Washington State Health Care Authority

Health Technology Assessment

Spinal Injections – Re-review

Final Evidence Report: Appendices

February 12, 2016

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Spinal Injections (Re-review)

Provided by:

Spectrum Research, Inc.

Final Report
APPENDICES

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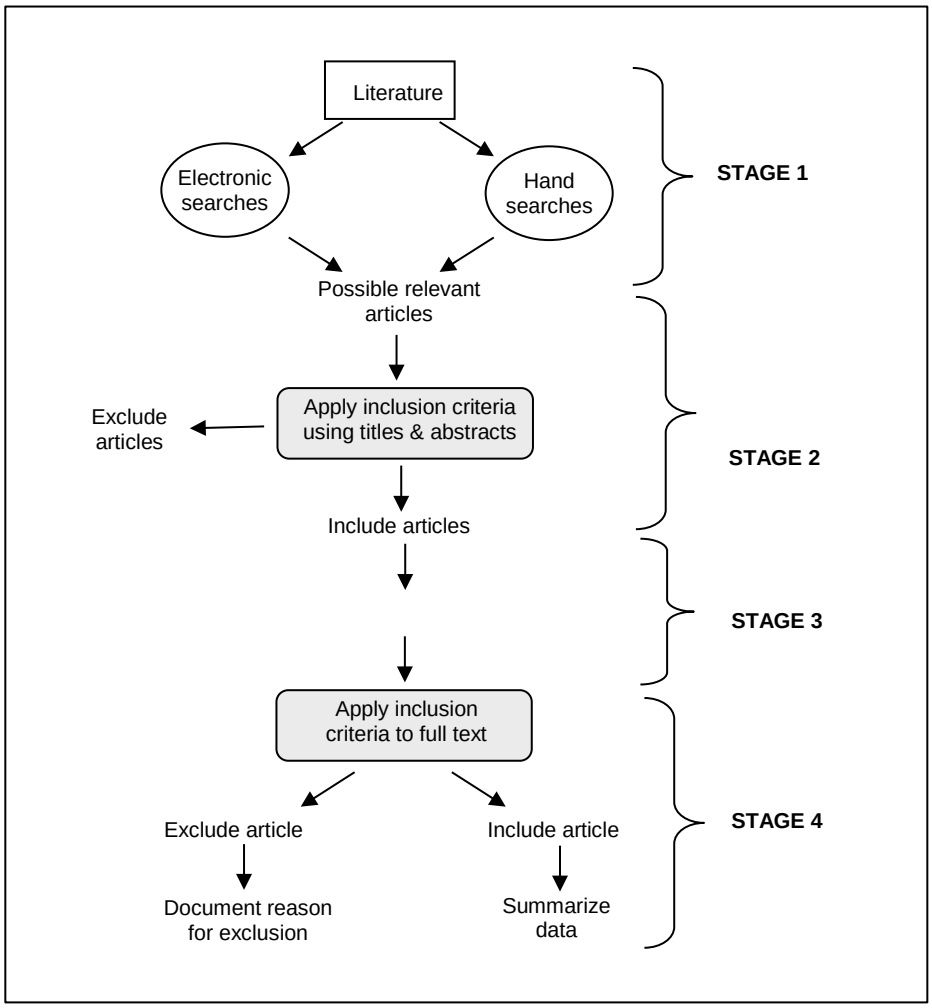
APPENDIX A. Algorithm for Article Selection



APPENDIX B. Search Strategies

Below is the search strategy for PubMed. Parallel strategies were used to search other electronic databases listed below. Keyword searches were conducted in the other listed resources.

Search strategy (PubMed)
Search date: 01/01/2010 to 07/24/2015
(2010 HTA: search done through August 2010)

Originally ran two searches and combined results
Total number of citations from both searches (conducted 07/24/2015 by RH): 1104

Filters: Abstract available, English
Database: Pubmed

		2015 HTA	2011 HTA
1.	"Injections, Spinal"[MESH]	1952	10,085
2.	Injection*	105,223	448,700
3.	Epidural OR facet OR sacroiliac OR intradiscal	10,982	34,438
4.	#2 AND #3	1554	5163
5.	"medial branch"	155	281
6.	#4 OR #5	1664	5392
7.	#1 AND #6	581	2157
8.	Pain	155,118	352,335
9.	Back OR neck OR spinal OR cervical OR lumbar OR sacral	196,184	537,833
10.	#8 AND #9	32,877	69,424
11.	#7 AND #10	402	1018
12.	#11 NOT (In Vitro[Publication Type] OR Cadaver*[tw] OR Case Reports[Publication Type] OR Infant[mh] OR Child[mh] OR Adolescent[mh] OR rat[tw] OR rats[tw] OR mouse[tw] OR mice[tw] OR dog[tw] or dogs[tw])	301	677

OR

Limit: Abstract available, English

		2015 HTA	2011 HTA
1.	Spine[mh] OR Spinal Nerve Roots[mh]	22024	86,137
2.	spine[tw] OR spinal[tw] OR back[tw] OR coccyx[tw] OR intervertebral disk[tw] OR lumbar vertebrae[tw] OR cervical vertebrae[tw] OR sacral[tw] OR sacrum[tw] OR spinal canal[tw] OR facet joint[tw] OR sacroiliac[tw] OR intradisc*[tw]	113,697	338,623
3.	#1 OR #2	114,615	341,398
4.	Injection*[tw] OR Injections, Spinal[mh]	105,299	449,042

		2015 HTA	2011 HTA
5.	"medial branch block*"[tw]	21	19
6.	(Spine*[tw] or spinal*[tw] or nerv*[tw]) AND block*[tw]	15,739	64,887
7.	Anesthesia, Conduction[mh]	5124	33,577
8.	Anesthetics[mh] OR Anti-Inflammatory Agents[mh]	35,583	132,872
9.	#4 OR #5 OR #6 OR #7 OR #8	149,891	632,739
10.	#9 NOT (extraspinal[tw] or Botulinum[tw] OR prolotherap*[tw] OR chemonucleolysis[tw] or chemonucleolysis[mh] OR radiofrequency denerv*[tw] OR intradiscal electrothermal*[tw] OR coblation[tw])	147,541	627,815
11.	Spinal Diseases[mh] OR Peripheral Nervous System Diseases[mh]	30,148	124,181
12.	Spinal disease*[tw] OR hyperostosis[tw] OR spinal stenosis[tw] OR intervertebral disk displacement[tw] OR spinal osteophytosis[tw] OR hyperostosis[tw] OR diffuse idiopathic skeletal[tw] OR Sciatica[tw] OR radicul*[tw]	7161	31,588
13.	Back Pain[mh] OR Neck Pain[mh] OR Back Pain[tw]	12,673	24,812
14.	#11 OR #12 OR #13	42,560	150,069
15.	#14 NOT (Nervous System Neoplasms[mh] OR Spinal Neoplasms[mh] OR Neoplasms[mh] OR Labor, Obstetric[mh] OR labor[tw] OR labour[tw] OR cauda equina syndrome*[tw] OR fibromyalg*[tw] OR spondylo*[tw] OR spondyliti*[tw] OR vertebral compression fracture*[tw] OR osteoporo*[mh] OR Osteoporosis[mh])	31,975	104,454
14.	#3 AND #10 AND #15	2066	4583
15.	#14 NOT (In Vitro[Publication Type] OR Cadaver*[tw] OR Case Reports[Publication Type] OR Infant[mh] OR Child[mh] OR Adolescent[mh] OR rat[tw] OR rats[tw] OR mouse[tw] OR mice[tw] OR dog[tw] or dogs[tw])	1021	2352

Parallel strategies were used to search the Cochrane Library and others listed below. Keyword searches were conducted in the other listed resources.

Electronic Database Searches

The following databases have been searched for relevant information:

Agency for Healthcare Research and Quality (AHRQ)
Cumulative Index to Nursing and Allied Health (CINAHL)
Cochrane Database of Systematic Reviews
Cochrane Registry of Clinical Trials (CENTRAL)
Cochrane Review Methodology Database
Database of Reviews of Effectiveness (Cochrane Library)
EMBASE
PubMed
Informational Network of Agencies for Health Technology Assessment (INAHTA)
NHS Economic Evaluation Database
HSTAT (Health Services/Technology Assessment Text)
EconLIT

Additional Economics, Clinical Guideline and Gray Literature Databases

AHRQ - Healthcare Cost and Utilization Project
Canadian Agency for Drugs and Technologies in Health
Centers for Medicare and Medicaid Services (CMS)
Food and Drug Administration (FDA)
Google
Institute for Clinical Systems Improvement (ICSI)
National Guideline Clearinghouse

APPENDIX C. Excluded Articles

Articles excluded as primary studies after full text review, with reason for exclusion.

	Citation	Reason for exclusion after full-text review
	RCTs considered and excluded	
1.	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.	Wrong population: duration of LBP not reported
2.	Ghahreman, A. and N. Bogduk (2011). "Predictors of a favorable response to transforaminal injection of steroids in patients with lumbar radicular pain due to disc herniation." Pain Med **12**(6): 871-879.	Wrong study type: no control group, study not designed to evaluate harms.
3.	Kawu, A. A., et al. (2011). "Facet joints infiltration: a viable alternative treatment to physiotherapy in patients with low back pain due to facet joint arthropathy." Niger J Clin Pract **14**(2): 219-222.	Wrong study type: observational study not designed to evaluate harms.
4.	Kraemer, J., et al. (1997). "Lumbar epidural perineural injection: a new technique." Eur Spine J **6**(5): 357-361.	Wrong population: duration of LBP not reported
5.	Laiq, N., et al. (2009). "Comparison of Epidural Steroid Injections with conservative management in patients with lumbar radiculopathy." J Coll Physicians Surg Pak **19**(9): 539-543.	Wrong population: duration of LBP not reported; for inclusion duration was required to be 2 weeks
6.	Mathews, J. A., et al. (1987). "Back pain and sciatica: controlled trials of manipulation, traction, sclerosant and epidural injections." Br J Rheumatol **26**(6): 416-423.	Wrong population: duration of pain < 4 weeks in ~50% of patients (median duration of pain was 4 weeks)
7.	Nash, T. (1990). "Facet joints-intra-articular steroids or nerve block." Pain Clinic **3**(2): 77-82.	Wrong population: duration of LBP not reported
8.	Peng, B., et al. (2010). "A randomized placebo-controlled trial of intradiscal methylene blue injection for the treatment of chronic discogenic low back pain." Pain **149**(1): 124-129.	Wrong intervention: steroids not injected.
9.	Radcliff, K., et al. (2012). "The impact of epidural steroid injections on the outcomes of patients treated for lumbar disc herniation: a subgroup analysis of the SPORT trial." J Bone Joint Surg Am **94**(15): 1353-1358.	Wrong study type: observational study not designed to evaluate harms.
10.	Radcliff, K., et al. (2013). "Epidural steroid injections are associated with less improvement in patients with lumbar spinal stenosis: a subgroup analysis of the Spine Patient Outcomes Research Trial." Spine (Phila Pa 1976) **38**(4): 279-291.	Wrong study type: observational study not designed to evaluate harms.
11.	Spijker-Huiges, A., et al. (2014). "Steroid injections added to the usual treatment of lumbar radicular syndrome: a pragmatic randomized controlled trial in general practice." BMC	Wrong population: acute LBP only.

	Citation	Reason for exclusion after full-text review
	Musculoskelet Disord **15**: 341.	
12.	Valat, J. P., et al. (2003). "Epidural corticosteroid injections for sciatica: a randomised, double blind, controlled clinical trial." Ann Rheum Dis **62**(7): 639-643.	Wrong population: duration of pain < 4 weeks in >20% patients (mean duration of pain was 16 days)
13.	Grunnesjö, M. I., et al. (2011). "A randomized controlled trial of the effects of muscle stretching, manual therapy and steroid injections in addition to 'stay active' care on health-related quality of life in acute or subacute low back pain." Clin Rehabil 25(11): 999-1010.	Wrong intervention (# of treatment modalities)
14.	Zhang, Y., et al. (2013). "Treatment of the lumbar disc herniation with intradiscal and intraforaminal injection of oxygen-ozone." J Back Musculoskelet Rehabil 26(3): 317-322.	Wrong intervention (study of chemiodiscolysis using O2-O3)
15.	Kim, S. B., et al. (2012). "The effect of hyaluronidase in interlaminar lumbar epidural injection for failed back surgery syndrome." Ann Rehabil Med 36(4): 466-473.	Wrong intervention (study of hyaluronidase)
16.	Kim, S. B., et al. (2011). "The additional effect of hyaluronidase in lumbar interlaminar epidural injection." Ann Rehabil Med 35(3): 405-411.	Wrong intervention (study of hyaluronidase)
17.	Manchikanti L. et al (2009). “The preliminary results of a comparative effectivenesss evaluation of adhesiolysis and caudal epidural injections in managing chronic low back pain secondary to spinal stenosis: a randomized, equivalence controlled trial.” Pain Physician. 2009;12:E341-54.	Wrong intervention (adhesiolysis)
18.	Manchikanti L, et al. (2009) “A comparative effectiveness evaluation of percutaneous adhesiolysis and epidural steroid injections in managing lumbar post surgery syndrome: a randomized, equivalence controlled trial.” Pain Physician. 2009 Nov-Dec;12(6):E355-68.	Wrong intervention (adhesiolysis)
19.	Manchikanti L, et al. “Assessment of effectiveness of percutaneous adhesiolysis and caudal epidural injections in managing post lumbar surgery syndrome: 2-year follow-up of a randomized, controlled trial.” J Pain Res. 2012;5:597-608.	Wrong intervention (adhesiolysis)
	Cohort studies considered and excluded	
1.	Maus, T., et al. (2014). "Radiation dose incurred in the exclusion of vascular filling in transforaminal epidural steroid injections: fluoroscopy, digital subtraction angiography, and CT/fluoroscopy." Pain Med **15**(8): 1328-1333.	Does not report on patients, only anthropomorphic phantoms

	Citation	Reason for exclusion after full-text review
	Case series considered and excluded	
1.	Botwin, K. P., et al. (2001). "Radiation exposure to the physician performing fluoroscopically guided caudal epidural steroid injections." Pain Physician **4**(4): 343-348.	Does not report outcomes of interest
2.	El Abd OH, Amadera JE, Pimentel DC, Pimentel TS. Intravascular flow detection during transforaminal epidural injections: a prospective assessment. Pain Physician 2014;17:21-7.	No safety outcomes of interest (in this case, intravascular injection of steroid) reported.
3.	Furman, M. B., et al. (2000). "Incidence of intravascular penetration in transforaminal lumbosacral epidural steroid injections." Spine **25**(20): 2628-2632.	Does not specify if intravascular injections are of contrast, LA, or steroid
4.	Furman, M. B., et al. (2003). "Incidence of intravascular penetration in transforaminal cervical epidural steroid injections." Spine **28**(1): 21-25.	Classifies intravascular injection as injection/uptake of contrast, not injection of steroid
5.	Hanu-Cernat DE, Duarte R, Raphael JH, Mutagi H, Kapur S, Senthil L. Type of interventional pain procedure, body weight, and presence of spinal pathology are determinants of the level of radiation exposure for fluoroscopically guided pain procedures. Pain Pract 2012;12:434-9.	Case series with less than 100 patients receiving injections of interest.
6.	Hebl, J. R., et al. (2010). "Neuraxial blockade in patients with preexisting spinal stenosis, lumbar disk disease, or prior spine surgery: efficacy and neurologic complications." Anesth Analg **111**(6): 1511-1519.	Injections of LA only
7.	Kim YH, Park HJ, Moon DE. Rates of lumbosacral transforaminal injections interpreted as intravascular: fluoroscopy alone or with digital subtraction. Anaesthesia 2013;68:1120-3.	No safety outcomes of interest (in this case, intravascular injection of steroid) reported.
8.	Manchikanti, L., et al. (2004). "Evaluation of fluoroscopically guided caudal epidural injections." Pain Physician **7**(1): 81-92.	Reports that injections with improper needle placement were aborted
9.	Manchikanti L, Malla Y, Wargo BW, Cash KA, Pampati V, Fellows B. A prospective evaluation of complications of 10,000 fluoroscopically directed epidural injections. Pain Physician 2012;15:131-40.	Unclear whether steroids were used; or what proportion of patients received steroid injections.
10.	Manchikanti L, Malla Y, Wargo BW, Cash KA, Pampati V, Fellows B. Complications of fluoroscopically directed facet joint nerve blocks: a prospective evaluation of 7,500 episodes with 43,000 nerve blocks. Pain Physician 2012;15:E143-50.	Unclear whether steroids were used; or what proportion of patients received steroid injections.

