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.