick leave)* <u>Pain</u> Leg pain (0-100 VAS): 71 vs. 75 at baseline; 39 vs. 54 at 2 w, difference -12 (95% CI -23.4 to 1.6); 37 vs. 44 at 4 w, difference -2.3 (95% CI -13.4 to 8.7); 31 vs. 34 at 3 m, difference 0.5 (95% CI -11 to 12); 31 vs. 22 at 6 m, difference 16 (95% CI 5.6 to 27); 24 vs. 24 at 12 m, difference 5.3 (-5.0 to 16); by MRI subgroups: bulges no differences at any time point; contained herniation difference -24 (95% CI -8 to -41) at 2 w; -19 (95% CI -36 to -3) at 4 w; -1.4 (95% CI -23 to 20) at 3 m; 22 (95% CI 5 to 40) at 6 m; 0.3 (95% CI -16 to 16) at 1 y Back pain (0-100 VAS): 53 vs. 60 at baseline; 26 vs. 36 at 2 w, difference -5.8 (95% CI -17 to 5.1); 27 vs. 31 at 4 w, difference 6.1 (95% CI -5.0 to 17); 26 vs. 23 at 3 m, difference 12 (95% CI 1.0 to 24); 23 vs. 20 at 6 m, difference 14 (95% CI 2.4 to 25); 19 vs. 19 at 12 m, difference 8.4 (95% CI -2.1 to 19); extrusions no differences except at 6 m, difference 17 (95% CI 1 to 32); disc level L3-L4/L4-L5 -25 difference -25 (955 CI -40 to -10) at 2w, -20 (95% CI -35 to 5) at 4 w, no differences at other time points >75% improvement in leg pain (only reported for some subgroups): contained herniations: 35% (9/26) vs. 9% (2/23) at 2 w (p=0.04), otherwise no differences; extrusions: No differences at any time point; disc level L3-L4/L4-L5: 68% (21/36) vs. 31% (16/51) at 4 w (p=0.02), otherwise no differences <u>Function</u> ODI (0-100): 43 vs. 44 at baseline; 29 vs. 34 at 2 w, difference -5.1 (95% CI -10 to 0.3); 27 vs. 29 at 4 w, difference -1.5 (95% CI -7.3 to 4.4); 23 vs. 23 at 3 m, difference 1.3 (95% CI -6.1 to 8.6); 19 vs. 16 at 6 m, difference 5.9 (95% CI -0.7 to 12); 16 vs. 16 at 12 m, difference 0.4 (95% CI -6.2 to 7.0); by MRI subgroups: bulges no differences at any time point; contained herniation difference -8.0 (-16 to 0.3) at 2 w, -2.7 (95% CI -10 to 5) at 4 w, 2.3 (95% CI -9 to 13) at 3 m, 14 (95% CI 3 to 24) at 6 m, 1.2 (95% CI -9 to 12) at 1 y; extrusion no differences at any time point; disc level L3-L4 or L4-L5 -9.6 (95% CI -17 to -2) at 2 w, no differences at other time points <u>Other outcomes</u> Sick leave (days/month): 8.9 vs.10 at 4 w, difference -0.5 (95% CI -3.9 to 4.9); 7.3 vs. 7.4 at 3 m, difference -0.2 (95% CI -4.4 to 3.9); 3.6 vs. 4.9 at 6 m, difference 1.7 (95% CI -1.7 to 5.1); 1.9 vs. 1.2 at 12 m, difference -0.6 (95% CI -2.4 to 1.2) Therapy visits: 0.4 vs. 1.9 at 4 w, difference 1.7 (95% CI -0.5 to 3.9); 3.7 vs. 5.9 at 12 m, difference 1.7 (95% CI -2.9 to 6.3) Underwent surgery: 22% (18/80) vs. 19% (15/80) at 12 m, RR 1.2 (95% CI 0.65 to 2.21); contained herniation subgroup 20% vs. 42% (p=0.10), extrusion subgroup 32% vs. 13% (p=0.05)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Karppinen, 2001 See also Karpinnen, 2001	1 year	A vs. B: 2/80 (2.5%) vs. 0/80 (0%); 3 other exclusions because neurogram findings were not typical	Complete	Retroperitoneal hematoma in one patient on anticoagulant therapy in group A	Private foundation and government agencies in Finland; International Spinal Intervention Society	Good

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Kennedy, 2014	RCT	USA Two centers Rehabilitation or spine surgery clinic	Unilateral radicular pain with pain intensity ≥4 on 0-10 scale; <6 months duration; MRI single level below L3 corresponding with symptoms; appropriate for surgery if injection failed	Back pain greater than leg pain; nonradicular pain; unclear diagnosis; more than one potential pain generator on MRI; lumbar stenosis; prior surgery; prior spine injection; conditions increasing injection risk (bleeding tendencies, workers compensation, pregnancy, litigation)	Approached: Not reported Eligible: 81 Randomized: 78 (41 vs. 37) Analyzed: Unclear at 6 months	A: Transforaminal epidural injection with 15 mg dexamethasone (1.5 ml) plus 1% lidocaine (2 ml), with fluoroscopic guidance B: Transforaminal epidural injection with 60 mg triamcinolone (1.5 ml) plus 1% lidocaine (2 ml), with fluoroscopic guidance
Kim, 2011	RCT	USA Single center Pain clinic	Lumbar radicular symptoms below the knee corresponding to MRI findings; ≥18 year of age; pain ≥6 months; failed medication and physical therapy	Litigation; history of psychopathology; Beck Depression Inventory <15; history of substance abuse; contraindications to intra-axial procedures	Approached: Not reported Eligible: Not reported Randomized: 61 (31 vs. 30) Analyzed: 60 (30 vs. 30)	A: Interlaminar epidural injection with 15 mg dexamethasone phosphate, 0.25% bupivacaine (2 ml), and saline (total 10 ml), with fluoroscopic guidance (n=30) B: Interlaminar epidural injection with 80 mg methylprednisolone acetate, 0.25% bupivacaine (2 ml), and saline (total 10 ml), with fluoroscopic guidance (n=30)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Kennedy, 2014	A vs. B: Age (mean): 36 vs. 36 years Male: 66% vs. 65% Duration of symptoms (weeks): 10 vs. 8.6 Baseline pain (0-10): 6.3 vs. 6.5 Baseline ODI (0-100): 46 vs. 42	A vs. B: Treatments prior to intervention: No differences between groups; no formal treatment program prior to intervention Treatments following intervention: Not specified L4/L5: 15% vs. 14% L5/S1: 56% vs. 54% S1/S2: 29% vs. 32% Disc extrusion: 27% vs. 46%	Number and frequency of injections: Up to 3 injections over 6 months; 54% vs. 62% received 1 injection, 29% vs. 32% 2 injections, 17% vs. 2.7% 3 injections Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification	Head-to-head comparison of alternative corticosteroids
Kim, 2011	A vs. B: Age (mean): 66 vs. 64 years Male: 13% vs. 20% Duration of symptoms: Not reported Baseline pain (0-100 VAS): 78 vs. 77 Baseline function: Not reported	A vs. B: Treatment prior to intervention: Not specified Treatments following intervention: not specified Other patient characteristics: Not reported	Number and frequency of injections: Two injections, within 1-2 months Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification in epidural space	Head-to-head comparison of alternative corticosteroids

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Kennedy, 2014	A vs. B: <u>Pain</u> Pain (mean 3 day average NRS, 0-10): 7.0 vs. 6.9 at baseline 4.1 vs. 4.1 at 7-14 days; 1.6 vs. 1.8 at 3 months; 1.4 vs. 1.2 at 6 months Pain improved >50%: 32% (13/41) vs. 43% (16/37) at 7-14 days, RR 0.73 (95% CI 0.41 to 1.31)27; 73% (30/41) vs. 73% (27/37) at 3 months, RR 1.0 (95% CI 0.77 to 1.31); 73% (30/41) vs. 76% (28/37) at 6 months, RR 0.97 (95 % CI 0.75 to 1.25) <u>Function</u> ODI improved >51%: 27% (11/41) vs. 35% (13/37) at 7-14 days, RR 0.60 (95% CI 0.30 to 1.92); 68% (28/41) vs. 68% (30/37) at 3 months, RR 0.84 (95% CI 0.65 to 1.09); 71% (27/41) vs. 65% (24/37) at 6 months, RR 1.07 (95% CI 0.78 to 1.46) <u>Other outcomes</u> Underwent surgery: 15% (6/41) vs. 19% (7/37) at 6 months, RR 0.77 (95% CI 0.29 to 2.09)
Kim, 2011	A vs. B: <u>Pain</u> Pain (0-100 VAS): 78 vs. 77 at baseline, 61 vs. 54 at 1-2 months; percent change from baseline -20% vs. -27% (p=0.37) Decrease in pain: 90% (27/30) vs. 87% (26/30), RR 1.04 (95% CI 0.86 to 1.25) <u>Other outcomes</u> Pain medication use, emergency room visits for pain, new treatment for pain: No differences, data not provided

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Kennedy, 2014	6 months after last injection	Unclear	Appears complete	Not reported	International Spine Intervention Society	Fair
Kim, 2011	1-2 months (mean 41 vs. 51 days)	A vs. B: 3.2% (1/31) excluded from analysis from dexamethasone group	Appears complete	"No complications were reported including new neurological symptoms or new areas of pain." 1 patient excluded for inadvertant dexamethasone injection intrathecally; no complications seen	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Klenerman, 1984	RCT	UK Single center Rheumatology clinic	Unilateral sciatica with or without objective neurological signs; no previous treatment in a hospital for backs; symptoms ≤6 months	Not reported	Approached: Not reported Eligible: Not reported Randomized: 74 Analyzed: 63 (19 vs. 16 vs. 16 vs. 12) at 2 months	A: Epidural injection with 80 mg methylprednisolone plus normal saline (20 ml total) (n=19) B: Epidural injection with 0.25% bupivacaine (20 ml) (n=16) C: Epidural injection with normal saline (20 ml) (n=16) D: Interspinous ligament needling without injection (n=12)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Klenerman, 1984	A vs. B vs. C vs. D: Age: Not reported Male: Not reported Duration of symptoms: Not reported (≤6 months by inclusion criteria) Baseline pain (0-100 VAS): 48 vs. 53 vs. 65 vs. 65 Baseline function: Not reported	A vs. B vs. C vs. D: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single Number of levels: Single level Provider experience: Not reported	Not reported	Epidural injection with local anesthetic of saline, or soft tissue needling without injection

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Klenerman, 1984	A vs. B vs. C vs. D: <u>Pain</u> Pain (0-100 VAS, estimated from graph): at baseline 48 vs. 53 vs. 65 vs. 65; at 2 weeks 30 vs. 39 vs. 39 vs. 53; at 2 months 25 vs. 19 vs. 20 vs. 25 <u>Global assessment</u> "Improved" or "cured" (failed, improved, cured) at 2 months: 79% (15/19) vs. 69% (11/16) vs. 69% (11/16) vs. 83% (10/12): A vs. B: RR 0.19 (95% CI 0.77 to 1.72); A vs. C RR 1.15 (95% CI 0.66 to 1.60); A vs. D RR 0.95 (95% CI 0.67 to 1.34); B vs. C: RR 1.00 (95% CI 0.77 to 1.72); B vs. D: RR 0.83 (95% CI 0.54 to 1.25); C vs. D RR 0.83 (95% CI 0.54 to 1.25) <u>Other outcomes</u> Underwent surgery: 0% (0/19) vs. 12% (2/16) vs. 0% (0/16) vs. 0% (0/12): A vs. B: RR 0.17 (95% CI 0.00 to 3.30); A vs. C RR 0.85 (95% CI 0.02 to 40.60); A vs. D RR 0.65 (95% CI 0.01 to 30.77); B vs. C: RR 5.00 (95% CI 0.26 to 96.59); B vs. D: RR 3.83 (95% CI 0.20 to 73.00); C vs. D RR 0.76 (95% CI 0.02 to 36.04)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Klenerman, 1984	2 months	A vs. B vs. C vs. D: 15% (11/74) excluded from analysis, including 1 lost to followup	Appears complete	Not reported	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Koh, 2013	RCT	Korea Single center Pain clinic	Age ≥20 years, chronic lumbosacral radiculopathy secondary to spinal stenosis lasting ≥12 weeks, dominant leg pain with less severe back pain, unilateral leg pain with symptoms restricted to 1-level of dermatome, and previous failure of conservative management including physiotherapy, exercise therapy, analgesic medication, and acupuncture; MRI findings of lateral canal spinal stenosis (including lateral recess and foraminal spinal stenosis)	Unbearable pain >9 on the NRS, pain <4 NRS, acute back or leg pain, patients who had developed signs of progressive motor weakness or neurologic deficits, patients with a history of prior spinal surgery, allergies to steroids or contrast dyes, coagulopathy, injection of steroids or hyaluronic acids within the previous 12 weeks, systemic infections, injection site infections, unstable medical or psychiatric condition; bilateral radiculopathy, spondylolisthesis, multilevel spinal stenosis, and radiographic confirmed severe central canal stenosis	Approached: 259 Eligible: 86 Randomized: 68 (34 vs. 34) Analyzed: 53 (27 vs. 53) at 3 m, 25 (13 vs. 12) at 6 m	A: Transforaminal epidural steroid injection with 20 mg triamcinolone acetonide plus 2 mL 10% hypertonic saline (sodium chloride solution) (n=27) B: Transforaminal epidural steroid injection with 20 mg triamcinolone acetonide plus 2 mL 0.9% normal saline (n=26)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Koh, 2013	A vs. B: Age (mean): 66 vs. 63.7 years Male: 30% vs. 27% Duration of symptoms (months): 18.3 vs. 22.3 Baseline NRS (0-10): 7.26 vs. 6.60 Baseline ODI (1-100): 42.6 vs. 37.5	A vs. B Treatments prior to intervention: Prior epidural steroid injections 2.41 vs. 2.35 Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Not reported Provider experience: Anesthesiologist with 10 year career in pain medicine	Fluoroscopic guidance	Transforaminal epidural injection with saline

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Koh, 2013	A vs. B <u>Pain</u> NRS (0-10): At baseline 7.26 vs. 6.60. Difference at 1 month -3.13 vs. -2.56 (p=0.25), at 2 months -3.22 vs. -1.94 (p=0.02), at 3 months -2.93 vs. -1.52 (p=0.01), at 4 months -2.78 vs. -1.50 (p=0.05), at 6 months -2.15 vs. -0.58 (p=0.17) <u>Global assessment</u> GPE mean values (1-7 Likert scale where 7=best ever and 1=worst ever). Difference at 1 month 5.82 vs. 5.65 (p=0.24), at 3 months 5.41 vs. 4.73 (p=0.02), at 6 months 4.59 vs. 4.22 (p=0.40) <u>Function</u> ODI, Korean version (0-100). At baseline 42.6 vs. 37.5. Difference at 1 month -13.22 vs. -10.08 (p=0.56), at 2 months -13.81 vs. -10.31 (p=0.45), at 3 months -12.70 vs. -8.08 (p=0.34), at 4 months -12.22 vs. -6.90 (p=0.41), at 6 months -6.85 vs. -3.83 (p=0.34)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Koh, 2013	6 months	A vs. B At 4 months 32% (11/34) vs. 41% (14/34), at 6 months 62% (21/34) vs. 65% (22/34)	Appears complete	1 withdrawal due to severe burning in the hypertonic saline group that resolved within 2 hours; no other reports of serious complications during injection and no other withdrawals due to adverse effects	None	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Kolsi, 2000	RCT	France Single center Rheumatology clinic	18 to 75 years of age; sciatica (L5 or S1) or femoral neuralgia (L4) with pain radiating at least to knee; positive straight leg raise or crossed straight leg raise; duration ≥15 days; baseline pain >5 on 0-10 scale; impingement of disc on nerve root by CT or MRI	Cauda equina syndrome; motor strength ≤2 on 0 to 5 scale; history of disc surgery or chemonucleolysis; epidural corticosteroid injection within 1 week; bleeding disorder or anticoagulant therapy; pregnant or breast-feeding; current infection; psychiatric disorders	Approached: Not reported Eligible: Not reported Randomized: 30 (17 vs. 13) Analyzed: 30 at 4 weeks	A: Transforaminal nerve root injection with 3.75 mg cortivazol (1.5 ml) plus 0.10 g lidocaine (2 ml), with fluoroscopic guidance (n=17) B: Interlaminar epidural injection with 3.75 mg cortivazol (1.5 ml) plus 0.10 g lidocaine (2 ml), with fluoroscopic guidance (n=13)
Kraemer, 1997, study 1	RCT	Germany Single center Clinical setting unclear	Inpatients with intractable unilateral sciatica extending below knee with paresthesia; positive SLR test; limited trunk movement and aggravation of pain by certain movements and coughing; disk protrusion with nerve root compression seen on MRI and/or CT; duration not specified	Presence of other concomitant disease like osteoporosis or diabetes; contraindications to steroids	Approached: Not reported Eligible: Not reported Randomized: 133 (47 vs. 40 vs. 46) Analyzed: 133 (includes patients with missing data, number unclear)	A: Epidural perineural injection via oblique interlaminar approach with 10 mg triamcinolone + local anesthetic (1 ml, drug not specified) (n=47) B: Interlaminar epidural steroid injection using conventional technique (medications and doses not reported) (n=40) C: Paravertebral local anesthetic injection (medications and doses not reported) (n=46)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Kolsi, 2000	A vs. B: Age (mean): 45 vs. 40 years Male: 41% vs. 38% Duration of symptoms (months): 3.7 vs. 4.4 Baseline leg pain (0-10 VAS): 7.0 vs. 6.3 Baseline back pain (0-10 VAS): 3.9 vs. 4.2 Baseline RDQ (French version) (0-24): 16 vs. 15	A vs. B: Treatment prior to intervention: Not specified Treatments following intervention: Not specified L5: 6/17 vs. 5/13 S1: 10/17 vs. 8/13 Intra- or extraforaminal nerve root impingement: 1/17 vs. 2/13 Midline herniation: 5/17 vs. 3/13 Herniation on side of pain: 11/17 vs. 7/13 Work-related injury: 24% (4/17) vs. 15% (2/13)	Number and frequency of injections: Number of injections not reported; open-label transforaminal nerve root steroid injection performed if <50% pain score decrease after first injection Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification	Head-to-head comparison of transforaminal vs. interlaminar steroid injection
Kraemer, 1997, study 1	A vs. B vs. C: Age (mean): Not reported Male: Not reported Duration of symptoms: Not reported Baseline pain: Not reported (Age, sex, duration of symptoms, baseline pain not reported by treatment group though reports no statistically significant difference) Function: Not reported	A vs. B vs. C: Treatments prior to intervention: Physiotherapy; back school; and dynamic flexion orthosis Other patient characteristics: Not reported	Number and frequency of injections: Single injection given three times in one week Number of levels: Single level Provider experience: Not reported	Not used routinely	Interlaminar epidural steroid injection (unclear if local anesthetic used) Soft tissue injection with local anesthetic

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Kolsi, 2000	A vs. B: <u>Pain</u> Radicular pain (0-10 VAS, estimated from graph): at 2 weeks 7.0 vs. 6.3 at baseline, 2.6 vs. 1.6; at 4 weeks 2.0 vs. 1.5 Radicular pain, percent improvement from baseline (estimated from graph): at 1 week 78% vs. 73%; at 4 weeks 70% vs. 78% Back pain (0-10 VAS, estimated from graph): at baseline 3.9 vs. 4.2; at 2 weeks 1.5 vs. 2.4; at 4 weeks1.6 vs. 2.0 <u>Function</u> RDQ (French version, 0-24): at 4 weeks 16 vs.16 at baseline, 10 vs. 7.6 <u>Other outcomes</u> Underwent surgery: at 8 months 18% (3/17) vs. 23% (3/13) RR 0.76 (95% CI 0.18 vs. 3.20)
Kraemer, 1997, study 1	A vs. B vs. C: <u>Pain</u> *(Based on modified MacNab criteria; p-values not reported)* Modified MacNab criteria "good" (leg <10%, back pain <20%, return to work, sports as before; some results estimated from graph): 68% (32/47) vs. 53% (21/40) vs. 26% (12/46) at 3 months: A vs. B: 68% (32/47) vs. 53% (21/40), RR, 1.30 (95% CI 0.91 to 1.85); A vs. C: 68% (32/47) vs. 26% (12/46), RR 2.61 (95 % CI 1.55 to 4.41): B vs. C: 53% (21/40) vs. 26% (12/46), RR 2.02 (95% CI 1.14 to 3.55) <u>Other outcomes</u> Surgery: 8.5% (4/47) vs. 18% (7/40) vs. 13% (6/46) at 3 months; A vs. B: (4/47) vs. 18% (7/40), RR, 0.49 (5% CI 0.15 to 1.54); A vs. C: 8.5% (4/47) vs. 13% (6/46), RR 0.65 (95% CI 0.20 vs. 2.16); B vs. C: 18% (7/40) vs. 13% (6/46), RR 1.34 (95% CI 0.51 to 3.54)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Kolsi, 2000	4 weeks for pain, function; mean 8 months for surgery	None reported	Appears complete	A vs. B: 1 case of acute hypertension in group A	Not reported	Fair
Kraemer, 1997, study 1	3 months	Not reported by study or treatment arm; eight patients withdrew across two trials	Appears complete	No serious adverse events reported in any group. Headache: 1.9% (including group A in trial 2) vs. 3.6% vs. <1%	Not reported	Poor

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Kraemer, 1997, study 2	Study 2: A "prospective double-blind study," not described as randomized	Germany Single center University hospital setting, departments of Orthopaedic Surgery and Radiology	Inpatients with intractable unilateral sciatica extending below knee with paresthesia; positive SLR test; limited trunk movement and aggravation of pain by certain movements and coughing; disk protrusion with nerve root compression seen on MRI and/or CT; duration not specified	Presence of other concomitant disease like osteoporosis or diabetes; contraindications to steroids	Approached: Not reported Eligible: Not reported Randomized: 49 (24 vs. 25) Analyzed: 49 (includes patients with missing data, number unclear)	A: Epidural perineural injection via oblique interlaminar approach with 10 mg triamcinolone plus saline (volume not reported) (n=24) B: Epidural perineural injection via oblique interlaminar approach with saline alone plus intramuscular injection with 10 mg triamcinolone (n=25)
Laiq, 2009	RCT	Pakistan Single Center Setting unclear	Lumbar radicular pain (including low back and unilateral or bilateral leg pain); VAS pain score ≥6/10 for >2 weeks; single lumbar intervertebral disc herniation on recent MRI corresponding to clinical symptoms	Previous lumbar epidural steroid injections; previous lumbar spine surgery; unstable neurological deficits; cauda equina syndrome; radiologically proven facet syndrome; known contraindications for epidural steroid injections; infection; bleeding tendency or malignancy	Approached: Not reported Eligible: Not reported Randomized: 52 (26 vs. 26) Analyzed: 50 (25 vs. 25)	A: Interlaminar epidural injection with 80 mg methylprednisolone plus 2% Xylocaine (3 ml), preceded by 2% lidocaine (3 ml) (n=26) B: Ibuprofen 400 mg tid x 1 m, tramadol SR 100 mg QD x 2 m, tizanidine 2 mg bid x 3 m, famotidine 40 mg throughout treatment, bed rest and limited activity x 1 m with gradual increase to waling 2-3 h/day, heavy lifting and strenuous exercise not permitted for 3-6 m (n=25)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Kraemer, 1997, study 2	A vs. B: Age (mean): Not reported Male: Not reported Duration of symptoms: Not reported Baseline pain: Not reported (Age, sex, duration of symptoms, baseline pain not reported by treatment group though reports no statistically significant difference) Function: Not reported	A vs. B: Treatments prior to intervention: Physiotherapy; back school; and dynamic flexion orthosis Other patient characteristics: Not reported	Number and frequency of injections: Single injection given three times in one week; epidural perineural injection with corticosteroid performed if patients did not improve Number of levels: Single level Provider experience: Not reported	Not used routinely	Epidural perineural injection via oblique interlaminar approach with saline plus soft tissue injection with corticosteroid
Laiq, 2009	A vs. B: Age (mean): 40 vs. 41 years Male: 68% vs. 60% Duration of symptoms: Not reported Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatment prior to intervention: Not reported Treatments following intervention: Not reported Other patient characteristics: Not reported	Number and frequency of injections: Appears to be single injection Number of levels: Appears to be single level Provider experience: "Expert" (no other details provided)	Not reported	Non-injection therapy

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Kraemer, 1997, study 2	A vs. B: <u>Pain</u> Modified MacNab criteria "good" (leg <10%, back pain <20%, return to work, sports as before; estimated from graph): at 3 months 54% (13/24) vs. 40% (10/25), RR 1.35 (95% CI 0.74 to 2.48) <u>Other outcomes</u> Surgery: at 3 months 4% (1/24) vs. 4% (1/25), RR 1.04 (95% CI 0.07 to 15.73)
Laiq, 2009	A vs. B: Pain (0-10 VAS): 2 vs. 4 at 2 weeks, (p<0.0001); 2 vs. 4.5 at 1 month, (p<0.0001); 4.5 vs. 5.0 at 3 months, (p=0.19); 6 vs. 6.5 at 6 months, (p=0.21) Pain score >=6 (0-10 VAS): 16% (4/25) vs. 24% (6/25), RR 0.67 (95% CI 0.22 to 2.1) Patient satisfaction with improvement in pain: at 2 weeks 80% (20/25) vs. 52% (13/25), RR 1.54 (95 % CI 1.01 to 2.35) (p=0.38); at 1 month 76% (19/25) vs. 48% (12/25), RR 1.59 (95% CI 1.00 to 2.52) (p=0.36); at 3 months 52% (13/25) vs. 56% (14/25), RR 0.93 (95 % CI 0.56 to 1.55) (p=1.0); at 6 months 68% (17/25) vs. 64% (16/25), RR 106 (95% CI 0.71 to 1.58) (p = 1.0)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Kraemer, 1997, study 2	3 months	Not reported by study or treatment arm; eight patients withdrew overall across two trials	Appears complete	See Kraemer, 1997 above	Not reported	Fair
Laiq, 2009	6 months	A vs. B: 3.8% (1/26) vs. 3.8% (1/26)	Appears complete	A vs. B: "Major complications": 0% (0/25) vs. 0% (0/25) Blood glucose > 180 mg/dl) with no history of diabetes): 12% (3/25) vs. NR Flushing: 16% (4/25) vs. NR Headache:16% (4/25) vs. NR Backache: 4% (1/25) vs. NR	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Manchikanti, 2014 Manchikanti, 2013 Manchikanti, 2010	RCT	US Single center Pain clinic	≥ 18 years of age; disc herniation or radiculitis; function-limiting low back and lower extremity pain for ≥6 months; imaging findings not specified	Previous lumbar surgery; radiculitis secondary to spinal stenosis without disc herniation; uncontrollable or unstable opioid use; uncontrolled psychiatric disorder or acute/chronic medical illness; pregnant or lactating; patients with history, potential for adverse reaction to study medications	Approached: 162 Eligible: 140 Randomized: 120 (60 vs. 60) Analyzed: 120 at 2 years, including 19 (10 vs. 9) with missing data	A: Interlaminar epidural injection with 6 mg betamethasone (1 ml) plus 0.5% lidocaine (5 ml), with fluoroscopic guidance (n=60) B: Interlaminar epidural injection with 0.5% lidocaine (6 ml), with fluoroscopic guidance (n=60)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Manchikanti, 2014 Manchikanti, 2013 Manchikanti, 2010	A vs. B: Age (mean): 41 vs. 49 years Male: 62% vs. 38% Duration of symptoms (months): 133 vs. 135 Baseline pain (0 to 10 NRS): 8.0 vs. 8.2 Baseline ODI (0-50): 30 vs. 30	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified L4/5: 13% vs. 3.3% L5/S1: 87% vs. 95% Other patient characteristics: Not reported	Number and frequency of injections: Mean 6.1 vs. 5.3 over 2 years, frequency not specified Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification in epidural space	Interlaminar epidural injection with local anesthetic

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Manchikanti, 2014 Manchikanti, 2013 Manchikanti, 2010	A vs. B: <u>Pain</u> Pain scores (0-10): at baseline 8.0 vs. 8.2; at 3 months 3.5 vs. 3.9; at 6 months 3.5 vs. 4.1; at 12 months 3.4 vs. 4.0; at 24 months 3.7 vs. 4.1 (p>0.05 at all time points) Pain relief >=50%: at 3 months 88% (53/60) vs. 78% (47/60), RR 1.13 (95% CI 0.96 to 1.33); at 6 months 88% (53/60) vs. 70% (42/60), RR 1.26 (95% CI 1.04 to 1.53); at 12 months 85% (51/60) vs. 72% (43/60), RR 1.19 (95% CI 0.98 to 1.44); at 24 months 70% (42/60) vs. 63% (38/60), RR 1.11 (95% CI 0.86 to 1.42) <u>Function</u> ODI (0-50): at baseline 30 vs. 30, at 3 months 14 vs. 16; at 6 months 14 vs. 16; at 12 months 13 vs. 16; at 24 months 14 vs. 16 (p>0.05 at all time points) ODI improved >=50%: at 3 months 82% (49/60) vs. 73% (44/60), RR 1.11 (95% CI 0.92 to 1.35); at 6 months 87% (52/60) vs. 63% (38/60), RR 1.37 (95% CI 1.10 to 1.70); at 12 months 87% (52/60) vs. 68% (41/60), RR 1.27 (95% CI 1.04 to 1.55); at 24 months 73% (44/60) vs. 63% (38/60), RR 1.16 (95% CI 0.91 to 1.48) <u>Other outcomes</u> Opioid use (mg MED/day): at baseline 47 vs. 50; at 3 months 42 vs. 34; at 6 months 36 vs. 37; at 12 months 36 vs. 37; at 24 months 37 vs. 36 (p>0.05 at all time points)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Manchikanti, 2014 Manchikanti, 2013 Manchikanti, 2010	24 months	A vs. B: 17% (10/60) vs. 15% (9/60) at 24 months	Appears complete	One dural puncture (treatment group not reported); no other major adverse events	Not reported	Poor