	Citation	Reason for exclusion after full-text review
11.	Nahm, F. S., et al. (2010). "Risk of intravascular injection in transforaminal epidural injections." Anaesthesia **65**(9): 917-921.	Does not indicate that epidural injections were done with steroids
12.	Rathmell JP, Michna E, Fitzgibbon DR, Stephens LS, Posner KL, Domino KB. Injury and liability associated with cervical procedures for chronic pain. Anesthesiology 2011;114:918-26.	Data obtained from claims
13.	Smuck M, Zheng P, Chong T, Kao MC, Geisser ME. Duration of fluoroscopic-guided spine interventions and radiation exposure is increased in overweight patients. PM R 2013;5:291-6; quiz 6.	Case series; no harms reported.
14.	Stretanski MF, Chopko B. Unintentional vascular uptake in fluoroscopically guided, contrast-confirmed spinal injections: a 1-yr clinical experience and discussion of findings. Am J Phys Med Rehabil 2005;84:30-5.	Unclear how many (what % of) patients had steroid injections.
15.	Sullivan, W. J., et al. (2000). "Incidence of intravascular uptake in lumbar spinal injection procedures." Spine **25**(4): 481-486.	Reports on intravascular injections of contrast only
	Econ studies considered and excluded	
1.	Fitzsimmons D, Phillips CJ, Bennett H, et al. Cost-effectiveness of different strategies to manage patients with sciatica. Pain 2014;155:1318-27.	Cannot separate out impact of ESI alone as ESI is only included in a stepwise care approach
2.	Manchikanti L, Falco FJ, Pampati V, Cash KA, Benyamin RM, Hirsch JA. Cost utility analysis of caudal epidural injections in the treatment of lumbar disc herniation, axial or discogenic low back pain, central spinal stenosis, and post lumbar surgery syndrome. Pain Physician 2013;16:E129-43.	ESI not compared to ENSI; outcomes and cost data for both injection types were not pooled.
3.	Whynes DK, McCahon RA, Ravenscroft A, Hardman J. Cost effectiveness of epidural steroid injections to manage chronic lower back pain. BMC Anesthesiol 2012;12:26.	Compares cost in relation to effects in same patient using a pre- vs. post-injection design.

APPENDIX D. Class of Evidence, Strength of Evidence, and QHES Determination

Each study is rated against pre-set criteria that resulted in a Risk of Bias (RoB) assessment and presented in a table. The criteria are listed in the Tables below.

Definition of the class of evidence and risk of bias for studies on therapy*

Risk of Bias	Studies of Therapy*	
	Study design	**Criteria***
Low risk: Study adheres to commonly held tenets of high quality design, execution and avoidance of bias	Good quality RCT	• Random sequence generation • Statement of allocation concealment • Intent-to-treat analysis • Blind or independent assessment for primary outcome(s) • Co-interventions applied equally • F/U rate of 80%+ and <10% difference in F/U between groups • Controlling for possible confounding‡
Moderately low risk: Study has potential for some bias; study does not meet all criteria for class I, but deficiencies not likely to invalidate results or introduce significant bias	Moderate quality RCT	• Violation of one or two of the criteria for good quality RCT
	Good quality cohort	• Blind or independent assessment for primary outcome(s) • Co-interventions applied equally • F/U rate of 80%+ and <10% difference in F/U between groups • Controlling for possible confounding‡
Moderately High risk: Study has significant flaws in design and/or execution that increase potential for bias that may invalidate study results	Poor quality RCT	• Violation of three or more of the criteria for good quality RCT
	Moderate or poor quality cohort	• Violation of any of the criteria for good quality cohort
	Case-control	• Any case-control design
High risk: Study has significant potential for bias; lack of comparison group precludes direct assessment of important outcomes	Case series	• Any case series design

* Additional domains evaluated in studies performing a formal test of interaction for subgroup modification (i.e., HTE) based on recommendations from Oxman and Guyatt[3]:

† Outcome assessment is independent of healthcare personnel judgment. Reliable data are data such as mortality or re-operation.

‡ Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

- Is the subgroup variable a characteristic specified at baseline or after randomization? (subgroup hypotheses should be developed a priori)

- Did the hypothesis precede rather than follow the analysis and include a hypothesized direction that was subsequently confirmed?
- Was the subgroup hypothesis one of a smaller number tested?

Determination of Overall Strength of Evidence

Following the assessment of the quality of each individual study included in the report, an overall "strength of evidence" for the relevant question or topic is determined. Methods for determining the overall strength of evidence are variable across the literature and are most applicable to evaluation of therapeutic studies.

SRI's method incorporates the primary domains of quality (CoE), quantity of studies and consistency of results across studies as described by AHRQ.

The following four possible levels and their definition will be reported:

- **High** – High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
- **Moderate** - Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
- **Low** - Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and likely to change the estimate.
- **Insufficient** – Evidence either is unavailable or does not permit a conclusion.

All AHRQ "required" and "additional" domains (risk of bias, consistency, directness, precision, publication bias) are assessed Bodies of evidence consisting of RCTs were initially considered as High strength of evidence, while those comprised of nonrandomized studies began as Low strength of evidence. The strength of evidence could be downgraded based on the limitations described above. There are also situations where the nonrandomized studies could be upgraded, including the presence of plausible unmeasured confounding and bias that would decrease an observed effect or increase an effect if none was observed, and large magnitude of effect (strength of association).

Example methodology outline for determining overall strength of evidence (SoE):

All AHRQ "required" and "additional" domains* are assessed. Only those that influence the baseline grade are listed in table.

Baseline strength: Risk of bias (including control of confounding) is accounted for in the individual article evaluations. HIGH = majority of articles RCTs. LOW = majority of articles cohort studies.

DOWNGRADE: Inconsistency** of results (1 or 2); Indirectness of evidence (1 or 2); Imprecision of effect estimates (1 or 2); Sub-group analyses not stated *a priori* and no test for interaction (2)

UPGRADE: Large magnitude of effect (1 or 2); Dose response gradient (1)

Outcome	Strength of Evidence	Conclusions & Comments	Baseline	DOWNGRADE	UPGRADE
Outcome	**HIGH**	Summary of findings	**HIGH** RCTs	**NO** consistent, direct, and precise estimates	**NO**
Outcome	**MODERATE**	Summary of findings	**LOW** Cohort studies	**NO** consistent, direct, and precise estimates	**YES** Large effect
Outcome	**LOW**	Summary of findings	**HIGH** RCTs	**YES (2)** Inconsistent Indirect	**NO**

*Required domains: risk of bias, consistency, directness, precision. Plausible confounding that would decrease observed effect is accounted for in our baseline risk of bias assessment through individual article evaluation. Additional domains: dose-response, strength of association, publication bias.

**Single study = "consistency unknown"

Assessment of Economic Studies

Full formal economic analyses evaluate both costs and clinical outcomes of two or more alternative interventions. The four primary types are cost minimization analysis (CMA), cost-utility analysis (CUA), cost-effectiveness analysis (CEA), and cost-benefit analyses (CBA). Each employs different methodologies, potentially complicating critical appraisal, but some common criteria can be assessed across studies.

No standard, universally accepted method of critical appraisal of economic analyses is currently in use. A number of checklists [Canadian, BMJ, AMA] are available to facilitate critique of such studies. The Quality of Health Economic Studies (QHES) instrument developed by Ofman, et al[2]. QHES embodies the primary components relevant for critical appraisal of economic studies[1,2]. It also incorporates a weighted scoring process and which was used as one factor to assess included economic studies. This tool has not yet undergone extensive evaluation for broader use but provides a valuable starting point for critique.

In addition to assessment of criteria in the QHES, other factors are important in critical appraisal of studies from an epidemiologic perspective to assist in evaluation of generalizability and potential sources of study bias.

Such factors include:

- Are the interventions applied to similar populations (e.g., with respect to age, gender, medical conditions, etc.)? To what extent are the populations for each intervention comparable and are differences considered or accounted for? To what extent are population characteristics consistent with "real world" applications of the comparators?
- Are the sample sizes adequate so as to provide a reasonable representation of individuals to whom the technology would be applied?
- What types of studies form the basis for the data used in the analyses? Data (e.g., complication rates) from randomized controlled trials or well-conducted, methodologically rigorous cohort studies for data collection are generally of highest quality compared with case series or studies with historical cohorts.
- Were the interventions applied in a comparable manner (e.g., similar protocols, follow-up procedures, evaluation of outcomes, etc.)?
- How were the data and/or patients selected or sampled (e.g., a random selection of claims for the intervention from a given year/source or all claims)? What specific inclusion/exclusion criteria or processes were used?
- Were the outcomes and consequences of the interventions being compared comparable for each? (e.g., were all of the relevant consequences/complications for each intervention considered or do they primarily reflect those for one intervention?)

Assessment of the overall strength of evidence for formal economic analyses does not appear to be documented in the literature.

REFERENCES

1. Chiou CF, Hay JW, Wallace JF, et al. Development and validation of a grading system for the quality of cost-effectiveness studies. Med Care 2003;41:32-44.
2. Ofman JJ, Sullivan SD, Neumann PJ, et al. Examining the value and quality of health economic analyses: implications of utilizing the QHES. J Manag Care Pharm 2003;9:53-61.
3. Oxman AD, Guyatt GH. A consumer's guide to subgroup analyses. Ann Intern Med 1992;116:78-84.

APPENDIX E. Study quality: CoE and QHES evaluation

CoE evaluation:

Lumbar spinal injection

Appendix Table E1. Risk of bias and class of evidence for RCTs evaluating spinal injections for lumbar radiculopathy due to disc pathology

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Arden 2005/Price 2005* Interlaminar	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Mod Low
Aronsohn 2010† NR	Unclear	Unclear	Yes	No	Unclear	Unclear	Unclear	Yes	Mod High
Buchner 2000‡ Interlaminar	Unclear	Unclear	Yes	No	Yes	Yes	Yes	No	Mod High
Burgher 2011§ Transforaminal	Unclear	Unclear	Yes	Yes	Yes	Yes	No	Yes	Mod High
Bush 1991§ Caudal	Unclear	Unclear	No	Yes	Unclear	Yes	No	No	Mod High
Butterman 2004† Interlaminar	Yes	Unclear	No	No	Yes	Yes	Yes	Yes	Mod High
Carette 1997§ Interlaminar	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Cohen 2012§ Transforaminal	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Mod Low
Cohen 2015* Interlaminar or transforaminal	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Cuckler 1985§** Interlaminar	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Mod High
Datta 2011§ Caudal	Yes	Unclear	No	Unclear	Yes	No	Yes	Yes	Mod High

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Dilke 1973* Interlaminar	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Mod High
el Zahaar 1991§** Caudal	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Mod High
Gertzen 2010† Transforaminal	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes	Mod Low
Ghahreman 2010§ Transforaminal	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Ghai 2015§ Interlaminar	Yes	Yes	Yes	Yes	Yes	Yes	Varies††	Yes	Mod Low
Helliwell 1985* Interlaminar	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear	No	Mod High
Iversen 2011††,‡‡ Caudal	Yes	Yes	Yes	Yes	Yes	Yes	Varies§§	Yes	Mod Low
Karppinen 2001§ Transforaminal	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Klenerman 1984‡‡ Interlaminar	Yes	Unclear	No	Unclear	Yes	Yes	Unclear	Yes	Mod High
Manchikanti 2012,2011,2008§ Caudal	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	No	Mod Low
Manchikanti 2014,2013,2010§ Interlaminar	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	No	Mod Low
Manchikanti 2014§ Transforaminal	Yes	Unclear	Yes	Yes	Yes	Varies***	Yes	Yes	Mod Low
Murakibhavi 2011‡ Caudal	Yes	Unclear	Yes	No	Unclear	Yes	Yes	Unclear	Mod High
Ridley 1988* Interlaminar	Yes	Unclear	Yes	No	Yes	Yes	Yes	Yes	Mod Low
Riew 2006,2000§ Transforaminal	No	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Mod Low

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Rogers 1992§ Interlaminar	Unclear	Unclear	Yes	Yes	Unclear	Unclear	Unclear	Yes	Mod High
Sayegh 2009§ Caudal	Unclear	Unclear	No	Yes	Yes	Yes	Varies†††	Yes	Mod High
Snoek 1977§ Interlaminar	No	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Mod High
Tafazal 2009/Ng 2005§ Transforaminal	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Mod Low
Wu 2015† Transforaminal	Yes	Unclear	Yes	Yes	Yes	Yes	No	Yes	Mod Low

*Provided data for ESI vs. NEI
†Provided data for ESI vs. disc procedures
‡Provided data for ESI vs. conservative care
§Provided data for ESI vs. ENSI
**Also included in spinal stenosis section.
†† Yes for 3 months (85% vs. 91%); No for 9 and 12 months (74% vs. 88% for both).
‡‡Provided data for ESI vs. ENSI and NEI
§§Epidural steroid injection vs. saline injection only vs. sham: 6 weeks (100% vs. 90% vs. 93%); 3 months (92% vs. 90% vs. 90%); and 12 months (92% vs. 85% vs. 80%).
*** Yes at 12 months, 84.2% (101/120); No at 24 months, 74.2% (89/120).
†††Yes at 1 month (96% vs. 94%); No at 6 months (89% vs. 78%); and Yes at 12 months (87% vs. 78%).

Appendix Table E2. Risk of bias and class of evidence for RCTs evaluating spinal injections for lumbar radiculopathy due to multiple causes

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Becker 2007* Interlaminar	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Mod Low
Breivik 1976* Caudal	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	No	Mod High
Wilson-MacDonald 2005† Interlaminar	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Mod Low

*Provided data for ESI vs. ENSI
†Provided data for ESI vs. NEI

Appendix Table E3. Risk of bias and class of evidence for RCTs evaluating spinal injections for lumbar spinal stenosis

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Brown 2012* Interlaminar	Unclear	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Mod low
Cuckler 1985†‡ Interlaminar	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Mod High
el Zahaar 1991†‡ Caudal	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Mod High
Friedly 2014/Suri 2015/Turner 2015† Interlaminar or Transforminal	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Fukusaki 1998† Interlaminar	Unclear	Unclear	Yes	No	Unclear	Unclear	Unclear	Yes	Mod High
Koc 2009§ Interlaminar	Unclear	Unclear	Yes	No	Yes	Yes	No	Yes	Mod High
Manchikanti 2012,2012,2008† Caudal	Yes	Unclear	Yes	Yes	Yes	Varies**	Yes	Yes	Mod Low

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Manchikanti 2015,2012† Interlaminar	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	No	Mod Low
Nam 2011† Transforaminal	Yes	Unclear	No	Unclear	Yes	No	Unclear	Yes	Mod High
Ohtori 2012†† Transforaminal	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Mod High

*Provided data for ESI vs. disc procedures
†Provided data for ESI vs. ENSI
‡Also included in radiculopathy due to disc pathology.
§Provided data for ESI vs. conservative care
**Yes at 3 months (97%) and 6 months (92%); No at 24 months (71%).
††Provided data for ESI vs. NEI.

Appendix Table E4. Risk of bias and class of evidence for RCTs evaluating spinal injections for lumbar nonradicular axial pain

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Butterman 2004* Intradiscal	Yes	Unclear	No	No	No	No	Unclear	Yes	Mod High
Cao 2011† Intradiscal	No	No	Yes	Yes	Unclear	Yes	Yes	No	Mod High
Khot 2004† Intradiscal	Unclear	Unclear	No	Yes	Unclear	Yes	Yes	Yes	Mod High
Manchikanti 2012,2011,2008† Caudal	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Mod Low
Manchikanti 2013,2012,2010† Interlaminar	Yes	Unclear	Yes	Yes	Yes	Varies‡	Yes	No	Mod Low
Peng 2010§ Intradiscal	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Mod Low
Simmons 1992† Intradiscal	No	No	Yes	Yes	Unclear	Unclear	Unclear	Unclear	Mod High

*Provided data for discography + ESI vs. discography alone.
†Provided data for ESI vs. ENSI.
‡Yes at 12 months 89% (107/120); No at 24 months 78% (94/120).
§Provided data for ENSI vs. ENSI.

Appendix Table E5. Risk of bias and class of evidence for RCTs evaluating spinal injections for failed back surgery syndrome

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Devulder 1999* Transforaminal	No	No	Yes	Unclear	Yes	Unclear	Unclear	Yes	Mod High
Manchikanti 2012,2010,2008* Caudal	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	No	Mod Low
Meadeb 2001† Caudal	Unclear	Unclear	No	Yes	Unclear	Yes	Unclear	No	Mod High
Rocco 1989* NR	Unclear	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes	Mod High

*Provided data for ESI vs. ENSI
†Provided data for ESI vs. NEI

Appendix Table E6. Risk of bias and class of evidence for RCTs evaluating spinal injections for lumbar facet joint pain

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Carette 1991*	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Mod Low
Civelek 2012†	Yes	Unclear	Yes	No	Yes	Yes	Yes	Yes	Mod Low
Fuchs 2005*	Yes	Unclear	Yes	No	No	Unclear	Unclear	Yes	Mod High
Lakemeier 2013‡	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Lilius 1989*§	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Yes	Unclear	Mod High
Manchikanti 2010, 2008**	Yes	Unclear	Yes	Yes	Yes	Yes	No	Yes	Mod Low
Manchikanti 2001**	Unclear	Unclear	No	No	Unclear	Unclear	Unclear	Yes	Mod High
Ribeiro 2013§	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low

*Provides data for IASI vs. IANSI
†Provides data for EASI vs. medical branch radiofrequency denervation.
‡Provides data for IASI vs. medical branch radiofrequency denervation.
§Provides data for IASI vs. EASI
**Provides data for EASI vs. EANSI

Appendix Table E7. Risk of bias and class of evidence for RCTs evaluating spinal injections for sacroiliac pain

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Luukkainen 2002*	Unclear	Unclear	Unclear	Yes	No	Unclear	Unclear	Yes	Mod High
Visser 2013†	Yes	Unclear	Yes	Yes	Unclear	No	Varies‡	Yes	Mod High

* Provides data for ESI vs. ENSI
†Provides data for ESI vs. conservative care
‡Epidural steroid injection vs. physiotherapy vs. manual therapy: 72% vs. 33% vs. 67% at 3 months.

Appendix Table E8. Risk of bias and class of evidence for RCTs evaluating cervical spinal injections

Study year	Random sequence generation	Statement of concealment	Intention to treat	Blind assessment	Co-interventions applied equally	Complete F/U of ≥80%	<10% difference in F/U between groups	Controlling for confounding	Risk of Bias
Cohen 2014	yes	unclear§§	yes	yes	yes	yes§§	yes	no§§	Mod Low
Manchikanti 2013 (Disc herniation)	yes	unclear*	yes	yes	yes	yes	yes	no*	Mod Low
Manchikanti 2014 (Nonradicular pain)	yes	unclear*	yes	yes	yes	yes	yes	no*	Mod Low
Stav 1993	unclear†	unclear†	no†	unclear†	yes	yes	no†	yes	Mod High
Manchikanti 2012 (Stenosis)	yes	unclear‡	no‡	unclear‡	yes	no‡	unclear‡	no‡	Mod High
Manchikanti 2012 (Postsurgery)	yes	unclear§	no§	unclear§	yes	no§	unclear§	no§	Mod High
Manchikanti 2010 (MBB)	yes	unclear**	yes	unclear**	yes	3 & 6 months: yes 24 months: unclear**	3 & 6 months: yes 24 months: unclear**	yes	Mod Low (3 & 6 months outcomes) Mod High (24 months outcomes)
Barnsley 1994	yes	unclear††	yes	yes	yes	yes	yes	yes	Mod Low
Park 2012	unclear‡‡	unclear‡‡	yes	unclear‡‡	no‡‡	no‡‡	yes	unclear‡‡	Mod High

§§Cohen 2014: No information on allocation concealment; note that patients who exited the study per protocol due to treatment failure were not considered as being lost to follow-up; Duration of pain was slightly longer in the CC alone group (median 12 months) compared with the ESI (median 10 months) or ESI + CC (median 8 months) groups; note that the CC group had a median duration of pain that was 50% longer than that of the ESI + CC group, and this difference was not controlled for

*Manchikanti 2013 (disc herniation) & Manchikanti 2014 (nonradicular pain): Unclear how allocation concealment was ensured; no controlling for confounding (a difference in weight between the groups at baseline was acknowledged, but not controlled for in analysis)

†Stav: Random sequence generation and allocation concealment: no information provided. Intention to treat: 8/50 patients began litigation of insurance claims during the f/u period and were excluded from all analysis; blind assessment of primary outcome (pain): unclear whether physician doing evaluation was blinded to treatment received; <10% difference in f/u between groups: 100% (25/25) (ESI) vs. 68% (17/25) (intramuscular steroid injections)

‡Manchikanti 2012 (stenosis): Unclear how allocation concealment was ensured; intention to treat principle not followed (98 patients randomized, 22 of which were excluded from all analyses because they did not meet the inclusion criteria); whether outcome assessment was done in a blinded manner was not reported; complete follow-up available for 56% of randomized patients (55/98); the percent of patients randomized to each group (from the 98 randomized) was not reported, thus we are unable to determine whether there was <10% difference in follow-up between groups; no controlling for confounding (a difference in weight between the groups at baseline was acknowledged, but not controlled for in analysis)
§Manchikanti 2012 (failed surgery syndrome): Unclear how allocation concealment was ensured; intention to treat principle not followed (102 patients randomized, 14 of which were excluded from all analyses because they did not meet the inclusion criteria and another 12 appeared to be participating in ongoing study but were not included in any analyses); whether outcome assessment was done in a blinded manner was not reported; complete follow-up available for 48% of randomized patients (49/102); the percent of patients randomized to each group (from the 102 randomized) was not reported, thus we are unable to determine whether there was <10% difference in follow-up between groups; no controlling for confounding (a difference in sex and height between the groups at baseline was acknowledged, but not controlled for in analysis)
**Manchikanti 2010/2008 (MBB): Unclear how allocation concealment was ensured; whether outcome assessment was done in a blinded manner was not reported; complete follow-up not reported for 24 months, thus we are unable to determine whether there was <10% difference in follow-up between groups for this time point
††Barnsley 1994 (MBB): No statement on how allocation concealment was ensured
‡‡Park 2012: No information reported regarding random sequence generation or allocation concealment; whether outcome assessment was done in a blinded manner was not reported; complete follow-up available for 76.5% of randomized patients (306/400); co-interventions were not applied equally (the injections group only could receive additional and Botox intra-muscular injections during the follow-up period); the baseline characteristics of patients randomized to each group was not reported, thus we are unable to determine whether there were differences in baseline characteristics between groups.

Appendix Table E9. Quality of Health Economic Studies (QHES) score of included RCTs for spinal injections

QHES Question (pts possible)		Udeh 2015	Karppinen 2001	Price 2005
1.	Was the study objective presented in a clear, specific, and measurable manner? (7 pts)	7	0	7
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated? (4 pts)	4	0	4
3.	Were variable estimates used in the analysis from the best available source (i.e. randomized controlled trial = best, expert opinion = worst)? (8 pts)	0	8	8
4.	If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study? (1 pt)	1	0	1
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions? (9 pts)	9	0	9
6.	Was incremental analysis performed between alternatives for resources and costs? (6 pts)	6	6	6
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated? (5 pts)	0	5	5
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate? (7 pts)	0	0	0
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described? (8 pts)	8	0	8
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes included? (6 pts)	6	6	0
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used? (7 pts)	0	7	7
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner? (8 pts)	8	8	8
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified? (7 pts)	7	0	7
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases? (6 pts)	6	6	0
15.	Were the conclusions/recommendations of the study justified and based on the study results? (8 pts)	8	0	8
16.	Was there a statement disclosing the source of funding for the study? (3 pts)	3	3	0
	Total score (out of possible 100):	**73**	**49**	**78**

APPENDIX F. Lumbar Radiculopathy Attributed to Disc Pathology RCT Study Characteristics and Results

Appendix Table F1. Lumbar Radiculopathy Attributed to Disc Pathology Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Epidural steroid injection vs. Control injection								
Arden 2005, Price 2005	N=228	Inclusion: 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 Exclusion: Spinal canal stenosis; previous back surgery; bleeding disorder or anticoagulation; bilateral symptoms; previous epidural injection; current litigation relating to sciatica; significant psychological disorder	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)	Levels: NR Repeat injections: Mean NR, ≤3 injections at 3 week intervals if ODI improved <75% from baseline	NR	Patients were free to use analgesics and NSAIDs, and they completed a diary; all patients had received a standardized physiotherapy package before the study, focusing mainly on education and exercise regimens	A vs. B: Age (mean): 43 ± 12 vs. 44 ± 12 years Male: 52% vs. 54% Duration of symptoms: Mean NR (4 weeks to 18 months by inclusion criteria); 38% vs. 35% duration of 4 weeks to 4 months Baseline leg pain (0-100 VAS): 52 ± 23 vs. 56 ± 22 Baseline back pain (0-100 VAS): 40 ± 24 vs. 44 ± 25 Baseline function (ODI 0-100): 44 ± 15 vs. 45 ± 18	UK National Health Service, Health Technology Assessment Programme
Bush 1991	N=28	Inclusion: Unilateral sciatica associated with paresthesia; positive straight leg raise; duration >1 month; imaging findings not required Exclusion: Cauda equina syndrome; nonorganic physical signs;	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	Levels: Caudal Repeat injections: 2 at 2 week intervals	NR	Additional measures in the form of bed rest, analgesics, corsets, and manipulation were allowed; however, only analgesics (NSAIDs) were permitted during the first 4 weeks of	A vs. B: Age (mean): 38 vs. 37 yrs. Male: 83% vs. 45% Duration of symptoms: mean 4.7 months (range, 1-13); not reported by group but p=NS	ER Squibb & Sons and the Boots Company PLC

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		other serious pathology; inadequate contraception in women of child-bearing age	injection with saline (25 ml) (n=11)			the study.	Baseline pain (VAS 0-100): 38.5 vs. 49.2 Baseline Function/ Lifestyle (6-18 scale): 13.4 vs. 12.9	
Carette 1997	N=158	Inclusion: >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 Exclusion: 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	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)	Levels: Single level L4-L5: 49% vs. 51% L5-S1: 45% vs. 48% Repeat injections: Mean 2.1 injections, repeated injections permitted at 3 and 6 weeks for failure to improve	NR	Acetaminophen, otherwise not specified	A vs. B: Age (mean ± SD): 39.0 ± 9.3 vs. 40.6 ± 11.3 years Male: 72% vs. 59% Duration of symptoms (weeks): 12.9 vs. 13.0 Disability compensation: 24% vs. 21% First episode of sciatica: 76% vs. 76% Baseline pain (0 to 100): 66 vs. 62 Baseline ODI (0 to 100): 50 vs. 50	Medical Research Council of Canada and the Canadian Arthritis Society
Cohen 2012	N=84	Inclusion: 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	A. Transforaminal epidural injection with 60 mg methylprednisolone acetate in 2 ml sterile water and 0.5% bupivacaine	Levels: 1-2 levels, dose divided for multiple levels L3-4: 10.7% (3/28) vs 7.7% (2/26) vs 0%	Fluoroscopic guidance with contrast verification of nerve	Analgesic medications	A vs. B vs. C: Age (mean): 41.46 ± 12.65 vs 43.19 ± 8.91 vs 42.47 ± 10.73 Male: 79% (22/28) vs. 69% (18/28)	John P. Murtha Neuroscience and Pain Institute, International Spinal