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Manchikanti, 2012 Manchikanti, 2011 Manchikanti, 2008	RCT	US Single center Pain clinic	Demonstrated disc herniation with radiculitis; >18 years of age; function-limiting low back and lower extremity pain for >6 months; imaging findings not specified	Previous lumbar surgery; radiculitis secondary to spinal stenosis or without disc herniation; uncontrollable or unstable opioid use; uncontrolled psychiatric disorders; uncontrolled medical illness; any conditions that could interfere with the interpretation of the outcome assessments; pregnant or lactating; history or potential for adverse reactions to local anesthetics or steroids	Approached: 178 Eligible: 132 Randomized: 120 (60 vs. 60) Analyzed: 120 (60 vs. 60) at 24 months, including 24 (12 vs. 12) with missing data	A: Caudal epidural injection with 6 mg betamethasone or 40 mg methylprednisolone plus 0.5% lidocaine (9 ml), with fluoroscopic guidance (n=60) B: Caudal epidural injection with 0.5% lidocaine (10 ml), with fluoroscopic guidance (n=60)
Matthews, 1987	RCT	UK Single center Specialty clinic	18 to 60 years of age; onset of most within 3 months; low back pain with asymmetrical restriction of lumbar spine movement; positive straight leg raise test and/or femoral nerve stretch test positive; radicular pain and uniradicular neurologic deficit; radiographs performed (imaging findings not specified)	Abnormalities or complicating problems after screening examination and investigations	Approached: 895 for 4 different trials (1 trial evaluated epidural injection) Eligible: Not reported Randomized: 57 (23 vs. 24) in trial of epidural injection Analyzed: 57 (23 vs. 34) at up to 12 months, including 3 (2 vs. 1) with missing data	A: Caudal epidural injection with 80 mg methylprednisolone (2 ml) and 0.125% bupivacaine (20 ml) (n=23) B: Soft tissue injection at sacral hiatus or tender point with lignocaine (2 ml, concentration not reported) (n=34)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Manchikanti, 2012 Manchikanti, 2011 Manchikanti, 2008	A vs. B: Age (mean): 43 vs. 49 years Male: 38% vs. 32% Duration of pain (months): 81 vs. 93 Baseline pain (0-10 NRS): 7.8 vs. 8.1 Baseline ODI (0 to 50): 28 vs. 29	A vs. B: Treatments prior to intervention: Not reported Treatments following intervention: Not reported Herniation level L3/4: 5% vs. 8% L4/L5: 70% vs. 67% L5/S1: 50% vs. 58% Other patient characteristics: Not reported	Number of injections: Mean 5.3 over 5.5 years, frequency not specified Number of levels: Caudal Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space	Caudal epidural injection with local anesthetic
Matthews, 1987	A vs. B: Age (median): 38 vs. 41 years Male: 83% vs. 71% Duration of symptoms (median, weeks): 4 vs. 4 weeks Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Acetaminophen as needed, opioid available on request; offered spinal corset and given instruction in 'posture' and 'back care' Other patient characteristics: Not reported	Number and frequency of injections: Injection repeated every 2 weeks, up to 3 times as needed Number of levels: Single level Provider experience: Not reported	Not reported	Soft tissue injection with local anesthetic

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Manchikanti, 2012 Manchikanti, 2011 Manchikanti, 2008	A vs. B: <u>Pain</u> Pain (mean NRS, 0 to 10): at baseline 7.8 vs. 8.1; at 3 months 3.4 vs. 4.1; at 6 months 3.5 vs. 3.9; at 12 months 3.5 vs. 4.1; at 24 months 3.6 vs. 4.2: (p=0.80 for group difference) Pain improved >=50% from baseline: at 3 months 80% (48/60) vs. 77% (46/60); at 6 months 82% (49/60) vs. 77% (46/60); at 12 months 77% (46/60) vs. 70% (42/60); at 24 months 68% (41/60) vs. 63% (38/60) <u>Function</u> ODI (0 to 50): at baseline 28 vs. 29; at 3 months 14 vs. 16; at 6 months 14 vs. 16; at 12 months 13 vs. 16; at 24 months 14 vs. 16: (p=0.71 for group difference) ODI improved >=50% from baseline: at 3 months 73% (44/60) vs. 62% (37/60); at 6 months 73% (44/60) vs. 72% (43/60), RR 1.02 (95% CI 0.82 vs. 1.28); at 12 months 72% (43/60) vs. 67% (40/60), RR 108 (95% CI 0.85 to 1.37); at 24 months 70% (42/60) vs. 60% (36/60), RR 1.08 (95% CI 0.82 to 1.43) <u>Other outcomes</u> Opioid use (mg MED/day): at baseline 45 vs. 52; at 3 months 30 vs. 33; at 6 months 31 vs. 33; at 12 months 31 vs. 33; at 24 months 31 vs. 33: (p=0.75 for group difference) Success (pain improved >=50% and ODI improved >=50%): at 6 months 73% (44/60) vs. 72% (43/60); at 12 months 72% (43/60) vs. 67% (40/60); at 24 months 65% (39/60) vs. 60% (36/60)
Matthews, 1987	A vs. B: <u>Pain</u> Pain score (6 point NRS): at 1 month 67% (14/21) vs. 56% (18/32), RR 1.67 (95% CI 1.23 to 2.28) (p>0.05); No further pain: at 1 year 39% (9/23) vs. 41% (14/34), RR 0.95 (95% CI 0.49 to 1.8) <u>Other outcomes</u> Spinal surgery: 4% (1/23) vs. 0% (0/34), RR 4.38 (95% CI 0.19 to 102.94)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Manchikanti, 2012 Manchikanti, 2011 Manchikanti, 2008	24 months	A vs. B: 20% (12/60) vs. 20% (12/60) at 24 months	Appears complete	No major adverse events	Not reported	Fair
Matthews, 1987	Up to 1 year	A vs. B: 8.7% (2/23) vs. 2.9% (1/34) at 1 year	Appears complete	Not reported	Department of Health and Social Security (UK) and St. Thomas' Hospital, London	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
McCahon, 2011	RCT with crossover design	UK Single center Anesthesiology clinic	Back and leg pain of any cause; ≥2 epidural steroid injections in the last 12 months; ODI score >20%; back or leg VAS >30 mm	Anticoagulant therapy; bleeding diathesis; sepsis	Approached: 83 Eligible: 78 Randomized: 38 (19 vs. 19) Analyzed: 33 at 12 weeks following crossover intervention	A: Caudal epidural injection with 80 mg methylprednisolone acetate (2 ml), 0.25% levobupivacaine (10 ml), and saline (8 ml) (n=19) B: Caudal epidural injection with 40 mg methylprednisolone acetate (1 ml), 0.25% levobupivacaine (10 ml), and saline (9 ml) (n=19)
Murakibhavi, 2011	RCT	India Single center Orthopedic clinic	≥18 years of age; low back pain with unilateral or bilateral sciatica for ≥3 months; not responding to rest and analgesics; MRI showed lumbar disc disease (disc degeneration or herniation)	History of surgery; severe motor weakness; rapidly progressive neurological deficit; cauda equina syndrome; neurogenic claudication; local infection at injection site; steroid use in last 3 weeks; allergy to steroids; bleeding diathesis; pregnant; uncontrolled hypertension; uncontrolled diabetes	Approached: 189 Eligible: 189 Randomized: 102 (52 vs. 50) Analyzed: 100 (50 vs. 50) at 6 months	A: Caudal epidural injection with 80 mg triamcinolone acetate (2 ml), 2% lidocaine (2 ml), and normal saline (20 ml), with fluoroscopic guidance B: Conservative treatment (tizanidine 6-12 mg/d, diclofenac 50-100 mg/d, amitriptyline 10-50 mg qhs, bilateral skin traction, physiotherapy including TENS, short-wave diathermy, back extension exercises)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
McCahon, 2011	A vs. B: Age (mean): 56 years Male: 39% Duration of pain (years): 19 Baseline leg pain (0-100 VAS): 57 vs. 54 Baseline back pain (0-100 VAS): 67 vs. 66 Baseline ODI (0-100): 55 vs. 54	A vs. B: Treatments prior to intervention: ≥2 epidural injections in last 12 months (median 3 prior injections in last 12 months) Treatment following intervention: Not reported Other patient characteristics: Not reported	Number and frequency of injections: Appears to be single Number of levels: Caudal Provider experience: Not reported	None	Head-to-head comparison of different corticosteroid doses
Murakibhavi, 2011	A vs. B: Age (mean): 45 years (overall) Male: 66% (overall) Race: Not reported Duration of symptoms (months): 21 (overall) Baseline pain (0-10 VAS): 8.1 vs. 8.1 Baseline ODI (0-100): 36 vs. 36	A vs. B: Treatment prior to intervention: 98% rest/analgesics; 78% traction; 76% lumbar belt; 76% physiotherapy; 18% epidural injection Treatments following intervention: Not specified MRI findings: 60% disc degeneration; 26% disc bulge; 14% disc herniation	Number and frequency of injections: Repeat injection permitted after 2-3 weeks if <20% improvement in VAS pain; 12% received repeat injection Number of levels: Caudal injection Provider experience: Not reported	Fluoroscopic guidance without contrast verification	Conservative therapy

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
McCahon, 2011	A vs. B: <u>Function</u> Change in ODI from baseline (0-100, estimated from graph): -7 vs. -7 at 4 weeks; 0.5 vs. -3 at 8 weeks; 1 vs. 0 at 12 weeks <u>Other outcomes</u> Analgesic use: No difference between groups
Murakibhavi, 2011	A vs. B: <u>Pain</u> Pain (0-10 VAS): 8.1 vs. 8.1 at baseline; 2.7 vs. 6.1 at 6 months <u>Function</u> ODI (0-100): 36 vs. 36 at baseline; 12 vs. 25 at 6 months Beck Depression Inventory (0-63): 18 vs. 19 at baseline; 8.6 vs. 13 at 6 months <u>Other outcomes</u> Complete pain relief (complete, partial, no relief): 92% (46/50) vs. 32% (16/50) at 3 weeks, RR 2.88 (95 % CI 1.90 to 4.34); 86% (43/50) vs. 24% (12/50) at 6 months, RR 3.58 (95% CI 2.16 to 5.94)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
McCahon, 2011	12 weeks	A vs. B: 13% (5/38) withdrew, did not maintain ODI booklet, or did not return diary	Appears complete	"No adverse events reported"	No external funding	Fair
Murakibhavi, 2011	6 months	Not reported	3.8% (2/52) excluded in group A due to hypotension during procedure	A vs. B: Dural puncture: 0% (0/50) Headache: 18% (9/50) Hypotension during procedure: 24% (12/50) Bleeding during procedure: 4% (2/50)	NIH/NIAMS and University of Washington (through gift from Synthes Spine)	Poor

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Owlia, 2007	RCT	Iran Single center Rheumatology clinic	Lumbar radicular pain for >2 weeks; MRI showing disc herniation with or without canal stenosis; refractory pain despite NSAIDS; opioids, and physical therapy for >2 weeks	Prior back surgery; radiologically proven facet syndrome; signs or symptoms of infection; bleeding tendency; or malignancy	Approached: Not reported Eligible: Not reported Randomized: 84 (43 vs. 41) Analyzed: 84 at 3 months	A: Interlaminar epidural injection with 80 mg methylprednisolone acetate (8-10 ml) plus 2% lidocaine (2-4 ml), with fluoroscopic guidance (n=43) B: Interlaminar epidural injection with 40 mg methylprednisolone acetate (8-10 ml) plus 2% lidocaine (2-4 ml), with fluoroscopic guidance (n=41)
Park, 2010	RCT	South Korea Single center Neurosurgery clinic	18 to 80 years of age, lumbar radicular pain; MRI showing nerve root compromise; duration not specified	Chronic use of oral steroids; oral, peripheral, or epidural steroid use in past 3 months; temperature >100.4 F; pregnant; cognitive impairment; use of aspirin, Plavix, Coumadin, or heparin in last 2 weeks; history of bleeding disorders; history of lumbar surgery	Approached: Not reported Eligible: Not reported Randomized: 106 (53 vs. 53) Analyzed: 106 at 4 weeks	A: Transforaminal injection with 7.5 mg dexamethasone plus 1% lidocaine (1 ml), with fluoroscopic guidance (n=53) B: Transforaminal injection with 40 mg triamcinolone acetonide plus 1% lidocaine (1 ml), with fluoroscopic guidance (n=53)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Owlia, 2007	A vs. B: Age (mean): 38 vs. 36 years Male: 51% vs. 66% Duration of symptoms (weeks): 12 vs. 9 Baseline pain: Not reported Limitation in daily activities: 28% vs. 49%	A vs. B: Treatments prior to intervention: NSAIDS, opioids, and physical therapy for >2 weeks Treatments following intervention: Rehabilitative management for 2 weeks Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification in epidural space	Head-to-head comparison of alternative corticosteroid doses
Park, 2010	A vs. B: Age (mean): 56 vs. 62 years Male: 49% vs. 45% Duration of symptoms: Not reported Baseline pain (0-10 VAS): 7.5 vs. 8.3 Baseline ODI (0-100: 52 vs. 58	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified L4: 21% vs. 17% L5: 47% vs. 55% S1: 32% vs. 25%	Number and frequency of injections: Appears to be single injection Number of levels: Appears to be single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification	Head-to-head comparison of alternative corticosteroids

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Owlia, 2007	A vs. B: <u>Pain</u> Improvement in pain (not defined): at 2 weeks, 70% (30/43) vs. 61% (25/41), RR 1.14 (95% CI 0.84 to 1.57); at 1 month, 74% (32/43) vs. 76% (31/41), RR 0.98 (95% CI 0.77 to 1.25); at 3 months, 65% (28/43) vs. 51% (21/41), RR 1.27 (95% CI 0.88 to1.84)
Park, 2010	A vs. B: <u>Pain</u> Pain (0-10 VAS): 7.4 vs. 8.3 at baseline, 4.1 vs. 2.4 at 1 month ($p<0.0005$) McGill Pain Questionnaire summary score (0-45): 15 vs. 13 at baseline, 13 vs. 20 at 1 month ($p>0.05$) <u>Function</u> ODI (0-100): 52 vs. 58 at baseline, 45 vs. 59 at 1 month ($p>0.05$)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Owlia, 2007	3 months	None reported	Appears complete	A vs. B: Major complications: None Hyperglycemia: 4.6% (2/43) vs. 0% (0/41) Flushing: 14% (6/43) vs. 2.4% (1/41) Post-injection flare: 4.6% (2/43) vs. 7.3% (3/41) CSF hypotension: 2.3% (1/43) vs. 7.3% (3/41)	Not reported	Poor
Park, 2010	1 month	Not reported	Appears complete	Not reported	Wooridul Institute	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Park, 2013	RCT	Korea Single center Pain clinic	Back pain with pain radiating to leg; duration not specified; imaging confirmation not required	Systemic inflammatory disease; anticoagulant; uncontrolled diabetes; allergic reaction to lidocaine or contrast media; suspected or diagnosed infection; poor general health; skin defects in the injection area; psychiatric problems preventing the completion of a questionnaire; injections within 3 months; pain-relieving anti-inflammatory medication other than acetaminophen; undergoing physical therapy during the study period that might impact treatment effects; cauda equina syndrome; additional peripheral injections; surgery	Approached: 156 Eligible: 144 Randomized: 120 (60 vs. 60) Analyzed: 110 (55 vs. 55) at 12 weeks	A: Caudal epidural injection with 10 mg dexamethasone (2 ml) plus 0.5% lidocaine (13 ml) and 5 ml of iodinated contrast, with Doppler ultrasound and fluoroscopy guidance B: Caudal epidural injection with 10mg dexamethasone (2 ml) plus 0.5% lidocaine (13 ml) with 5 ml of iodinated contrast, with fluoroscopic guidance

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Park, 2013	A vs. B Age (mean): 57 vs. 58 years Male: 29% vs. 44% Duration of symptoms (months): 6.6 vs. 7.0 Baseline pain (0-10 NRS): 6.4 vs. 6.4 Baseline ODI (0-100): 51 vs. 52	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Herniated lumbar disc: 42% vs. 34% Spinal stenosis: 58% vs. 66% Target root L4: 36% vs. 36% Target root L5: 44% vs. 44% Target root S1: 9.1% vs. 20%	Number and frequency of injections: 51% vs. 53% received 2 injections within 2 week interval; 2nd injection performed if <50% reduction in pain NRS after 1st injection Number of levels: Caudal Provider experience: Not reported	Doppler ultrasound with contrast verification in epidural space, also fluoroscopic confirmation vs. fluoroscopy with contrast verification in epidural space (without ultrasound)	Head-to-head comparison of alternative imaging guidance methods

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Park, 2013	A vs. B: <u>Pain</u> Pain (0-10 NRS): 6.4 vs. 6.4 at baseline; 3.1 vs. 3.2 at 2 weeks; 2.5 vs. 2.6 at 12 weeks, (p>0.05) <u>Function</u> ODI (0-100): 51 vs. 52 at baseline; 33 vs. 31 at 2 weeks; 29 vs. 29 at 12 weeks, (p>0.05) <u>Global assessment</u> Pain score improvement >50% and ODI improvement >40%: at 2 weeks 87% (48/55) vs. 89% (49/55), RR 0.98 (95% CI 0.85 to 1.12); at 12 weeks 76% (42/55) vs. 74% (41/55), RR 1.02 (95% CI 0.83 to 1.27)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Park, 2013	12 weeks	None reported	6 (4 vs. 2) discontinued interventions due to lack of response or worsening of pain, 4 excluded due to peripheral injections or use of non-permitted medications	A vs. B: Vasovagal reaction: 3.6% (2/55) vs. 5.4% (3/55) Headache: 3.6% (2/55) vs. 1.8% (1/55) Pain exacerbation: 9.1% (5/55) vs. 7.3% (4/55) Post lumbar puncture syndrome: None Infection or hematoma: None Intravascular injection: 0% (0/55) vs. 3.6% (2/55)	Inje University, South Korea	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Rados, 2011	RCT	Croatia Single center Pain clinic	Unilateral lumbosacral radicular leg pain greater than back pain; duration <1 year; unresponsive to ≥6 weeks of conservative management; pain score ≥5; underwent MRI and EMG	Motor or bowel/bladder impairment; lumbar canal stenosis on MRI or x-ray that could explain symptoms; pregnant; allergic to steroids; bleeding history; infections; on anticoagulants; neurological deficits secondary to spine pathology; previous lumbar spinal surgery; previous caudal or lumbar epidural steroid injection; history of opioid abuse or currently on long acting opioids	Approached: Not reported Eligible: Not reported Randomized: 70 (35 vs. 35) Analyzed: 64 (32 vs. 32) at 24 weeks	A: Transforaminal epidural injection with 40 mg methylprednisolone plus 0.5% lidocaine (3 ml), with fluoroscopic guidance B: Interlaminar epidural injection with 80 mf methylprednisolone plus 0.5% lidocaine (8 ml), with fluoroscopic guidance
Ridley, 1988	RCT	UK Single center Rheumatology clinic	Clinical history consistent with sciatic nerve root compression with numbness or paresthesia or objective neurologic deficit	Prior epidural injection; spinal surgery	Approached: Not reported Eligible: Not reported Randomized: 39 Analyzed: 35 (19 vs. 15) at 2 weeks	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) and saline (10 ml) (n=19) B: Interspinous ligament injection with saline (2 ml) (n=16)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Rados, 2011	A vs. B: Age (mean): 49 vs. 49 years Male: 62% vs. 66% Duration of symptoms: Not reported (<1 year and >6 weeks by inclusion criteria) Baseline pain (0-10 VAS): 6.7 vs. 7.4 Baseline ODI (0-100): 53 vs. 52	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: tramadol 50 mg 1-2 T po q 6 h prn L4-5: 43% vs. 41% L5-S1: 57% vs. 59% Other patient characteristics: Not reported	Number and frequency of injections: 3 injections at 2 week intervals Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification	Head-to-head comparison of transforaminal vs. interlaminar steroid injection
Ridley, 1988	A vs. B: Age (mean): 40 vs. 39 years Male: 42% vs. 44% Duration of symptoms >6 months: 47% vs. 56% Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single injection repeated after 1 week if no improvement Number of levels: Single level Provider experience: Not reported	Not reported	Non-epidural saline injection

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Rados, 2011	A vs. B: <u>Pain</u> Pain (0-10 VAS, estimated from graph): at baseline 6.7 vs. 7.4; at 2 weeks, 5.0 vs. 5.0; at 4 weeks, 4.2 vs. 4.0; 12 weeks, 3.8 vs. 4.0 Pain improved >=2 (0-10 VAS): 84% (27/32) vs. 75% (24/32): RR, 1.13 (95% CI 0.88 to 1.44) Pain improved >50%: 63% (20/32) vs. 53% (17/32) at 24 weeks: RR, 1.18 (95% CI 0.77 to 1.79) <u>Function</u> ODI (0-100, estimated from graph): at baseline, 53 vs. 52; at 2 weeks, 47 vs. 47; at 4 weeks, 46 vs. 44; at 12 weeks, 42 vs. 42; at 24 weeks, 39 vs. 40 ODI improved >10 points: 66% (21/32) vs. 50% (16/32), RR, 1.31 (95% CI 0.86 to 2.01)
Ridley, 1988	A vs. B: <u>Pain</u> Rest pain, improvement from baseline (median, 0-10 VAS): at 2 weeks 46% vs. 0%, ($p<0.01$) Walking pain, improvement from baseline (median, 0-10 VAS): at 2 weeks 69% vs. 0%, ($p<0.01$)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Rados, 2011	24 weeks	A vs. B: 8.6% (3/5) vs. 8.6% (3/35) at 6 months (excluded because they did not undergo 3 injections)	Appears complete	Not reported	No external funding	Fair
Ridley, 1988	2 weeks	A vs. B: 5% (2/39) at 2 weeks	14 crossovers in placebo group; timing unclear	None reported	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Riew, 2000 Riew, 2006	RCT	USA Single center Spine surgery clinic	>21 years of age; degenerative lumbar radicular pain with disc herniation or spinal stenosis confirmed by MRI or CT; completed course of nonoperative management (NSAID, PT, activity modification) for at least 6 weeks without adequate benefit, unless in intractable pain despite maximum NSAID plus opioid; surgery considered appropriate	Acute trauma; cauda equina syndrome; progressive neurological deficit; motor deficit; pathologic or infectious etiology; not an operative candidate; Workers' Compensation claim; history of an adverse reaction to corticosteroids or local anesthetics; lack of a radiographically detectable abnormality; more than two radiographically abnormal and symptomatic levels on either side; absence of substantial radicular pain as the presenting symptom	Approached: Not reported Eligible: Not reported Randomized: 55 (28 vs. 27) Analyzed: 55 at 13-28 months, 55 at >5 years, including 8 (8 vs. 0) with missing data	A: Transforaminal nerve root injection with 6 mg betamethasone (1 ml) plus 0.25% bupivacaine (1 ml), with fluoroscopic guidance (n=28) B: Transforaminal nerve root injection with 0.25% bupivacaine (1 ml), with fluoroscopic guidance (n=27)
Rogers 1992	RCT	UK Single center Pain clinic	Clinical diagnosis of sciatica with positive straight leg raise at less than 60 degrees; duration and imaging findings not specified	Not reported	Approached: Not reported Eligible: Not reported Randomized: 30 (15 vs. 15) Analyzed: 30 Lost to followup: Not reported	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) plus 2% lignocaine (14 ml) plus saline (4 ml) (n=15) B: Interlaminar epidural injection with 2% lignocaine (14 ml) + saline (6 ml) (n=15)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Riew, 2000 Riew, 2006	A vs. B: Age: Not reported (states no difference) Male: 49% overall (states no difference) Duration of symptoms: Not reported Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: NSAIDs; PT; and activity modification for ≥6 weeks; +/- opioid Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single injection with 4 additional injections during followup period-19 had >1; frequency not specified (range 6 days to 10.5 months) Number of levels: One or two (determined by surgeon based on patient's history) Provider experience: Radiologists experienced in the injection technique	Fluoroscopic guidance with contrast verification of nerve root site	Transforaminal nerve root injection with local anesthetic
Rogers 1992	A vs. B: Age (mean): 42 vs. 41 years Male: 47% vs. 47% Duration of symptoms (months): 23 vs. 25 Baseline pain "severe" or "very severe": 87% vs. 67% Baseline function: Not reported	A vs. B: Treatments prior to intervention: Prior surgery: 1/15 vs. 0/15 Prior epidural injection: 4/15 vs. 2/15 Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: Not reported	Not reported	Interlaminar epidural injection with local anesthetic

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Riew, 2000 Riew, 2006	A vs. B: <u>Other outcomes</u> Underwent surgery: 29% (8/28) vs. 67% (18/27) at 13 to 28 months, RR 0.43 (95% CI 0.22 to 0.82); 39% (11/28) vs. 70% (19/27) at >=5 years, RR 0.56 (95% CI 0.33 to 0.94) (assuming none lost to follow-up had surgery); 68% (19/28) vs. 70% (19/27), RR 0.96 (95% CI 0.66 to 1.4) (assuming all lost to follow-up had surgery)
Rogers 1992	A vs. B: <u>Pain</u> Pain "none" (none, mild, moderate, severe): 20% (3/15) vs. 6.7% (1/15), RR 3.0 (95% CI 0.35 to 26) Pain "none" or "mild": 47% (7/15) vs. 20% (3/15), RR 2.33 (95% CI 0.74 to 7.35) <u>Function</u> Full ability to work: 53% (8/15) vs. 33% (5/15), RR 1.6 (95% CI 0.68 to 3.80) <u>Other outcomes</u> Reduced analgesic intake: 53% (8/15) vs. 40% (6/15, RR 1.33 (95% CI 0.61 to 2.9) Subsequent surgery: 27% (4/15) vs. 27% (4/15), RR 1.0 (95% CI 0.31 to 3.28)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Riew, 2000 Riew, 2006	Mean 23 months, range 13 to 28 months for initial followup; ≥5 years for second followup	A vs. B: None at 13 to 28 months; 29% (8/28) vs. 0% (0/27) at ≥5 years	Appears complete	Not reported	Barnes-Jewish Christian Health System's Innovations in Health Care Grant and Washington University School of Medicine	Fair
Rogers 1992	1 month for all outcomes except subsequent surgery, which was evaluated at 20-21 months	Not reported	Appears complete	Not reported	Not reported	Poor

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Sayegh, 2009	RCT	Greece Single center Orthopedic Department	Low back pain for ≥ 1 month with or without unilateral or bilateral sciatica; failure to respond to conservative measures; disc degeneration or herniation on MRI	Cauda equina or spinal stenosis; psychosomatic diseases or any other pathology	Approached: Not reported Eligible: 191 Randomized: 183 (93 vs. 90) Analyzed: 151 (81 vs. 70) at 1 year	A: Caudal epidural injection with betamethasone (2 mg/dL betamethasone dipropionate + 5 mg/dL betamethasone phosphate) (1 ml) + 2% Xylocaine (12 ml) (n=93) B: Caudal epidural injection with 2% Xylocaine (12 ml) + water for injection (8 ml) (n=90)
Snoek, 1977	RCT	Norway Single center Neurology and anesthesiology clinic	Radiating pain in the distribution of the sciatic or femoral nerve; neurologic deficit that correlated with compression of L4, L5, or S1 nerve root; myelographic findings at the appropriate level and side; duration not specified	Acute severe motor paresis; cauda equina syndrome; intolerable pain; previous lumbar spine surgery; contraindications to corticosteroids; doubts about myelography findings	Approached: >200 Eligible: Not reported Randomized: 51 (27 vs. 24) Analyzed: Unclear	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) (n=27) B: Interlaminar epidural injection with saline (2 ml) (n=24)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Sayegh, 2009	A vs. B: Age (mean): 51 vs. 48 years Male: 65% vs. 70% Duration of symptoms (days): 53 vs. 51 Baseline pain: Not reported Baseline ODI (0-100): 39 vs. 39	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Acetaminophen allowed during first 4 weeks of study, but not NSAIDs Other patient characteristics: Not reported	Number and frequency of injections: 51/183 (28%) received 2nd injection 1-2 weeks after 1st for failure to improve Number of levels: Caudal injection Provider experience: Not reported	No fluoroscopic guidance	Caudal epidural injection with local anesthetic
Snoek, 1977	A vs. B: Age (mean): 44 vs. 46 years Male: 48% vs. 54% Duration of symptoms (weeks): 12 vs. 11 Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: Not reported	Not reported	Interlaminar epidural injection with saline

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Sayegh, 2009	A vs. B: <u>Function</u> ODI (scale NR): 39 vs. 39 at baseline (p=0.75); 13 vs. 6.2 at 1 week (p<0.0005); 12 vs. 9.6 at 1 month (p<0.0005); 5.8 vs. 14 at 6 months (p<0.0005); 4.9 vs. 13 at 1 year (p<0.0005) <u>Other outcomes</u> Surgery (overall): 16% (13/83) vs. 22% (19/85) at 1 month, RR 0.70 (95% CI 0.37 to 1.3) Surgery (disc herniation group): 17% (7/42) vs. 24% (8/33) at 1 month, RR 0.69 (95% CI 0.28 to 1.70)
Snoek, 1977	A vs. B: <u>Other outcomes</u> Subsequent surgery: 52% (14/27) vs. 58% (14/24), RR 0.89 (95% CI 0.54 to 1.5)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Sayegh, 2009	1 year	A vs. B: 13% (12/93) vs. 22% (20/90) at 1 year	Appears complete	A vs. B: Transient lower extremity numbness: 13% (12/93) vs. 8.9% (8/90) "No patient reported any major immediate or late complications"	Not reported	Fair
Snoek, 1977	Mean not reported; range 8-20 months after injection	Not reported	Unclear	A few patients who felt increased pain of sciatic distribution	Not reported	Poor