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		pathologic disc condition correlating with symptoms Exclusion: Coagulopathy; systemic infection; unstable medical or psychiatric condition; previous spinal surgery; previous epidural steroid injection; allergy to contrast dye	(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)	(0/30) L4-5: 29% (8/28) vs. 35% (9/26) vs. 27% (8/30) L5-S1: 43% (12/28) vs. 50% (13/26) vs. 47% (14/30) S1-2 0% (0/29) vs 0% (0/26) vs 3.3% (1/30) 2 levels: 17.9% (5/28) vs 7.7% (2/26) vs 2.3% (7/30) Repeat injections: 86% vs. 88% vs. 93% received 2 injections (2nd injection two weeks after first)	root and epidural space		vs. 63% (19/30) Duration of symptoms (months): 2.61 ± 1.82 vs. 2.67 ± 1.67 vs. 2.82 ± 1.7 Disability/worker's compensation/medical board: 4% (1/28) vs. 12% (3/26) vs. 10% (3/30) Opioid therapy: 39% (11/28) vs. 39% (10/26) vs. 47% (14/30) Baseline leg pain (0-10): 5.71 ± 1.93 vs. 6.62 ± 1.66 vs. 6.31 ± 2.02 Baseline back pain (0-10): 5.30 ± 2.50 vs. 6.08 ± 2.51 vs. 4.75 ± 2.49 Baseline function (ODI 0-100): 42.93 ± 15.57 vs. 41.12 ± 18.29 vs. 40.87 ± 17.50	Intervention Society, the Center for Rehabilitation Sciences Research
Cuckler 1985 Included in spinal stenosis condition also	N=73	Inclusion: Radicular pain in the lower limb; acute unilateral sciatica and well defined, discrete neurological findings; failure to improve	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) and 1%	Levels: Single level Repeat injections: 43% (18/42) vs. 58%	NR	All patients were advised to take mild analgesics (aspirin or acetaminophen) during the post-	A vs. B: Age (years): 49 vs. 50 Male: 48% vs. 55% Duration of	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		with at least two weeks of non- invasive therapy; required to have findings on myelography, CT or epidural venography that were consistent with symptoms and neurological findings; duration of symptoms not specified Exclusion: Lumbar surgery for similar symptoms or any lumbar surgery within 6 months	procaine (5 ml) (n=42) B: Interlaminar epidural injection with saline (2 ml) and 1% procaine (5 ml) (n=31)	(18/31) received second injection with corticosteroid and local anesthetic after 24 hours due to no relief after initial injection		injection period; no special exercise program or other physical therapy was employed; patients instructed to continue activities as symptoms permitted	symptoms (months): 17.3 vs. 13.8 Previous surgery: 2% (1/42) vs. 7% (2/31) Herniated disc: 52% vs. 45% Spinal stenosis: 48% vs. 55% Baseline pain: NR Baseline function: NR	
Datta 2011	N=207	Inclusion: 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 Exclusion: Requiring surgery, structural spinal deformities; symptoms from causes other than herniated disc; spinal injection in last year; prior low back surgery, chemo-nucleolysis or nucleotomy; pregnant; allergy to corticosteroids; use of tricyclic antidepressants or lithium	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)	Levels: Single disc: 82% vs. 86% vs. 88% vs. 86% 2+ 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% Repeat injections: Up to 3 injections over 12 months At 3 weeks: 33.3% (13/39) vs. 25.7% (11/42) vs. 35.5% (14/40) vs. 59.5% (25/42) At 6 weeks: 58.5%	"No imaging used but the "Swoosh test", a modification of the Whoosh test, was used in all patients to confirm accurate drug placement; all cases had a postitive "Swoosh test".	Analgesics other than diclofenac prohibited; no injections during followup; physiotherapy permitted	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 Diclofenac use (tablets/week): 51 vs. 49 vs. 47 vs. 48 Baseline pain (0-10 VAS): 7.4 ± 0.95 vs. 7.4 ± 0.57 vs. 7.3 ± 0.65 vs. 7.2 ± 0.79 Baseline RDQ (0-24): 21 vs. 22 vs. 21 vs. 22	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
				(23/39) vs. 68.5% (29/42) vs. 50.8% (20/40) vs. 22.5% (9/42) At 9 weeks: 12.4% (5/39) vs. 5.5% (2/42) vs. 6.5% (3/40) vs. 3.5% (1/42)				
Dilke 1973	N=100	Inclusion: Unilateral sciatica with painful limitation of sciatic or femoral nerve stretch; sciatic scoliosis, appropriate neurologic deficit; duration not specified; imaging findings not required Exclusion: Diagnostic uncertainty; bilateral manifestations; prior lumbar spine surgery; medical conditions affecting rehabilitation; doubt about the technical success of an injection	A: Interlaminar epidural injection with 80 mg methylprednisolone in saline (10 ml) (n=50) B: Interspinous ligament injection with saline (1 ml) (n=50)	Levels: Single level Repeat injections: Mean not reported, second injection permitted after 1 week if no improvement	NR	Mefenamic acid; diazepam; bed rest; graded rehabilitation with hydrotherapy; postural exercise; and spinal mobilizing exercise	A vs. B: Age (mean, range): 38.7 (18-75) vs. 42.3 (18-66) years Male: 53% vs. 58% Duration of symptoms >4 weeks: 90% vs. 90% Baseline pain: NR Baseline function: NR	NR
el Zahaar 1991 Note: this study also included in caudal epidural steroid injection versus placebo for stenosis	N=63	Inclusion: Radicular pain in the lower limb; acute unilateral sciatica with neurological findings; failure to improve with at least 2 weeks of conservative therapy; findings on MRI or CT consistent with clinical presentation Exclusion: Surgery for similar symptoms	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)	Levels: Single injection Repeat injections: NR	NR	Advised to take aspirin; no physical therapy or exercise program	A vs. B: Age (mean): 46 vs. 49 years Male: 54% vs. 65% Duration of symptoms (months): 17 vs. 14 Herniated disc: 51% (n=19) vs. 54% (n=14) Spinal stenosis:	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		or within 6 months					49% (n=18) vs. 46% (n=12) Baseline pain: NR Baseline function: NR	
Ghahreman 2010	N=150	Inclusion: 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; demonstration of a disc herniation by CT or MRI at a segmental level consistent with the clinical features; neurological signs of radiculopathy were not required, but served to consolidate the diagnosis when they were present; duration not specified Exclusion: 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)	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	Levels: 1 or 2 L2: 0% (0/28) vs 2.7% (1/37) vs 0% (0/27) vs 0% (0/28) vs 0% (0/30) L3: 0% (0/28) vs 2.7% (1/37) vs 7.4% (2/27) vs 0% (0/28) vs 3.3% (1/30) L4: 10.7% (3/28) vs 5.4% (2/37) vs 11.1% (3/27) vs 25.0% (7/28) vs 6.7% (2/30) L5: 46.4% (13/28) vs 40.5% (15/37) vs 37.0% (10/27) vs 32.1% (9/28) vs 50.0% (15/30) S1: 35.7% (10/28) vs 43.2% (16/57) vs 44.4% (12/27) vs 36% (10/28) vs 33.3% (10/30) L3 and L5: 0% (0/28) vs 0% (0/37) vs 0% (0/27) vs 0% (0/28) vs 3.3% (1/30) L4 and L5: 3.6% (1/28) vs 5.4% (2/37) vs 0% (0/27) vs 7.1% (2/28) vs 0% (0/30) L5 and S1: 3.6%	Fluoroscopic guidance with contrast verification of nerve root for transforaminal injections	NR	A vs. B vs. C vs. D vs. E: Age (median years, IQR): 49 (39-61) vs. 44 (33-54) vs. 43 (35-66) vs. 49 (38-62) vs. 46 (37-64) Male: 61% (17/28) vs. 51% (19/37) vs. 63% (17/27) vs. 54% (15/28) vs. 70% (21/30) Acute Pain 68% (19/28) vs 57% (21/37) vs 48% (13/27) vs 43% (12/28) vs 50% (15/30) Chronic Pain 32% (9/28) vs 43% (16/37) vs 52% (14/27) vs 57% (16/28) vs 50% (15/30) Duration of symptoms (weeks, Median (IQR)): Acute: 6 (2 to 12) vs 6 (4-8) vs 4 (1 to 8) vs 3 (1 to 6) vs 8 (4 to 12) Chronic: 96 (42 to	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
			saline (2 ml), with fluoroscopic guidance (n=30)	(1/28) vs 0% (0/37) vs 0% (0/27) vs 0% (0/28) vs 0% (0/30) <u>Repeat injections:</u> single			560) vs 42 (24 to 138) vs 48 (23 to 120) vs 32 (24 to 48) vs 72 (24 to 96) Baseline leg pain (median, IQR, 0-10): 7 (5 to 8) vs. 7 (5 to 8) vs. 7 (6 to 10) vs. 7 (6 to 8) vs. 8 (6 to 9) Baseline Roland Morris score (median, IQR 0-24): 17 (11 to 20) vs. 17 (13 to 20) vs. 19 (14 to 21) vs. 17 (13 to 21) vs. 15 (11 to 18), p range: 0.028 to 0.942 SF-36 (median, IQR) Physical functioning: 20 (6 to 39) vs 20 (10 to 35) vs 35 (15 to 45) vs 20 (10 to 43) vs 30 (24 to 46), p range: 0.062 to 0.987 Social functioning: 38 (25 to 50) vs 38 (19 to 50) vs 25 (25	

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
							to 63) vs 30 (25 to 63) vs 38 (25 to 60), p range: (0.188 to 0.926) Bodily pain: 22 (10 to 29) vs 22 (12 to 31) vs 21 (10 to 31) vs 22 (12 to 32) vs 22 (12 to 32) (0.287 to 0.960) General health: 52 (40 to 65) vs 60 (41 to 67) vs 72 (42 to 77) vs 47 (36 to 77) vs 57 (44 to 83), p range: 0.114 to 0.844 Vitality: 28 (16 to 40) vs 35 (12 to 43) vs 35 (20 to 65) vs 40 *16 to 49) vs 35 (23 to 45), p range: 0.08 to 0.827 Mental health: 50 (40 to 75) vs 52 (32 to 68) vs 48 (36 to 84) vs 58 (45 to 79) vs 50 (36 to 73), p range: 0.196 to 0.949	
Ghai 2015	N=69	Inclusion: either gender aged 18 to 60 years with chronic low back pain and unilateral lumbrosacral radicular pain of ≥ 12 weeks duration not responding to medications and physical therapies, having pain score of ≥ 5 on 0-10 NRS	A: Epidural injection of 6 mL 0.5% lidocaine mixed with 80 mg (2 mL) of methylprednisolone acetate using a parasaggital interlaminar	Levels: 3— L3-L4: 4% (3/69), L4-L5: 52% (36/69), L5-S1: 44% (30/69) A vs B: L3-L4— 6% (2/35) vs 3% (1/34)	Fluoroscopic guidance	All patients received conservative management including analgesics (adjuvant, pregabalin, amitriptyline,	A vs B Age (mean ± SD) in years: 45.9 ± 13.3 vs 44.7 ± 10.5, p = 0.65 Male (%, n/n): 54% (19/35) vs 44% (15/34), p = 0.47	Funding NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		at the time of enrollment; the diagnostic criteria for lumbrosacral radicular pain were discussed previously. A trained specialist performed a detailed clinical examination to determine the most probable nerve root affected. MRI was performed in all patients to correlate the symptoms and disc level protrusion. Inclusion criteria focused on unilateral radiculitis and disc herniation. Exclusion: if patients had severe spinal pathology (large disc herniation occupying more than 60% of spinal canal, severe central spinal stenosis, spondylolisthesis, tumor, or synovial cysts). Patients with any sensory or motor loss; referred pain because of facet or sacroiliac joint arthropathy, unstable neurological deficits, cauda equine syndrome; previous lumbar spine surgery, clinically significant or unstable medical or psychiatric illness; inability to understand questionnaires; those having received EI in the past, corticosteroids or anesthetics allergies, those taking anticoagulants or bleeding diathesis, systemic	approach B: Epidural injection of 8 mL of 0.5% lidocaine using a parasaggital interlaminar approach	L4-L5— 51% (18/35) vs 53% (18/34) L5-S1— 43% (15/35) vs 44% (15/34) Repeat injections: 62% (43/69) received a second injection; median injection interval was 42 days (IQR 15-68). 26% (18/69) received a third injection; median injection interval was 24 days (IQR 15-61)		opioid, or non-opioid) and/or exercise program during the study. Dose titration of analgesis was done as per patient requirement.	Weight (kg, mean ± SD): 68.7 ± 12.5 vs 66.3 ± 10.1, p = 0.07 BMI (kg/m2): 24.9 ± 4.1 vs 24.8 ± 3.6, p = 0.88 Duration of pain (months): Mean ± SD— 21.5 ± 14.8 vs 19.6 ± 12.5, p = 0.58 Median (IQR): 12 (12-36) vs 15 (10-25) VAS: Mean ± SD— 8.0 ± 1.6 vs 8.0 ± 1.4, p = 0.94 Median (IQR): 8 (8-9) vs 8 (8-9) Modified ODI: Mean ± SD— 46.8 ± 14.3 vs 49.6 ± 12.8, p = 0.94 Median (IQR)— 46 (37-58) vs 49 (42-60) Level of injection: L3-L4— 6% (2/35) vs 3% (1/34) L4-L5— 51% (18/35) vs 53% (18/34) L5-S1— 43% (15/35) vs 44% (15/34)	

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		corticosteroids; pregnant and lactating women, being treated with investigational drug within 30 days of trial.						
Helliwell 1985	N=39	Inclusion: 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 Exclusion: Diagnostic uncertainty; pregnant; prior lumbar spine surgery or the development of progressive neurologic impairment	A: Interlaminar epidural injection with 80 mg methylprednisolone in saline (10 ml) (n=20) B: Interspinous ligament injection with saline (5 ml) (n=19)	Levels: Single level Repeat injections: none	NR	No other form of treatment was introduced; patients already wearing lumbo-sacral supports were allowed to continue using them if they wished; patients were also given the choice of reducing their analgesic consumption and returning to work or other full-time activities.	A vs. B: Age (mean, range): 44.6 (20-69) vs. 47.4 (23-68) years Male: 25% vs. 20% Duration of symptoms (months): 8.5 vs. 13 Baseline pain: NR Baseline function: NR	NR
Iversen 2011	N=116	Inclusion: 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, however, inclusion in the trial was not dependent on the results from the MRI and CT; the results did not have to correspond with those from the clinical examination; to be included, the patients had to have clinically proved radiculopathy).	A: Caudal epidural injection with 40 mg triamcinolone in 0.9% saline (29 ml) (n=37) B: Caudal epidural injection with 0.9% saline (30 ml) (n=39) C: Subcutaneous injection superficial to the sacral hiatus and outside spinal canal with 0.9%	Levels: NR Repeat injections: 2 injections within 2 weeks on all patients unless pain recovered prior to 2nd injection	Ultrasound	Use of physiotherapy was recorded during followup but not routinely offered to patients, though patients were encouraged to engage in physical activity; use of NSAIDs was discontinued	A vs. B vs. C: Age (mean): 40 vs. 43 vs. 43 years Male: 54% vs. 62% vs. 60% Duration of leg pain (weeks): 42.5 ± 62.6 vs. 57.1 ± 158.0 vs. 26.7 ± 22.4 Duration of back pain (weeks): 50.4 ± 64.3 vs. 63.1 ± 157.8 vs. 46.6 ± 86.3 Physically	North Norway Regional Health Authority and Health Region Nord-Trondelag, Norway

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		Exclusion: 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	saline (2 ml) (n=40)				demanding work: 57% vs. 46% vs. 47% Received sickness benefit: 68% vs. 67% vs. 55% Baseline back pain, mean (95% CI) (0-100 VAS): 46.8 (39.0 to 54.6) vs. 49.6 (40.3 to 58.2) vs. 46.3 (39.2 to 54.1) Baseline leg pain, mean (95% CI) (0-100 VAS): 50.1 (42.5 to 57.7) vs. 53.5 (45.6 to 61.3) vs. 48.3 (39.6 to 56.9) Baseline ODI (0-50): 32 vs. 31 vs. 26 Fear Avoidance Beliefs Questionnaire (FABQ) work: 24 vs. 25 vs. 22 FABQ physical activity: 12 vs. 14 vs. 13	
Karppinen 2001, 2001	N=163	Inclusion: 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	A: Transforaminal (periradicular) injection with 2-3 cc of methylprednisolone 40 mg/cc plus bupivacaine 5 mg/cc,	Levels: Appears single Levels affected on MRI: L3-4: 3% (2/80) vs 5% (4/80)	Fluoroscopic guidance with contrast verification of nerve	Back school instructions by physiotherapist at 2 weeks; pain medication and physiotherapy for persisting sciatic	A vs. B: Age (mean ± SD): 44.8 ± 13 vs. 43.7 ± 13 years Male: 64% (51/80) vs. 58% (46/80) Duration of	Private foundation and government agencies in Finland; Internationa

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		inclusion not specified) Exclusion: 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	with fluoroscopic guidance (n=80) B: Transforaminal (periradicular) injection with isotonic (0.9%) saline (2-3 cc), with fluoroscopic guidance (n=80)	L4-5: 61% (49/80) vs 32/80) L5-S1: 36% (29/80) vs 55% (44/80) Repeat injections: single	root site	pain; referral to neurosurgeon for severe sciatic pain and disability	symptoms (months): 2.4 ± 1.5 vs. 2.6 ± 1.5 Baseline leg pain (0 to 100 VAS): 71.0 ± 18 vs. 75 ± 19 Baseline back pain (0 to 100 VAS): 52.8 ± 25 vs. 59.8 ± 25 Baseline function (ODI 0-100): 42.9 ± 16 vs. 43.5 ± 15 Work-related features: Employed: 73% (58/80) vs 72% (62/80) Retired: 11% (9/80) vs 11% (9/80) Other (unemployed, student): 16% (13/80) vs 11% (9/80) Straight leg raising test (mean °, SD) 58 ± 18 vs 60 ± 19 4.8 ± 1.5 vs 4.9 ± 1.5 Lumbar flexion (mean ± SD cm) 4.8 ± 1.5 vs 4.9 ± 1.5	l Spinal Intervention Society

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
							Motor deficit 24% vs 20% Sick leave (mean days ± SD) 14.4 ± 18 vs 22.1 ± 26	
Klenerman 1984 Also included for epidural injection (approach NR) vs. placebo for LBP + radiculopathy	N=74	Inclusion: Unilateral sciatica with or without objective neurological signs; no previous treatment in a hospital for their back; symptoms ≤6 months Exclusion: NR	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)	Levels: Single level Repeat injections: Single injection	NR	Patients whose symptoms were still severe during the follow-up period were given supplementary treatment usually in the form of physiotherapy (p=NS between groups in number of patients that received additional therapy)	A vs. B vs. C vs. D: Age: NR Male: NR Duration of symptoms: NR (≤6 months by inclusion criteria) Baseline pain (0-100 VAS): 48 vs. 53 vs. 65 vs. 65 Baseline function: NR	NR
Manchikanti 2012, 2011, 2008	N=120	Inclusion: Demonstrated disc herniation with radiculitis; >18 years of age; function-limiting low back and lower extremity pain for >6 months; imaging findings not specified Exclusion: Previous lumbar surgery; radiculitis secondary to spinal stenosis or without disc herniation; uncontrollable or unstable	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%	Levels: Caudal Herniation level: L3/4: 5% vs. 8% L4/L5: 70% vs. 67% L5/S1: 50% vs. 58% Repeat injections: Mean 5.3 ± 2.4 vs. 5.5 ± 2.8 over 24 months (mean 3.6 ±	Fluoroscopy with contrast verification in epidural space	No specific cointerventions or additional interventions; however, all patients continued previous exercise programs, drug therapy, and work	A vs. B: Age (mean): 43 vs. 49 yrs. Male: 38% vs. 32% Duration of pain (months): 81 vs. 93 Baseline pain (0-10 NRS): 7.8 ± 0.9 vs. 8.1 ± 0.9 Baseline function (ODI, 0 to 50): 28	There was no external funding in the preparation of this manuscript

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		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	lidocaine (10 ml), with fluoroscopic guidance (n=60)	1.1 vs. 3.8 ± 1.4 within first 12 months), p=NS; frequency not specified			vs. 29	
Manchikanti 2014	N=120	Inclusion: Age ≥18 years; disc herniation (L4-5 and L5-S1) and unilateral radiculitis; chronic low back and lower extremity pain of at least 6 months with pain intensity limiting function and an NRS score above 5 on a scale of 0 to 10; must have been capable of understanding the trial protocol, able to provide voluntary written informed consent, and had an unrestricted ability to participate in outcomes assessments Exclusion: history of previous lumbar surgery; radiculitis secondary to spinal stenosis, either foraminal or central; radiculitis without disc herniation; bilateral radiculitis; uncontrolled medical illnesses; unstable	A: Transforaminal epidural injection of betamethasone 0.5 mL plus lidocaine 1.5 mL (1%), with fluoroscopic guidance (n=60) B: Transforaminal epidural injection of lidocaine 1.5 mL (1%) and sodium chloride, with fluoroscopic guidance (n=60)	Levels (single or multiple) L4-5: 48% (29/60) vs 50% (30/60) L5-S1: 72% (43/60) vs 65% (39/60) Repeat injections: Mean 3.5 ± 1.3 vs 3.6 ± 1.4 over 1 year, 4.8 ± 2.7 vs. 5.2 ± 2.7 over 2 years, frequency not specified	Fluoroscopic guidance with contrast verification	Similar co-interventions were provided for all patients, including a structured exercise program; those employed continued working or returned to work when possible; all patients continued drug therapy with opioids or NSAIDs, although generally, at a lower level than their initial doses; medications or dosages were changed based on necessity or discontinued if no longer needed; if an increase in opioid dosage was required, the patient was withdrawn; no	A vs. B: Age (mean): 42.6 ± 11.2 vs. 43.1 ± 11.8 years Male: 45% (27/60) vs. 17% (10/60); p=0.001 Duration of symptoms (months): 103.8 ± 92.5 vs. 98.4 ± 83.4 Baseline pain (0 to 10 NRS): 8.2 ± 0.9 vs. 8.3 ± 0.9 Baseline function (ODI 0-50): 28.0 ± 5.3 vs 29.9 ± 4.8; p=0.04	No external funding

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		psychiatric disorders; extremely high dose opioid users not amenable to reductions; inability to participate in outcomes assessments; pregnant and lactating women; history of or potential for any type of adverse reactions to steroids or local anesthetics				additional physical therapy, occupational therapy, or any other interventions were offered beyond the protocol.		
Manchikanti 2014, 2013, 2010	N=120	Inclusion: ≥ 18 years of age; disc herniation or radiculitis; function-limiting low back and lower extremity pain for ≥6 months; imaging findings not specified Exclusion: 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	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)	Levels: Single level: L4/5: 13% vs. 3.3% L5/S1: 87% vs. 95% Repeat injections: Mean 6.1 vs. 5.3 over 2 years, frequency not specified	Fluoroscopic guidance with contrast verification in epidural space	No specific physical therapy, occupational therapy, bracing, or interventions, other than the assigned study intervention, were offered; all patients continued their previously directed exercise programs, as well as their employment, and most patients were already taking opioids, non-opioid analgesics, and adjuvant analgesics; these medications were either discontinued or the dosages increased dependent on the patients individual medical need.	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 function (ODI 0-50): 30 vs. 30	"No external support or funding; this study was conducted with internal resources of the practice of the first author"
Ridley 1988	N=39	Inclusion: Clinical history consistent	A: Interlaminar epidural injection	Levels: Single level	NR	NR	A vs. B: Age (mean ± SD):	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		with sciatic nerve root compression with numbness or paresthesia or objective neurologic deficit Exclusion: Prior epidural injection; spinal surgery	with 80 mg methylprednisolone (2 ml) and saline (10 ml) (n=19) B: Interspinous ligament injection with saline (2 ml) (n=16)	Repeat injections: Single injection repeated after 1 week if no improvement			40 ± 9 vs. 39 ± 12 years Male: 42% vs. 44% Duration of symptoms >6 months: 47% vs. 56% Baseline pain: NR Baseline function: NR	
Riew 2006, 2000	N=55	Inclusion: >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, demonstrated persistent or new neurological compression Exclusion: 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	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)	Levels: Single injection with 4 additional injections during follow up period: 19 had >1; frequency not specified (range 6 days to 10.5 months), no significant differences in number of levels between groups was found. Repeat injections: One or two (determined by surgeon based on patient's history)	Fluoroscopic guidance with contrast verification of nerve root site	NR	A vs. B: Age: NR (states no difference) Male: 49% overall (states no difference) Duration of symptoms: Mean NR (minimum 6 weeks according to inclusion criteria) Baseline pain: NR Baseline function: NR *States no significant differences between groups with respect to the baseline North American Spine Society outcome measurements*.	Barnes-Jewish Christian Health System's Innovations in Health Care Grant and Washington University School of Medicine

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		radiographically detectable abnormality; more than two radiographically abnormal and symptomatic levels on either side; absence of substantial radicular pain as the presenting symptom						
Rogers 1992	N=30	Inclusion: Clinical diagnosis of sciatica with positive straight leg raise at less than 60 degrees; duration and imaging findings not specified Exclusion: NR	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)	Levels: Single level Repeat injections: NR	None – applied the loss of resistance to air or saline technique	NR	A vs. B: Age (mean): 42 vs. 41 years Male: 47% vs. 47% Duration of symptoms (months): 23 vs. 25 Prior surgery: 1/15 vs. 0/15 Prior epidural injection: 4/15 vs. 2/15 Baseline pain "severe" or "very severe": 87% vs. 67% Baseline function: NR	NR
Sayegh 2009	N=183	Inclusion: Low back pain for ≥ 1 month ± unilateral or bilateral sciatica; failure to respond to conservative measures; disc degeneration or herniation on MRI Exclusion: Cauda equina or spinal stenosis; symptoms for <1 month duration;	A: Caudal epidural injection with betamethasone (2 mg/dL betamethasone dipropionate + 5 mg/dL betamethasone phosphate) (1 ml) + 2% Xylocaine (12 ml)	Levels: Caudal Repeat injections: 51/183 (28%) received 2nd injection 1-2 weeks after 1st for failure to improve	No fluoroscopic guidance (Gentle aspiration confirmed the proper position)	Acetaminophen allowed during first 4 weeks of study, but not NSAIDs	A vs. B: Age (mean): 51 vs. 48 yrs. Male: 65% vs. 70% Duration of symptoms (days): 53 vs. 51 Baseline pain: NR Baseline ODI (0-100): 39 vs. 39	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		psychosomatic diseases or any other pathology	(n=93) B: Caudal epidural injection with 2% Xylocaine (12 ml) + water for injection (8 ml) (n=90)					
Snoek 1977	N=51	Inclusion: Radiating pain in the distribution of the sciatic or femoral nerve; neurologic deficit that correlated with compression of L4, L5, or S1 nerve root; Radiologically, diagnostic features were indentation of the dural sac, and/or increased width of the root and shortening of the root sleeve; myelographic findings at the appropriate level and side; duration not specified Exclusion: Acute severe motor paresis; cauda equina syndrome; intolerable pain; previous lumbar spine surgery; contraindications to corticosteroids; doubts about myelography findings	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) (n=27) B: Interlaminar epidural injection with saline (2 ml) (n=24)	Levels: Single level Repeat injections: none	None - extradural space was identified by the "loss of resistance test" of Dogliotti (1933)	Physiotherapy, mainly consisting of instruction and isometric training of the appropriate muscle groups, was identical for all patients; patients were given analgesics on request only	A vs. B: Age (mean): 44 vs. 46 years Male: 48% vs. 54% Duration of symptoms (weeks): 12 vs. 11 Baseline pain: NR Baseline function: NR	NR
Tafazal 2009, Ng 2005	N=150	Inclusion: 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	A: Transforaminal periradicular injection with 40 mg methylprednisolone plus 0.25% bupivacaine (2 ml), with fluoroscopic	Levels: Single level Repeat injections: 13% (8/64) vs. 15% (10/65) at 1 year	Fluoroscopy with contrast verification	NR	A vs. B: Age (mean): 52.8 vs. 51.0 years Male: 60% vs. 54% Duration of symptoms (months): 20 (IQR: 7 to 24.5) vs. 17.8	None

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		Exclusion: 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	guidance (n=74) B: Transforaminal periradicular injection with 0.25% bupivacaine (2 ml), with fluoroscopic guidance (n=76)				(IQR: 6 to 24) Baseline leg pain (0-100 VAS): 72.7 (IQR: 60 to 80) vs. 76.4 (IQR: 70 to 90) Baseline back pain (0-100 VAS): 44.3 (IQR: 20 to 73) vs. 47.5 (IQR: 20 to 80) Baseline function (ODI 0-100): 43.4 (IQR: 32 to 54) vs. 46.6 (IQR: 34 to 58)	
Epidural steroid injection vs. Control injection with other medication								
Burgher 2011	N=26	Inclusion: ≥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 Exclusion: Pain intensity was less than 3 of 10 or more than 8 of 10 on PI-NRS if already taking opioids; recent spinal trauma; cauda equina syndrome; progressive motor deficit; chronic anticoagulation; infectious etiology; workers'	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)	Levels: Single level Repeat injections: Mean 2.3 vs. 2.0 injections, repeated at 10-14 day intervals Injection location L3: 7% (1/15) vs 0% (0/11) L4: 27% (4/15) vs 18% (2/11) L5: 20% (3/15) vs 36% (4/11) S1: 27% (4/15) vs 45% (5/11) Overall p = 0.865	Fluoroscopic guidance (digital subtraction angiography) with contrast verification	Patients were provided prescriptions or referrals for oral anti-inflammatories, oral anticonvulsant or antidepressant pain medications, oral opioid analgesics, physical therapy or more intensive medical or surgical therapy as indicated	A vs. B: Age (mean years ± SD): 50.3 ± 11.0 vs. 44.1 ± 12.4, p = 0.161 Male: 67% (10/15) vs. 82% (9/11), p = 0.658 Duration of symptoms (weeks): 5.3 ± 3.7 vs. 5.0 ± 2.5, p = 0.649 Opioid use prior to intervention: 67% (10/15) vs. 91% (10/11), p = 0.197 PI-NRS: (0-10 NRS): 7.0 ± 2.0 vs. 7.0 ± 1.9	Grant from National Center for Research Resources (NCRR), component of the National Institutes of Health