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Tafazal, 2009; Ng, 2005	RCT	UK Single center Spine clinic	Unilateral leg pain with intensity comparable to back pain intensity; MRI diagnosis of lumbar disc herniation or foraminal stenosis; ≥ 6 weeks of failed conservative treatment	Acute back trauma; cauda equina syndrome; active local skin infection; previous back operation; periradicular infiltration during previous 12 months; epidural injection in last 3 months; pregnant; allergy to treatment agents; anticoagulation treatment	Approached: Not reported Eligible: Not reported Randomized: 150 (74 vs. 76) Analyzed: 124 (65 vs. 59) at 3 months)	A: Transforaminal periradicular injection with 40 mg methylprednisolone plus 0.25% bupivacaine (2 ml), with fluoroscopic guidance (n=74) B: Transforaminal periradicular injection with 0.25% bupivacaine (2 ml), with fluoroscopic guidance (n=76)
Tauheed, 2014	RCT	India Single center Pain clinic	Ages 18-55 years, weight between 40-70 kg, ASA grade I or II, suffering from sciatica due to disc herniation, and symptomatic for ≥6 weeks; 1 or 2 level disc herniation at L3-L4, L4-L5, L5-S1 on MRI	Large HNP with severe central or foraminal stenosis on MRI, progressive neurologic deficits, cauda-equina syndrome, blood coagulation disorder, valvular heart diseases, hypotension, emotional instability, known history of allergy to local anesthetics, corticosteroids or clonidine or received prior epidural steroid injection or lumbar surgery	Approached: Not reported Eligible: Not reported Randomized: 180 (60 vs. 60 vs. 60) Analyzed: 177 (60 vs. 58 vs. 59) at 12 w	A: Transforaminal sleeve root injection with 60 mg methylprednisolone (n=60) B: Transforaminal sleeve root injection with 60 mg methylprednisolone plus 0.5 mcg/kg clonidine (n=60) C: Transforaminal sleeve root injection with 60 mg methylprednisolone plus 1 mcg/kg clonidine (n=60)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Tafazal, 2009; Ng, 2005	A vs. B: Age (mean): 52 vs. 51 years Male: 60% vs. 54% Duration of symptoms (months): 20 vs. 18 months Baseline leg pain (0-100 VAS): 73 vs. 76 Baseline back pain (0-100 VAS): 44 vs. 48 Baseline ODI (0-100): 43 vs. 47	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: 13% vs. 15% received subsequent injections, mean number not reported, frequency not specified Number of levels: Single level Provider experience: Senior surgeon	Fluoroscopy with contrast verification	Transforaminal periradicular injection with local anesthetic
Tauheed, 2014	A vs. B vs. C: Age (mean): 39 vs. 42 vs. 41 Male: 63% vs. 72% vs. 67% Duration of pain: 128 vs. 130 vs. 127 days	A vs. B vs. C: Treatments prior to intervention: Not specified Treatments following intervention: Not reported Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Two levels, depending upon the level of disc herniation Provider experience: Not reported	Fluoroscopic guidance	Transforaminal epidural injection with clonidine

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Tafazal, 2009; Ng, 2005	A vs. B: <u>Pain</u> Leg pain, change from baseline (mean, 0-100 VAS): 26 vs. 19 at 6 weeks, 24 vs. 23 at 12 weeks (p=0.74) Back pain, change from baseline (mean, 0-100 VAS): 9.8 vs. 6.4 at 6 weeks, 6.9 vs. 9.9 at 12 weeks (p=0.57) Leg pain improved >=20 points (0-100 VAS) (from Ng): at 12 weeks 42% (18/43) vs. 48% (20/43): RR, 0.90 (95% CI 0.56 to 1.50) <u>Function</u> ODI, change from baseline (mean, 0-100 VAS): 9.3 vs. 11 at 12 weeks (p=0.69) Low Back Outcome Score, change from baseline (mean, 0-75): 8.8 vs. 8.5 at 6 weeks, 9.1 vs. 9.4 at 12 weeks (p=0.93) ODI improved ≥ 10% (from Ng): at 12 weeks 35% (15/43) vs. 55% (24/43; RR 0.63 (95% CI 0.38 to 1.0) Change in walking distance from baseline (yards) (from Ng): at 6 weeks 89 vs. 220 (0.12); 200 vs. 240 at 12 weeks (p=0.72) <u>Global assessment</u> Satisfaction excellent or good (from Ng): at 12 weeks 45% (18/40) vs. 49% (20/4) RR, 0.92 (95% CI 0.58 to 1.5) <u>Other outcomes</u> Subsequent peri-radicular injection: 13% (8/64) vs. 15% (10/65) at 1 year, RR 0.81 (95% CI 0.34 to 1.93) Surgery a 12 weeks (from Ng): 2.5% (1/40) vs. 0% (0/41): RR, 3.07 (95% CI 0.13 to 73.28) (4 of 5 patients who withdrew at 6 weeks also had surgery, not reported by treatment arm) Surgery at 1 year: 14% (9/64) vs. 22% (14/65)], RR 0.65 (95% CI 0.30 to 1.40)
Tauheed, 2014	A vs. B vs. C: <u>Pain</u> Global pain score (VAS, 0-100): At baseline 7.83 vs. 7.60 vs. 7.72, at 1 week 5.41 vs. 4.62 vs. 4.41, at 2 weeks 3.97 vs. 3.61 vs. 2.02, at 4 weeks 4.37, 3.91 vs. 2.23, at 6 weeks 4.46 vs. 4.11 vs. 2.41, and 12 weeks 4.66 vs. 4.24 vs. 2.65 (p >0.05 at all followup)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Tafazal, 2009; Ng, 2005	12 weeks (pain and function); 1 year (need for surgery or additional interventions)	A vs. B: 14% (21/150)	Appears complete	2 deaths; not stratified by treatment group	Not reported	Fair
Tauheed, 2014	12 weeks	A vs. B vs. C: 0 vs. 1 vs. 0	Appears complete	No serious adverse events or complication rates reported in any group	Not reported	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Thomas, 2003	RCT	France Single center Rheumatology clinic	>18 years of age; radicular pain <3 months; disc herniation of L4-L5 or L5-S1 confirmed by CT or MRI; radicular pain intensity >30 on 0 to 100 VAS	Epidural corticosteroid injection within 1 month; history of spinal surgery; motor or sphincter dysfunction requiring emergency surgery; iodine allergy; anticoagulant intake; depression; employment disruption >6 months; occupational injury	Approached: Not reported Eligible: Not reported Randomized: 31 (15 vs. 16) Analyzed: 22 (10 vs. 12) at 6 months	A: Transforaminal injection with 5 mg dexamethasone acetate (2 ml), with fluoroscopic guidance (n=15) B: Interlaminar epidural injection with 5 mg dexamethasone acetate (2 ml), with fluoroscopic guidance (n=16)
Valat, 2003	RCT	France Single center Rheumatology clinic	First or recurrent episode of sciatica (pain in one leg, radiation below knee, at least one nerve root compression, sign); duration 15 to 180 days; pain >30 on 0-100 mm VAS	Requiring surgery; structural spinal deformities; symptoms from causes other than herniated disc; spinal injection in past month; prior low back surgery; chemonucleolysis; or nucleotomy; pregnant; allergy to corticosteroid; treated with tricyclic antidepressant or lithium; out of work >1 year; worker's compensation	Approached: Not reported Eligible: Not reported Randomized: 85 (43 vs. 42) Analyzed: 63 (33 vs. 30) at 35 days	A: Interlaminar epidural injection with 50 mg prednisolone acetate (2 ml) (n=43) B: Interlaminar epidural injection with saline (2 ml) (n=42)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Thomas, 2003	A vs. B: Age (mean): 50 vs. 51 years Male: 53% vs. 31% Duration of symptoms (weeks): 6.5 vs. 6.8 Baseline leg pain (0-100 VAS): 74 vs. 72 Baseline RDQ (0-24): 12 vs. 14	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Rest and physical therapy (not otherwise specified) Lateral (vs. posterior) herniation: 33% vs. 25% Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level (L4-5) Provider experience: Not reported	Fluoroscopic guidance with contrast verification of nerve root (transforaminal) or epidural space (interlaminar)	Head-to-head comparison of different approaches for epidural injections
Valat, 2003	A vs. B: Age (mean): 44 vs. 38 years Male: 60% vs. 62% Duration of symptoms (days): 15 vs. 17 Baseline pain (0-100 VAS): 58 vs. 58 Baseline RDQ (0-24): 15 vs. 14	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: 3 injections at 2 day intervals Number of levels: Single Provider experience: Not reported	None reported	Interlaminar epidural injection with saline

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Thomas, 2003	A vs. B: Pain Leg pain (0-100 VAS): 74 vs. 72 at baseline; at 1 month 17 vs. 31(p=0.04); at 6 months 22 vs. 44 (p=0.04) Function RDQ (0-24): 12 vs. 14 at baseline; at 1 month, 7.9 vs. 9.6 (p>0.05); at 6 months, 5.3 vs.10 at (p=0.05) Dallas Daily Activities: 84 vs. 84 at baseline; at 1 month 52 vs. 59 (p>0.05); at 6 months, 46 vs. 69 (p=0.05) Dallas Work and Leisure Activities: at baseline 99 vs. 96, (p>0.05); at 6 months, 37 vs. 60 (p=0.02) Dallas Anxiety-Depression: at baseline 50 vs. 64; at 1 month 36 vs. 40, (p>0.05); at 6 months 34 vs. 55, (p=0.04) Dallas Sociability: at baseline 47 vs. 54; at 1 month 33 vs. 32, (p>0.05); at 6 months 30 vs. 44, (p>0.05) Other outcomes Surgery at 6 months:33% (5/15) vs. 25% (4/16), RR, 1.33 (95% CI 0.44 to 4.05)
Valat, 2003	A vs. B: Pain Pain (0-100 VAS): 58 vs. 58 at baseline; 28 vs. 40 at day 20, difference -11 (95% CI -23 to 1.3); 22 vs. 25 at day 35, difference -5.1 (95% CI -19 to 8.4) Success (recovery or marked improvement on four category scale and not requiring NSAID): 51% (22/43) vs. 36% (15/42), RR 1.43 (95% CI (p=0.15) at day 20; 49% (21/43) vs. 48% (20/42) at day 35, RR 1.03 (95% CI 0.66 to 1.59) Function RDQ (0-24): 15.1 vs. 14.2 at baseline; 10.9 vs. 11.7 at day 20, difference -1.8 (95% CI -4.6 to 1.0); 8.5 vs. 9.1 at day 35, difference -2.1 (95% CI -5.0 to 0.8) Dallas Daily Activities: 66 vs. 69 at baseline; 41 vs. 49 at day 20, difference -3 (95% CI -18 to 5.7), 31 vs. 40 at day 35, difference -5.7 (95% CI -18 to 7.1) Dallas Work and Leisure Activities: at baseline 73 vs. 78; 50 vs. 62 at day 20, difference -7.2 (95% CI -21 to 6.2); 41 vs. 47at day 35 , difference -7.3 (95% CI -22 to 7.1) Dallas Anxiety-Depression: 29 vs. 34 at baseline; 21 vs. 30 at day 20, difference -3.2 (95% CI -16 to 9.8); 16 vs. 26 at day 35, difference -5.3 (95% CI -19 to 8.4) Dallas Sociability: 29 vs. 25 at baseline; 18 vs. 20 at day 20, difference -10 (95% CI -20 to -0.9); 14 vs. 20 at day 35, difference -12 (95% CI -22 to -2.5) Other outcomes Surgery: 2.3% (1/43) vs. 4.7% (2/42), RR 0.49 (95% CI 0.05 to 5.19)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Thomas, 2003	6 months	A vs. B: None; 9 patients who underwent surgery excluded from 6 month analysis	Appears complete	Not reported	Not reported	Fair
Valat, 2003	35 days	A vs. B: 23% (10/43) vs. 29% (12/42) at 35 days	Appears complete	A vs. B: Headache: 9.3% (2/43) vs. 5% (2/40)	Ministry of Health	Fair

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)
Wilson-MacDonald, 2005	RCT	UK Single center Surgery clinic	Lumbosacral nerve root pain >6 weeks of sufficient intensity to warrant surgery; MRI showing disc prolapse and/or spinal stenosis	Not a surgical candidate; cauda equina syndrome; deteriorating neurological function	Approached: Not reported Eligible: Not reported Randomized: 93 (44 vs. 48) Analyzed: 72 (36 vs. 36) at 3 months	A: Interlaminar epidural steroid injection with 80 mg methylprednisolone (2 ml) plus 40 mg 0.5% bupivacaine (8 ml) (n=44) B: Intramuscular/interspinous ligament injection with 80 mg methylprednisolone (2 ml) plus 40 mg 0.5% bupivacaine (8 ml) (n=48)
el Zahaar, 1991	RCT	Egypt Single center Surgery clinic	Acute unilateral sciatica with neurological findings or neurogenic claudication without specific neurologic deficits; failure to improve with at least 2 weeks of conservative therapy; findings on MRI or CT consistent with clinical presentation	Surgery for similar symptoms or within 6 months	Approached: Not reported Eligible: Not reported Randomized: 63 (37 vs. 26) Analyzed: Unclear	A: Caudal epidural injection with hydrocortisone (5 ml), 4% Carbocaine (4 ml), and saline (21 ml) (n=37) B: Caudal epidural injection with 4% Carbocaine (4 ml) plus saline (26 cc) (n=26)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Wilson-MacDonald, 2005	A vs. B: Age (mean): 49 vs. 49 years Male: 40% (entire cohort) Herniated disc: 52% vs. 40% Spinal stenosis: 41% vs. 29% Both: 7% vs. 31% Duration of symptoms: Not reported (>6 weeks for all) Baseline pain: Not reported Baseline ODI (0-100): 44 vs. 40	A vs. B: Treatment prior to intervention: 16% (7/44) vs. 19% (9/48) previous epidural injection, chemonucleolysis, or surgery Treatment following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: 16% (7/44) vs. 19% (9/48) received a second epidural following the 6 week visit Number of levels: Appears to be single Provider experience: Not reported	Not reported	Nonepidural injection with corticosteroid plus local anesthetic
el Zahaar, 1991	A vs. B: Age (mean): 46 vs. 49 years Male: 54% vs. 65% Duration of symptoms (months): 17 vs. 14 Herniated disc: 51% vs. 54% Spinal stenosis: 49% vs. 46% Baseline pain: Not reported Baseline function: Not reported	A vs. B: Treatment prior to intervention: Not specified Treatment following intervention: Advised to take aspirin; no physical therapy or exercise program Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: Not reported	Not reported	Caudal epidural injection with local anesthetic

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Results
Wilson-MacDonald, 2005	A vs. B: <u>Pain</u> Pain relief: Favored intervention A (p<0.004), data not provided <u>Other outcomes</u> Underwent surgery: 41% (18/44) vs. 31% (15/48) at >=2 years, RR: 1.31 (95% CI 0.76 to 2.27)
el Zahaar, 1991	A vs. B: <u>Other outcomes</u> Treatment success (>75% improvement in pre-injection symptoms and no spinal surgery): 49% (18/37) vs.50% (13/26) at 13-36 months, RR 0.97 (95% CI 0.59 to 1.62); 58% (11/19) vs. 64% (9/14) in patients with herniated disc, RR 0.90 (95% CI 0.52 to 1.56) Subsequent surgery: 13/37 (35%) vs. 10/26 (38%) at 13-36 months, RR 0.91 (95% CI 0.47 to 1.76); 26% (5/19) vs. 21% (3/14) in patients with herniated disc, RR 1.23 (95% CI 0.35 to 4.30)

Appendix E1. Epidural Steroid Injections for Radiculopathy and Herniated Disc

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Wilson-MacDonald, 2005	At least 2 years	Unclear	19% (9/19) in nonepidural injection group received epidural corticosteroid injection due to continued symptoms	Not reported	Not reported	Fair
el Zahaar, 1991	Mean 20 to 21 months	Unclear	Appears complete	Not reported	Not reported	Poor

ACS=acute coronary syndrome; BMI=body mass index; cc=cubic centimeters; CI=confidence interval; CT=computed tomography; DLG=poly(DL-lactide-co-glycolide); DLR=digital luminescence radiography; EMG=electromyography; ER=emergency room; ESI=epidural steroid injection; F=female; FABQ=Fear-Avoidance Beliefs Questionnaire; FL=fetal length; gD=growth and development; h=hours; HAD=healthcare alternatives development; IL=interlaminar; L=angular momentum; m=months; MED=minimal effective dose; MIL=midline interlaminar; MRI=magnetic resonance imaging; NIAMS=National Institute of Arthritis and Musculoskeletal and Skin Diseases; NIH=National Institutes of Health; NR=no results; OR=not reported; NRS=numeric rating scale; NS=not significant; NSAID=nonsteroidal antiinflammatory drug; ODI=Oswestry Disability Index; PIL=pre illness level; PLC=pityriasis lichenoides chronica; PT=physical therapy; RCT=randomized controlled trial; RDQ=Roland Disability Questionnaire; RR=relative risk; S=Diabetes; SF-36=Short Form (36) Health Survey; SLR=straight leg raise; SR=systematic review; TENS=Toxic Epidermal Necrosis Syndrome; TFESI=transformational epidural steroid injection; tid=three times daily; VA=Veteran's Affairs; VAS=visual analogue scale; w=week; y=year.

Please see Appendix C. Included Studies for full study references.

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria
Brown, 2012	RCT	USA Single center Pain clinic	Degenerative lumbar spinal stenosis with painful lower limb neurogenic claudication and hypertrophic ligamentum flavum; with MRI or CT correlation; >18 years of age; failed conservative therapy; ODI >20; able to walk >10 feet unaided; duration not specified	Prior surgery at the intended treatment level, previous epidural steroids, recent spinal fractures, disabling back or leg pain from causes other than lumbar spinal stenosis, fixed spondylolisthesis > grade 1, disk protrusion or osteophyte formation, excessive facet hypertrophy, bleeding disorders, current use of anticoagulants, ASA or NSAID within 5 days, pregnant or breastfeeding, unable to lie prone, on Workman's Compensation or considering litigation
Cuckler, 1985	RCT	USA >1 center Type of clinics not reported	Acute unilateral sciatica; well defined, discrete neurological findings or neurogenic claudication; failure to improved with at least two weeks of noninvasive therapy; duration of symptoms not specified; imaging findings not required	Lumbar surgery for similar symptoms or any lumbar surgery within 6 months

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)	Subject Characteristics
Brown, 2012	Approached: 50 Eligible: 46 Randomized: 38 (17 vs. 21) Analyzed: 38 at 6 weeks	A: Interlaminar epidural steroid injection with 80 mg triamcinolone acetate (40 mg in diabetic patients) plus NS (6 ml), with fluoroscopic guidance (n=17) B: Minimally invasive lumbar decompression (mild) procedure using device to access the interlaminar space and remove portions of the lamina and ligamentum flavum, with fluoroscopic guidance (n=21)	Age (mean): 74 vs. 79 years Male: 62% vs. 47% Duration of medical management >6 months: 76% vs. 62% Baseline pain: Not reported Baseline function: Not reported
Cuckler, 1985	Approached: Not reported Eligible: Not reported Randomized: 37 (23 vs. 14) Analyzed: 37 at 20-22 months	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) and 1% procaine (5 ml) (n=23) B: Interlaminar epidural injection with saline (2 ml) and 1% procaine (5 ml) (n=14)	Age (years): 49 vs. 50 Male: 48% vs. 55% Duration of symptoms (months): 17.3 vs. 13.8 Baseline pain: Not reported Baseline function: Not reported

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Brown, 2012	Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of treatments: One treatment up to 6 weeks, then patient unblinded and given option of additional treatments, including nonallocated treatment Number of levels: 7/17 epidural steroid vs. 7/21 had one level treated Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space	Noninjection intervention
Cuckler, 1985	Treatments prior to intervention: Not specified Treatments following intervention: Not specified Previous surgery: 2% (1/42) vs 7% (2/31), RR 0.38 (95% CI 0.04 to 4.05) Herniated disc: 52% vs 45% Spinal stenosis: 48% vs. 55%"	Number of injections: 43% (18/42) vs. 58% (18/31), RR 0.82 (95% CI 0.48 to 1.39) received second injection with corticosteroid and local anesthetic after 24 h due to no relief after initial injection Number of levels: Single level Provider experience: Not reported	Interlaminar epidural injection with corticosteroid and local anesthetic	Interlaminar or transforaminal epidural injection with local anesthetic

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Results
Brown, 2012	A vs. B <u>Pain</u> >=2 point improvement in VAS pain (0-10): 35% (6/17) vs. 76% (16/21) at 2 weeks, RR 0.46 (95% CI 0.23 to 0.92) Pain (mean, 0-10 VAS): 6.4 vs. 6.4 at baseline, 6.3 vs. 3.8 at 6 weeks <u>Function</u> Oswestry Disability Index: 40 vs. 39 at baseline, 35 vs. 27 at 6 weeks <u>Other Outcomes</u> Zurich Claudication Questionnaire patient satisfaction (mean, 1-6): 2.8 vs. 2.2 at 6 weeks, patient satisfaction <=2.5: 41% (7/17) vs. 59% (12/21) at 6 weeks, RR 0.72 (95% CI 0.36 to 1.74)
Cuckler, 1985	A vs B (spinal stenosis subgroup) <u>Pain</u> Pain improved >=75%: 22% (5/23) vs. 14% (2/14) at mean 20 months, RR 1.52 (95% CI 0.34 to 6.81) <u>Other Outcomes</u> Surgery: 26% (6/23) vs. 29% (4/14) at mean 20 months, RR 0.91 (95% CI 0.31 to 2.68)

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating	Comments
Brown, 2012	6 weeks	None reported	No crossover prior to 6 weeks	Mortality: None "No major procedure-related or device-related complications reported in either treatment group"	Vertos Medical	Fair	
Cuckler, 1985	13 to 30 months (mean 20 .2 vs. 21.5 months)	None reported	Appears complete	Not reported	Not reported	Fair	

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria
Friedly, 2014	RCT	USA Multicenter	≥50 years of age; central lumbar spinal stenosis on MRI or CT; average pain rating >4 on 0 to 10 scale; pain in lower back, buttock, or on standing, walking, or spinal extension in the past week; worse pain in the buttock, leg or both than in the back; score ≥7 on RDQ; duration not specified	Spondylolisthesis requiring surgery, history of lumbar surgery or epidural injections within past 6 months

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)	Subject Characteristics
Friedly, 2014	Approached: 2224 Eligible: 422 Randomized: 400 (200 vs. 200) Analyzed: 386 (193 vs. 193) at 6 weeks	A: Interlaminar (n=143) or transforaminal (n=57) injection with 1 to 3 ml triamcinolone (60 to 120 mg), betamethasone (6 to 12 mg), dexamethasone (8 to 10 mg), or methylprednisolone (60 to 120 mg) plus 0.25% to 1% lidocaine (3 ml), with fluoroscopic guidance (n=200) B: Interlaminar (n=139) or transforaminal (n=61) injection with 0.25% to 1% lidocaine, with fluoroscopic guidance (2 to 6 ml) (n=200)	Age (mean): 68 vs. 68 years Male: 42% vs. 48% Nonwhite: 32% vs. 30% Duration of symptoms: <3 months 12% to 20%; 3 to < 12 months 25% to 28%; 1 to 5 years 29.5 to 31.2% ; >5 years 21.1 to 33.5% Baseline leg pain (0-10 NS): 7.2 vs. 7.2 Baseline RDQ (0-24): 16 vs. 16

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Friedly, 2014	Treatments prior to intervention: Not specified Treatments following intervention: Not specified Employed full-time or part-time: 28% vs. 36% Smoker: 12% vs. 16% Diabetes on insulin: 8.0% vs. 7.5% Expectation of pain relief (0-10): 7.7 vs. 7.8	Number of injections: Up to two injections in 1st six weeks Number of levels: Multilevel and bilateral injections allowed (numbers not reported) Provider experience: Board-certified anesthesiologists, physiatrist, and radiologists with expertise in epidural injections, trained to administer injections in standardized manner	Fluoroscopy	Interlaminar or transforaminal epidural injection with local anesthetic

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Results
Friedly, 2014	A vs. B <u>Pain</u> Leg pain improved >=30%: 49.2% (96/193) vs. 49.7% at 6 weeks (96/193), RR 1.0 (95% CI 0.82 to 1.22 Leg pain improved >=50%: 38.3% (74/193) vs. 38.3% (74/193) at 6 weeks, RR 1.0 (95% CI 0.78 to 1.29) Leg pain (0-10): 7.2 vs. 7.2 at baseline; 4.4 vs. 5.0 at 3 weeks, difference -0.6 (95% CI -1.2 to -0.10; 4.4 vs. 4.6 at 6 weeks, 95% CI -0.2 (95% CI -0.8 to 0.4) BPI, SSSQ symptoms and physical function, EQ-5D, GAD-7: No differences <u>Function</u> RDQ (0-24): 16 vs. 16 at baseline; 12 vs. 13 at 3 weeks, difference -1.8 (95% CI -2.8 to -0.9); 12 vs. 12 at 6 weeks, difference -1.0 (95% CI -2.1 to 0.1) RDQ improved >=30%: 37.3% (72/193) vs. 31.6% (61/193) at 6 weeks, RR 1.18 (95% CI 0.90 to 1.56) RDQ improved >=50%: 23.8% (46/193) vs. 20.2% (39/193) at 6 weeks RR 1.14 (95% CI 0.78 to 1.69) <u>Other Outcomes</u> PHQ-8: More improvement in group A (p=0.007) SSQ satisfaction "very" or "somewhat" satisfied: 67% (129/193) vs. 54% (104/191), RR 1.23 (95% CI 1.04 to 1.45) Interlaminar <u>Pain</u> Leg pain (0-10): 7.3 vs. 7.4 at baseline; 4.1 vs. 5.0 at 3 weeks, difference -0.9 (95% CI -1.5 to -0.3); 4.2 vs. 4.5 at 6 weeks, difference -0.3 (95% CI -1.0 to 0.4) <u>Function</u> RDQ (0-24): 17 vs. 16 at baseline; 11 vs. 13 at 3 weeks, difference -2.5 (95% CI -3.7 to -1.3); 12 vs. 13 at 6 weeks, difference -1.4 (95% CI -2.8 to -0.1) Transforaminal <u>Pain</u> Leg pain (0-10): 7.0 vs. 7.0 at baseline; 5.0 vs. 5.1 at 3 weeks, difference 0.0 (95% CI -0.9 to 0.9); 4.9 vs. 4.9 at 6 weeks, difference 0.1 (95% CI -0.9 to 1.0)

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating	Comments
Friedly, 2014	6 weeks	3.5% (7/200) vs. 3.% (7/200) at 6 weeks	Appears complete	A vs. B At least 1 adverse event: 22% (43/200 vs. 16% (31/200), RR 1.39 (95% CI 0.91 to 2.11) Adverse event rate, interlaminar approach: 0.22 (32/143) vs. 0.10 (14/139), RR 2.22 (95% CI 1.24 to 3.98) Adverse event rate, transforaminal approach: 0.46 (26/57) vs. 0.33 (20/61), RR 1.39 (95% CI 0.88 to 2.20) Excessive pain: 2.5% (5/200) vs. 3.5% (7/200), RR 0.71 (95% CI 0.23 to 2.21) Headache: 4% (8/200) vs. 1.5% (3/200), RR 2.67 (95% CI 0.72 to 9.91) Fever and/or infection: 5% (10/200) vs. 1.0% (2/200), RR 5.0 (95% CI 1.11 to 22.53) Dizziness/lightheadedness: 2% (4/200) vs. 2% (4/200), RR 1.0 (95% CI 0.25 to 3.94) Dural puncture: 0.5% (1/200) vs. 0.5% (1/200), RR 10. (95% CI 0.6 to 15.88) Serious adverse event: 2.5% (5/200) vs. 2.0% (4/200), RR 1.25 (95% CI 0.34 to 4.59)	Agency for Healthcare Research and Quality	Good	

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria
Fukusaki, 1998	RCT	Japan Single center Pain clinic	Pseudoclaudication and diagnosed by an orthopedist as having lumbar degenerative spinal canal stenosis with imaging correlation; duration not specified	Not reported
Huda, 2010	RCT	India Single center Orthopedics clinic	Clinical signs and symptoms of lumbar canal stenosis, refractory pain after full dose NSAIDs or physical therapy for >2 weeks; imaging findings not specified	Prior back surgery, back or leg pain due to other causes, pregnant, breast feeding, serious medical comorbidities

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)	Subject Characteristics
Fukusaki, 1998	Approached: Not reported Eligible: Not reported Randomized: 53 (19 vs. 18 vs. 16) Analyzed: 53 at 3 months	A: Interlaminar epidural injection with 40 mg methylprednisolone and 1% mepivacaine (8 ml) B: Interlaminar epidural injection with 1% mepivacaine (8 ml) C: Interlaminar epidural injection with normal saline (8 ml)	Mean age (years): 72 vs. 69 vs. 70 Male: 68% vs. 72% vs. 75% Duration of symptoms: Not reported Baseline pain: Not reported Baseline function: Not reported Walking distance (m): 9 vs. 11 vs. 10
Huda, 2010	Approached: Not reported Eligible: Not reported Randomized: 70 (35 vs. 35) Analyzed: 70	A: Caudal epidural injection with 80 mg methylprednisolone (2 ml) plus 0.125% bupivacaine (5 ml) and normal saline (13 ml) (n=35) B: Caudal epidural injection with 80 mg triamcinolone acetate (80 mg) plus 0.125% bupivacaine (5 ml) and normal saline (13 ml) (n=35)	Age (mean): 45 vs. 42 years Male: 54% vs. 66% Duration of symptoms (months): 18 vs. 17 Baseline pain (0-10 VAS): 6.4 vs. 6.3 Baseline function: Not reported

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Fukusaki, 1998	Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: 2 injections in first week Number of levels: Not specified (L3/4 or L4/5 interspace) Provider experience: "Experienced anesthesiologist"	No use of imaging guidance reported	Epidural local anesthetic Epidural saline
Huda, 2010	Treatments prior to intervention: Not specified Treatments following intervention: Not specified Baseline claudication distance (m) 170 vs. 163	Number and frequency of injections: 2 injections with 2nd injection after 2 weeks Number of levels: Caudal Provider experience: Not reported	Not reported	Head-to-head comparison of different corticosteroids