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		compensation claim; history of adverse reaction to study medications; 1 or more corticosteroid injection in the preceding 4 months; pregnant; severe medical disease					Baseline function (ODI 0-50): 29 vs. 31 RMDQ (mean ± SD) 11.0 ± 5.2 vs 14.0 ± 3.8, p = 0.124 MPI (mean ± SD) 52.9 ± 9.1 vs 57.4 ± 12.7 CESD (mean ± SD) 12.5 ± 7.7 vs 15.2 ± 13.0	
Cohen 2012	N=84	Inclusion: 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 Exclusion: Coagulopathy; systemic infection; unstable medical or psychiatric condition; previous spinal surgery; previous epidural steroid injection; allergy to contrast dye	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)	Levels: 1-2 levels, dose divided for multiple levels L3-4: 10.7% (3/28) vs 7.7% (2/26) vs 0% (0/30) L4-5: 29% (8/28) vs. 35% (9/26) vs. 27% (8/30) L5-S1: 43% (12/28) vs. 50% (13/26) vs. 47% (14/30) S1-2 0% (0/29) vs 0% (0/26) vs 3.3% (1/30) 2 levels: 17.9% (5/28) vs 7.7% (2/26) vs 2.3% (7/30) Repeat injections: 86% vs. 88% vs. 93% received 2 injections (2nd injection two weeks after first)	Fluoroscopic guidance with contrast verification of nerve root and epidural space	Analgesic medications	A vs. B vs. C: Age (mean): 41.46 ± 12.65 vs 43.19 ± 8.91 vs 42.47 ± 10.73 Male: 79% (22/28) vs. 69% (18/28) vs. 63% (19/30) Duration of symptoms (months): 2.61 ± 1.82 vs. 2.67 ± 1.67 vs. 2.82 ± 1.7 Disability/worker's compensation/medical board: 4% (1/28) vs. 12% (3/26) vs. 10% (3/30) Opioid therapy: 39% (11/28) vs. 39% (10/26) vs. 47% (14/30) Baseline leg pain	John P. Murtha Neuroscience and Pain Institute, International Spinal Intervention Society, the Center for Rehabilitation Sciences Research

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
			, with fluoroscopic guidance (n=30)				(0-10): 5.71 ± 1.93 vs. 6.62 ± 1.66 vs. 6.31 ± 2.02 Baseline back pain (0-10): 5.30 ± 2.50 vs. 6.08 ± 2.51 vs. 4.75 ± 2.49 Baseline function (ODI 0-100): 42.93 ± 15.57 vs. 41.12 ± 18.29 vs. 40.87 ± 17.50	
Cohen 2015	N=145	Inclusion: age ≥17 years; average radicular leg pain score ≥4 (0-10) in the preceding week, or 3/10 if leg pain as bad or worse than back pain; current symptoms last ≥past 6 weeks, ≤4 years; s/sx of lumbrosacral radicular pain; AND findings of herniated disk or spinal stenosis on MRI imaging concordant with their presentation. Exclusion: neuropathic pain for ≥4 years; previous negative experience with gabapentin or pregabalin; ESI in the past 3 years, cauda equina syndrome; referrals for surgical evaluation; previous lumbar spine surgery; pregnancy; allergic reaction to contrast dye; known secondary gain; active	A: Epidural Spinal Injection, 60 mg depomethylprednisolone + 1 mL of 0.25% bupivacaine (interlaminar diluted to 4 mL in saline [n=11] or transforaminal diluted to 3 mL in saline [n=62] approach) plus oral placebo medication; (n=73) B: Posterior ligament injection of 3 mL saline (interlaminar [n=12] or transforaminal [n=60]) plus oral gabapentin 300 mg (n=72) (sham procedure)	Number of levels: Single level (specific spinal location [e.g. L4-L5] NR) Repeat injections: NR	Fluoroscopic guidance	Tramadol and NSAID prescribed prn as rescue medications, OR opioids could be increased by up to 20%	*A vs B* Age ± SD: 43.8 ± 14.0 vs 41.7 ± 11.9 years Men: 66% (48/73) vs 82% (59/72) Duration of pain: <3 months—15% (11/73) vs 21% (15/72) 3 months-1year—36% (26/73) vs 21% (15/72) >3 years—12% (9/73) vs 10% (7/72) Treatment with opioids: None—74% (54/73) vs 77% (55/72) <60 morphine equivalents/day—22% (16/73) vs 19% (14/72)	Center for Rehabilitation Sciences Research, Bethesda, MD (congressional grant)

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		infection; serious medical or psychiatric condition					≥60 morphine equivalents/day—4% (3/73) vs 4% (3/72) Mean ± SD oral morphine equivalents among opioid users (mg/day)—28.7 ± 34.8 vs 38.5 ± 53.0. Diagnosis: herniated nucleus pulposus— 85% (63/73) vs 90% (65/72) Spinal stenosis—14% (10/73) vs 10% (7/72) Current smoker: 21% (15/73) vs 18% (13/72) Obese: 18% (13/73) vs 26% (19/73) Baseline pain scores (mean ± SD): Average leg pain: 5.4 ± 2.1 vs 5.4 ± 1.9 Worst leg pain—7.9 ± 1.7 vs 7.8 ± 2.0 Average back pain—5.0 ± 2.6 vs 4.7 ± 2.4 Worst back pain—7.0 ± 2.6 vs 7.0 ± 2.9	

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
							Owestry Disability score: 39.8 ± 15.3 vs 39.8 ± 14.7	
Epidural steroid injection vs. Disc procedure								
Aronsohn 2010	N=50	Inclusion: 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 Exclusion: NR	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)	Levels: Single level Repeat injections: Single injection	Fluoroscopic guidance	NR	A vs. B: Age (mean): 51.2 ± 12.4 vs. 41.36 ± 10.3 years Male: 56% vs. 64% Duration of symptoms: NR Baseline back pain (0-10): 7.1 vs. 7.5 Baseline radicular pain (0-10): 9.3 vs. 9.1 Baseline function: NR	NR
Buttermann 2004	N=100	Inclusion: 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 Exclusion: Cauda equina syndrome; pars defect at the level of the herniation; far-lateral disc herniation; multilevel symptomatic disc herniation; recurrent disc herniation	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)	Levels: Single level Repeat injections: Mean NR, patients could receive 1-3 at one week intervals based on response	Fluoroscopic guidance in 76% of patients undergoing epidural injection	NR	A vs. B: Age (mean): 41 vs. 40 years Male: NR Duration of symptoms (months): 3.3 vs. 3.8 Smokers: 30% vs. 36% Size of disc herniation: 42% vs. 43% Motor deficit: 82% vs. 88% Baseline back pain (0-10): 5.4 vs. 5.2	None

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
							Baseline leg pain (0-10): 7.4 vs. 7.0 Baseline function (ODI 0-100): 47 vs. 48	
Gerstzen 2010	N=90	Inclusion: 18 to 75 years of age; BMI <40; radicular pain score >50 on 0 to 100 VAS; 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 Exclusion: 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	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. The spinal cannula was introduced into the disc using a posterolateral extrapedicular approach (n=46)	Levels: Single level L2-3: 0% (0/40) vs 2% (1/45) L3-4: 5% (2/40) vs 11% (5/45) L4-5: 30% (12/40) vs 31% (14/45) L5-S1: 65% (26/40) vs 56% (25/45) Overall p = 0.63 Repeat injections: Up to 2 injections 3 weeks apart;75% (30/40) underwent 2 epidural injections 13 patients in group B received epidural injection	Fluoroscopic guidance	Allowed to receive additional conservative therapies, including bed rest, braces, physical therapy, narcotic analgesics, or NSAIDs at the discretion of the treating investigator.	A vs. B: Age (mean ± SD): 42 ± 11 vs. 46 ± 12 years, p = 0.13 Male: 52% (21/40) vs. 47% (21/45), p = 0.65 Duration of symptoms (months, median (range)): 24 (2.5 to 156) vs. 12 (1 to 192), p = 0.04 Full or part-time employment: 65% (26/40) vs. 62% (28/45), employment status p = 0.98 Opioid use prior to intervention: 55% (22/40) vs. 47% (21/45), medication use p = 0.40 Baseline leg pain (0-100 VAS): 75 ± 14 vs. 72 ± 13, p = 0.48 Baseline back pain (0-100 VAS):	ArthoCare Corp

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		comorbidities; Workman's Compensation or ongoing litigation					53 ± 23 vs. 44 ± 24, p = 0.10 <u>Baseline function</u> (ODI 0-100): 43 ± 17 vs. 42 ± 14 <u>BMI</u> 27.3 ± 5.1 vs 26.9 ± 4.7, p = 0.59 <u>Mean SF-36 scores</u> Physical functioning: 32 ± 9 vs 31 ± 9, p = 0.43 Role, physical: 29 ± 10 vs 29 ± 10, p = 0.92 Bodily pain: 32 ± 6 vs 31 ± 6, p = 0.69 General health perceptions: 47 ± 7 vs 47 ± 10, p = 0.71 Vitality: 43 ± 10 vs 42 ± 10, p = 0.52 Social function: 35 ± 12 vs 33 ± 12, p = 0.47 Role emotional: 37 ± 16 vs 35 ± 15, p = 0.51 Mental health: 45 ± 8 vs 42 ± 13, p = 0.21 Physical components summary: 32 ± 7 vs 32 ± 7, p = 0.81 Mental components	

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
							summary: 46 ± 10 vs 43 ± 14, p = 0.25	
Wu 2015	N=118	Inclusion: Patients with ≥6 months' radicular pain caused by single-level lumbar disc herniation; age 20-60 years; MRI confirmation of disc herniation that correlated with clinically identified segment (<6 mm with ≥50% normal disc height); absence of neurological deficits; unresponsive to conservative treatment (physical therapy, manual therapy, non-opioid medications); NRS ≥5 (on 0-10 scale); no history of surgical treatment. Exclusion: Infection; spine tumor or fracture; history of drug abuse; multilevel symptoms or MRI evidence thereof; psychological or cognitive disorder that could influence outcome; structural spinal deformities or vertebral canal stenosis; severe degenerative disc material or complete annular disruption on MRI; intervertebral disc herniations ≥6 mm or sequestered intervertebral disc herniations and leg pain greater than back pain; pregnancy; allergy to contrast or drugs used in	A: Transforaminal injection of betamethasone (2.0 mL, dosage NR) plus 1.0% lidocaine (1.0 ml) with 1.0 mL contrast and fluoroscopic guidance (n=40) B: Nucleoplasty plus nerve root injection: nucleoplasty as below (C) immediately followed by nerve root injection of betamethasone (2.0 mL, dosage NR) plus 1.0% lidocaine (1.0 ml) (n=39) C: Nucleoplasty: discography with 0.5 ml contrast to verify annular integrity followed by nucleoplasty using radiofrequency (temperature and length of ablation NR) at six position with	Levels: Single (A vs. B vs. C; L4-L5: 69% (20/29) vs. 69% (24/35) vs. 67% (22/33); L5-S1: 31% (9/29) vs. 31% (11/35) vs. 33% (11/33) Repeat injections: Single	CT guidance with fluoroscopy	A: Lumbar stabilization exercises beginning 3 weeks post-injection B & C: 6 hours bed rest post-procedure; unlimited walking, standing, sitting but avoidance of lifting, bending, or stooping for 2 weeks post-procedure; lumbar stabilization exercises beginning 3 weeks post-injection	A vs. B vs. C: Age (mean): 40.5 ± 10.5 vs. 41.2 ± 9.9 vs. 42.4 ± 10.1 Male: 62% (18/29) vs. 63% (22/35) vs. 64% (21/33) Duration of symptoms: mean NR; 6-12 mos.: 7% (2/29) vs. 6% (2/35) vs. 9% (3/33); 12-24 mos.: 21% (6/29) vs. 20% (7/35) vs. 21% (7/33); >24 mos.: 72% (21/29) vs. 74% (26/35) vs. 70% (23/33) Baseline pain (0-10 NRS): 7.3 ± 1.00 vs. 7.3 ± 1.01 vs. 7.2 ± 1.15 Baseline function (ODI, 0-100) 48.1 ± 11.29 vs. 47.7 ± 11.7 vs. 47.7 ± 10.3	NR (authors declared no conflict of interest)

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		the study.	fluoroscopic guidance (n=39)					
Epidural steroid injection vs. Conservative Care								
Buchner 2000	N=36	Inclusion: 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 Exclusion: Previous lumbar surgery; lumbar spinal stenosis by MRI; cauda equina syndrome; acute severe motor paresis	A: Interlaminar epidural injection with 100 mg methylprednisolone in 0.25% bupivacaine (10 ml) plus conservative care (see "B" for details) (n=17) B: Conservative care: Bed rest; analgesics; NSAIDS or tramadol; graded rehabilitation including hydrotherapy, electroanalgesia, spinal mobilization physiotherapy (n=19)	Levels: Single level Repeat injections: 3 injections within 14 days	NR	NR	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 Baseline function: Hannover Functional Ability Questionnaire: 39% vs. 40%	NR
Murakibhavi 2011	N=102	Inclusion: ≥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) Exclusion: History of surgery; severe motor weakness; rapidly progressive neurological deficit; cauda equina	A: Caudal epidural injection with 80 mg triamcinolone acetate (2 ml), 2% lidocaine (2 ml), and normal saline (20 ml), with fluoroscopic guidance (n=50) B: Conservative treatment (tizanidine 6-12 mg/d, diclofenac	Levels: NR Repeat injections: Repeat injection permitted after 2-3 weeks if <20% improvement in VAS pain; 12% received repeat injection	Fluoroscopic guidance without contrast verification	NR	A vs. B: Age (mean): 45 years (overall) Male: 66% (overall) Race: NR MRI findings: 60% disc degeneration; 26% disc bulge; 14% disc herniation Treatment prior to intervention: 98% rest/analgesics; 78% traction; 76%	NIH/NIAMS and University of Washington (through gift from Synthes Spine)

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		syndrome; neurogenic claudication; local infection at injection site; steroid use in last 3 weeks; allergy to steroids; bleeding diathesis; pregnant; uncontrolled hypertension; uncontrolled diabetes	50-100 mg/d, amitriptyline 10-50 mg qhs, bilateral skin traction, physiotherapy including TENS, short-wave diathermy, back extension exercises) (n=50)				lumbar belt; 76% physiotherapy; 18% epidural injection Duration of symptoms (months): 21 (overall) Baseline pain (0-10 VAS): 8.1 vs. 8.1 Baseline ODI (0-100): 36 vs. 36	

Appendix Table F2. Lumbar Radiculopathy Attributed to Disc Pathology Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injection vs. Control injection							
Arden 2005, Price 2005	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)	12 months 89% (203/228)	A vs. B: Leg pain Baseline scores: 5.2 ± 2.3 vs. 5.6 ± 2.2 Mean change from baseline, 0-100 VAS: -12 ± 28 vs. -10 ± 28 at 3 weeks; -15 ± 32 vs. -15 ± 32 at 6 weeks; -13 ± 33 vs. -18 ± 33 at 12 weeks; -17 ± 36 vs. -20 ± 34 at 52 weeks (p>0.05 at all time points) Leg pain improved >50%: 35% (42/120) vs. 26% (28/108) at 3 weeks; 47% (56/120) vs. 41% (44/108) at 6 weeks; 43% (52/120) vs. 46% (50/108) at 12 weeks; 48% (58/120) vs. 44% (48/108) at 52 weeks	A vs. B: ODI Baseline scores: 44 ± 15 vs. 45 ± 18 Mean change from baseline, 0-100: -10.3 ± 14.8 vs. -6.6 ± 15.6 at 3 weeks; -13 ± 17 vs. -10 ± 18 at 6 weeks; -12 ± 19 vs. -12 ± 21 at 12 weeks; -16 ± 23 vs. -14 ± 24 at 52 weeks (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%: 12.5% (15/120) vs. 3.7% (4/108) at 3 weeks; 15% (18/120) vs. 13% (14/108) at 6	SF-36: p=NS (data NR)	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 Surgery: 13% (15/120) vs. 13% (14/108) through 52 weeks, RR, 0.96 (95% CI 0.49 to 1.9) Other injections: 13% vs. 11% over 52 weeks Other: Physiotherapy: 26% vs. 23% over 52 weeks Anxiety (mean improvement from baseline): 2 vs. 2 at 3 weeks; 2 vs. 2 at 6 weeks; 2 vs. 3 at	A vs. B: Post-dural puncture headache: 0.8% (1) vs. 0% Non-specific headache: 3% (4) vs. 4% (4) Nausea: 1.6% (2) vs. 1.8% (2) Transient side effects, not further defined: 4.1% (5) vs. 4.6% (5)