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Results
Fukusaki, 1998	A vs. B vs. C <u>Function</u> Walking distance: 87 vs. 92 vs. 23 at 1 week, 26 vs. 28 vs. 18 at 1 month, 10 vs. 13 vs. 11 at 3 months ($p<0.05$ for A and B vs. C at week 1 only) Good or excellent results (walk >20 meters): 63% (12/19) vs. 56% (10/18) vs. 12% (2/16) at 1 week: A vs. B, RR 1.14 (95% CI 0.66 to 1.94); A vs C, RR 5.05 (95% CI 1.32 to 19.31); B vs. C, RR 4.44 (95% CI 1.14 to 17.33); 16% (3/19) vs. 17% (3/18) vs. 6.3% (1/16) at 1 month: A vs. B, RR 0.94 (95% CI 0.22 to 4.10); A vs. C, RR 2.53 (95% CI 0.29 to 21.98); B vs. C RR 2.67 (95% CI 0.30 to 23.14); 5.3% (1/19) vs. 5.6% (1/18) vs. 6.3% (1/16) at 3 months: A vs. B, RR 0.95 (95% CI 0.06 to 14.03); A vs. C RR 0.84 (95% CI 0.06 to 12.41); B vs. C, RR 0.89 (95% CI 0.06 to 13.07)
Huda, 2010	A vs. B <u>Pain</u> Pain (0-10 VAS): 6.3 vs. 6.4 at baseline; 5.6 vs. 5.4 at 1 month; 4.9 vs. 4.7 at 3 months; 3.6 vs. 4.8 at 6 months (p values not reported and SD's not provided) Pain score improved >2 points on 0-10 VAS: 94% (33/35) vs. 86% (30/35) at 1 month, RR 1.10 (95% CI 0.94 to 1.30); 30/35 (86%) vs. 26/35 (74%) at 3 months, RR 1.15 (95 % CI 0.91 to 1.46); 28/35 (80%) vs. 21/35 (60%) at 6 months, RR 1.33 (95% CI 0.97 to 1.83) <u>Function</u> Claudication distance (m): 163 vs. 170 at baseline; 467 vs. 280 at 1 month; 587 vs. 312 at 3 months; 637 vs. 350 at 6 months (p-values not reported)

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating	Comments
Fukusaki, 1998	3 months	Unclear	Appears complete	"No incidence of dural puncture, hypotension, or subarachnoid injection in any group."	Not reported	Poor	
Huda, 2010	6 months	Not reported	Appears complete	"No serious complications like epidural abscess, infection, or hematoma…during the study period of 12 months"	Not reported	Fair	

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria
Koc, 2009	RCT	Turkey Single center Clinic setting unclear	Lumbar spinal stenosis based on medical history; physical and neurologic exam and MRI; duration not specified	Coronary artery or peripheral artery disease; spinal surgery; recent vertebral fracture; progression neurologic deficit; cauda equina syndrome
Manchikanti, 2009	RCT	USA Single center Pain clinic	≥ 50 yrs of age; evidence of lumbar spinal stenosis with radicular pain; chronic (≥ 6 months) function-limiting low back and lower extremity pain; failed fluoroscopically directed epidural injections; failed to improve substantially with conservative management; imaging findings not specified	Previous lumbar surgery; central spinal stenosis without radicular pain; uncontrollable or unstable opioid use; uncontrolled psychiatric disorder or acute/chronic medical illness; pregnant or lactating; history or potential for adverse reaction to study medications

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)	Subject Characteristics
Koc, 2009	Approached: Unclear Eligible: Unclear Randomized: 33 (10 vs. 13 vs. 10) Analyzed: 29 (10 vs. 10 vs. 9) at 6 months	A: Interlaminar epidural injection with 60 mg triamcinolone acetonide (1.5 ml), 15 mg 0.5% bupivacaine (3 ml), and 0.9% NS (5.5 ml), with fluoroscopic guidance B: Physical therapy 5 days/week for 2 weeks, including ultrasound for 10 minutes, hot pack for 20 minutes, and TENS for 20 minutes C: No injection or physical therapy	Age (mean): 61 vs. 63 vs. 53 years Male: 80% vs. 50% vs. 89% Duration of pain (years): 5.0 vs. 5.7 vs. 5.7 Baseline pain (0-100 VAS): 56 vs. 54 vs. 59 Baseline Roland Morris Disability Index (estimated from graph): 18 vs. 19 vs. 15
Manchikanti, 2009	Approached: 116 Eligible: 106 Randomized: 82 (not reported by group) Analyzed: 50 (25 vs. 25) at 12 months, including 8 patients (8 vs. 0) missing data (preliminary analysis)	A: Caudal epidural injection with 6 mg betamethasone, normal saline (6 mL), and 2% lidocaine (5 ml), with fluoroscopic guidance B: Epidural adhesiolysis with fluoroscopic guidance, followed by injection of 6 mg betamethasone, 10% sodium chloride (6 ml), and 2% lidocaine (5 ml), with fluoroscopic and lumbar epidurogram guidance	Age (mean): 62 vs. 61 years Male: 44% vs. 40% Duration of pain (months): 114 vs. 164 Baseline pain (0-10 NRS): 8.0 vs. 7.8 Functional status: Not reported

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Koc, 2009	Treatments prior to intervention: Training to perform home-based therapeutic exercise program and oral diclofenac sodium 75 mg bid x 2 weeks Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space	Physical therapy without injection No injection or physical therapy
Manchikanti, 2009	Treatments prior to intervention: Epidural injection with fluoroscopic guidance Treatments following intervention: Not specified Other patient characteristics: Not reported	Number of injections: 1.8 vs. 3.5 per year, frequency not reported Number of levels: Caudal approach Provider experience: Not reported	Fluoroscopy with lumbar epidurogram	Epidural adhesiolysis with corticosteroid and local anesthetic

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Results
Koc, 2009	A vs. B vs. C <u>Pain</u> Pain intensity (mean VAS, 0 to 100; estimated from graph): 53 vs. 55 vs. 58 at baseline; 20 vs. 31 vs. 47 at 2 weeks; 21 vs. 32 vs. 56 at 1 month; 23 vs. 24 vs. 38 at 3 months; 26 vs. 22 vs. 33 at 6 months <u>Function</u> Roland Morris Disability Index (mean, 0-24; estimated from graph): 18 vs. 19 vs. 15 at baseline; 8 vs. 12 vs. 12 at 2 weeks; 13 vs. 14 vs. 11 at 1 month; 11 vs. 11 vs. 10 at 3 months; 13 vs. 12 vs. 9 at 6 months Nottingham Health Profile (NHP), pain (median, 0-100): 56 vs. 54 vs. 59 at baseline; 7.3 vs. 19 vs. 33 at 2 weeks; 36 vs. 31 vs. 20 at 1 month, 20 vs. 18 vs. 28 at 3 months; 23 vs. 23 vs. 20 at 6 months NHP, physical mobility (median, 0-100): 42 vs. 42 vs. 42 at baseline; 22 vs. 31 vs. 31 at 2 weeks; 32 vs. 37 vs. 20 at 1 month; 31 vs. 32 vs. 31 at 3 months; 31 vs. 37 vs. 20 at 6 months NHP, energy (median, 0 to 100): 100 vs. 88 vs. 63 at baseline; 61 vs. 30 vs. 63 at 2 weeks; 100 vs. 24 vs. 61 at 1 month; 62 vs. 30 vs. 100 at 3 months; 82 vs. 49 vs. 63 at 6 months, (p>0.05 at all time points) NHP, sleep (median, 0 to 100): 58 vs. 56 vs. 56 at baseline; 26 vs. 32 vs. 12 at 2 weeks; 45 vs. 12 vs. 12 at 1 month; 14 vs. 12 vs. 29 at 3 months; 26 vs. 12 vs. 29 at 6 months, (p>0.05 at all time points) NHP, social isolation (median, 0 to 100): 42 vs. 29 vs. 0 at baseline; 22 vs. 18 vs. 0 at 2 weeks; 22 vs. 19 vs. 0 at 1 months; 32 vs. 11 vs. 0 at 3 months; 32 vs. 0 vs. 0 at 6 months, (p>0.05 at all time points)
Manchikanti, 2009	A vs. B <u>Pain</u> Pain (mean NRS, 0 to 10): 8.0 vs. 7.8 at baseline (p=0.47); 5.4 vs. 3.6 at 3 months, (p<0.0005); 6.0 vs. 3.8 at 6 months, (p<0.0005); 6.2 vs. 3.9 at 12 months Pain relief >=50% from baseline: 28% (7/25) vs. 80% (20/25) at 3 months, RR 0.35 (95% CI 0.18 to 0.67); 12% (3/25) vs. 80% (20/25) at 6 months, RR 0.15 (95% CI 0.50 to 0.44); 4% (1/25) vs. 76% (19/25) at 12 months RR 0.05 (95% CI 0.00 to 0.36) <u>Function</u> ODI (0 to 50): 30 vs. 31 at baseline (p=0.80), 23 vs. 16 at 3 months, (p<0.0005), 25 vs. 16 at 6 months, (p<0.0005), 25 vs. 16 at 12 months, (p<0.0005) ODI improved >=40% from baseline: 24% (6/25) vs. 80% (20/25) at 3 months, RR 0.30 (95% CI 0.14 to 0.62); 8% (2/25) vs. 76% (19/25) at 6 months RR 0.11 (95% CI 0.03 to 0.41); 0% (0/25) vs. 80% (20/25) at 12 months RR 0.02 (95% CI 0.00 to 0.38)

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating	Comments
Koc, 2009	6 months	0% (0/10) vs. 23% (3/13) vs. 10% (1/10) at 6 months, RR 0.18 (95% CI 0.01 to 3.16)	Appears complete	2 withdrawals due to adverse events, group not described	None	Fair	
Manchikanti, 2009	12 months	32% (8/25) vs. 0% (0/25) at 12 months	Unclear; 18/25 patients in caudal epidural injection group unblinded early and received additional interventions	Subarachnoid placement of catheter: 0% (0/25) vs. 4% (1/25), RR 0.33 (5% CI 0.01 to 7.81)	None reported	Poor	All of the patients failed the control treatment prior to enrollment, preliminary analysis

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria
Manchikanti, 2012	RCT	USA Single center Pain clinic	>30 years of age, chronic function-limiting low back pain and lower extremity pain of at least 6 on a scale of 0-10 for >6 months; diagnosis of central spinal stenosis with radicular pain; failure to improve with conservative management; imaging findings not specified	Spinal stenosis without radicular pain; foraminal stenosis without central stenosis; uncontrolled psychiatric disorders; a history of lumbar surgery; uncontrollable or unstable opioid use; pregnant or lactating women; uncontrolled medical illness (either acute or chronic); patients with a history or potential for adverse reaction(s) to local anesthetics or steroids
Manchikanti 2012 Manchikanti 2012 Manchikanti 2008	RCT	USA Single center Pain clinic	Spinal stenosis with radicular pain, ≥30 years of age; history of function-limiting low back pain and lower extremity pain >6 on a scale of 0-10 for >6 months; failed to improve with conservative management; imaging findings not specified	History of lumbar surgery, spinal stenosis without radicular pain; uncontrollable or unstable opioid use; uncontrolled psychiatric disorders; uncontrolled medical illness, pregnant or lactating; patients with a history or potential for adverse reaction to study medications

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)	Subject Characteristics
Manchikanti, 2012	Approached: 164 Eligible: 138 Randomized: 120 Analyzed: 60 (30 vs. 30) at 12 months, including 6 (3 vs. 30) with missing data (preliminary analysis)	A: Interlaminar epidural injection with betamethasone (1 ml, dose not specified) plus 0.5% lidocaine (5 ml), with fluoroscopic guidance B: Interlaminar epidural injection with 0.5% lidocaine (6 ml), with fluoroscopic guidance	Age (mean): 50 vs. 54 years Male: 63% vs. 40% Duration of pain (months): 121 vs. 138 Baseline pain (0 to 10 NRS): 8.1 vs. 8.1 Baseline ODI (0 to 50): 29 vs. 31
Manchikanti 2012 Manchikanti 2012 Manchikanti 2008	Approached: 140 Eligible: 112 Randomized: 100 (50 vs. 50) Analyzed: 100 (50 vs. 50) at 24 months including 29 (14 vs.15) with missing data	A: Caudal epidural injection with betamethasone 6 mg (1 ml) plus lidocaine 0.5% (9 ml) with fluoroscopic guidance B: Caudal epidural injection with lidocaine 0.5% (10 ml) with fluoroscopic guidance	Age (mean): 56 vs. 57 years Male: 50% vs. 32% Race: Not reported Duration of pain (months): 105 vs. 94 Baseline pain (NRS 0 to 10): 7.6 vs. 7.9 Baseline ODI (0 to 50): 28 vs. 40

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Manchikanti, 2012	Treatments prior to intervention: Not specified Treatment following intervention: Not specified Other patient characteristics: Not reported	Number of injections: Mean 3.5 vs. 3.6 per year, Frequency not specified Number of levels: Appears to be single Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space	Interlaminar epidural injection with local anesthetic
Manchikanti 2012 Manchikanti 2012 Manchikanti 2008	Treatments prior to intervention: Not specified Treatment following intervention: Not specified Other patient characteristics: Not reported	Number of injections: Mean 3.8 vs. 4.2 over 2 years, Frequency not specified Number of levels: Caudal Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space	Caudal epidural local anesthetic

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Results
Manchikanti, 2012	A vs. B <u>Pain</u> Pain (mean NRS, 0 to 10): 8.1 vs. 8.1 at baseline, (p=0.90); 4.1 vs. 3.7 at 3 months, (p=0.37); 4.2 vs. 3.8 at 6 months, (p=0.38); 4.2 vs. 4.0 at 12 months, (p=0.67) Pain relief >=50% from baseline: 77% (23/30) vs. 77% (23/30) at 3 months, RR 1.0 (95% CI 0.76 to 1.32); 73% (22/30) vs. 73% (22/30) at 6 months, RR 1.0 (95% CI 0.74 to 1.36); 63% (19/30) vs. 70% (21/30) at 12 months, RR 0.90 (95% CI 0.63 to 1.30) <u>Function</u> ODI (0 to 50): 29 vs. 31 at baseline, (p=0.18); 16 vs.15 at 3 months, (p=0.73); 15 vs.16 at 6 months, (p=0.92); 16 vs.16 at 12 months, (p=0.84) ODI improved >=50% from baseline: 63% (19/30) vs. 80% (24/30) at 3 months, RR 0.79 (95% CI 0.57 to 1.10); 67% (20/30) vs. 67% (20/30) at 6 months, RR 1.0 (95% CI 0.70 to 1.43); 60% (18/30) vs. 70% (21/30) at 12 months, RR 0.86 (95% CI 0.59 to 1.25)
Manchikanti 2012 Manchikanti 2012 Manchikanti 2008	**A vs. B** <u>Pain</u> Pain (mean NRS, 0 to 10): 7.6 vs. 7.9 at baseline; 4.1 vs. 4.1 at 3 months; 4.2 vs. 4.1 at 6 months; 4.3 vs. 4.4 at 12 months; 4.7 vs. 4.6 at 24 months, (p=0.80 for group difference) Pain relief >=50% from baseline: 62% (31/50) vs. 66% (33/50) at 3 months RR 0.94 (95% CI 0.70 to 1.26); 56% (28/50) vs. 58% (29/50) at 6 months, RR 0.97 (95% CI 0.63 to 145); 46% (23/50) vs. 48% (24/50) at 12 months, RR 0.97 (95% CI 0.63 to 145); 44% (22/50) vs. 42% (21/50) at 24 months, RR 1.05 (95% CI 0.67 to 1.65) <u>Function</u> ODI (0 to 50): 28 vs. 30 at baseline; 17 vs. 17 at 3 months; 7 vs.17 at 6 months; 17 vs.18 at 12 months; 17 vs.18 at 24 months, (p=0.60 for group difference) ODI improved >=50% from baseline: 49% (24/50) vs. 58% (29/50) at 3 months, RR 0.83 (95% CI 0.57 to 1.20); 50% (25/50) vs. 54% (27/50) at 6 months RR 0.93 (95% CI 0.64 to 1.35); 50% (25/50) vs. 50% (25/50) at 12 months RR 1.0 (95 % CI 0.68 to 1.48); 46% (23/50) vs. 42% (21/50) at 24 months RR 1.10 (95 % CI 0.70 to 1.71) <u>Global Assessment</u> Success (pain improved >=50% and ODI improved >=50%): 48% (24/50) vs. 58% (29/50) at 3 months; 50% (25/50) vs. 54% 927/50) at 6 months; 46% (23/50) vs. 44% (22/50) at 12 months; 44% (22/50) vs. 38% (19/50) at 24 months <u>Other Outcomes</u> Opioid use (mg MED/day): 49 vs. 46 at baseline; 33 vs. 33 at 3 months; 34 vs. 34 at 6 months; 33 vs. 36 at 12 months; 32 vs. 36 at 24 months, (p>0.05 at all time points)

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating	Comments
Manchikanti, 2012	12 months	10% (3/30) vs. 10% (3/30) at 12 months, RR 1.0 (95% CI 0.22 to 4.56)	Appears complete	3 subarachnoid punctures (not reported by group)	None reported	Fair	Preliminary analysis
Manchikanti 2012 Manchikanti 2012 Manchikanti 2008	24 months	28% (14/50) vs. 30% (15/50) at 24 months, RR 0.93 (95% CI 0.51 to 1.72)	Appears complete	"No major adverse events"	None reported	Fair	

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria
Nam, 2011	RCT	South Korea Single center Physical medicine and rehabilitation clinic	≥50 years of age; pain increased with lumbar extension and decreased with lumbar flexion; pain radiating below knee; thoracolumbar scoliosis greater than 10 degrees, visible on x-rays; spinal stenosis on CT or MRI; duration not specified	Systemic inflammatory disease or diabetes; on anticoagulants; prior side effects from lidocaine or contrast dye; suspected infectious disease; steroid injection within 3 months; degenerative spondylolisthesis, osteoporosis, or compression fracture; surgical treatment of thoracolumbar region or cancer metastasis to thoracolumbar site or with spinal deformity caused by metabolic disease
Ohtori, 2012	RCT	Japan Single center Orthopedic surgery clinic	Low back and leg pain >1 month, lumbar spinal stenosis (central stenosis, lateral recess, or foraminal stenosis) on x-ray and MRI and physical examination	Monoradiculopathy, cauda equina syndrome, polyradiculopathy
el Zahaar, 1991	RCT	Egypt Single center Surgery clinic	Acute unilateral sciatica with neurological findings or neurogenic claudication without specific neurologic deficits; failure to improve with at least 2 weeks of conservative therapy; findings on MRI or CT consistent with clinical presentation	Surgery for similar symptoms or within 6 months

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)	Subject Characteristics
Nam, 2011	Approached: Not reported Eligible: Not reported Randomized: 48 Analyzed: 36 (17 vs. 19) at 12 weeks	A: Transforaminal epidural injection with 20 mg triamcinolone (0.5 ml) plus 0.5% lidocaine (1.5 ml), with fluoroscopic guidance (n=17) B: Transforaminal epidural injection with 0.5% lidocaine (2 ml), with fluoroscopic guidance (n=19)	Age (mean): 75 vs. 71 years Male: 24% vs. 26% Duration of symptoms (months): 7.7 vs. 6.7 Baseline pain (0-10 VAS): 7.3 vs. 7.4 Baseline ODI (0-100): 63 vs. 63
Ohtori, 2012	Approached: Not reported Eligible: Not reported Randomized: 80 (40 vs. 40) Analyzed: Not reported	A: Transforaminal epidural injection with 3.3 mg dexamethasone plus 1% lidocaine (2 ml), with fluoroscopic guidance (n=40) B: Transforaminal epidural injection with 10 mg etanercept plus 1% lidocaine (2 ml), with fluoroscopic guidance (n=40)	Age (mean): 67 vs. 65 years Male: 45% vs. 55% Race: Not reported Duration of symptoms (months): 2.3 vs. 2.5 Baseline pain (0-10 VAS): 7.5 vs. 7.9 Baseline ODI (0-100): 40 vs. 38
el Zahaar, 1991	Approached: Not reported Eligible: Not reported Randomized: 30 (18 vs. 12) Analyzed: 30	A: Caudal epidural injection with hydrocortisone (5 ml), 4% Carbocaine (4 ml), and saline (21 ml) (n=18) B: Caudal epidural injection with 4% Carbocaine (4 ml) plus saline (26 cc) (n=12)	Age (mean): 46 vs. 49 years Male: 54% vs. 65% Duration of symptoms (months): 17 vs. 14 Herniated disc: 51% vs. 54% Spinal stenosis: 49% vs. 46% Baseline pain: Not reported Baseline function: Not reported

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Nam, 2011	Treatments prior to intervention: Not specified Treatments following intervention: Physical therapy not allowed Other patient characteristics: Not reported	Number and frequency of injections: 2nd injection after 3 weeks for partial improvement (53% vs. 47% received 2 injections) Number of levels: Single level (L5-S1 35% vs. 42%; L4-L5 41% vs. 37%) Provider experience: Not reported	Fluoroscopic guidance with contrast verification	Transforaminal epidural injection with local anesthetic
Ohtori, 2012	Treatment prior to intervention: Not specified (85% vs. 88% used meloxicam) Treatments following intervention: Not reported Spondylosis on x-ray: 60% vs. 65% Spondylolisthesis on x-ray: 40% vs. 35% Central stenosis on MRI: 70% vs. 78% Foraminal stenosis on MRI: 15% vs. 10% L4: 18% vs. 12% L5: 60% vs. 60^ S1: 22% vs. 28%	Number of injections: Single injection Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification of nerve	Transforaminal epidural injection with etancercept
el Zahaar, 1991	Treatment prior to intervention: Not specified Treatment following intervention: Advised to take aspirin, no physical therapy or exercise program Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: Not reported	Not reported	Caudal epidural injection with local anesthetic

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Results
Nam, 2011	A vs. B <u>Pain</u> Pain (mean, 0-10 VAS): 7.3 vs. 7.4 at baseline; 3.4 vs. 4.0 at 2 weeks; 3.5 vs. 4.4 at 1 month; 3.8 vs. 4.7 at 3 months (p<0.05 a 2 weeks, 1 month, and 3 months) <u>Function</u> ODI (mean, 0-100): 63 vs. 63 at baseline; 42 vs. 44 at 2 weeks; 39 vs. 46 at 1 month; 37 vs. 49 at 3 months (p<0.05 at 2 weeks; 1 month; and 3 months) <u>Global Assessment</u> Success (pain improved >40%, ODI improved >20%, patient satisfaction good or excellent): 76% (13/17) vs. 42% (8/19), RR 1.82 (95% CI 1.0 to 3.27) In multiple regression, sex, age, BMI, duration, and radiographic findings not associated with likelihood of success
Ohtori, 2012	A vs. B <u>Pain</u> Leg pain (0-10 VAS): 7.5 vs. 7.9 at baseline, 5.2 vs. 3.5 at 1 m (p=0.026) Leg numbness (0-10 VAS): 6.0 vs. 6.9 at baseline, 4.9 vs. 4.8 at 1 m (p>0.05) <u>Function</u> ODI (0-100): 40 vs. 38 at baseline, 30 vs. 28 at 1 m (p>0.05)
el Zahaar, 1991	A vs B (spinal stenosis subgroup) <u>Global Assessment</u> Treatment success (>75% improvement in pre-injection symptoms and no spinal surgery): 38% (7/18) vs. 33% (4/12) at 13-36 months; RR 1.17 (95% CI 0.43 to 3.13) <u>Other Outcomes</u> Subsequent surgery: 44% (8/18) vs. 58% (7/12) at 13-36 months, RR 0.68 (95% CI 0.33 to 1.40)

Appendix E2. Epidural Steroid Injections for Spinal Stenosis

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating	Comments
Nam, 2011	3 months	12 patients excluded from analysis for various reasons; 13 others excluded after "enrollment" (unclear if randomized)	Appears complete	Not reported	Inje University	Poor	
Ohtori, 2012	1 month	Not reported	Appears complete	No cases of infection, hematoma, spinal nerve injury, or other complications reported	No funding received	Fair	
el Zahaar, 1991	Mean 20 to 21 months	Unclear	Appears complete	Not reported	Not reported	Poor	

ASA = aspirin; CI = confidence interval; CT = CT=computed tomography; MRI = magnetic resonance imaging; NSAID = nonsteroidal antiinflammatory drug, ODI = Oswestry Disability Index; RCT = randomized controlled trial; RDQ = Roland Disability Questionnaire; RR = relative risk; VAS = visual analogue scale

Please see Appendix C. Included Studies for full study references.

Appendix E3. Epidural Steroid Injections for Nonradicular Pain

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental and control groups, dose, duration of treatment)
Lee, 2009	RCT	South Korea Single center Physical medicine clinic	Axial back pain without radiation for >3 months, due to herniated intervertebral disc or spinal stenosis	Unilateral or bilateral leg pain, arterial vascular disease, lumbar epidural steroid injection in last 2 months, prior lumbar spine surgery, presence of neurological deficits	Approached: Not reported Eligible: Not reported Randomized: 202 Analyzed: 192 (116 vs. 76) at 2 weeks to 4 months	A: Transforaminal epidural injection with 20 mg triamcinolone acetonide (0.5 ml) with lidocaine 0.5% (4 ml) with fluoroscopic guidance (n=116) B: Interlaminar epidural injection with 40 mg triamcinolone acetonide (1 ml) with lidocaine 0.5% (8 ml) with fluoroscopic guidance (n=76)
Manchikanti, 2012 Also Manchikanti 2011 Manchikanti 2008	RCT	USA Single center Pain clinic	No evidence of disc herniation and negative controlled local anesthetic blocks for facet or sacroiliac joint pain; ≥18 years of age; history of chronic function-limiting low back pain for >6 months; failure to improve with conservative management; imaging findings not specified	Facet joint pain; previous lumbar surgery; uncontrolled or unstable opioid use; uncontrolled psychiatric disorders; uncontrolled medical illness, either acute or chronic; pregnant or lactating; history or potential for an adverse reaction or reactions to study medications	Approached: 147 Eligible: 133 Randomized: 120 (60 vs. 60) Analyzed: 120 (60 vs. 60) at 24 months, including 22 (10 vs. 12) lost to followup	A: Caudal epidural with 6 mg betamethasone or 40 mg methylprednisolone (1 ml) with lidocaine 0.5% (9 ml) with fluoroscopic guidance (n=60) B: Caudal epidural with lidocaine 0.5% (10 ml) with fluoroscopic guidance (n=60)

Appendix E3. Epidural Steroid Injections for Nonradicular Pain

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance
Lee, 2009	A vs. B: Age (mean): 42 vs. 42 in herniated disc group, 62 vs. 62 years in spinal stenosis group Male: 61% vs. 50% in herniated disc group, 35% vs. 26% in spinal stenosis group Duration of pain: 4.5 vs. 3.7 m in herniated disc group, 14 vs. 16 months in spinal stenosis group Baseline pain (0-10 NRS): 6.5 vs. 6.8 in herniated disc group, 6.6 vs. 6.6 in spinal stenosis group Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: 52% herniated disc, 58% spinal stenosis (analyzed separately)	Number of injections: Mean not reported, maximum of three interlaminar injections at minimum 2 week intervals, maximum number of transforaminal injections not reported (injection performed bilaterally) Number of levels: Appears to be single Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space
Manchikanti, 2012 Also Manchikanti 2011 Manchikanti 2008	A vs. B: Age (mean): 44 vs. 48 years Male: 37% vs. 22% Duration of pain (months): 92 vs. 100 Baseline pain (0 to 10 NRS): 7.9 vs. 8.0 Baseline ODI (0 to 50): 28 vs. 28	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number of injections: Mean 5.5 vs. 4.5 over 2 years, frequency not specified Number of levels: Caudal Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space

Appendix E3. Epidural Steroid Injections for Nonradicular Pain

Author, Year Title	Type of Comparison	Results (acute and subacute, or chronic, or mixed)
Lee, 2009	Transforaminal versus interlaminar epidural injection with corticosteroid plus local anesthetic	Herniated disc group Roland pain score (0 to 5): 3.34 vs. 3.25 at baseline, 1.55 vs. 1.53 at 2 w, 1.57 vs. 1.59 at 2 m, 1.66 vs. 1.72 at 4 m Patient Satisfaction Index score 1 or 2 (1 to 4 scale): 78% (46/59) vs. 85% (29/34) at 2 w, RR 0.91 (95% CI 0.75 to 1.11); 83% (49/59) vs. 85% (29/34) at 2 m, RR 0.97 (95% CI 0.81 to 1.17); 76% (45/59) vs. 85% (29/34) at 4 m, RR 0.89 (95% CI 0.73 to 1.09) Pain score improved ≥2 points (0-10 pain NRS): 68% (40/59) vs. 65% (22/34) at 2 w, RR 1.05 (95% 0.77 to 1.42); 75% (44/59) vs. 65% (22/34) at 2 m, RR 1.15 (95% CI 0.86 to 1.54); 66% (39/59) vs. 50% (17/34) at 4 m, RR 1.32 (95% CI 0.90 to 1.94) Spinal stenosis group Roland pain score (0 to 5): 3.39 vs. 3.31 at baseline, 1.6 vs. 2.19 at 2 w, 1.67 vs. 2.12 at 2 m, 1.79 vs. 2.19 at 4 m ($p<0.05$ at 2 w, 2 m, and 4 m) Patient Satisfaction Index score 1 or 2 (1 to 4 scale): 75% (43/57) vs. 64% (27/42) at 2 w, RR 1.17 (95% CI 0.90 to 1.54); 70% (40/57) vs. 57% (25/42) at 2 m, RR 1.18 (95% CI 0.87 to 1.59); 67% (38/57) vs. 52% (22/42) at 4 m, RR 1.27 (95% CI 0.90 to 1.79) Pain score improved ≥2 points (0-10 pain NRS): 54% (31/57) vs. 36% (15/42) at 2 w, RR 1.52 (95% CI 0.95 to 2.44); 61% (35/57) vs. 36% (15/42) at 2 m, RR 1.72 (95% CI 1.09 to 2.71); 51% (29/57) vs. 31% (13/42) at 4 m, RR 1.64 (95% CI 0.98 to 2.76)
Manchikanti, 2012 Also Manchikanti 2011 Manchikanti 2008	Caudal epidural injection with local anesthetic	A vs. B <u>Pain</u> Pain (mean NRS, 0 to 10): 7.9 vs. 8.0 at baseline, 3.6 vs. 4.2 at 3 months, 3.7 vs. 4.1 at 6 months, 3.8 vs. 4.3 at 12 months, 4.0 vs. 4.4 at 24 months (p=0.52 for group difference) Pain relief >=50% from baseline: 80% (48/60) vs. 68% (41/60) at 3 months, 80% (48/60) vs. 68% (41/60) at 6 months, 72% (43/60) vs. 63% (38/60) at 12 months, 65% (39/60) vs. 57% (34/60) at 24 months <u>Function</u> ODI (0 to 50): 28 vs. 28 at baseline, 14 vs. 16 at 3 months, 14 vs. 16 at 6 months, 14 vs. 16 at 12 months, 15 vs. 16 at 24 months (p=0.21 for group difference) ODI improved >=50% from baseline: 75% (45/60) vs. 60% (36/60) at 3 months, 75% (45/60) vs. 62% (37/60) at 6 months, 72% (43/60) vs. 56% (34/60) at 12 months, 63% (38/60) vs. 56% (34/60) at 24 months <u>Other Outcomes</u> Opioid use (mg MED/day): 36 vs. 34 at baseline, 30 vs. 29 at 3 months, 31 vs. 32 at 6 months, 30 vs. 32 at 12 months, 30 vs. 31 at 24 months (p=0.45 for group difference)