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
				weeks; 16% (19/120) vs 22% (24/108) at 12 weeks; 32.5% (38/120) vs. 29.6% (32/108) at 52 weeks		12 weeks; 3 vs. 3 at 52 weeks 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 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	
Bush 1991	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)	12 months 82% (23/28)	A vs. B: Pain (0-100 VAS): 38.5 vs. 49.2 at baseline; 16 vs. 45 at 1 month (p not reported); 14.2 vs. 29.6 at 12 months (p>0.05)	A vs. B: Function/Lifestyle (6-18 scale; specific symptomology questionnaire designed by Grogono and Woodgate): 13.4 vs. 12.9 at baseline; 15.8 vs. 13.7 at 1 month (p not reported); 16.6 vs. 15.6 at 12 months (p>0.05)	NR	A vs. B: Opioid use: NR Surgery: 8.3% (1/12) vs.18% (2/11), RR 0.39 (95% CI 0.04 to 3.80) Other: NR	A vs. B: Irregular menses: 8% (1/12) vs. 0% "no major side effects were reported"

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Carette 1997	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)	3 months 99% f/u (156/158)	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)* Pain (0-100 VAS): 65.6 ± 21.6 vs. 61.5 ± 21.4 at baseline; 44.9 vs. 49.1 at 3 weeks, difference -8.6 (95% CI -18 to 0.3); 38.9 vs. 39.5 at 3 months, change from baseline -26.5 ± 36.0 vs. -22.5 ± 34.4 at 3 months, difference -4.0 (95% CI -15 to 7.2) at 3 months McGill Present Pain Intensity (0-5): 2.6 ± 1.1 vs. 2.8 ± 1.0 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): 27.8 ± 12.0 vs. 26.2 ± 10.7 at baseline;	A vs. B: ODI (mean ± SD, 0-100): 59.6 ± 15.7 vs. 50.0 ± 15.5 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 (perceived degree of overall improvement rated on a 7 item scale that ranged from very marked improvement to very marked	NR	Use of drugs other than acetaminophen (i.e., narcotics, NSAIDs, anxiolytic agents, or muscle relaxants): 34.6% (27/78) vs. 40.0% (32/80), p=0.55 Surgery: Cumulative probability of undergoing surgery in 12 months post randomization: 25.8% vs. 24.8% (p=0.90, log-rank test) Other: Non-pharmacologic treatment (i.e., physiotherapy or chiropractic treatment): 11.5% (9/78) vs. 5.0% (4/80); p=NS Lack of efficacy	A vs. B: Dural puncture: 1.3% (1/78) vs. 1.2% (1/80); RR = 1.02 (95% CI, 0.06 to 16.1), p=0.98 Transient headache: 27% (21/78) vs. 20% (16/80); RR = 1.34 (95% CI, 0.76 to 2.38), p=0.30

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			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)	deterioration [not defined further]): 33% (25/76) vs. 30% (23/78) at 3 weeks, 55% (41/74) vs. 56% (43/77) at 3 months Sickness Impact Profile, Overall (0 to 100): 21.7 ± 10.5 vs. 21.4 ± 9.7 at baseline; 16 vs. 18 at 3 weeks; 12 vs. 13 at 3 months (no differences on physical or psychosocial dimensions subscales) Restricted activity in previous 2 weeks (number of days): 9.9 ± 6.1 vs. 9.7 ± 6.1 at baseline; 8.9 vs. 7.9 at 3 weeks; 5.9 vs. 5.4 at 3 months		withdrawal: 15% (12/78) vs. 25% (20/80) at 3 months, RR 0.62 (95% CI 0.32 to 1.17)	
Cohen 2012	A. Transforaminal epidural injection with 60 mg methylprednisolone acetate in 2 ml	6 months; surgery and remained on active duty assessed	A vs. B. vs. C: *(difference ANCOVA adjusted for study site, sex, duration of pain, opioid use, baseline*	A vs. B. vs. C: *(difference ANCOVA adjusted for study site, sex, duration of pain, opioid use,*	A vs. B. vs. C: *(difference ANCOVA adjusted for study site, sex, duration of pain, opioid use, baseline outcome score)*	A vs. B. vs. C: *(difference ANCOVA adjusted for study site, sex,*	A vs. B. vs. C: Worsening pain: 4% (1/28) vs. 19% (5/26) vs. 20% (6/30)

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	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)	through 1 year % f/u: 100% (84/84)	*outcome score)* Leg Pain (0-10 NRS, SD or 95% CI) 5.71 ± 1.93 vs. 6.62 ± 1.66 vs. 6.31 ± 2.02 at baseline; 2.54 1.36 to 3.69) vs. 3.56 (2.35 to 4.72) vs. 3.78 (2.72 to 4.85) 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 ± 2.50 vs. 6.08 ± 2.51 vs. 4.75 ± 2.49 at baseline, 3.49 (2.48 to 4.50) vs. 4.41 (3.37 to 5.44) vs. 4.01 (3.08 to 4.93) 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 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. B	*baseline outcome score)* ODI (0-100): 42.93 ± 15.57 vs. 41.12 ± 18.29 vs. 40.87 ± 17.50 at baseline, 24.1 (16.64 to 31.55) vs. 40.3 (32.91 to 47.61) vs. 30.0 (23.2 to 36.69) 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	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, s63% vs. 45% vs. 48% at 6 months	*duration of pain, opioid use, baseline outcome score)* Medication reduction (cessation of nonopioid analgesic or ≥20% decrease in opioid use): 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)	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%

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			adjusted OR 3.63 (95% CI 1.10 to 12.0), A vs. C 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)			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) Other: 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) Positive categorica outcome 75% (21/28) vs 42% (11/26) vs 50% (15/30) at 1	

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
						month (p = 0.09) 50% (14/28) vs 42% (11/26) vs 43% (13/30) at 3 months, 38% (8/28) vs 38% (10/26) vs 40% (12/30) at 6 months.	
Cuckler 1985	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)	13-30 mos. (mean 20.2 vs. 21.5 months) 100% (73/73)	A vs. B: 24-hours, pain improved ≥75%, all patients: 28.5% (12/42) vs. 25.8% (8/31); RR = 1.1 (95% CI, 0.5 to 2.3), p = 0.79 24 hours, pain improved ≥75%, herniated disc patients: 31.8% (7/22) vs. 35.7% (5/14); RR = 0.8 (95% CI, 0.35 to 2.2), p = 0.8 24 hours, pain improved ≥75%, stenosis patients: 25% (5/20) vs. 17.6% (3/17); RR = 1.4 (95% CI, 0.39 to 5.0), p = 0.59 24 hours, average improvement (%), all patients: 41.6 ± 6.2 vs. 43.6 ± 6.6, t = NS 24 hours, average improvement (%), herniated disc patients: 39.8 ± 9 vs. 43.9 ± 11.2, t = NS 24 hours, average	NR	NR	A vs. B: 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) Surgery, spinal stenosis: 26% (6/23) vs. 28.5% (4/14) at mean 20 months, RR = 0.91 (95% CI, 0.31 to 2.6), p = 0.87 Other: NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			improvement (%), stenosis patients: 43.5 ± 8.7 vs. 43.2 ± 8.0, t = NS Long-term, pain improved ≥75%, all patients: 26% (11/42) vs. 13% (4/31) at mean 20 months Long-term, pain improved ≥75%, herniated disc patients: 26% (6/23) vs. 15% (2/13) at mean 20 months Long-term, pain improved ≥75%, stenosis patients: 21.7% (5/23) vs. 14.2% (2/14)				
Datta 2011	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)	3 months 78.7% (163/207)	A vs. B vs. C vs. D: Pain (0-10 VAS): 7.4 ± 0.95 vs. 7.4 ± 0.57 vs. 7.3 ± 0.65 vs. 7.2 ± 0.79 at baseline; 6.3 ± 0.79 vs. 6.3 ± 0.79 vs. 6.4 ± 0.79 vs. 6.8 ± 0.79 at 3 weeks; 4.9 ± 1.29 vs. 4.8 ± 0.92 vs. 5.2 ± 1.59 vs. 6.2 ± 0.79 at 3 months Complete pain relief (<6 diclofenac tablets/week) at 3 months: 43.5% (17/39) vs. 42.9% (18/42) vs. 37.5% (15/40) vs. 26.2% (11/42)	A vs. B vs. C vs. D: RDQ improved >5 points (percent improvement, 0-24): 41% (16/39) vs. 40% (17/42) vs. 35% (14/40) vs. 38% (16/42) at 3 weeks; 69% (27/39) vs. 71% (30/42) vs. 62% (25/40) vs. 24% (10/42) at 3 months	NR	A vs. B vs. C vs. D: Use of diclofenac (tablets/day): 6.0 vs. 5.9 vs. 6.0 vs. 5.7 at baseline; 3.8 vs. 3.3 vs. 4.0 vs. 4.8 at 3 weeks; 18 vs. 17 vs. 18 vs. 26 at 3 months Surgery: 6.0% (3/50) vs. 7.7% (4/52) vs. 6.0% (3/50) vs. 16% (9/55) at 3 months	A vs. B vs. C vs. D: Local pain >24 hrs.: 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.

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	D: Caudal epidural injection with 0.125% bupivacaine (10-15 ml) (n=55)					Other: 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 at 3 months: 12.8% (5/39) vs. 21.4% (9/42) vs. 27.5% (11/40) vs. 47.6% (20/42) Motor deficits at 3 months: 13.8% (5/39) vs. 16.3% (7/42) vs. 16.1% (6/40) vs. 23.4% (10/42)	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) Sensory deficits: 13% (5/39) vs. 21% (9/42) vs. 28% (11/40) vs. 48% (20/42) at 3 months Epidural hematoma: 0% for all groups Intravascular injection: 0% for all groups Nerve root injury: 0% for all groups Subarachnoid injection: 0% for all groups Meningitis: 0% for all groups
Dilke 1973	A: Interlaminar epidural injection with 80 mg	3 months 82% (82/100)	A vs. B: Pain clearly relieved during admission (clearly	NR	NR	A vs. B: Analgesic consumption	"There were no complications attributable to

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	methylprednisolone in saline (10 ml) (n=50) B: Interspinous ligament injection with saline (1 ml) (n=50)		relieved, clearly not relieved, or intermediate): 31% (16/51) vs. 8% (4/43) Pain assessment "none" (none, not severe, severe): 36% (16/44) vs. 21% (8/38) at 3 months Pain assessment "none" or "not severe": 91% (40/44) vs. 74% (28/38) at 3 months			"none" (none, less than daily, daily) at 3 months: 50% (19/38) vs. 38% (11/29) Surgery: 14% (7/51) vs. 21% (10/48) at 3 mos. Other: 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 (p=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) Underwent other conservative treatment at 3 months: 18% (9/51) vs. 29% (14/48)	the injections" "Cerebrospinal fluid was inadvertently tapped on 6 occasions in the course of this trial; the needle was withdrawn and an extradural injection was carried out immediately through an adjacent interspinous space"

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
						Underwent second injection at 3 months: 31% (16/51) vs. 48% (23/48)	
el Zahaar 1991	A: Caudal epidural injection with hydrocortisone (5 ml), 4% Carbocaine (4 ml), and saline (21 ml) (n=19 with acute HNP)* B: Caudal epidural injection with 4% Carbocaine (4 ml) plus saline (26 cc) (n=14 with acute HNP)* *A total of 37 patients were randomized to epidural steroid injection and 26 to placebo; only results for those diagnosed with a herniated disc are reported here.	Mean 20.9 months (20.2 vs. 21.5 months) (range, 13-36 months) % f/u NR	A vs. B: Treatment success, short term (≥75% improvement (no formal definition – all patients asked quantitate the % improvement) in pre-injection back, leg, and thigh symptoms after 24 hours): 73.6% (14/19) vs. 71.4% (10/14) Treatment success, long term (≥75% improvement (no formal definition – all patients asked quantitate the % improvement) in pre-injection symptoms at mean 20.9 months, range 13-36 months): 57.8% (11/19) vs. 64.2% (9/14) Total failures: 42.1% (8/19) vs.	NR	NR	Surgery: 26.3% (5/19) vs. 21.4% (3/14)	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			35.7% (5/14)				
Ghahreman 2010	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)	12 months 79% f/u (118/150) Differential loss to f/u for 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	A vs. B vs. C vs. D vs. E: Pain (mean, 0-10): at baseline 7.0 ± 1.7 vs. 7.4 ± 2.1 vs. 6.6 ± 2.2 vs. 7.6 ± 2.0 vs. 7.0 ± 1.5; at 1 month 4.1 ± 3.0 vs. 6.7 ± 2.8 vs. 5.5 ± 2.6 vs. 5.9 ± 3.4 vs. 6.0 ± 2.5, 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	A vs. B vs. C vs. D vs. E: Patient-specified Functional Outcome Scale (median, 0-12): at 1 month 8 (6 to 9) vs. 6 (2 to 12) vs. 6 (4 to 9) vs. 10 (6 to 12) vs. 10 (6 to 12) (p>0.05)	NR	A vs. B vs. C vs. D vs. E: 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) Other:	No complications occurred that could be attributed to the treatment, 1 case of bladder incontinence after transforaminal injection of local anesthetic

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			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			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)	

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
						No differences in health care utilization	
Ghai 2015	A: Epidural injection of 6 mL 0.5% lidocaine mixed with 80 mg (2 mL) of methylprednisolone acetate using a parasaggital interlaminar approach B: Epidural injection of 8 mL of 0.5% lidocaine using a parasaggital interlaminar approach	12 months Overall: 81.1% (56/69) A vs B: 88.6% (31/35) vs 73.5% (25/34)	**Effective pain relief** 3 months 86% (30/35) vs 50% (17/34), p = 0. 6 months 86% (30/35) vs 56% (19/34), p = 0.008 9 months 89% (31/35) vs 53% (18/34) p = 0.001 12 months 89% (31/35) vs 59% (20/34) at 12 months **NRS (0-10):** Baseline 8.0 ± 1.6 vs 8.0 ± 1.4, p = 0.92 3 months 3.1 vs. 4.5, p < 0.001 6 months 3.0 vs. 4.4 , p < 0.001 9 months 2.7 vs. 4.6, p < 0.001 at 12 months 2.6 vs. 4.4, p < 0.001 (3, 6, 9, 12 months estimated from graph)	**Modified Owestry Disability Questionnaire** Score Baseline 46.8 ± 14.3 vs 49.6 ± 12.8, p = 0.94 3 months 21 vs. 27, p < 0.001 6 months 20 vs. 26, p < 0.001 9 months 18 vs. 26, p < 0.001 12 months 19 vs. 27, p < 0.001 (3, 6, 9, 12 months estimated from graph)	NR	NR	One patient in group B developed vasovagal response at the time of drug injection and was managed successfully with an injection of atropine. No other complications were noted.
Helliwell 1985	A: Interlaminar epidural injection with 80 mg methylprednisolone in saline (10 ml)	3 months % f/u NR	A vs. B: Pain, mean change from baseline (0-10 VAS, estimated from figure): at 1 month -2.6 vs. -0.7;	NR	A vs. B: Overall outcome "definite improvement" (vs. no improvement): at 3 months 70% 14/20 vs. 26% (5/19)	A vs. B: Analgesic consumption decreased by ≥50%: at 3	"No complications during injection procedures. All patients given