Appendix E3. Epidural Steroid Injections for Nonradicular Pain

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating	Comments
Lee, 2009	4 months	10/192 at 2 weeks to 4 months	Not reported	Not reported	Wooridul Spine Foundation	Fair	
Manchikanti, 2012 Also Manchikanti 2011 Manchikanti 2008	24 months	A vs. B: 17% (10/60) vs. 20% (12/60) at 24 months	Appears complete	"None of the patients reported significant adverse events"	None reported	Fair	Primary ITT analysis based on baseline data or last followup for patients lost to followup

Appendix E3. Epidural Steroid Injections for Nonradicular Pain

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental and control groups, dose, duration of treatment)
Manchikanti, 2013 Also Manchikanti 2012 Manchikanti 2010	RCT	USA Single center Pain clinic	Lumbar axial or discogenic pain; age ≥18 years; function-limiting low back pain for >6 months; failure to improve with conservative management; imaging findings not specified	Lumbar facet joint or sacroiliac joint pain based on controlled, comparative local anesthetic blocks; previous lumbar surgery; uncontrollable or unstable opioid use; uncontrolled psychiatric disorders; uncontrolled medical illness; pregnant or lactating; history or potential for adverse reactions to study medications	Approached: 164 Eligible: 134 Randomized: 120 (60 vs. 60) Analyzed: 120 (60 vs. 60) at 24 months, including 13 (9 vs. 4) with missing data	A: Interlaminar epidural injection with 6 mg betamethasone (1 ml) and lidocaine 0.5% (5 ml) with fluoroscopic guidance (n=60) B: Interlaminar epidural injection with lidocaine 0.5% (6 ml) with fluoroscopic guidance (n=60)

Appendix E3. Epidural Steroid Injections for Nonradicular Pain

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance
Manchikanti, 2013 Also Manchikanti 2012 Manchikanti 2010	A vs. B: Age (mean): 43 vs. 41 years Male: 40% vs. 23% Race: Not reported Duration of pain (months): 129 vs. 104 Baseline pain (NRS 0 to 10): 7.7 vs. 8.0 Baseline ODI (0 to 50): 29 vs. 31	A vs. B: Treatments prior to intervention: Not specified Treatment following intervention: Not specified Other patient characteristics: Not reported	Number of injections: Mean 3.8 vs. 3.7 per year, frequency not specified Number of levels: Caudal Provider experience: Not reported	Fluoroscopy with contrast verification in epidural space

Appendix E3. Epidural Steroid Injections for Nonradicular Pain

Author, Year Title	Type of Comparison	Results (acute and subacute, or chronic, or mixed)
Manchikanti, 2013 Also Manchikanti 2012 Manchikanti 2010	Interlaminar epidural steroid injection with local anesthetic	A vs. B <u>Pain</u> Pain (mean NRS, 0 to 10): 7.7 vs. 8.0 at baseline, 3.5 vs. 3.6 at 3 months, 3.6 vs. 3.9 at 6 months, 3.7 vs. 3.7 at 12 months, 3.6 vs. 3.9 at 24 months (p=0.38 for group difference) Pain relief >=50% from baseline: 80% (48/60) vs. 68% (41/60) at 3 months, 80% (48/60) vs. 68% (41/60) at 6 months, 72% (43/60) vs. 63% (38/60) at 12 months, 65% (39/60) vs. 57% (34/60) at 24 months <u>Function</u> ODI (0 to 50): 29 vs. 31 at baseline, 15 vs. 15 at 3 months, 14 vs. 15 at 6 months, 15 vs. 15 at 12 months, 15 vs. 15 at 24 months (p=0.29 for group difference) ODI improved >=50% from baseline: 75% (45/60) vs. 60% (36/60) at 3 months, 75% (45/60) vs. 62% (37/60) at 6 months, 72% (43/60) vs. 56% (34/60) at 12 months, 63% (38/60) vs. 56% (34/60) at 24 months <u>Other Outcomes</u> Opioid use (mg MED/day): 53 vs. 57 at baseline, 40 vs. 36 at 3 months, 42 vs. 36 at 6 months, 42 vs. 36 at 12 months, 42 vs. 36 at 24 months (p=0.45 for group difference)

Appendix E3. Epidural Steroid Injections for Nonradicular Pain

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating	Comments
Manchikanti, 2013 Also Manchikanti 2012 Manchikanti 2010	24 months	A vs. B: 27% (16/60) vs. 17% (10/60) at 24 months	Appears complete	4 subarachnoid punctures without headache and one case of nerve root irritation, not reported by group	None reported	Fair	Primary ITT analysis based on baseline data or last followup for patients lost to followup

E=electronic; ITT=intention-to-treat; m=month; MED=minimal effective dose; n=number; NCS=Nerve Conduction Study; NRS=Numerical Rating Scale; ODI=Oswestry Disability Index; p=p value; RCT=randomized controlled trial; SI=sacroiliac

Please see Appendix C. Included Studies for full study references.

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental and control groups, dose, duration of treatment)
Devulder, 1999	RCT	Belgium Single center Pain clinic	20-70 years of age; persistent pain following spinal surgery for disc herniation; EMG showing chronic nerve pathology without acute irritation; pronounced nerve fibrosis on epidurogram and MRI (considered primary source of pain and neurophysiological abnormalities); 1-2 pathologic nerve roots; duration not specified	Lumbar instability; recurrent lumbar disc herniation; spinal stenosis	Approached: Not reported Eligible: Not reported Randomized: 60 (20 vs. 20 vs. 20) Analyzed: 60	A: Transforaminal epidural injection to nerve root sleeve with 40 mg methylprednisolone, 0.5% bupivacaine (1 ml) (total 2 ml) (n=20) B: Transforaminal epidural injection to nerve root sleeve with 40 mg methylprednisolone, 1,500 U hyaluronidase, and 0.5% bupivacaine (1 ml) (total 2 ml) (n=20) C: Transforaminal epidural injection to nerve root sleeve with 1,500 U hyaluronidase and 0.5% bupivacaine (1 ml), with fluoroscopic guidance (total 2 ml) (n=20)

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Devulder, 1999	A vs. B vs. C: Age (mean): 48 vs. 47 vs. 44 years Male: 50% vs. 40% vs. 30% Race: Not reported Duration of symptoms: Not reported Baseline pain: Not reported Baseline function: Not reported	A vs. B vs. C: Treatments prior to intervention: Surgery for disc herniation Treatment following intervention: Not specified Other patient characteristics: Not reported	Number of injections: Two injections 1 week apart Number of levels: Appears to be single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification in nerve root sleeve	Transforaminal epidural injection with corticosteroid, hyaluronic acid, and local anesthetic or hyaluronic acid and local anesthetic

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Results (acute and sub-acute, or chronic, or mixed)	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Devulder, 1999	A vs. B vs. C Pain Pain improved >50%: 40% (8/20) vs. 35% (7/20) vs. 35% (7/20) at 1 month (p=0.71), 40% (8/20) vs. 25% (5/20) vs. 25% (5/20) at 3 months (p=0.69), 35% (7/20) vs. 20% (4/20) vs. 25% (5/20) at 6 months (p=0.66)	6 months	Not reported	Appears complete	Not reported	Not reported	Poor

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental and control groups, dose, duration of treatment)
Manchikanti, 2012	RCT	United States Single center Pain clinic	>18 years of age; lumbar surgery ≥6 months prior; function-limiting low back pain for >6 months with or without lower extremity pain; no evidence of facet joint pain; failed to improve substantially with conservative management; imaging findings not specified	>400 mg morphine equivalents/day; uncontrolled psychiatric disorder or acute/chronic medical illness; pregnant or lactating; history or potential for adverse reaction to study medications	Approached: 242 Eligible: 214 Randomized:180 Analyzed: 120 (60 vs. 60) at 12 months in preliminary analysis, including 35 (33 vs. 2) with missing data	A: Caudal epidural injection with 6 mg betamethasone, 2% lidocaine (5 ml), normal saline (6 ml), with fluoroscopic guidance (n=60) B: Caudal epidural adhesiolysis with 6 mg betamethasone, 2% lidocaine (5 ml), and hypertonic (10%) saline (6 ml) (n=60)

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Manchikanti, 2012	A vs. B: Age (mean): 52 vs. 52 years Male: 42% vs. 42% Duration of symptoms (months): 186 vs. 196 Baseline pain (0-10 NRS): 7.9 vs. 8.1 Baseline ODI (0-50): 29 vs. 31	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Mean 2.2 vs. 3.5 per year; adhesiolysis performed after 3 months Number of levels: Single level Provider experience: Not reported	Fluoroscopic guidance with contrast verification in epidural space	Caudal adhesiolysis

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Results (acute and sub-acute, or chronic, or mixed)	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Manchikanti, 2012	A vs. B <u>Pain</u> Pain scores (0-10): 7.9 vs. 8.1 at baseline (p=0.22), 4.9 vs. 3.4 at 3 months (p<0.0005), 5.8 vs. 3.7 at 6 months (p<0.0005), 6.1 vs. 4.0 at 12 months (p<0.0005), 6.2 vs. 3.6 at 24 months Pain relief >50%: 35% (21/60) vs. 90% (54/60) at 3 months; 18% (11/60) vs. 85% (51/60) at 6 months; 12% (7/60) vs. 73% (44/60) at 12 months <u>Function</u> ODI (0-50): 29 vs. 31 at baseline (p=0.001), 20 vs. 15 at 3 months (p<0.0005), 22 vs. 15 at 6 months (p<0.0005), 23 vs. 16 at 12 months (p<0.0005), 23 vs. 14 at 24 months ODI improved >40%: 37% (22/60) vs. 92% (55/60) at 3 months; 25% (15/60) vs. 88% (53/60) at 6 months; 13% (8/60) vs. 77% (46/60) at 12 months <u>Global Assessment</u> Success (pain relief >=50% and ODI improved <u>></u>50%): 23% (14/60) vs. 78% (47/60) at 3 months, 7% (4/60) vs. 73% (44/60) at 6 months, 5% (3/60) vs. 70% (42/60) at 12 months, 5% (3/60) vs. 82% (49/60) at 24 months <u>Other Outcomes</u> Opioid intake (mg MED/day): 41 vs. 64 at baseline (p=0.001), 42 vs. 42 at 3 months (p=0.67), 47 vs. 49 at 6 months (p=0.71), 40 vs. 41 at 12 months (p=0.72)	24 months	A vs. B: 62% (43/60) vs. 3% (2/60) were unblinded and did not complete trial at 1 year; 87% (52/60) and 10% (6/60) at 2 years	Complete	"No adverse events noted"	Not reported	Poor

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental and control groups, dose, duration of treatment)
Meadeb, 2001	RCT	France Multicenter Rheumatology clinic	18 to 75 years of age; postoperative sciatica with or without low back pain; duration not specified; imaging findings not required though nerve root compression by residual disc tissue or lumbar spinal stenosis or of a nondegenerative disease on CT or MRI included as an exclusion criterion	Clotting disorders; skin lesion at injection site; hypersensitivity to iodine	Approached: Not reported Eligible: Not reported Randomized: 58 Analyzed: 47 (16 vs.16 vs. 15) at 120 days	A: Caudal epidural injection with 125 mg prednisolone acetate, with fluoroscopic guidance (n=16) B: Forceful caudal epidural injection with saline (20 ml), with fluoroscopic guidance (n=16) C: Forceful caudal epidural injection with saline (20 ml) plus 125 mg prednisolone acetate, with fluoroscopic guidance (n=15)
Rahimzadeh, 2014	RCT	Iran Single center Pain clinic	Patients ages 20-75 years old suffering from persistent (>6 months) back pain following laminectomy for spinal canal stenosis and/or discectomy for herniated nucleus pulposus documented by MRI (Failed back surgery syndrome defined as pain and or disability following laminectomy with or without sensory-motor neurological deficits or any form of urinary or bowel incontinence for at least 6 months)	Sacroiliac joint disease, facet joint arthritis, severe cardiopulmonary disease, uncontrolled diabetes, morbid obesity, addiction, infection, and coagulation disorders that prohibited lumber epidural injections	Approached: 33 Eligible: Not reported Randomized: 25 Analyzed: 25	A. Transforaminal lumbar epidural injection of bupivacaine 5 mg (1 mL) + triamcinolone 40 mg (1 mL) + saline solution 10% (2 mL) + hyaluronidase 1500 IU reconstituted in 1 mL distilled water (n=12) B. Transforaminal lumbar epidural injection of bupivacaine 5 mg (1 mL) + triamcinolone 40 mg (1 mL) + saline solution 10% (2 mL) + 1 mL distilled water (n=13)

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Meadeb, 2001	A vs. B vs. C: Age (mean): 43 vs. 47 vs. 45 years Male: 44% vs. 50% vs. 27% Duration of symptoms (months): 31 vs. 35 vs. 20 Baseline pain (0-100 VAS): 55 vs. 70 vs. 60 Dallas ADL (0-100: 66 vs. 71 vs. 61)	A vs. B vs. C: Treatments prior to intervention: Discectomy, time since surgery 38 vs. 43 vs. 34 months; prior epidural steroid injection 12/15 vs. 12/15 vs. 12/14 Treatments following intervention: Not specified Other patient characteristics: Not reported	Number and frequency of injections: Single injection Number of levels: Single level (caudal) Provider experience: Not reported	Fluoroscopic guidance with contrast verification in epidural space	Forceful caudal injection with saline or saline plus corticosteroid
Rahimzadeh, 2014	A vs. B : Age (mean): 46 vs. 48 years Male: 58% vs. 54% Duration of symptoms (months): 7 vs. 8 Baseline pain (0-10 VAS): 3.1 vs. 3.4	A vs. B Treatments prior to intervention: Laminectomy for spinal canal stenosis and/or discectomy for herniated nucleus pulposus Treatment following intervention: Not reported Other patient characteristics: Not reported	Number and frequency of injections: 1 Number of levels: Not reported Provider experience: Interventional pain specialist	Fluoroscopic guidance	Epidural injection with hyaluronidase

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Results (acute and sub-acute, or chronic, or mixed)	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Meadeb, 2001	A vs. B vs. C Pain Pain (mean, 0-100 VAS): 55 vs. 70 vs. 60 at baseline; 48 vs. 66 vs. 58 at 30 days; 53 vs. 62 vs. 52 at 60 days; 45 vs. 60 vs. 58 at 120 days Pain improved >=15%: 25% (4/16) vs. 44% (7/16) vs. 20% (3/215) at 120 days Function Dallas ADL (mean, 0-100 VAS): 66 vs. 71 vs. 61 at baseline; 58 vs. 69 vs. 62 at 30 days; 60 vs. 68 vs. 60 at 60 days; 58 vs. 67 vs. 65 at 120 days	120 days	A vs. B vs. C: 18.9%(11/58) excluded due to incomplete evaluation at baseline or failure to respond to injections	Appears complete	A vs. B vs. C: Pain induced by injection: 76% vs. 73% vs. 70%	French Society for Rheumatology	Poor
Rahimzadeh, 2014	A vs. B Pain VAS (median IQR, 0-10): 0 vs. 0 at baseline, 1 vs. 1 at week 1, 1 vs. 1.5 at week 2, 1.5 vs. 2.5 at week 4 ($p<0.001$ at week 4) % patients with >50% decrease in numerical rating of pain score (NRS): 100% (12/12) vs. 100% (13/13) at baseline, 92% (11/12) vs. 77% (10/13) at week 1, 92% (11/12) vs. 54% (7/13) at week 2, 83% (10/12) vs. 46% (6/13) at week 4	4 weeks	Not reported	Appears complete	A vs. B Experienced any adverse event (specifically monitored for development of inadvertent subarachnoid injection, prolonged sensory-motor block, long-term weakness of the limbs, epidural hematoma, infection, bladder dysfunction, and arachnoiditis): 0% vs. 0%	No external funding	Poor

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental and control groups, dose, duration of treatment)
Rocco, 1989	RCT	USA Single center Pain clinic	Prior laminectomy, still symptomatic; duration not specified; imaging findings not specified	Not reported	Approached: Not reported Eligible: Not reported Randomized: 24 Analyzed: 22 (8 vs. 7 vs. 7) at 6 months	A: Epidural injection with 75 mg triamcinolone diacetate (1.9 ml) plus 5% lidocaine (2 ml) and normal saline (8 ml) (n=8) B: Epidural injection with 8 mg morphine (8 ml) plus 5% lidocaine (2 ml) (n=7) C: Epidural injection with 75 mg triamcinolone diacetate (1.9 ml) and 8 mg morphine (8 ml) plus 5% lidocaine (2 ml) (n=7)

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison
Rocco, 1989	A vs. B vs. C: Age (mean): 49 vs. 50 vs. 52 years Male: 50% vs. 29% vs. 57% Duration of symptoms: Not reported Baseline pain: Not reported Baseline function: Not reported	A vs. B vs. C: Treatments prior to intervention: Laminectomies 2.1 vs. 2.4 vs. 2.1; epidural steroid 4 vs. 4 vs. 4 Treatments following intervention: Not specified Other patient characteristics: Primary diagnosis epiduroarachnoiditis: 75% vs. 71% vs. 71%	Number and frequency of injections: Up to 3 injections at 1 month intervals; 62^ vs. 67% vs. 86% received 3 blocks Number of levels: Not specified Provider experience: Not reported	Not reported	Epidural injection with morphine or morphine plus corticosteroid

Appendix E4. Epidural Steroid Injections for Post-Surgery Syndrome

Author, Year Title	Results (acute and sub-acute, or chronic, or mixed)	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Rocco, 1989	A vs. B vs. C Pain Pain (mean, 0-10 VAS): 6.4 vs. 4.0 vs. 5.0 at baseline; 4.2 vs. 5.7 vs. 5.8 at 6 months (p>0.05); Pain improved: better, no change, worse, based on number of injections: 12% (1/8) vs. 0% (0/7) vs. 0% (0/7) at 6 months	6 months	A vs. B vs. C: 8.3% (2/24) lost to followup or inadvertant subarachnoid injection (1)	Appears complete	A vs. B vs. C: Required naloxone: 0% vs. 0% vs. 43% (3/7) Urinary retention: 0% (0/8) vs. 14% (1/7) vs. 71% (5/7) Nausea and vomiting: 12% (1/8) vs. 71% (5/7) vs. 57% (4/7) Pruritus: 12% (1/8) vs. 57% (4/7) vs. 57% (4/7)	Not reported	Fair

ADL=Activities of Daily Living; AE=adverse event; CT=computerized tomography; d=day; EMG=electromyogram; m=month; MED=minimal effective dose; MRI=magnetic resonance imaging; n=number; NRS=numerical rating scale; ODI=Oswestry Disability Index; p=p value; RCT=randomized controlled trial; VAS=visual analog scale

Please see Appendix C. Included Studies for full study references.

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Facet Joint Block (percent pain relief) Requirements	Imaging Requirements for Patient Selection	Duration of Symptoms at Enrollment
Ackerman, 2008	RCT	USA Single center Pain clinic	18 to 55 years of age; nonradicular low back pain, SPECT positive for lumbar facet joint involvement; excluded patients with normal MRI imaging	Not required	Required (SPECT, excluded if MRI normal)	<6 months (mean 7.6 weeks)
Carette, 1991	RCT	Canada Single center Pain clinic	18 to 65 years of age; first or recurrent episode of low back pain, buttock pain, or both for ≥6 months; pain present on day of enrollment; normal neurological exam; at least 50% reduction in pain following uncontrolled facet joint block at L4-L5 and/or L5-S1 followed by return of pain by 2 weeks after block (imaging findings not required)	Single intraarticular facet joint block (≥50% pain relief)	Not required	≥6 months (median 18-24 months)

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Subject Age, Sex, Diagnosis, Duration of Pain, Severity of Pain	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)
Ackerman, 2008	Allergy to study drugs, radicular symptoms, pregnant, steroid exposure within 4 weeks, workman's compensation or motor vehicle accident, anticoagulant therapy, lumbar disc herniation, spinal stenosis, lumbar compression fracture, positive bleeding history, pain longer than 6 months, schedule II opioid use	Approached: Not reported Eligible: Not reported Randomized: 46 (23 vs. 23) Analyzed: 46 at 12 w	A vs. B Age (mean): 41 vs. 38 years Male: 52% vs. 61% Duration of pain: Not reported by group, mean 7.6 w overall Baseline pain (0-10 NRS): 7.8 vs. 8.1 Baseline function (0-100 ODI): 31 vs. 34	Treatment prior to intervention: Not reported Treatments following intervention: Not reported Other patient characteristics: Not reported
Carette, 1991	Nonmechanical low back pain (e.g., tumor, infection, or spondylitis); previous injections into the facet joints or low back surgery; pregnant; known allergy to local anesthetic or radiologic contrast agents; blood coagulation disorder.	Approached: Not reported; 190 underwent diagnostic facet joint block Eligible:108 Randomized: 101 (51 vs. 50) Analyzed: 95 (48 vs. 47) at 6 m	A vs. B: Age (mean): 42 vs. 43 years Male: 51% vs. 58% Duration of pain (median, months): 18 versus 24 Baseline pain (0-10 VAS): 6.3 vs. 6.2 Baseline Sickness Impact Profile (0 to 100): 11 vs. 13	A vs. B: Treatments prior to intervention: Restricted to acetaminophen Treatments following intervention: Physicians asked to limit concurrent treatments to acetaminophen; 11 vs. 6 patients received other treatments (antidepressant, physical therapy, additional injection) through 6 months Other patient characteristics: Not reported

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Type of Intervention (experimental & control groups, dose, duration of treatment)	Number and Frequency of Injections, Number of Levels, Provider Experience	Imaging Guidance	Type of Comparator
Ackerman, 2008	A: Intra-articular facet joint injection with 8 mg triamcinolone (0.2 ml) and 1% lidocaine (0.5 ml), with fluoroscopic guidance B: Medial branch block with at medial branches of doral rami with 8 mg triamcinolone (0.2 ml) and 1% lidocaine (0.5 ml), with fluoroscopic guidance	Number and frequency of injections: Injections appeared to be performed once Number of levels: 5 levels bilaterally Provider experience: Physician fellowship trained and board certified in anesthesiology and pain medicine	Fluoroscopic guidance	Intra-articular versus medial branch corticosteroid injection
Carette, 1991	A: Intra-articular facet joint injection with 20 mg methylprednisolone acetate (1 ml) plus isotonic saline (1 ml), with fluoroscopic guidance B: Intra-articular facet joint injection with isotonic saline (2 ml), with fluoroscopic guidance	Number and frequency of injections: Mean 3.6 vs. 3.6 injections, frequency not specified Number of levels: 2 vs. 2 (L4/L5 and L5/S1), bilateral 80% vs. 79%	Fluoroscopic guidance	Intraarticular injection of saline

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Results (acute and subacute, or chronic, or mixed)
Ackerman, 2008	A vs. B Pain (0-10 NRS): 7.8 vs. 8.1 at baseline, 3.2 vs. 5.4 at 12 w (p<0.05) Pain relief ≥50% (0-10 NRS): 61% (14/23) vs. 26% (6/23) at 12 w, RR 2.33 (95% CI 1.09 to 5.00) ODI (0-100): 31 vs. 34 at baseline, 12 vs. 23 at 12 w (p<0.05)
Carette, 1991	A vs. B <u>Pain</u> Pain (0-10 VAS): 4.5 vs. 4.7 at 1 m, 4.0 vs. 5.0 at 6 m (p<0.05) McGill pain questionnaire, pain rating index (scale NR): 19.0 vs. 22.8 at 1 m (p>0.05); 17.1 vs. 21.6 at 6 m (p>0.05) McGill pain questionnaire, present pain intensity (0 to 5): 2.3 vs. 2.6 at 1 m (p>0.05); 2.1 vs. 2.9 at 6 m (p>0.05) <u>Function</u> Sickness Impact Profile, overall (0-100): 9.3 vs. 9.8 at 1 m (p>0.05), 7.8 vs. 10.8 at 6 m (p>0.05) Sickness Impact Profile, physical dimension (0-100): 5.2 vs. 6.3 at 1 m (p>0.05), 4.3 vs. 7.9 at 6 m (p<0.05) Sickness Impact Profile, psychosocial dimension: 8.2 vs. 9.0 at 1 m (p>0.05); 7.7 vs. 9.0 at 6 m (p>0.05) Bed rest in past 2 weeks (days): 0.3 vs. 0.1 at 1 m (p>0.05), 0.2 vs. 0.4 at 6 m (p>0.05) Complete restriction in main activity in past 2 weeks (days): 3.2 vs. 2.2 at 1 m (p>0.05); 1.3 vs. 2.9 at 6 m (p>0.05) <u>Global Assessment</u> Overall effect (7 category scale), "very marked" or "marked improvement": 42% (20/48) vs. 33% (16/48) at 1 m (p=0.53), 46% (22/48) vs. 15% (7/47) at 6 m (p=0.002)

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawals due to Adverse Events	Quality Rating	Sponsor
Ackerman, 2008	12 weeks	0% at 12 w	Appears complete	Not reported	Fair	Not reported
Carette, 1991	6 months	A vs. B 5.9% (3/51) vs. 6.0% (3/50) at 6 m	No patient in saline injection group received methylprednisolone injection	"No adverse events reported, other than transient local pain at the injection sites."	Fair	Not reported

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Facet Joint Block (percent pain relief) Requirements	Imaging Requirements for Patient Selection	Duration of Symptoms at Enrollment
Civelek, 2012	RCT	Turkey Number of centers not reported Neurosurgery clinic	Chronic and debilitating low back pain thought due to lumbar facet syndrome, not responding to conservative treatment for up to 6 weeks (mean duration 19 months), pain relief after facet joint injection for radiofrequency denervation patients (methods of facet joint block not reported, facet joint block not reported as required for facet joint injection patients, imaging findings of facet joint arthritis described but not clearly required)	Facet joint injection group: Not required Facet denervation group: Facet joint block, methods not reported (% pain relief NR)	Unclear	19 months (mean)
Fuchs, 2005	RCT	Germany Single center Pain clinic	Low back pain for at least 3 months; radiologic evidence of facet joint osteoarthritis with osteophyte formation (Kellgreen grade 2/3); facet joint block not required	Not required	Required (CT)	>3 months
Galiano, 2007	RCT	Germany Single center Neurosurgery and radiology clinic	Chronic low back pain > 6 months; CT or MRI imaging of lumbar spine (findings not specified); >18 years of age	Not required	Required (CT or MRI)	>6 months

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Subject Age, Sex, Diagnosis, Duration of Pain, Severity of Pain	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)
Civelek, 2012	Radicular pain; neurogenic claudication; neurologic deficits; acute or uncontrolled medical illness; history of adverse reaction to local anesthetics; pregnant or lactating	Approached: Not reported Eligible: Not reported Randomized: 100 (50 vs. 50) Analyzed: 100 at 1 y	A vs. B: Age (mean): 56 vs. 52 years Male: 29% vs. 30% Duration of symptoms (mean months): 19 vs. 19 Baseline pain score (0-10 NRS): 8.5 vs. 8..2 Baseline EQ-5D (5-15): 14 vs. 15	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Spine rehabilitation program for 4-6 weeks in patients who responded favorably to procedure at 1 week, surgery or physical therapy offered to patients who did not respond at 1 week Other patient characteristics: Not reported
Fuchs, 2005	Hypersensitivity or contraindication to study medications; contraindication to intraarticular treatment; anticoagulation, radicular pain, or other specific conditions on clinical examination or CT scan	Approached: Not reported Eligible: Not reported Randomized: 60 (30 vs. 30) Analyzed: 59 (30 vs. 29)	A vs. B: Age (mean): 66 vs. 65 years Male: 20% vs. 40% Duration of symptoms: Not reported (minimum 3 mos.) Baseline pain score (0-100 VAS): 69 vs. 69 Baseline RDQ (0-24): 12 vs. 12	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported
Galiano, 2007	Local or systemic infection; allergy to steroids or anesthetics; uncorrectable coagulopathy; pregnancy	Approached: Not reported Eligible: Not reported Randomized: 40 (20 vs. 20) Analyzed: Not reported	A vs. B: Age (mean): 49 vs. 49 years Male: 35% vs. 70% Duration of symptoms: Not reported (minimum 6 m) Baseline pain score (0-10 VAS): 71 vs.73 Baseline function: Not reported	A vs. B: Treatments prior to intervention: Lumbar surgery (35% vs. 35%) Treatments following intervention: Not specified Other patient characteristics: Not reported

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Type of Intervention (experimental & control groups, dose, duration of treatment)	Number and Frequency of Injections, Number of Levels, Provider Experience	Imaging Guidance	Type of Comparator
Civelek, 2012	A: Extra-articular facet joint injection to site of medial branch of the dorsal spinal ramus with 40 mg methylprednisolone (1 ml) and 1% lidocaine (8 ml), with fluoroscopic guidance B: Radiofrequency facet denervation at medial branch of the dorsal spinal ramus performed at 80° C for 120 s, with fluoroscopic guidance and electrostimulation confirmation	Number and frequency of injections: Appears to be one Number of levels 1-level: 54% vs. 52% 2-level: 26% vs. 28% 3-level: 16% vs. 16% 4-level: 4% vs. 4% Provider experience: 2 providers with 5+ years experience	A: Fluoroscopic guidance B: Fluoroscopic guidance with electrostimulation confirmation	Radiofrequency denervation
Fuchs, 2005	A: Intraarticular facet joint injection with 10 mg triamcinolone acetonide (1 ml), with CT fluoroscopic guidance B: Intraarticular facet joint injection with 10 mg sodium hyaluronate (1 ml), with CT fluoroscopic guidance	Number and frequency of injections: 3 injections performed at different levels at weekly intervals Number of levels: 3 over 3 weeks (bilateral) Provider experience: Not reported	CT fluoroscopic guidance	Intraarticular facet join injection of hyaluronic acid
Galiano, 2007	A: CT-guided intraarticular facet joint injection with 4 mg betamethasone (1 ml), 1% lidocaine (1 ml), and 0.5% bupivacaine hydrochloride (1 ml) B: Ultrasound-guided intraarticular facet joint injection with 4 mg betamethasone (1 ml), 1% lidocaine (1 ml), and 0.5% bupivacaine hydrochloride (1 ml)	Number and frequency of injections: Single injection Number of levels: Single level Provider experience: Not reported	A: CT guidance (contrast verification not reported) B: Ultrasound guidance (contrast verification not reported)	Type of guidance (CT vs. ultrasound)

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Results (acute and subacute, or chronic, or mixed)
Civelek, 2012	A vs. B <u>Pain</u> Pain (0-10 VNS): 8.5 vs. 8.2 at baseline, 3.4 vs. 2.2 at 1 m, 4.4 VS. 2.5 at 6 m, 4.9 vs. 2.6 at 12 m (p<0.01 at all time points except baseline) Pain improved >50%: 80% vs. 100% at 1 m, 68% vs. 90% at 6 m, 62% vs. 88% at 12 m <u>Other Outcomes</u> NASS patient satisfaction questionnaire (1-4): 1.3 vs. 1.3 at 1 m (p>0.05), 1.7 vs. 1.4 at 6 m (p>0.05), 2.0 vs. 1.5 at 12 m (p=0.04) NASS score 1 or 2: 88% vs. 100% at 1 m, 75% vs. 90% at 6 m, 66% vs. 88% at 12 m EQ-5D (scale, 5-15): 15 vs. 14 at baseline, 6.0 vs. 5.6 at 1 m, 7.2 vs. 6.5 at 6 m, 8.0 vs. 6.7 at 12 m (p>0.05 at all time points) EQ-5D <9: 89% vs. 98% at 1 m, 75% vs. 92% at 6 m, 69% vs. 90% at 12 m
Fuchs, 2005	A vs. B <u>Pain</u> Pain (0-100 VAS): 69 vs. 69 at baseline, 30 vs. 41 at 1 m, 33 vs 38 at 6 m (p>0.05) <u>Function</u> Roland Morris (0-24): 12 vs. 12 at baseline, 7.2 vs. 8.4 at 1 m, 8.3 vs. 7.1 at 6 m (p>0.05) ODI (0-50): 18 vs. 21 at baseline, 12 vs. 14 at 1 m, 13 vs. 13 at 6 m (p>0.05) Low Back Outcome Score (0-75): 33 vs. 32 at baseline, 44 vs. 43 at 1 m, 44 vs. 46 at 6 m (p>0.05) <u>Other Outcomes</u> SF-36: "Similar improvement" between groups on all subscales
Galiano, 2007	A vs. B <u>Pain</u> Pain (0-100 VAS, data estimated from graph): 46 vs. 38 at 6 w (p<0.01)

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawals due to Adverse Events	Quality Rating	Sponsor
Civelek, 2012	12 months	0% at 12 m	Appears complete	A vs. B Infection: 0% vs. 0% New motor deficit: 0% vs. 0% New sensory deficit: 0% vs. 0% Increase in severity of low back pain: 0% vs. 4% (resolved within 6-8 weeks)	Fair	Not reported
Fuchs, 2005	6 months	A vs. B 0% (0/30) vs. 3.3% (1/29) at 6 m	Appears complete	"No significant adverse events"	Fair	Not reported
Galiano, 2007	6 weeks	Not reported	Appears complete (4 ultrasound patients received CT guidance after ultrasound could not provide adequate resolution)	Fluid retention with edema: 1 (group not reported)	Fair	Not reported

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Facet Joint Block (percent pain relief) Requirements	Imaging Requirements for Patient Selection	Duration of Symptoms at Enrollment
Lakemeier, 2013	RCT	Germany Single center Orthopedic clinic	Lumbar facet joint-related low back pain for at least 24 months; ≥18 years of age; pain reduction ≥50% with uncontrolled intraarticular facet joint block; lumbar facet joint osteoarthritis and hypertrophy in the L3/L4-L5/S1 segments on MRI	Single intraarticular facet joint block (≥50% pain relief)	Required (MRI)	>24 months
Lilius, 1989	RCT	Finland Single center Clinic setting unclear	Back pain >3 months, localized to one side with tenderness and local muscle spasm over the facet joints; negative straight leg raise (response to facet joint block and imaging findings not required)	Not required	Not required	>3 months

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Subject Age, Sex, Diagnosis, Duration of Pain, Severity of Pain	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)
Lakemeier, 2013	History of osteoporosis or malignancies; allergies to local anesthetics; pregnant or lactating; lumbar spinal stenosis or spinal instability; vertebral fractures; symptomatic radiculopathies; uncontrolled psychiatric disorders, uncontrolled medical illness; history of adverse reactions to corticosteroids.	Approached: 89 Eligible: 69 Randomized: 56 (29 vs. 27) Analyzed: 52 (26 vs. 26) at 6 m	A vs. B: Age (mean): 56 vs. 58 years Male: 62% vs. 65% Duration of symptoms: Not reported (≥24 months required for inclusion) Baseline pain score (0-10 VAS): 7.0 vs. 6.6 Baseline ODI (0-100): 39 vs. 41	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported
Lilius, 1989	Not described	Approached: Not reported Eligible: Not reported Randomized: 109 (28 vs. 39 vs. 42) Analyzed: 104 at 3 m	A vs. B vs. C: Age (mean): 44 years overall Male: 44% overall Duration of symptoms: Not reported Baseline pain (0 to 100 VAS): 49 overall Baseline function: Not reported "No important differences between groups for age, sex, duration of symptoms, previous operations"; data not reported by group	A vs. B vs. C: Treatments prior to intervention: Not reported Treatments following intervention: Not reported Other patient characteristics: Not reported

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Type of Intervention (experimental & control groups, dose, duration of treatment)	Number and Frequency of Injections, Number of Levels, Provider Experience	Imaging Guidance	Type of Comparator
Lakemeier, 2013	A: Intraarticular facet injection with betamethasone 3 mg (1 ml) plus 0.5% bupivacaine (0.5 ml), with fluoroscopic guidance; sham denervation (electrodes not connected to generator) B: Radiofrequency denervation of facet joint: 0.5% bupivacaine (1ml), radiofrequency applied to site of the dorsal ramus medial branch of the target facet joint at 80°C for 90 seconds, with fluoroscopic guidance and electrostimulation confirmation	Number and frequency of injections: Unclear Number of levels: Unclear Provider experience: "Experienced spinal surgeon"	A: Fluoroscopic guidance with contrast verification in facet joint B: Fluoroscopic guidance to site of the dorsal ramus medial branch of the relevant lumbar facet joint, confirmed with electrostimulation	Radiofrequency denervation
Lilius, 1989	A: Intraarticular facet joint injection with 80 mg methylprednisolone acetate (2 ml) plus 30 mg bupivacaine (6 ml), with fluoroscopic guidance B: Extra-articular (pericapsular) facet joint injection with 80 mg of methylprednisolone (2 ml) + 30 mg bupivacaine (6 ml), with fluoroscopic guidance C: Intra-articular facet join injection with 8 ml saline, with fluoroscopic guidance	Number and frequency of injections: Appears to be single injection Number of levels: Unilateral, 2 levels per patient (L3/4 and L4/5 in15 patients and L4/5 and L5/S1 in 94 patients) (Provider experience: Not reported	Fluoroscopic guidance	Pericapsular injection of steroid + local anesthetic Intraarticular injection of saline

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Results (acute and subacute, or chronic, or mixed)
Lakemeier, 2013	A vs. B Pain Pain (0-10 VAS): 7.0 vs. 6.6 at baseline, 5.4 vs. 4.7 at 6 m; improvement 1.6 vs. 1.9 (p=0.35) Function Roland Morris Disability Questionnaire (0-24): 1.32 vs. 12.8 at baseline, 9.0 vs. 9.1 at 6 m; improvement 4.2 vs. 3.7 (p=0.51) ODI (0-100): 39 vs. 41 at baseline, 33 vs. 28 at 6 m, improvement 5.7 vs. 13 (p=0.46) Other Outcomes Analgesic intake: "No measurable differences," data not provided
Lilius, 1989	A vs. B vs. C Pain Pain (VAS, 0-100, estimated from graph): 45 vs. 52 vs. 52 at baseline, 31 vs. 35 vs. 41 at 2 w, 40 vs. 40 vs. 42 at 6 w, 44 vs. 42 vs. 43 at 3 m (p=0.33 vs. A vs. B, p=0.72 for A + B vs. C) Function Disability score: Data not reported (p=0.99 for A vs. B, p=0.89 for A + B vs. C) Return to work: No difference between groups (data not reported)

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawals due to Adverse Events	Quality Rating	Sponsor
Lakemeier, 2013	6 months	A vs. B 10.3% (3/29) vs. 3.7% (1/27) at 6 m	10% (3/29) vs. 3.7% (1/27) did not undergo allocated procedure or underwent additional procedure (nucleotomy)	"No major adverse events reported"	Good	No funding
Lilius, 1989	3 months	A vs. B 3.6% (1/28) vs. 0% (0/39) vs. 4.8% (2/42)	Appears complete	Not reported by intervention group; unspecified "side effects" reported in 7/106 overall	Poor	None

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Facet Joint Block (percent pain relief) Requirements	Imaging Requirements for Patient Selection	Duration of Symptoms at Enrollment
Manchikanti, 2010 Manchikanti, 2008	RCT	USA Single center Pain clinic	History of chronic function-limiting low back pain for >6 months; >18 years of age; positive results on controlled diagnostic lumbar facet joint nerve blocks (≥80% concordant pain relief and ability to perform previously painful movements); Imaging findings not required	Two medial branch blocks (≥80% pain relief)	Not required	>6 months (mean 108 months)
Manchikanti, 2001	RCT	USA Single center Pain clinic	Low back pain for >6 months with or without lower extremity pain; positive response to comparative facet joint blocks (criteria for positive response not reported); imaging findings not required	Two facet joint blocks (% pain relief NR)	Not required	> 6 months (mean 21 months)

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Subject Age, Sex, Diagnosis, Duration of Pain, Severity of Pain	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)
Manchikanti, 2010 Manchikanti, 2008	Radicular pain, lumbar spine surgery within 3 months, uncontrolled major depression or psychiatric disorders, heavy opioid usage (300 mg MED/day), acute or uncontrolled medical illness, pregnant or lactating, unable to be positioned in the prone position, history of adverse reactions to study medications	Approached: 144 (152 in 2008 report) Eligible: 128 Randomized: 120 (60 vs. 60) Analyzed: 120 (including 24 patients with missing data) at 24 m	A vs. B: Age (mean): 46 vs. 48 years Male: 45% vs. 35% Duration of symptoms (months): 108 vs. 108 Baseline pain (0-10 NRS): 7.9 vs. 8.2 Baseline ODI (0-50): 26 vs. 27	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Prior lumbar surgery: 13% vs. 20% Other patient characteristics: Not reported
Manchikanti, 2001	<18 or >90 years, neurological deficits, response to conservative treatment, previous nerve block	Approached: 212 Eligible: 84 Randomized: 84 (42 vs. 42) Analyzed: 73 (41 vs. 32) at 2.5 y	A vs. B: Age (mean): 47 vs. 46 years Male: 44% vs. 36% Duration of symptoms (years): 1.7 vs. 1.8 Baseline pain (0-10 NRS): 7.7 vs. 7.6 Functional status (scale not reported): 3.7 vs. 3.6	A vs. B: Treatments prior to intervention: Prior laminectomy 17% vs. 31% Treatments following intervention: Not reported Occupational: 12% vs. 16% Depression: 73% vs. 81% Generalized anxiety disorder: 76% vs. 72% Somatization disorder: 56% vs. 41% Disabled: 47% vs. 34%

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Type of Intervention (experimental & control groups, dose, duration of treatment)	Number and Frequency of Injections, Number of Levels, Provider Experience	Imaging Guidance	Type of Comparator
Manchikanti, 2010 Manchikanti, 2008	A: Extra-articular facet joint injection with 0.5-1.5 ml solution of 0.15 mg/ml betamethasone and 0.25% bupivacaine or bupivacaine plus Sarapin in equal amounts, with fluoroscopic guidance B: Extra-articular facet joint injection with 0.5-1.5 ml solution of 0.25% bupivacaine or bupivacaine and Sarapin in equal amounts, with fluoroscopic guidance	Number and frequency of injections: 6.1 vs. 5.6 over 2 years (allowed for patients with initial >50% pain relief with subsequent deterioration in pain relief to <50%, timing not reported) Number of levels: Unclear (blocks performed on minimum of 2 nerves) Provider experience: Not reported	Fluoroscopic guidance	Facet joint nerve block with local anesthetic and Sarapin
Manchikanti, 2001	A: Extra-articular facet joint injection of the medial branch of the medial branch block with 0.5-1 ml of 1 mg/ml methylprednisolone and 0.5% lidocaine or 0.25% bupivacaine plus equal volume of Sarapin, with fluoroscopic guidance B: Extra-articular facet joint injection of the medial branch of the medial branch block with 0.5-1 ml of 0.5% lidocaine or 0.25% bupivacaine plus equal volume of Sarapin, with fluoroscopic guidance	Number and frequency of procedures: Mean 7.3 vs. 6.6 over 2.5 years, frequency not specified Number of levels:4 per patient (L1/2 to L4/5) (bilateral for bilateral pain and ipsilateral for unilateral pain) Provider experience: Not reported	Fluoroscopic guidance	Extra-articular facet joint injection with local anesthetic and Sarapin

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Results (acute and subacute, or chronic, or mixed)
Manchikanti, 2010 Manchikanti, 2008	A vs. B <u>Pain</u> Pain (mean NRS, 0 to 10): 7.9 vs. 8.2 at baseline, 3.5 vs. 3.8 at 3 m, 3.3 vs. 3.6 at 6 m, 3.5 vs. 3.7 at 12 m, 3.2 vs. 3.5 at 24 m (p>0.05 at all time points) Pain relief >=50% from baseline: 82% (49/60) vs. 83% (50/60) at 3 m, 93% (56/60) vs. 83% (50/60) at 6 m, 85% (51/60) vs. 82% (49/60) at 12 m, 90% (54/60) vs. 85% (51/60) at 24 m <u>Function</u> ODI (0 to 50): 26 vs. 27 at baseline, 14 vs. 13 at 3 m, 12 vs. 13 at 6 m, 12 vs. 12 at 12 m, 11 vs. 12 at 24 m (p>0.05 at all time points) ODI improved >=40% from baseline: 72% (43/60) vs. 82% (49/60) at 3 m, 78% (47/60) vs. 83% (50/60) at 6 m, 78% (47/60) vs. 85% (51/60) at 12 m, 88% (53/60) vs. 87% (52/60) at 24 m <u>Other Outcomes</u> Opioid use (mg MED/day): 37 vs. 31 at baseline (p=0.29), 33 vs. 29 at 12 m (p=0.41), 30 vs. 27 at 24 m (p=0.55)
Manchikanti, 2001	A vs. B <u>Pain</u> Pain (0-10 NRS): 7.7 vs. 7.6 at baseline, 3.3 vs. 3.5 post-treatment (duration unclear) (p>0.05) Pain relief >50%: 100% (41/41) vs. 100$ (32/32) at 3 m, 88% (36/41) vs. 75% (24/32) at 6 m, 17% (7/41) vs. 25% (8/32) at 1 y, 5% (2/41) vs. 16% (5/32) at >12 m <u>Function</u> Functional status: (scale not reported) 3.7 vs. 3.6 at baseline, 5.7 vs. 5.3 post-treatment (duration unclear) (P>0.05) <u>Other Outcomes</u> Use of schedule II opioids: 15% (6/41) vs. 19% (6/32) post-treatment (duration unclear) Physical health (scale not reported): 5.1 vs. 4.7 at baseline, 7.1 vs. 6.7 post-treatment (duration unclear) (p>0.05) Mental health (scale not reported): 4.7 vs. 4.2 at baseline; 6.7 vs. 6.3 post-treatment (duration unclear) (p>0.05) Depression (criteria not reported): 73% (30/41) vs. 81% (26/32) (baseline); 58% (24/41) vs. 72% (23/32) (follow-up unclear) (p>0.05) Generalized anxiety disorder (criteria not reported): 76% (31/41) vs. 72% (23/32) (baseline); 61% (25/41) vs. 63% (20/32) (follow-up unclear) (p>0.05) Somatization disorder (criteria not reported): 56% (23/41) vs. 41% (13/32) (baseline); 32% (13/41) vs. 18% (9/32) (p<0.05) Symptom magnification (criteria not reported): 34% (14/41) vs. 28% (9/32) (baseline); 22% (9/41) vs. 19% (6/32) (p>0.05)

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawals due to Adverse Events	Quality Rating	Sponsor
Manchikanti, 2010 Manchikanti, 2008	24 months	A vs. B 20.0% (12/60 vs. 20.0% (12/60) at 24 m	4/60 vs. 5/60 unblinded prematurely due to lack of treatment response	"No adverse events reported"	Fair	No funding
Manchikanti, 2001	Unclear (up to 2.5 years)	A vs B 2.3% (1/42) vs. 23.8% (10/42) at 2.5y	Appears complete	"None of the various types of complications...were observed"	Poor	Not reported

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Facet Joint Block (percent pain relief) Requirements	Imaging Requirements for Patient Selection	Duration of Symptoms at Enrollment
Marks, 1992	RCT	Australia Single center Pain clinic	Lumbar or lumbarsacral pain and referred pain in an extra-spinal region; pain present most of the time for >6 months; unresponsive to non-narcotic analgesics and physical therapy; pain aggravated by sustained postures; imaging not specified	Not required	Not required	>6 months (median 8.5 years)
Nash, 1990	RCT	UK Single center Pain clinic	Primary low back pain; diffuse lesser intensity pain over the buttocks and posterolateral thigh and occasional radiation to the calf aggravated by sustained positions such as sitting, lying, or standing (diagnostic blocks not performed and no imaging findings required)	Not required	Not required	Not reported
Pneumaticos, 2006	RCT	USA Single center Orthopedic and radiology clinic	Presumed facet joint pain with nonradicular low back pain; symptoms present >6 months; low back pain with extension of lumbar spine; imaging evidence of facet joint abnormalities; response to facet joint block not required	Not required	Required (imaging method not specified)	>6 months

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Subject Age, Sex, Diagnosis, Duration of Pain, Severity of Pain	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)
Marks, 1992	Precise radicular pattern of motor or sensory changes in either lower limb (ignoring changes in tendon reflexes); straight leg raising limited to less than 60 degrees by lower limb pain; evidence of progressive spinal disorder of nondegenerative origin; gross psychological distress	Approached: Not reported Eligible: Not reported Randomized: 86 (42 vs. 44) Analyzed: 86 at 3 m, including 3 (1 vs. 2) with missing data	A vs. B: Age: Not reported Male: Not reported Duration of symptoms: Not reported Baseline pain "severe" or "very severe": 61% vs. 59% Baseline function: Not reported	A vs. B: Treatments prior to intervention: Spinal surgery 11.9% vs. 11.3% Treatments following interventions: Not specified Other patient characteristics: Not reported
Nash, 1990	Not specified	Approached: Not reported Eligible: Not reported Randomized: 67 (33 vs. 34) Analyzed: 56 (30 vs. 26) at 1 m	A vs. B: Age: Not reported Male: Not reported Duration of symptoms: Not reported Baseline pain "severe" or "very severe": 61% vs. 59% Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following interventions: Not specified Other patient characteristics: Not reported
Pneumaticos, 2006	Prior spinal surgery or facet joint injection, other spinal abnormalities, unable to tolerate SPECT, pregnant	Approached: Not reported Eligible: 47 Randomized: 47 (31 vs. 16) Analyzed: 46 (31 vs. 15) at 6 m	A vs. B: Age (mean): 43 vs. 44 years Male: 48% vs. 50% Duration of symptoms: Not reported (minimum 6 months) Baseline AAOS pain score (0 to 100): 46 across groups (NS for between-group difference, data not reported) Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Type of Intervention (experimental & control groups, dose, duration of treatment)	Number and Frequency of Injections, Number of Levels, Provider Experience	Imaging Guidance	Type of Comparator
Marks, 1992	A: Intraarticular facet joint injection with 20 mg methylprednisolone acetate (0.5 ml) and 1% lignocaine (1.0 to 1 .5 ml), with fluoroscopic guidance B: Extra-articular facet joint injection at medial articular branch of posterior primary ramus with 20 mg methylprednisolone acetate (0.5 ml) and 1% lignocaine (1.0 to 1 .5 ml) , with fluoroscopic guidance	Number and frequency of injections: Not reported Number of levels: Not reported Provider experience: Not reported	Fluoroscopic guidance, contrast verification not reported	Extra-articular facet joint injection with corticosteroid and local anesthetic
Nash, 1990	A: Intraarticular facet join injection with 20 mg methylprednisolone and 2% lignocaine (1 ml) and 0.5% bupivacaine (1 ml), with fluoroscopic guidance B: Extra-articular facet joint injection at medial branch of posterior ramus with 2% lignocaine (1 ml) and 0.5% bupivacaine (1 ml), with fluoroscopic guidance	Number and frequency of injections: Not reported Number of levels: Not reported (extra-articular injections performed at target level and level above) Provider experience: Not reported	A: Fluoroscopic guidance with intraarticular contrast confirmation B: Fluoroscopic guidance with contrast confirmation at site	Extra-articular facet joint injection with local anesthetic
Pneumaticos, 2006	A: Intra-articular and extra-articular facet joint injection with 3 mg betamethasone (0.5 ml) and 0.5% bupivacaine (2.5 ml) (half within joint and half around posterior facet capsule), guided by single photon electronic computed tomography (at positive sites when present or at levels specified by referring physician if no positive sites on SPECT), with fluoroscopic guidance B: Intra-articular and extra-articular facet joint injection with 3 mg betamethasone (0.5 ml) and 0.5% bupivacaine (2.5 ml) (half within joint and half around posterior facet capsule), at levels specified by referring physician, with fluoroscopic guidance	Number and frequency of injections: Not reported Number of levels: Mean 4 joints/patient (not reported by treatment group) Provider experience: 2 providers with 7 and 10 years of experience	Fluoroscopic guidance	Comparison of SPECT vs. no SPECT to guide site of facet joint injections

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Results (acute and subacute, or chronic, or mixed)
Marks, 1992	A vs. B <u>Pain</u> Pain response excellent (none, slight, good, excellent): 7.1% (3/42) vs. 0% (0/44) at 1 m, 4.8% (2/42) vs. 0% (0/44) at 3 m Pain response good or excellent: 36% (15/42) vs. 20% (9/44) at 1 m; 22% (9/42) vs. 14% (6/44) at 3 m
Nash, 1990	A vs. B <u>Pain</u> Pain moderate to very severe (nil to very severe): 83% (25/30) vs. 85% (22/26) at 1 m <u>Function</u> Functional status full (nil, limited, full): 57% (17/30) vs. 58% (15/26) at 1 m <u>Other Outcomes</u> Drug intake decreased: 30% (9/30) vs. 38% (10/26) at 1 m
Pneumaticos, 2006	A vs. B <u>Pain</u> AAOS pain score, change from baseline (0-100, estimated from graph): 20 vs. 12 at 1 m, 23 vs. 15 at 3 m, 16 vs. 11 at 6 m AAOS pain score improved >17 points: 48% (15/31) vs. 45% (5/16) at 1 m, 45% (14/31) vs. 45% (5/16) at 3 m, 39% (12/31) vs. 36% (5/14) at 6 m

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawals due to Adverse Events	Quality Rating	Sponsor
Marks, 1992	3 months	2.4% (1/42) vs. 4.8% (2/44) at 3 m	Appears complete	A vs, B: "Serious complications": 0% (0/42) vs. 0% (0/44) Headache: 9.5% (4/42) vs. 6.8% (3/44) Paraesthesia of one leg below knee without motor signs: 2.4% (1/42) vs. 2.3% (1/44) Nausea: 2.4% (1/42) vs. 2.3% (1/44) Worsening of pain (1 month): 21.4% (9/42) vs. 29.5% (13/44)	Fair	Not reported
Nash, 1990	1 month	A vs. B 9.1% (3/33) vs. 24% (8/34) at 1 m	Not reported	A vs. B Dermatomal analgesia (periprocedural): 0% vs. 0% Motor weakness (periprocedural): 0% vs. 0%	Poor	Not reported
Pneumaticos, 2006	6 months	A vs. B 0% (0/31) vs. 2/15 (13%) at 6 months	Appears complete	Not reported	Fair	Roderick Duncan MacDonald Research Fund of St Luke's Episcopal Hospital and Institute of Orthopedic Research and Education

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Facet Joint Block (percent pain relief) Requirements	Imaging Requirements for Patient Selection	Duration of Symptoms at Enrollment
Ribeiro, 2013	RCT	Brazil Single center University outpatient clinic	18 to 80 years of age; continuous or intermittent low back pain for 3 months or longer; baseline pain intensity between 4 to 8 (on a 10-point VAS scale); diagnosis of facet joint syndrome based on the following criteria: local paraspinal tenderness (with or without radiation to the groin or thigh); pain on hyperextension, rotation or lateral bending; absence of neurological deficit; findings of degenerative facet disease (osteophyte and bone sclerosis) on lumbar spine radiograph	Not required	Required (lumbar radiograph)	4.3 years (mean, minimum 3 months)

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Subject Age, Sex, Diagnosis, Duration of Pain, Severity of Pain	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)
Ribeiro, 2013	Known diagnosis of low back pain of an origin other than the facet joints; prior spine surgery; uncontrolled diabetes, systemic arterial hypertension, or glaucoma; diabetes with insulin use; fibromyalgia; changes in medications used for low back pain during the previous 2 months; allergy to the contrast medium; pregnancy or suspected pregnancy; current involvement in litigation	Approached: 82 Eligible: 69 Randomized: 60 (31 vs. 29) Analyzed: 60 (31 vs. 29) at 6 m	A vs. B: Age (mean): 63 vs. 64 years Male: 19% vs. 17% Duration of pain (mean, months): 50 vs. 53 Baseline pain (0-10 VAS): 7.0 vs. 6.8 (p=0.8) Baseline pain on extension (0-10 VAS): 6.8 vs. 6.5 (p=0.53) Baseline RDQ (0-24): 15 vs. 16 (p=0.31)	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Patients to remain at rest for 48 hours, take acetaminophen as needed (maximum 750 mg 4x daily) or diclofenac tablets as needed (maximum 50 mg 3x daily), no other medications should be taken or nonpharmacological therapy was to be taken for back pain Other patient characteristics: Diabetes: 13% vs. 17%, systemic arterial hypertension: 20% vs. 21%

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Type of Intervention (experimental & control groups, dose, duration of treatment)	Number and Frequency of Injections, Number of Levels, Provider Experience	Imaging Guidance	Type of Comparator
Ribeiro, 2013	A: Intra-articular facet joint injection with 20 mg triamcinolone hexacetonide (1 ml) and lidocaine (dose not reported, 1 ml), with fluoroscopic guidance B: Intramuscular injections in the lumbar paravertebral musculature with 20 mg triamcinolone hexacetonide (1 ml) and lidocaine (dose not reported, 1 ml)	Number and frequency of injections: Appeared to be administered once Number of levels: 6 injections performed bilaterally at L3 to S1, each level injected bilaterally Injections performed by a rheumatologist with experience in minimally invasive procedures	Fluoroscopic guidance	Intramuscular injection

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Results (acute and subacute, or chronic, or mixed)
Ribeiro, 2013	A vs. B <u>Pain</u> Pain (0-10 VAS): 7.0 vs. 6.8 at baseline (p=0.54), 4.0 vs. 4.0 at 1 week (p=0.92), 4.0 vs. 3.6 at 1 m (p=0.92), 4.7 vs. 6.1 at 3 m (p=0.06), 5.3 vs. 5.8 at 6 m (p=0.54) Pain on extension (0-10 VAS): 6.8 vs. 6.5 at baseline (p=0.53), 3.6 vs. 4.4 at 1 week (p=0.30), 4.0 vs. 5.1 at 1 m (p=0.17), 5.1 vs. 6.4 at 3 m (p=0.10), 5.3 vs. 6.1 at 6 m (p=0.32) <u>Function</u> RDQ (0-24): 15 vs. 16.4 at baseline (p=0.31), 11.5 vs. 13.4 at 1 week (p=0.24), 10.2 vs. 12.2 at 1 m (p=0.21), 10.6 vs. 14.7 at 3 m (p=0.01), 10.9 vs. 13.4 at 6 m (p=0.17) <u>Global</u> Improvement (5-point Likert scale, options were "much worse, a little worse, unchanged, a little better, or much better), percentage of patients who were "much better": 58% vs. 31% at 1 week (intergroup p=0.029), 55% vs. 52% at 1 m (p=0.4), 55% vs. 45% at 3 m (p=0.82), 48% vs. 24% at 6 m (p=0.26) <u>Quality of life</u> SF-36 Physical Functioning: p=0.21 between the groups over time (data NR) SF-36 Role Physical: p=0.023 between the groups over time (favors group A) (data NR) SF-36 Body Pain: p=0.15 between the groups over time (data NR) SF-36 General Health: p=0.52 between the groups over time (data NR) SF-36 Vitality: p=0.45 between the groups over time (data NR) SF-36 Social Functioning: p=0.16 between the groups over time (data NR) SF-36 Role Emotional: p=0.35 between the groups over time (data NR) SF-36 Mental Health: p=0.68 between the groups over time (data NR) <u>Medication usage</u> Acetaminophen daily intake (unit of measurement not reported): 5.2 vs. 3.7 at 1 week (p=0.34), 6.0 vs. 9.4 at 1 m (p=0.40), 19.5 vs. 19.7 at 3 m (p=0.98), 26.4 vs. 28.8 at 6 m (p=0.83) Diclofenac daily intake (unit of measurement not reported): 1.5 vs. 1.4 at 1 week (p=0.98), 4.3 vs. 5.4 at 1 m (p=0.72), 3.1 vs. 10.4 at 3 m (p=0.06), 5.9 vs. 14.9 at 6 m (p=0.04) No differences between groups in terms of the number of patients between groups who used other treatments, including pharmacological treatments, physical therapy, and spine surgery.

Appendix E5. Epidural Steroid Injections for Facet Joint Pain

Author, Year Title	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawals due to Adverse Events	Quality Rating	Sponsor
Ribeiro, 2013	6 months	A vs. B 6.5% (2/31) vs. 6.9% (2/29) at 6 months (but all 60 patients included in the intention to treat analysis)	Appears that all patients received injection as randomized.	Gastrointestinal bleeding (considered serious) and endoscopic surgery: 0% (0/31) vs. 3% (1/29) between 3 and 6 m Spinal arthrodesis for aggravation of back pain after a fall: 3% (1/31) vs. 0% (0/29) (after 1 m visit) Death (cause not reported): 3% (1/31) vs. 0% (0/29) between 3 and 6 m "No significant differences were found between the groups regarding the number of adverse [local and systemic] events." Events included: Postprocedure pain: 9 patients total Cutaneous hypochromia: 1 patient total Increased blood glucose: 5 patients total Vaginal bleeding: 3 patients total Dizziness: 3 patients total Nausea: 3 patients total	Good	Grant funding (from Fundacao de Amparo a Pesquisa do Estado de Sao Paulo)

AAOS = American Academy of Orthopedic Surgeons; CI = confidence interval; CT=computed tomography; EQ-5D = EuroQoL five-level version; MED = minimal effective dose; MRI = magnetic resonance imaging; NASS = North American Spine Society; NR = not reported; NRS = numeric rating scale; ODI = Oswestry Disability Index; RCT = randomized controlled trial; SPECT = single photon electronic computed tomography; VAS = visual analogue scale

Please see Appendix C. Included Studies for full study references.

Appendix E6. Epidural Steroid Injections for Sacroiliac Pain

Author, Year Title	Study Design	Country Setting	Inclusion Criteria	Exclusion Criteria	Number of Treatment and Control Subjects (number approached, number eligible, number enrolled)	Type of Intervention (experimental & control groups, dose, duration of treatment)	Subject Characteristics	Other Patient Characteristics (expectations of treatment benefit, confidence in clinician, worker's compensation status, ongoing litigation, smoking status, other treatments received)
Luukkainen, 2002	RCT	Finland Single center Rheuama-tology clinic	18-70 years of age; pain >3 months in sacroiliac joint region; positive results on one of the following: Gaenslen's test, Patrick's test, thigh flexion test; no signs of infection or neoplasm; no radiological signs of sacroiliitis; no signs of spondyloarthropathy; imaging findings not specified	Not reported	Approached: Not reported Eligible: Not reported Randomized: 24 (13 vs. 11) Analyzed: 24	A: Periarticular sacroiliac joint injection with 60 mg methylprednisolone (1.5 ml) and 20 mg/ml lidocaine (1.5 ml) (n=13) B: Periarticular sacroiliac joint injection with 20 mg/ml lidocaine (1.5 ml) (n=11)	A vs. B: Age (mean): 50 vs. 49 years Male: 23% vs. 36% Race: Not reported Duration of symptoms (years): 5.4 vs. 4.4 Baseline pain (median, 0-100 VAS): 53 vs. 53 Baseline function: Not reported	A vs. B: Treatments prior to intervention: Not specified Treatments following intervention: Not specified Other patient characteristics: Not reported

Appendix E6. Epidural Steroid Injections for Sacroiliac Pain

Author, Year Title	Number and Frequency of Injections Number of Levels Provider Experience	Imaging Guidance	Type of Comparison	Results	Duration of Followup	Loss to Followup	Compliance to Treatment	Adverse Events and Withdrawal due to Adverse Events	Sponsor	Quality Rating
Luukkainen, 2002	Number of injections: Single injection Number of levels: Sacroiliac Provider experience: Not reported	No use of imaging guidance reported	Periarticular sacroiliac joint injection with local anesthetic	A vs. B: Pain Improvement in pain (median, 0-100 VAS): -40 vs. -13 at 1 m (p=0.046)	1 month	Not reported	Appears complete	Not reported	Not reported	Fair

m=month; RCT=randomized controlled trial; SIJ=sacroiliac joint; VAS=visual analogue scale

Please see Appendix C. Included Studies for full study references.

Appendix F1. Quality Assessment of Epidural Steroid Injections for Radicular Pain and Herniated Disc

Author, year Title	Randomization Adequate?	Allocation Concealment Adequate?	Groups Similar at Baseline?	Eligibility Criteria Specified?	Outcome Assessors Masked?	Care Provider Masked (injection/ post-injection)
Ackerman, 2007	Yes	Unclear	Yes	Yes	Yes	Unclear
Ahadian, 2011	Yes	Unclear	No	Yes	Yes	No
Arden, 2005/ Price, 2005	Yes	Unclear	Yes	Yes	Yes	No/Unclear
Aronsohn, 2010	Unclear	Unclear	Yes	Yes	Unclear	No
Becker, 2007	Yes	Unclear	Unclear	Yes	Unclear	Yes
Beliveau 1971	No	No	Unclear	Yes	Unclear	Unclear
Breivik, 1976	Yes	Unclear	Unclear	Yes	Yes	Unclear
Buchner, 2000	Unclear	Unclear	No	Yes	Unclear	Unclear
Burgher, 2011	Unclear	Unclear	Yes	Yes	Yes	Yes
Bush, 1991	Unclear	Unclear	No	Yes	Yes	Unclear
Buttermann, 2004	Yes	Unclear	Yes	Yes	No	No
Candido, 2013	Yes	Unclear	Yes	Yes	Unclear	No
Candido, 2008	Yes	Unclear	Unclear	Yes	Unclear	Unclear
Carette, 1997	Yes	Yes	No	Yes	Yes	Yes
Cocelli, 2009	Unclear	Unclear	No	Yes	Unclear	Unclear
Cohen, 2012a	Yes	Unclear	Yes	Yes	Yes	Yes
Cohen, 2012b	Yes	Unclear	Yes	Yes	Yes	Yes
Cuckler, 1985	Unclear	Unclear	Yes	Yes	Yes	Yes
Dashfield, 2005	Unclear	Unclear	Yes	Yes	Yes	Yes

Appendix F1. Quality Assessment of Epidural Steroid Injections for Radicular Pain and Herniated Disc

Author, year Title	Patient Masked?	Attrition and Withdrawals Reported?	Attrition Acceptable and Comparable?	Analyze People in the Groups in Which They Were Randomized?	Primary Outcome Specified and Reported?	Quality Rating
Ackerman, 2007	Unclear	Yes	Yes	Yes	No	Fair
Ahadian, 2011	Yes	Yes	Yes	Yes	Yes	Fair
Arden, 2005/ Price, 2005	Yes	Yes	Yes	Yes	Yes	Fair
Aronsohn, 2010	No	No	Unclear	Yes	No	Poor
Becker, 2007	Yes	Yes	Yes	Yes	Yes	Fair
Beliveau 1971	Unclear	No	Unclear	Yes	No	Poor
Breivik, 1976	Yes	No	Unclear	Yes	No	Poor
Buchner, 2000	No	Yes	Yes	Yes	No	Fair
Burgher, 2011	Yes	Yes	Yes	Yes	Yes	Fair
Bush, 1991	Yes	Yes	Yes	Yes	No	Fair
Buttermann, 2004	No	Yes	Yes	No	No	Poor
Candido, 2013	Unclear	Yes	Yes	Yes	No	Fair
Candido, 2008	No	No	Unclear	Yes	Yes	Fair
Carette, 1997	Yes	Yes	Yes	Yes	Yes	Fair
Cocelli, 2009	Unclear	Yes	Yes	Yes	No	Fair
Cohen, 2012a	Yes	Yes	Yes	Yes	Yes	Good
Cohen, 2012b	Yes	Yes	Yes	Yes	Yes	Fair
Cuckler, 1985	Yes	Yes	Yes	Unclear	Unclear	Fair
Dashfield, 2005	Yes	Yes	No	No	Yes	Fair

Appendix F1. Quality Assessment of Epidural Steroid Injections for Radicular Pain and Herniated Disc

Author, year Title	Randomization Adequate?	Allocation Concealment Adequate?	Groups Similar at Baseline?	Eligibility Criteria Specified?	Outcome Assessors Masked?	Care Provider Masked (injection/ post-injection)
Datta, 2011	Yes	Yes	Yes	Yes	Unclear	Unclear
Dilke, 1973	Unclear	Unclear	Yes	Yes	Yes	No
Gerstzen, 2010	Unclear	Unclear	No	Yes	Unclear	No
Ghahreman, 2010 Ghahreman, 2011	Yes	Yes	Yes	Yes	Yes	No
Ghai, 2014	Yes	Yes	Yes	Yes	Yes	Yes
Ghai, 2013	Yes	Unclear	Yes	Yes	Unclear	Yes
Gharibo, 2011	Yes	Unclear	Unclear	Yes	Unclear	No
Habib, 2013	No	No	Yes	Yes	No	No
Helliwell, 1985	Unclear	Unclear	No	Yes	No	No
Iversen, 2011	Yes	Yes	Yes	Yes	Yes	No
Jeong, 2007	Unclear	Unclear	Unclear	Yes	Yes	No
Kang, 2011	Yes	Unclear	Yes	Yes	Yes	Yes
Karppinen, 2001 Karppinen, 2001	Yes	Yes	Yes	Yes	Yes	Yes
Kennedy, 2014	Yes	Unclear	No	Yes	Yes	Unclear
Kim, 2011	Yes	Unclear	Yes	Yes	Yes	No
Klenerman, 1984	Yes	Yes	Unclear	Yes	Yes	Unclear
Koh, 2013	Yes	Unclear	Yes	Yes	Yes	Yes
Kolsi, 2000	Unclear	Unclear	Yes	Yes	Yes	No
Kraemer, 1997 study 1	Unclear	Unclear	Yes	Yes	Unclear	Unclear
Kraemer, 1997 study 2	Unclear	Unclear	Yes	Yes	Unclear	Unclear

Appendix F1. Quality Assessment of Epidural Steroid Injections for Radicular Pain and Herniated Disc

Author, year Title	Patient Masked?	Attrition and Withdrawals Reported?	Attrition Acceptable and Comparable?	Analyze People in the Groups in Which They Were Randomized?	Primary Outcome Specified and Reported?	Quality Rating
Datta, 2011	Unclear	Yes	No	No	No	Poor
Dilke, 1973	Yes	Yes	Unclear	Yes	Unclear	Fair
Gerstzen, 2010	No	Yes	Yes	Yes	Yes	Fair
Ghahreman, 2010 Ghahreman, 2011	Yes	Yes	Yes	Yes	Yes	Good
Ghai, 2014	Yes	Yes	Yes	Yes	Yes	Good
Ghai, 2013	Yes	No	Unclear	Yes	Yes	Fair
Gharibo, 2011	No	No	Unclear	Yes	Yes	Fair
Habib, 2013	Yes	Yes	Yes	Unclear	Yes	Poor
Helliwell, 1985	Yes	No	Unclear	Yes	No	Poor
Iversen, 2011	Yes	Yes	Yes	Yes	Yes	Good
Jeong, 2007	Yes	Yes	Yes	Yes	Unclear	Fair
Kang, 2011	Yes	Yes	Yes	Yes	No	Fair
Karppinen, 2001 Karppinen, 2001	Yes	Yes	Yes	Yes	No	Good
Kennedy, 2014	Yes	No	Unclear	Yes	Yes	Fair
Kim, 2011	Yes	Yes	Yes	Yes	No	Fair
Klenerman, 1984	Unclear	Yes	Yes	No	No	Fair
Koh, 2013	Yes	Yes	No	Yes	Yes	Fair
Kolsi, 2000	Yes	Yes	Yes	Yes	No	Fair
Kraemer, 1997 study 1	Unclear	No	Unclear	Yes	Unclear	Poor
Kraemer, 1997 study 2	Unclear	No	Unclear	Yes	Unclear	Fair

Appendix F1. Quality Assessment of Epidural Steroid Injections for Radicular Pain and Herniated Disc

Author, year Title	Randomization Adequate?	Allocation Concealment Adequate?	Groups Similar at Baseline?	Eligibility Criteria Specified?	Outcome Assessors Masked?	Care Provider Masked (injection/ post-injection)
Laiq, 2009	Yes	Yes	Unclear	Yes	No	Unclear
Manchikanti, 2014 Manchikanti, 2013 Manchikanti, 2010	Yes	Unclear	No (large differences on multiple characteristics)	Yes	Unclear	Yes
Manchikanti, 2012 Manchikanti 2011 Manchikanti 2008	Yes	Unclear	Yes	Yes	Yes	Unclear
Matthews, 1987	Unclear	Unclear	Yes	Yes	Yes	No/Unclear
McCahon, 2011	Yes	Unclear	Yes	Yes	Yes	Unclear
Murakibhavi, 2011	Yes	Unclear	Unclear	Yes	No	No
Owlia, 2007	Unclear	Unclear	Unclear	Yes	Unclear	Unclear
Park, 2010	Unclear	Unclear	Yes	Yes	Unclear	Unclear
Park, 2013	Yes	Unclear	Yes	Yes	Yes	Unclear
Rados, 2011	Yes	Unclear	Yes	Yes	No	Unclear
Ridley, 1988	Yes	Unclear	Unclear	Yes	No	No/No
Riew, 2000; Riew, 2006	Unclear	Unclear	Unclear	Yes	Unclear	Yes/Yes
Rogers, 1992	Unclear	Unclear	Yes	Yes	Yes	Unclear
Sayegh, 2009	Unclear	Unclear	Unclear	Yes	Unclear	Yes
Snoek, 1977	Unclear	Unclear	Unclear	Yes	Yes	Unclear
Tafazal, 2009;Ng, 2005	Yes	Unclear	Yes	Yes	Unclear	Yes
Tauheed, 2014	Yes	Unclear	Yes	Yes	Unclear	Unclear
Thomas, 2003	Unclear	Unclear	No	Yes	Unclear	Unclear

Appendix F1. Quality Assessment of Epidural Steroid Injections for Radicular Pain and Herniated Disc

Author, year Title	Patient Masked?	Attrition and Withdrawals Reported?	Attrition Acceptable and Comparable?	Analyze People in the Groups in Which They Were Randomized?	Primary Outcome Specified and Reported?	Quality Rating
Laiq, 2009	No	Yes	Yes	Yes	No	Fair
Manchikanti, 2014 Manchikanti, 2013 Manchikanti, 2010	Yes	Yes	Yes	Yes	Yes	Poor
Manchikanti, 2012 Manchikanti 2011 Manchikanti 2008	No	Yes	Yes	Yes	Yes	Fair
Matthews, 1987	Yes	Yes	Yes	Yes	No	Fair
McCahon, 2011	Yes	Yes	Yes	Yes	Yes	Fair
Murakibhavi, 2011	No	No	Unclear	Yes	No	Poor
Owlia, 2007	Unclear	No	Unclear	Yes	Yes	Poor
Park, 2010	Unclear	No	Unclear	Yes	No	Fair
Park, 2013	No	Yes	Yes	Yes	Yes	Fair
Rados, 2011	Yes	Yes	Yes	Yes	Yes	Fair
Ridley, 1988	No	Yes	Yes	Yes	Unclear	Fair
Riew, 2000; Riew, 2006	Yes	Yes	Yes	Yes	Unclear	Fair
Rogers, 1992	Yes	No	Unclear	Yes	Unclear	Poor
Sayegh, 2009	Yes	Yes	Yes	Yes	Unclear	Fair
Snoek, 1977	Yes	No	Unclear	Yes	Unclear	Poor
Tafazal, 2009;Ng, 2005	Yes	Yes	Yes	Yes	Yes	Fair
Tauheed, 2014	Yes	Yes	Yes	Yes	Unclear	Fair
Thomas, 2003	Yes	Yes	No	Yes	No	Fair

Appendix F1. Quality Assessment of Epidural Steroid Injections for Radicular Pain and Herniated Disc

Author, year Title	Randomization Adequate?	Allocation Concealment Adequate?	Groups Similar at Baseline?	Eligibility Criteria Specified?	Outcome Assessors Masked?	Care Provider Masked (injection/ post-injection)
Valat, 2003	Yes	Yes	Yes	Yes	Yes	Unclear
Wilson-MacDonald, 2005	Yes	Yes	Unclear	Yes	Unclear	Yes
el Zahaar, 1991	Unclear	Unclear	Unclear	Yes	Unclear	Unclear

Appendix F1. Quality Assessment of Epidural Steroid Injections for Radicular Pain and Herniated Disc

Author, year Title	Patient Masked?	Attrition and Withdrawals Reported?	Attrition Acceptable and Comparable?	Analyze People in the Groups in Which They Were Randomized?	Primary Outcome Specified and Reported?	Quality Rating
Valat, 2003	Yes	Yes	No	Yes	Yes	Fair
Wilson-MacDonald, 2005	Yes	Unclear	Unclear	Yes	No	Fair
el Zahaar, 1991	Yes	No	Unclear	Yes	Unclear	Poor

Please see Appendix C. Included Studies for full study references.

Appendix F2. Quality Assessment of Epidural Steroid injections for Spinal Stenosis

Author, year Title	Randomization Adequate?	Allocation Concealment Adequate?	Groups Similar at Baseline?	Eligibility Criteria Specified?	Outcome Assessors Masked?	Care Provider Masked (injection/ postinjection)
Brown, 2012	Unclear	Yes	Yes	Yes	Yes	Yes
Cuckler, 1985	Unclear	Unclear	Yes	Yes	Yes	Yes
Friedly, 2014	Yes	Yes	Yes	Yes	Yes	Yes/Yes
Fukasaki, 1998	Unclear	Unclear	Yes	Yes	Yes	Unclear
Huda, 2011	Yes	Unclear	Yes	Yes	Unclear	Unclear
Koc, 2009	Unclear	Unclear	Yes	Yes	Yes	Unclear
Manchikanti, 2009	Yes	Unclear	Yes	Yes	Unclear	Unclear
Manchikanti, 2012	Yes	Yes	Yes	Yes	Yes	Yes
Manchikanti 2012 Manchikanti 2012 and Manchikanti 2008	Yes	Unclear	Yes	Yes	Yes	Unclear Yes
Nam, 2011	Yes	Unclear	Yes	Yes	Unclear	Unclear
Ohtori, 2012	Yes (minimization)	NA (minimization method)	Yes	Yes	Unclear	Unclear/Unclear
El Zahaar, 1991	Unclear	Unclear	Unclear	Yes	Unclear	Unclear

Appendix F2. Quality Assessment of Epidural Steroid injections for Spinal Stenosis

Author, year Title	Patient Masked?	Attrition and Withdrawals Reported?	Attrition Acceptable and Comparable?	Analyze People in the Groups in Which They Were Randomized?	Primary Outcome Specified and Reported?	Quality Rating
Brown, 2012	Yes	Yes	Yes	Yes	Yes	Fair
Cuckler, 1985	Yes	Yes	Yes	Unclear	Unclear	Fair
Friedly, 2014	Yes	Yes	Yes	Yes	Yes	Good
Fukasaki, 1998	No	No	Unclear	Yes	No	Poor
Huda, 2011	Yes	No	Unclear	Yes	Yes	Fair
Koc, 2009	No	Yes	No	Yes	No	Fair
Manchikanti, 2009	No	Yes	No	Yes	Yes	Poor
Manchikanti, 2012	Yes	Yes	No	Yes	Yes	Fair
Manchikanti 2012 Manchikanti 2012 and Manchikanti 2008	Yes	Yes	Yes	Yes	No	Fair
Nam, 2011	Unclear	Yes	No	No	No	Poor
Ohtori, 2012	Unclear	No	Unclear	Unclear	No (not specified)	Fair
El Zahaar, 1991	Yes	No	Unclear	Yes	Unclear	Poor

Please see Appendix C. Included Studies for full study references.

Appendix F3. Quality Assessment of Epidural Steroid Injections for Nonradicular Pain

Author, year	Randomization Adequate?	Allocation Concealment Adequate?	Groups Similar at Baseline?	Eligibility Criteria Specified?	Outcome Assessors Masked?	Care Provider Masked (injection/ postinjection)
Lee, 2009	Unclear	Unclear	Yes	Yes	Unclear	Unclear
Manchikanti, 2012 (J Pain Research 2012;5:381-90) Manchikanti 2011 (Pain Physician 2011;14:25-36)) Manchikanti 2008 (Pain Physician 2008;11:785-800)	Yes	Yes	Yes	Yes	Yes	Yes/Yes
Manchikanti, 2013 (Pain Physician 2013;16:E491-E504) Also Manchikanti 2012 (J Pain Research 2012; 5:301-11; Manchikanti 2010	Yes	Unclear	Yes	Yes	Yes	Unclear

Appendix F3. Quality Assessment of Epidural Steroid Injections for Nonradicular Pain

Author, year	Patient Masked?	Attrition and Withdrawals Reported?	Attrition Acceptable and Comparable?	Analyze People in the Groups in Which They Were Randomized?	Primary Outcome Specified and Reported?	Quality Rating
Lee, 2009	Unclear	Yes	Yes	Yes	Unclear	Fair
Manchikanti, 2012 (J Pain Research 2012;5:381-90) Manchikanti 2011 (Pain Physician 2011;14:25-36)) Manchikanti 2008 (Pain Physician 2008;11:785-800)	Yes	Yes	Yes	Yes	Yes	Fair
Manchikanti, 2013 (Pain Physician 2013;16:E491-E504) Also Manchikanti 2012 (J Pain Research 2012; 5:301-11; Manchikanti 2010	Yes	Yes	Yes	Yes	No	Fair

Please see Appendix C. Included Studies for full study references.

Appendix F4. Epidural Steroid Injections for Postsurgery Pain

Author, year	Randomization Adequate?	Allocation Concealment Adequate?	Groups Similar at Baseline?	Eligibility Criteria Specified?	Outcome Assessors Masked?	Care Provider Masked (injection/ post-injection)
Devulder, 1999	Unclear	Unclear	Unclear	Yes	Unclear	Unclear
Manchikanti, 2012	Yes	Unclear	Yes	Yes	Unclear	Unclear
Meadeb, 2011	Unclear	Unclear	No	Yes	Unclear	No
Rahimzadeh, 2014	Yes	Yes	Yes	Yes	Unclear	Yes
Rocco, 1989	Unclear	Unclear	No	Yes	Yes	Yes

Appendix F4. Epidural Steroid Injections for Postsurgery Pain

Author, year	Patient Masked?	Attrition and Withdrawals Reported?	Attrition Acceptable and Comparable?	Analyze People in the Groups in Which They Were Randomized?	Primary Outcome Specified and Reported?	Quality Rating
Devulder, 1999	Unclear	No	Unclear	Yes	No	Poor
Manchikanti, 2012	Unclear	Yes	No	Yes	Yes	Poor
Meadeb, 2011	Unclear	Yes	No	No	Yes	Poor
Rahimzadeh, 2014	Yes	Unclear	Unclear	Unclear	Yes	Poor
Rocco, 1989	Yes	Yes	Yes	Yes	No	Fair

Please see Appendix C. Included Studies for full study references.

Appendix F5. Quality Rating of Facet Joint Steroid Injections

Author, year	Randomization Adequate?	Allocation Concealment Adequate?	Groups Similar at Baseline?	Eligibility Criteria Specified?	Outcome Assessors Masked?	Care Provider Masked (injection/ postinjection)
Ackerman, 2008	Yes	Unclear	Yes	Yes	Unclear	No
Carette, 1991	Yes	Unclear	Yes	Yes	Unclear	Unclear
Civelek, 2012	Yes	Unclear	Yes	Yes	Yes	Unclear
Fuchs, 2005	Unclear	Unclear	Yes	Yes	Yes	Unclear
Galiano, 2007	Yes	Unclear	No	Yes	No	Unclear
Lakemeier, 2013	Yes	Yes	Yes	Yes	Yes	Yes
Lilius, 1989	Unclear	Unclear	Unclear	Yes	Unclear	Unclear
Manchikanti, 2010 Manchikanti, 2008	Yes	Unclear	Yes	Yes	Yes	Yes
Manchikanti, 2001	Unclear	Unclear	Yes	Yes	No	Unclear
Marks, 1992	Yes	Unclear	Unclear	Yes	Yes	Yes
Nash, 1990	Unclear	No	Unclear	Yes	Unclear	Unclear
Pneumaticos, 2006	Yes	Unclear	Unclear	Yes	Unclear	Unclear
Ribeiro, 2013	Yes	Yes	Yes	Yes	Yes	No (injectionist), yes (care provider)

Appendix F5. Quality Rating of Facet Joint Steroid Injections

Author, year	Patient Masked?	Attrition and Withdrawals Reported?	Attrition Acceptable and Comparable?	Analyze People in the Groups in Which They Were Randomized?	Primary Outcome Specified and Reported?	Quality Rating
Ackerman, 2008	Yes	Yes	Yes	Yes	Unclear	Fair
Carette, 1991	Yes	Yes	Yes	Yes	No	Fair
Civelek, 2012	No	Yes	Yes	Yes	No	Fair
Fuchs, 2005	No	No	Unclear	Yes	Yes	Fair
Galiano, 2007	No	No	Unclear	Yes	Yes	Fair
Lakemeier, 2013	Yes	Yes	Yes	Yes	Yes	Good
Lilius, 1989	No	Yes	Yes	Yes	No	Poor
Manchikanti, 2010 Manchikanti, 2008	Yes	Yes	No	Yes	Unclear	Fair
Manchikanti, 2001	No	No	No	Yes	No	Poor
Marks, 1992	Yes	Yes	Yes	Yes	No	Fair
Nash, 1990	No	Yes	Yes	Yes	Unclear	Poor
Pneumaticos, 2006	No	Yes	Yes	Yes	No	Fair
Ribeiro, 2013	Yes	Yes	Yes	Yes	Yes	Good

Please see Appendix C. Included Studies for full study references.

Appendix F6. Quality Rating of Epidural Steroid Injections for Sacroiliac Pain

Author, year	Randomization Adequate?	Allocation Concealment Adequate?	Groups Similar at Baseline?	Eligibility Criteria Specified?	Outcome Assessors Masked?
Luukkainen, 2002	Unclear	Unclear	Unclear	Yes	Yes

Appendix F6. Quality Rating of Epidural Steroid Injections for Sacroiliac Pain

Author, year	Care Provider Masked (injection/ postinjection)	Patient Masked?	Attrition and Withdrawals Reported?	Attrition Acceptable and Comparable?	Analyze People in the Groups in Which They Were Randomized?	Primary Outcome Specified and Reported?	Quality Rating
Luukkainen, 2002	Unclear	Yes	No	Unclear	Yes	No	Fair

Please see Appendix C. Included Studies for full study references.

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Key Question 1. In patients with low back pain, what is the effectiveness of epidural corticosteroid injections, facet joint corticosteroid injections, medial branch blocks, and sacroiliac joint corticosteroid injections versus epidural nonsteroid injection, nonepidural injection, no injection, surgery or non-surgical therapies on outcomes related to pain, function and quality of life?							
Epidural injections for radiculopathy							
Epidural corticosteroid injections versus placebo interventions							
Mean improvement in pain, immediate-term	6 trials N=701	Moderate	No serious inconsistency	Direct	Precise	Moderate	Epidural corticosteroid injections associated with greater improvement versus placebo interventions (6 trials, WMD -7.55 on 0 to 100 scale, 95% CI -11.4 to -3.74, I2=30%)
Mean improvement in pain, short-term	14 trials N=1537	Moderate	Inconsistent	Direct	Precise	Low	No difference (14 trials, WMD -3.94, 95% CI -9.11 to 1.24, I2=82%)
Mean improvement in pain, intermediate-term	4 trials N=436	Moderate	Inconsistent	Direct	Imprecise	Low	No difference (4 trials, WMD 0.07, 95% CI -8.41 to 8.26, I2=82%)
Mean improvement in pain, long-term	6 trials N=767	Moderate	Consistent	Direct	Precise	Moderate	No difference (6 trials, WMD -0.86, 95% CI -3.78 to 2.06, I2=0%)
Successful pain outcome, short-term	8 trials N=897	Moderate	Inconsistent	Direct	Precise	Low	No difference (8 trials, RR 1.21, 95% CI 0.98 to 1.49, I2=67%)
Successful pain outcome, intermediate-term	3 trials N=298	Moderate	Inconsistent	Direct	Precise	Low	No difference (3 trials, RR 1.12, 95% CI 0.93 to 1.36, I2=41%)
Successful pain outcome, long-term	4 trials N=504	Moderate	Consistent	Direct	Precise	Moderate	No difference (4 trials, RR 1.10, 95% CI 0.94 to 1.28, I2=0%)
Mean improvement in function, immediate-term	4 trials N=464	Moderate	Inconsistent	Direct	Imprecise	Low	No difference, based on all trials (4 trials, SMD -0.75, 95% CI -1.62 to 0.11, I2=94%). Excluding an outlier trial eliminated statistical heterogeneity and resulted in a statistically significant effect favoring epidural corticosteroid injections (3 trials, SMD -0.33, 95% CI -0.56 to -0.09, I2=0%)

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Mean improvement in function, short-term	11 trials N=1226	Moderate	Inconsistent	Direct	Precise	Moderate	No difference (11 trials, SMD -0.03, 95% CI -0.20 to 0.15, I2=53%)
Mean improvement in function, intermediate-term	5 trials N=619	Moderate	Inconsistent	Direct	Imprecise	Low	No difference (5 trials, SMD -0.30, 95% CI -0.74 to 0.15, I2=86%)
Mean improvement in function, long-term	8 trials N=950	Moderate	Inconsistent	Direct	Precise	Low	No difference (7 trials, SMD -0.23, 95% CI -0.55 to 0.10, I2=82%)
Successful functional outcome, short-term	6 trials N=873	Moderate	Inconsistent	Direct	Imprecise	Low	No difference (6 trials, RR 1.01, 95% CI 0.74 to 1.38, I2=76%)
Successful functional outcome, intermediate-term	2 trials N=240	Moderate	Inconsistent	Direct	Imprecise	Low	No difference (2 trials, RR 1.18, 95% CI 0.89 to 1.57, I2=71%)
Successful functional outcome, long-term	3 trials N=468	Moderate	Consistent	Direct	Precise	Low	No difference (3 trials, RR 1.15, 95% CI 0.97 to 1.35, I2=0%)
Risk of surgery, short-term	5 trials N=845	Moderate	Consistent	Direct	Imprecise	Low	Epidural corticosteroid injections were associated with lower risk versus placebo interventions (8 trials, RR 0.62, 95% CI 0.41 to 0.92, I2=0%), but the estimate was no longer statistically significant after exclusion of poor-quality trials (5 trials, RR 0.69, 95% CI 0.42 to 1.13, I2=0%)
Risk of surgery, intermediate-term	1 trial N=36	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	No difference (1 trial, RR 0.56, 95% CI 0.12 to 2.68)
Risk of surgery, long-term	14 trials N=1208	Moderate	Consistent	Direct	Precise	Moderate	No difference (14 trials, RR 0.97, 95% CI 0.75 to 1.25, I2=23%)
Successful composite outcome, short-term	9 trials N=604	Moderate	Consistent	Direct	Precise	Moderate	No difference (9 trials, RR 1.13, 95% CI 0.98 to 1.32, I2=3.5%)
Successful composite outcome, intermediate-term	1 trial N=58	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	No difference (1 trial, RR 0.71, 95% CI 0.34 to 1.48)
Successful composite outcome, long-term	2 trials N=153	Moderate	Consistent	Direct	Imprecise	Low	No difference (2 trials, 1.04, 95% CI 0.81 to 1.34, I2=0%)
Epidural corticosteroid injections versus other interventions							
Pain, function, surgery	2 trials N=150	High	Inconsistent	Direct	Imprecise	Insufficient	There was insufficient evidence from two trials to determine effects of epidural corticosteroid injections versus discectomy, due to methodological shortcomings in the trials

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Pain function, surgery	1 trial N=90	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found epidural corticosteroid injections associated with lower likelihood than minimally invasive lumbar decompression of achieving ≥ 25 point improvement in leg pain (RR 0.49, 95% CI 0.24 to 1.0), ≥13 point improvement in ODI (RR 0.34, 95% CI 0.34 to 0.95), and ≥5 point improvement in SF-36 (RR 0.34, 95% CI 0.12 to 0.95) through 2 years. There was no difference in risk of undergoing surgery (RR 0.45, 95% CI 0.09 to 2.19)
Pain, function, surgery	1 trial N=26	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Insufficient	There was insufficient evidence from one small, fair-quality trial to determine effects of epidural corticosteroid injections versus epidural clonidine injection
Pain, function, analgesic use	1 trial N=132	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found transforaminal epidural corticosteroid injection superior to etanercept on the ODI at 1 month (difference -16 on 0 to 100 scale, 95% CI -26.0 to -6.27). There were no differences on other outcomes, including pain and analgesic use
Pain, function	1 trial N=72	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no differences between epidural corticosteroid versus autologous conditioned serum administered via the oblique interlaminar approach in improvement in pain or ODI scores after 22 weeks
Pain, function, surgery	2 trials N=151	High	Inconsistent	Direct	Imprecise	Insufficient	There was insufficient evidence from two trials to determine effects of epidural corticosteroid injections versus non-surgical, non-interventional therapies due to methodological shortcomings in the trials and differences in the non-surgical, non-interventional therapies evaluated
Pain, function	1 trial N=53	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found transforaminal epidural corticosteroid injection with corticosteroid plus hypertonic saline associated with greater decrease in pain intensity through 4 months than a corticosteroid injection alone (difference from baseline -2.78 vs. -1.50 on 0 to 10 NRS, p=0.05), though the effect was smaller and no longer statistically significant at 6 months. There were no differences in global

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
							assessment or the ODI
Pain, function	1 trial N=177	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no difference between transforaminal epidural injection with corticosteroid versus corticosteroid plus low-dose clonidine in pain scores through 12 weeks in patients with subacute low back pain
Epidural injections for spinal stenosis							
Epidural corticosteroid injections versus placebo interventions							
Mean improvement in pain, immediate-term	1 trial N=29	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	Epidural corticosteroid injection was superior to placebo at intermediate-term (1 trial, WMD -22.0, 95 % -36.0 to -8.0)
Mean improvement in pain, short-term	5 trials N=615	Moderate	Consistent	Direct	Precise	Moderate	No difference (5 trials, WMD 0.62, 95% CI -2.87 to 4.11, I2=0%)
Mean improvement in pain, intermediate-term	3 trials N=179	Moderate	Consistent	Direct	Imprecise	Low	No difference (3 trials, WMD 3.73, 95% CI -0.81 to 8.26, I2=0%)
Mean improvement in pain, long-term	1 trial N=100	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	No difference (1 trial, mean difference 4.00, 95% CI -2.87 to 10.9)
Successful pain outcome, short-term	3 trials N=546	Moderate	Consistent	Direct	Imprecise	Low	No difference (3 trials, RR 0.98, 95% CI 0.84 to 1.15, I2=0%)
Successful pain outcome, intermediate-term	2 trials N=160	Moderate	Consistent	Direct	Imprecise	Low	No difference (2 trials, RR 0.98, 95% CI 0.78 to 1.24, I2=0%)
Successful pain outcome, long-term	3 trials N=197	Moderate	Consistent	Direct	Imprecise	Low	No difference (3 trials, RR 0.97, 95% CI 0.74 to 1.28, I2=0%)
Mean improvement in function, immediate-term	2 trials N=55	Moderate	Consistent	Direct	Imprecise	Low	No difference (2 trials, SMD -0.32, 95% CI -0.85 to 0.22, I2=0%)
Mean improvement in function, short-term	5 trials N=615	Moderate	Consistent	Direct	Precise	Moderate	No difference (5 trials, SMD -0.03, 95% CI -0.31 to 0.26, I2=60%)

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Mean improvement in function, intermediate-term	3 trials N=179	Moderate	Consistent	Direct	Imprecise	Low	No difference (3 trials, WMD 2.81, 95% CI -0.44 to 6.06, I2=0%)
Mean improvement in function, long-term	2 trials N=160	Moderate	Consistent	Direct	Imprecise	Low	No difference (2 trials, WMD 2.78, 95% CI -1.24 to 6.79, I2=0%)
Successful functional outcome, short-term	3 trials N=546	Moderate	Consistent	Direct	Imprecise	Low	No difference (3 trials, RR 0.91, 95% CI 0.70 to 1.18, I2=37%)
Successful functional outcome, intermediate-term	2 trials N=160	Moderate	Consistent	Direct	Imprecise	Low	No difference (2 trials, RR 0.96, 95% CI 0.74 to 1.25, I2=0%)
Successful functional outcome, long-term	2 trials N=160	Moderate	Consistent	Direct	Imprecise	Low	No difference (2 trials, RR 0.95, 95% CI 0.71 to 1.26, I2=0%)
Successful composite outcome, short-term	2 trials N=136	Moderate	Inconsistent	Direct	Imprecise	Low	No difference (2 trials, RR 1.18, 95% CI 0.55 to 2.55, I2=80%)
Successful composite outcome, intermediate-term	1 trial N=100	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	No difference (1 trial, RR 0.93, 95% CI 0.63 to 1.35)
Successful composite outcome, long-term	2 trials N=130	Moderate	Consistent	Direct	Imprecise	Low	No difference (2 trials, RR 1.16, 95% CI 0.76 to 1.78, I2=0%)
Risk of surgery, long-term	1 trial N=30	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	No difference (1 trial, RR 0.76, 95% CI 0.38 to 1.54)
Epidural corticosteroid injections versus other interventions							
Pain, function	1 trial N=38	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found an epidural corticosteroid injection associated with lower likelihood of experiencing ≥2 point improvement in pain at 2 weeks versus the minimally invasive lumbar decompression procedure, but the difference was no longer present at 6 weeks. There was no difference in function
Pain, function	1 trial N=23	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no differences between and epidural corticosteroid injection versus intense physical therapy in pain intensity or functional outcomes at 2 weeks through 6 months
Pain, function	1 trial N=80	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found epidural corticosteroid injection associated with worse leg pain than epidural etanercept injection at 1 month, with no difference in functional outcomes

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Pain, function	1 trial N=50	High	Cannot determine (1 trial)	Direct	Imprecise	Insufficient	There was insufficient evidence from one poor-quality trial to determine effects of epidural corticosteroid injections versus epidural adhesiolysis
Epidural corticosteroid injections versus placebo interventions for non-radicular low back pain							
Pain, function, opioid use	2 trials N=240	Moderate	Consistent	Direct	Imprecise	Low	Two trials found no differences between epidural corticosteroid injections and epidural local anesthetic injections in pain, function, or opioid use
Epidural injections for chronic post-surgical pain							
All outcomes	0 trials	No evidence	No evidence	No evidence	No evidence	Insufficient	No trial compared an epidural injection with corticosteroid versus a placebo intervention
All outcomes	5 trials N=274	High	Inconsistent	Direct	Imprecise	Insufficient	Evidence from 5 trials was insufficient to determine effects of epidural corticosteroid injections versus other interventions, due to methodological limitations, differences in the comparators evaluated, and small sample sizes
Facet joint injections							
Pain, function	2 trials N=171	Moderate	Consistent	Direct	Imprecise	Low	Two trials found no clear differences between an intra-articular facet joint injection with corticosteroid versus saline in pain or function at one to three months
All outcomes	1 trial N=67	High	Cannot determine (1 trial)	Direct	Imprecise	Insufficient	Evidence from one small, poor-quality trial was insufficient to determine effects of an intra-articular corticosteroid facet joint injection versus medial branch local anesthetic injection
All outcomes	1 trial N=81	High	Cannot determine (1 trial)	Direct	Imprecise	Insufficient	Evidence from one poor-quality trial was insufficient to determine effects of an extra-articular facet joint corticosteroid injection versus intra-articular saline injection

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Pain, function, opioid use	2 trials N=204	Moderate	Consistent	Direct	Imprecise	Low	Two trials found no differences between medial branch corticosteroid injection versus medial branch local anesthetic injection in pain, function, or opioid use through 12 to 24 months
Pain, function, quality of life	1 trial N=60	Low	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no clear differences between an intra-articular facet joint versus an intramuscular corticosteroid injection in pain, function, or quality of life through 6 months
Pain, function, quality of life	1 trial N=60	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no differences between intra-articular facet injection with triamcinolone acetonide versus hyaluronic acid in pain or function at 1 month or in health-related quality of life at 1 week
Pain, function, analgesic use	1 trial N=56	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no differences between intra-articular corticosteroid injection plus sham neurotomy versus medial branch radiofrequency facet neurotomy plus local anesthetic injection in pain, function, or analgesic use at six months
Pain, quality of life	1 trial N=100	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One fair-quality trial found medial branch corticosteroid injection inferior to radiofrequency facet denervation on pain at 1, 6, and 12 months, with no differences in quality of life (1, 6, and 12 months), but results may have been confounded by differential use of diagnostic blocks to select patients for inclusion
Sacroiliac joint injections							
All outcomes	1 trial N=24	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Insufficient	There was insufficient evidence from one small (n=24) trial to determine effects of periarticular sacroiliac corticosteroid injection versus local anesthetic injection

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Key Question 1a. How does effectiveness vary according to the medication (corticosteroid, local anesthetic) used, the dose or frequency of injections, the number of levels treated, or degree of provider experience?							
Epidural injections							
Epidural corticosteroid injections for radiculopathy							
Effects of different corticosteroids: all outcomes	4 trials[a] N=329	Moderate	Inconsistent	Direct	Imprecise	Low	Four trials that directly compared epidural corticosteroid injections for radiculopathy with different corticosteroids found few differences in outcomes including pain and function, but conclusions were limited by differences in the corticosteroids compared, doses, and some inconsistency
Effects of different local anesthetics: all outcomes	0 trials[a]	No direct evidence	No direct evidence	Indirect	No direct evidence	Insufficient	No trial directly compared effects of epidural corticosteroid injections with one local anesthetic versus another
Effects of corticosteroid dose: all outcomes	6 trials[a] N=506	Moderate	Consistent	Direct	Imprecise	Low	Six trials that directly compared epidural injections for radiculopathy using different corticosteroid doses found no clear differences in outcomes including pain and function
Effects of number of injections, number of levels injected, or provider experience: all outcomes	2 trials N=334	Moderate	Consistent	Indirect	Imprecise	Low for number of injections, insufficient for number of levels and provider experience	No trial directly compared the effectiveness of epidural corticosteroid injections based on the number of injections, number of levels injected, or provider experience. Two trials found no association between receipt of more injections and better outcomes

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Epidural corticosteroid injections for spinal stenosis							
Effects of corticosteroids: pain, claudication distance	1 trial N=70	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no clear differences between caudal epidural injection for spinal stenosis with methylprednisolone versus triamcinolone in pain or claudication distance through 6 months, though results favored methylprednisolone
Facet joint injections							
Effects of different corticosteroids, local anesthetics, doses, frequency or number of injections, or degree of provider experience	0 trials[a]	No direct evidence	No direct evidence	Indirect	No direct evidence	Insufficient	No trial of facet joint injections directly compared effects of different corticosteroids, different local anesthetics, different doses, different frequency or number of injections, or degree of provider experience. Indirect evidence was too limited to reach reliable conclusions
Key Question 1b. How does effectiveness vary according to use of imaging guidance or route of administration (e.g., for epidural injections interlaminar, transforaminal, caudal for epidural injections and for facet joint injections intra-articular, extra-articular [pericapsular] or medial branch injections)?							
Epidural injections							
Use of imaging							
Effects of imaging guidance versus no imaging guidance: All outcomes	0 trials[a]	No direct evidence	No direct evidence	Indirect	No direct evidence	Insufficient	No trial directly compared the effectiveness of epidural injections for radiculopathy performed with or without imaging guidance. Indirect evidence was not useful for evaluating effects of imaging guidance on estimates of effects because use of imaging guidance was highly associated with the epidural technique used
Effects of fluoroscopic plus Doppler versus fluoroscopic imaging guidance: Pain, function	1 trial N=110	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial of caudal epidural corticosteroid injections for radiculopathy found no difference between fluoroscopic plus Doppler guidance versus fluoroscopic guidance alone in pain or ODI scores through 12 weeks

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Effects of imaging to guide epidural injection targets: Pain, function, medication use	1 trial N=132	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no difference between use of MRI versus history and physical examination without MRI to guide epidural corticosteroid injection treatment and targets on pain, function, or medication use
Transforaminal versus interlaminar corticosteroid injections[a]							
Mean improvement in pain, immediate-term	5 trials N=227	Moderate	Inconsistent	Direct	Imprecise	Low	No difference (5 trials, WMD -10.1, 95% CI -24.8 to 4.63, I2=83%)
Mean improvement in pain, short-term	3 trials N=125	Moderate	Inconsistent	Direct	Imprecise	Low	No difference (3 trials, WMD -1.29, 95% CI -12.6 to 10.1, I2=54%)
Mean improvement in pain, intermediate-term	2 trials N=95	Moderate	Inconsistent	Direct	Imprecise	Low	No difference (2 trials, WMD -11.3, 95% CI -44.8 to 22.2, I2=87%)
Mean improvement in function, immediate-term	4 trials N=197	Moderate	Inconsistent	Direct	Imprecise	Low	No difference (4 trials, SMD 0.03, 95% CI -0.48 to 0.53, I2=68%)
Mean improvement in function, short-term	3 trials N=125	Moderate	Inconsistent	Direct	Imprecise	Low	No difference (3 trials, SMD 0.39, 95% CI -0.36 to 1.13, I2=74%)
Mean improvement in function, long-term	1 trial N=64	Low	Cannot determine (1 trial)	Direct	Imprecise	Low	No difference (1 trial, WMD -2.00, 95% CI -8.77 to 4.77)
Likelihood of undergoing surgery, intermediate-term	2 trials N=61	Moderate	Inconsistent	Direct	Imprecise	Low	There were no differences between transforaminal versus interlaminar epidural corticosteroid injections for radiculopathy in risk of undergoing surgery at intermediate-term in two trials (RR 0.76, 95% CI 0.18 to 3.19 and RR 1.33, 95% CI 0.44 to 4.05)

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Comparisons of other approaches							
Epidural injections for radiculopathy							
Caudal versus other approaches: Pain, function, depression	1 trial N=60	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found the transforaminal epidural corticosteroid injections for radiculopathy associated with better pain outcomes than the caudal approach, with no differences in measures of function or depression, but no differences between the interlaminar versus caudal approaches in measures of pain or depression
Oblique versus standard interlaminar approaches: Successful composite outcome, surgery	1 trial N=87	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no differences between epidural corticosteroid injections for radiculopathy using the oblique interlaminar versus standard interlaminar approaches in likelihood of achieving a successful outcome or undergoing surgery
Lateral parasagittal versus standard interlaminar approaches: Pain, function	2 trials N=143	Moderate	Consistent	Direct	Imprecise	Low	One trial of epidural corticosteroid injections for radiculopathy found the lateral parasagittal interlaminar approach associated with greater likelihood of achieving >50% pain relief (RR 4.1, 95% CI 1.4 to 12) and greater improvement in pain and function than the standard interlaminar approach through 6 months; a second trial also reported results that favored the lateral parasagittal approach, but differences were smaller and not statistically significant
Lateral parasagittal versus transforaminal approaches: Pain	2 trials N=119	Moderate	Consistent	Direct	Imprecise	Low	Two trials found no differences between epidural corticosteroid injections for radiculopathy using the lateral parasagittal versus transforaminal approaches in pain or function through 6 or 12 months
Ganglionic versus preganglionic transforaminal injections: Successful composite outcome	1 trial N=239	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found transforaminal epidural corticosteroid injections for radiculopathy at the ganglionic versus preganglionic approaches associated with a lower likelihood of a successful outcome at 1 month (RR 0.80, 95% CI 0.70 to 0.91), though differences were no longer present after 5 months

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Epidural injections for spinal stenosis							
Transforaminal versus interlaminar: Leg pain, function	1 trial (subgroup analysis) N=400	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	No trial randomized patients with spinal stenosis to different approaches for performing epidural corticosteroid injections. One trial in which epidural corticosteroid injections could be performed by the interlaminar or transforaminal approaches found that interlaminar corticosteroid injections were associated with greater improvement in leg pain and function versus local anesthetic injections at 3 weeks, but there were no differences between transforaminal corticosteroid versus local anesthetic injections
Facet joint injections							
Intra-articular facet joint corticosteroid injection: Pain	1 trial N=46	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found intra-articular facet joint corticosteroid injection in patients with subacute low back pain selected on the basis of positive facet joint SPECT findings associated with lower pain intensity (3.2 vs. 5.4 on 0 to 10 NRS, $p<0.05$), greater likelihood of ≥50% pain relief (61% vs. 26%, RR 2.33, 95% CI 1.09 to 5.00), and better ODI score (12 vs. 23, $p<0.05$). versus medial branch injection at 12 weeks
Intra-articular facet joint versus medial branch corticosteroid injection for chronic low back pain (imaging findings not required): Pain	1 trial N=86	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found intra-articular facet joint corticosteroid injection associated with higher likelihood of pain relief versus medial branch injection at 1 month (RR 1.68, 95% CI 1.03 to 2.73), but results were no longer statistically significant at 3 months, and there was no difference in likelihood of experiencing good or excellent pain relief
Intra-articular versus extra-articular (pericapsular) facet joint corticosteroid injection: All outcomes	1 trial N=67	High	Cannot determine (1 trial)	Direct	Imprecise	Insufficient	There was insufficient evidence from one poor-quality trial to determine effectiveness of intra- versus extra-articular (pericapsular) facet joint corticosteroid injections
Effects of imaging guidance versus no imaging guidance: All outcomes	0 trials	No evidence	No evidence	No evidence	No evidence	Insufficient	No trial directly compared the effectiveness of epidural injections for radiculopathy performed with or without imaging guidance

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Effects of CT- versus ultrasound imaging guidance: Pain	1 trial N=40	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no difference between CT- versus ultrasound-guided intra-articular facet joint corticosteroid injections with betamethasone and local anesthetic in pain at 6 weeks
Key Question 2. In patients with low back pain, what patient characteristics predict responsiveness to injection therapies on outcomes related to pain, function, and quality of life?							
Epidural injections							
Effects of duration: Pain, function	6 trials N=869	Moderate	Consistent	Indirect	Precise	Low	Five of six trials of patients with radiculopathy found no association between duration of symptoms and responsiveness to epidural corticosteroid injections
Effects of age, sex, anxiety/depression, opioid use, baseline function, presence of neurological abnormalities, previous episodes, or work status: Pain, function	6 trials N=869	Moderate	Consistent	Indirect	Precise	Low	Trials or patients with radiculopathy found no association between age, sex, anxiety/depression, opioid use, baseline function, presence of neurological abnormalities, previous episodes, or work status and responsiveness to epidural corticosteroid injections
Effects of cause of radicular symptoms: Pain, function	4 trials N=406	Moderate	Inconsistent	Indirect	Imprecise	Insufficient	There was insufficient evidence from 4 trials to determine effects of the cause of radicular symptoms on responsiveness to epidural corticosteroid injections for radiculopathy, due to inconsistent results
Effects of smoking status, body mass index, use of opioid therapies: Pain, function	0 trials	No evidence	No evidence	No evidence	No evidence	Insufficient	No study evaluated the association between smoking status, body mass index, or opioid therapies on responsiveness to epidural corticosteroid injection therapies for radiculopathy
Effects of pain, function	29 trials used in meta-regression analyses N=2792	Moderate	Consistent	Indirect	Imprecise	Low	Based on meta-regression analyses of trials of epidural corticosteroid injections versus placebo interventions for radiculopathy, there was no clear association between prior lumbar surgery, requirement for imaging correlation with symptoms, or requirement for presence of herniated disc on imaging and estimates of treatment effect

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Effects of race: All outcomes	1 trial N=400	Moderate	Cannot determine (1 trial)	Indirect	Imprecise	Low	One trial of patients with spinal stenosis found no interaction between race and responsiveness to epidural corticosteroid injections
Effects of pain, patient satisfaction	1 trial N=192	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial of patients with non-radicular low back pain found no differences between transforaminal versus interlaminar epidural corticosteroid injection in pain or a patient satisfaction index in the subgroup of patient with imaging findings of a herniated disc, but in patients with spinal stenosis effects on pain favored the transforaminal approach (1.79 vs. 2.19 on the 0 to 5 Roland pain score, $p<0.05$; likelihood of improving ≥2 points 51% vs. 31%, RR 1.64, 95% CI 0.98 to 2.76)
Facet joint injections							
Effects of use of SPECT versus no SPECT to identify targets for facet joint injections: Pain	1 trial N=46	Moderate	Cannot determine (1 trial)	Direct	Imprecise	Low	One trial found no difference between use of SPECT bone scans versus no SPECT to identify targets for intra- and extra-articular facet joint corticosteroid injections in pain outcomes through 6 months

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Key Question 3. In randomized trials of low back pain injection therapies, how does effectiveness vary according to the control therapy used (e.g., epidural nonsteroid injection, nonepidural injection, no injection)?							
Epidural injections							
Effects of type of placebo intervention in patients with radiculopathy: Pain, function	29 trials included in stratified analyses N=2792	Moderate	Consistent	Indirect	Imprecise	Low	In trials of epidural corticosteroid injections versus placebo injections for radiculopathy, there were no clear differences in estimates for improvement in pain or function, likelihood of a successful pain or functional outcome, or likelihood of undergoing surgery when trials were stratified according to the type of placebo intervention
Effects of type of control intervention in patients with radiculopathy: All outcomes	11 trials N=896	Moderate	Consistent	Indirect	Imprecise	Insufficient	Trials of epidural corticosteroid injections versus other interventions were too limited to determine effects on outcome estimates, due to variability in the interventions evaluated, small numbers of trials, and methodological limitations
Effects of type of placebo intervention in patients with other back conditions: All outcomes	20 trials N=1880	Moderate	Consistent	Indirect	Imprecise	Insufficient	There was insufficient evidence from trials of epidural corticosteroid injections for spinal stenosis, non-radicular back pain, or chronic post-surgical pain, to determine effects of comparators on estimates of effect, due to small numbers of trials for specific comparisons

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Facet joint injections							
Effects of type of placebo therapy:	8 trials N=589	Moderate	Consistent	Indirect	Imprecise	Insufficient	There was insufficient evidence from trials facet joint injections to determine effects of comparators on estimates of effect, due to small numbers of trials for specific comparisons
Key Question 3a. How do response rates vary according to the specific comparator evaluated (e.g., saline epidural, epidural with local anesthetic, nonepidural injection, no injection, surgery, non-surgical therapies)?							
Epidural injections for radiculopathy							
Epidural corticosteroid injections versus placebo interventions (direct comparisons): Pain, function, successful outcome	3 trials N=340	Moderate	Consistent	Direct	Imprecise	Low	Three trials found no differences between epidural local anesthetic versus epidural saline injections (3 trials) or soft tissue injections (2 trials) in mean improvements in pain or function or the proportion experiencing pain relief or a successful outcome
Epidural corticosteroid injections versus placebo interventions (indirect comparisons): Pain function	29 trials included in stratified analyses N=2792	Moderate	Inconsistent	Indirect	Precise	Low	In trials of epidural corticosteroid injections for radiculopathy, improvement in pain was smaller in patients who received epidural local anesthetic injections (3 trials, WMD –6.51, 95% CI –11.9 to –1.16, I2=45%) than epidural saline injections (4 trials, WMD –19.8, 95% CI –25.1 to –14.3, I2=56%) at immediate-term; there were no clear differences at other time points, but analyses were limited by small numbers of trials and statistical heterogeneity
Epidural corticosteroid injections versus other interventions: Pain, function	11 trials N=896	Moderate	Consistent	Indirect	Imprecise	Insufficient	Trials were too limited to determine effects on response rates, due to variability in the interventions evaluated, small numbers of trials, and methodological limitations

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Key Question 4. What are the harms of epidural corticosteroid, facet joint corticosteroid injections, medial branch blocks, and sacroiliac joint corticosteroid injection compared to epidural nonsteroid injection, nonepidural injection, no injection, surgery, or non-surgical therapies?							
Epidural injections							
Harms	29 trials N=2792	High	Consistent	Direct	Precise	Moderate	29 trials of epidural corticosteroid injections versus placebo for radiculopathy reported no serious adverse events and few harms, but methods for assessing harms were not well reported and harms data were sparse. Observational studies were consistent with the trials in showing a low risk of serious adverse events
Harms	11 trials N=896	High	Consistent	Direct	Precise	Moderate	Eleven trials of epidural corticosteroid injections versus other therapies for radiculopathy reported no serious adverse events and few harms
Harms	2 trials N=120	High	Consistent	Direct	Imprecise	Low	Two trials of transforaminal versus interlaminar epidural corticosteroid injections for radiculopathy reported no serious adverse events
Harms	4 trials N=324	High	Inconsistent	Direct	Imprecise	Insufficient	There was insufficient evidence from four trials that compared epidural injections for radiculopathy with different corticosteroids to determine effects on harms
Harms	5 trials N=452	High	Inconsistent	Direct	Imprecise	Insufficient	There was insufficient evidence from five trials of epidural corticosteroid injections for radiculopathy that compared different doses to determine effects on harms
Harms	8 trials N=821	High	Consistent	Direct	Precise	Low	Eight trials of epidural corticosteroid injections versus placebo injections for spinal stenosis reported no serious harms and few adverse events, but methods for assessing harms were not well reported and harms data were sparse

Appendix G. Strength of Evidence

Key Question Outcome	Study Design Number of Studies (N)	Risk of bias	Consistency	Directness	Precision	Strength of Evidence	Conclusion
Harms	2 trials N=240	High	Consistent	Direct	Imprecise	Low	Two trials of epidural corticosteroid injections for non-radicular back pain reported no serious harms
Harms	4 trials N=322	High	Inconsistent	Direct	Imprecise	Insufficient	There was insufficient evidence from four trials of epidural corticosteroid injections for chronic post-surgical back pain to determine effects on harms
Facet joint injections							
Harms	10 trials N=823	High	Consistent	Direct	Imprecise	Low	Ten trials of facet joint corticosteroid injections reported no serious harms and few adverse events, but methods for assessing harms were not well reported and harms data sparse
Sacroiliac joint injections							
Harms	1 trial N=24	High	Cannot determine (1 trial)	Direct	Imprecise	Insufficient	Harms were not reported in one small trial of periarticular sacroiliac joint injections

[a] Study number based on number of trials directly evaluating the comparison of interest

CI=confidence interval; ODI= Oswestry Disability Index; RR=relative risk; SMD=standard mean difference; SPECT= single photon electronic computed tomography; WMD=weighted mean difference

Please see Appendix C. Included Studies for full study references.