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	(n=20) B: Interspinous ligament injection with saline (5 ml) (n=19)		at 3 months -2.7 vs. -0.4 (p<0.01 at both time points)			months 64% (7/11) vs. 40% (4/10) Surgery: NR Other: NR	an epidural injection experienced pain in one or both legs for some minutes afterwards; this symptom was taken to indicate the correct placement of the injection"
Iversen 2011	A: Caudal epidural injection with 40 mg triamcinolone in 0.9% saline (29 ml) (n=37) B: Caudal epidural injection with 0.9% saline (30 ml) (n=39) C: Subcutaneous injection superficial to the sacral hiatus and outside spinal canal with 0.9% saline (2 ml) (n=40)	12 months 94% (109/116) at 6 weeks; 91% (105/116) at 3 months; 85% (99/116) at 12 months	A vs. B vs. C Low back pain (VAS 0-100): 46.8 (95% CI 39.0 to 54.6) vs. 49.6 (40.3 to 58.2) vs. 46.3 (39.2 to 54.1) at baseline; Difference in low back pain (95% CI) at followup (Crude analysis†): A vs. C: −4.8 (−16.2 to 6.6) at 6 weeks; 6.6 (−5.0 to 18.2) at 3 months; 0.0 (−12.1 to 12.2) at 12 months. B vs. C: −5.0 (−16.7 to 6.7) at 6 weeks; −7.8 (−19.3 to 3.8) at 3 months; −2.0 (−14.3 to 10.2) at 12 months Difference in low back pain (95% CI) at followup (Adjusted analysis‡):	A vs. B vs. C ODI (0-100): 32.5 (95% CI 28.6 to 36.4) vs. 31.4 (26.9 to 35.9) vs. 26.3 (22.0 to 30.6) at baseline; 23 vs. 25 vs. 23 at 6 weeks; 25 vs. 21.5 vs. 17.5 at 3 months; 19 vs. 14.5 vs. 13 at 12 months (6 weeks, 3 and 12 months estimated from graph) Difference (95% CI) in ODI at followup (Crude analysis†): A vs. C: −2.9 (−8.7 to 3.0) at 6 weeks; 4.0 (−1.9 to 9.9) at 3 months; 1.9 (−4.2 to 8.0) at 12 months	A vs. B vs. C EQ5D (-0.594 to 1): 0.54 (95% CI 0.45 to 0.62) vs. 0.46 (0.35 to 0.56) vs. 0.54 (0.47 to 0.56) at baseline Difference (95% CI) in EQ5D at followup (Crude analysis†): A vs. C: −0.05 (−0.16 to 0.06) at 6 weeks; −0.12 (−0.23 to −0.00) at 3 months; −0.05 (−0.17 to 0.06) at 12 months B vs. C: −0.02 (−0.13 to 0.09) at 6 weeks; −0.05 (−0.17 to 0.06) at 3 months; −0.01 (−0.12 to 0.11) at 12 months Difference (95% CI) in EQ5D at followup (Adjusted analysis‡): A vs. C: −0.04 (−0.15 to 0.07) at 6 weeks; −0.11 (0.22 to 0.00) at 3 months; −0.05 (−1.62 to 0.07) at 12 months	A vs. B. vs. C: Morphine use: 8.1% (3/37) vs. 17.1% (6/35) vs. 10.8% (4/37) at 6 weeks; p=0.70 Paracetamol use: 24.3% (9/37) vs. 20.0% (7/35) vs. 24.3% (9/37) at 6 weeks; p=0.26 NSAID use: 16.2% (6/37) vs. 11.4% (4/35) vs. 5.4% (2/37) at 6 weeks; p=0.45 Back surgery at 12 months: 2.7% (1/37) vs. 15% (6/39) vs. 20% (8/40); p=0.07	5% (6/116) had local pain with injection; "no serious complications due to injections"

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			A vs. C: −6.4 (−17.9 to 5.1) at 6 weeks; 5.1 (−6.5 to 16.8) at 3 months; −1.4 (−13.6 to 10.8) at 12 months. B vs. C: −6.9 (−18.8 to 5.1) at 6 weeks; −9.3 (−21.2 to 2.5) at 3 months; −4.1 (−16.5 to 8.4) at 12 months Leg pain (VAS 0-100): 50.1 (95% CI 42.5 to 57.7) vs. 53.5 (45.6 to 61.3) vs. 48.3 (39.6 to 56.9) at baseline; 37.5 vs. 41.5 vs. 37.5 at 6 weeks; 41.0 vs. 34.0 vs. 29.0 at 3 months; 22.0 vs. 27.0 vs. 20.0 at 12 months (6 weeks, 3 and 12 months estimated from graph) Difference in leg pain (95% CI) at followup (Crude analysis†): A vs. C: −1.3 (−13.3 to 10.7) at 6 weeks; 11.2 (−1.0 to 23.4) at 3 months; −0.2 (−12.9 to 12.5) at 12 months. B vs. C: 3.2 (−9.1 to 15.5) at 6 weeks; 2.5 (−9.6 to 14.6) at 3 months; 3.1 (−9.6 to 15.8) at 12 months	B vs. C: −0.5 (−6.3 to 5.4) at 6 weeks; 1.4 (−4.5 to 7.2) at 3 months; −1.9 (−8.0 to 4.3) at 12 months Difference (95% CI) in ODI at followup (Adjusted analysis‡): A vs. C: −3.2 (−9.1 to 2.7) at 6 weeks; 3.7 (−2.3 to 9.7) at 3 months; 1.7 (−4.5 to 7.8) at 12 months B vs. C: −0.6 (−6.6 to 5.4) at 6 weeks; 1.5 (−4.5 to 7.5) at 3 months; −2.6 (−8.9 to 3.6) at 12 months †Adjusted for baseline values. ‡Adjusted for duration of leg pain, back pain, and sick leave.	B vs. C: −0.01 (−0.13 to 0.10) at 6 weeks; −0.05 (−0.16 to 0.06) at 3 months; 0.01 (−1.06 to 0.13) at 12 months FABQ physical: 11.9 (95% CI 10.2 to 13.6) vs. 13.5 (12.1 to 14.9) vs. 13.0 (11.3 to 14.7) at baseline Difference (95% CI) in FABQ physical at followup:§ A vs. C: 0.60 (−1.84 to 3.03) at 6 weeks; −0.67 (−3.22 to 1.87) at 3 months; 0.60 (−1.84 to 3.03) at 12 months B vs. C: −0.24 (−2.69 to 2.21) at 6 weeks; −2.10 (−4.66 to −4.5) at 3 months; −0.24 (−2.69 to 2.21) at 12 months FABQ work: 23.5 (95% CI 20.5 to 26.5) vs. 25.0 (21.9 to 28.1) vs. 21.6 (17.9 to 25.3) at baseline Difference (95% CI) in FABQ work at followup:§ A vs. C: 2.31 (−1.48 to 6.11) at 6 weeks; 2.40 (−1.55 to 6.34) at 3 months; 2.31 (−1.48 to 6.11) at 12 months B vs. C: 0.72 (−3.10 to 4.55) at 6 weeks; 0.47 (−3.51 to 4.44) at 3 months; 0.72 (−3.10 to 4.55) at 12 months	Other: Physiotherapy: 11% (12/109) at 6 weeks; 17% (18/105) at 3 months; and 11% (11/99) at 12 months; p=0.69 between groups (% not reported by group) 5 patients did not receive allocated intervention (1 vs. 3 vs. 1), 7 discontinued intervention (2 vs. 4 vs. 1); no crossovers	

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			Difference in leg pain (95% CI) at followup (Adjusted analysis‡): A vs. C: −2.6 (−14.6 to 9.4) at 6 weeks; 10.0 (−2.2 to 22.3) at 3 months; −1.4 (−14.1 to 11.4) at 12 months. B vs. C: 2.7 (−9.8 to 15.2) at 6 weeks; 1.7 (−10.7 to 14.0) at 3 months; 0.5 (−12.4 to 13.4) at 12 months †Adjusted for baseline values. ‡Adjusted for duration of leg pain, back pain, and sick leave.		Patient satisfaction: NR †Adjusted for baseline values. ‡Adjusted for duration of leg pain, back pain, and sick leave. § Do not give results by Crude and Adjusted Analysis (like EQ5D); Assumed Crude.		
Karppinen 2001, 2001	A: Transforaminal (periradicular) injection with 2-3 cc of methylprednisolone 40 mg/cc plus bupivacaine 5 mg/cc, with fluoroscopic guidance (n=80) B: Transforaminal (periradicular) injection with isotonic (0.9%) saline (2-3 cc), with fluoroscopic guidance (n=80)	12 months 97% (158/163) at 3 (79 vs. 79), 6 (n=78 vs. 80) and 12 (n=78 vs. 80) months (2 patients lost to f/u; 3 patients withdrawn – envelopes unsealed-because	A vs. B: *(difference ANCOVA adjusted for level of symptomatic disc and days on sick leave)* Leg pain (0-100 VAS): 71.0 ± 18 vs. 75.2 ± 19 at baseline; 39.1 vs. 54.1 at 2 weeks, difference -12.5 (95% CI -23.4 to -1.6); 36.9 vs. 43.9 at 4 weeks, difference -2.3 (95% CI -13.4 to 8.7); 31.3 vs. 34.3 at 3 months, difference 0.5 (95% CI -11 to 12); 30.7	A vs. B: *(difference ANCOVA adjusted for level of symptomatic disc and days on sick leave)* ODI (0-100): 42.9 ± 16 vs. 43.5 ± 15 at baseline; 28.8 vs. 34.0 at 2 weeks, difference -5.1 (95% CI -10 to 0.3); 26.8 vs. 29.1 at 4 weeks, difference -1.5 (95% CI -7.3 to 4.4); 22.9 vs. 22.6 at	NR	A vs. B: *(difference ANCOVA adjusted for level of symptomatic disc and days on sick leave)* Opioid use: NR Surgery: 22% (18/80) vs. 19% (15/80) at 12 m, RR 1.2 (95% CI 0.65 to 2.21) Other:	Retroperitoneal hematoma in one patient on anticoagulant therapy in group A

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
		neurogram findings were not typical)	vs. 21.6 at 6 months, difference 16 (95% CI 5.6 to 27); 23.9 vs. 24.2 at 12 months, difference 5.3 (-5.0 to 16) Back pain (0-100 VAS): 52.8 ± 25 vs. 59.8 ± 25 at baseline; 25.5 vs. 36.3 at 2 weeks, difference -5.8 (95% CI -17 to 5.1); 27.4 vs. 31.3 at 4 weeks, difference 6.1 (95% CI -5.0 to 17); 26.2 vs. 22.8 at 3 m, difference 12 (95% CI 1.0 to 24); 22.6 vs. 20.1 at 6 m, difference 14 (95% CI 2.4 to 25); 18.8 vs. 19.0 at 12 m, difference 8.4 (95% CI -2.1 to 19)	3 m, difference 1.3 (95% CI -6.1 to 8.6); 18.9 vs. 15.8 at 6 m, difference 5.9 (95% CI -0.7 to 12); 15.9 vs. 16.3 at 12 m, difference 0.4 (95% CI -6.2 to 7.0) Straight Leg Raising Test (degrees) 58 ± 18 vs 60 ± 19 4.8 ± 1.5 vs 4.9 ± 1.5 at baseline; 73 vs 70 at 2 weeks, difference -6 (95% CI -12 to -1); 77 vs 74 at 4 weeks, difference -5 (-11 to 1); 82 vs 81 at 3 months, difference -1 (-9 to 5); 83 vs 85 at 6 months, difference 2 (-5 to 9); 87 vs 84 at 12 months, difference -5 (-11 to 2) Lumbar flexion 4.8 ± 1.5 vs 4.9 ± 1.5 at baseline, 4.9 vs 4.8 at 2 weeks, difference -0.4 (-0.8 to -0.1); 4.9 vs 4.9 at 4 weeks, difference 0 (-0.5 to 0.4); 4.9 vs 5.2 at 3		Sick leave (days/month): 8.9 vs.10 at 4 weeks, 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 weeks, 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)	

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
				months, difference 0.2 (-0.4 to 0.7); 5.4 vs 5.3 at 6 months, difference -0.3 (-1.4 to 0.8); 5.4 vs 5.4 at 12 months, difference -0.5 (-1.0 to 0.1)			
Klenerman 1984 Also included for epidural injection (approach NR) vs. placebo for LBP + radiculopathy	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)	2 months 85% f/u (63/74) (15% (11/74) excluded from analysis, including 1 lost to followup)	A vs. B vs. C vs. D: 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	NR	A vs. B vs. C vs. D: Global assessment "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)	Opioid use: NR 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) Other outcomes: NR	"no complications from the treatment administered"
Manchikanti 2012, 2011, 2008	A: Caudal epidural injection with 6 mg betamethasone or 40 mg	24 months 95.0% (114/120) at 3 months;	A vs. B: Pain (mean NRS, 0 to 10): 7.8 ± 0.9 vs. 8.1 ± 0.9 at	A vs. B: ODI (0 to 50): 27.9 ± 4.8 vs. 29.2 ± 4.6 at baseline	NR	A vs. B: Opioid use (mg MED/day): 45.0 ± 57.8 vs.	"No major adverse events"

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	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)	87.5% (105/120) at 6 months; 82.5% (99/120) at 12 months; 80.0% (96/120) at 24 months	baseline (p=0.08); 3.4 ± 1.7 vs. 4.1 ± 1.8 at 3 months (p=0.02); 3.5 ± 1.7 vs. 3.9 ± 1.8 at 6 months (p=0.21); 3.5 ± 1.9 vs. 4.1 ± 1.8 at 12 months (p=0.06); at 24 months 3.6 ± 1.8 vs.4.2 ± 1.8 (p=NR) (p=0.80 for group difference overall) <u>Pain improved ≥50% from baseline</u>: at 3 months 80.0% (48/60) vs. 76.7% (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>Success (pain improved ≥50% and ODI improved ≥50%)</u>: 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)	(p=0.16); 13.6 ± 6.5 vs. 16.5 ± 7.2 at 3 months (p=0.02); 13.7 ± 7.0 vs. 15.5 ± 7.3 at 6 months, (p=0.17); 13.1 ± 7.0 vs. 15.5 ± 7.74 at 12 months (p=0.07); 13.5 ± 7.2 vs. 15.6 ± 7.3 at 24 months (p=NR) (p=0.71 for group difference overall) <u>ODI improved ≥50% from baseline</u>: at 3 months 73% (44/60) vs. 62% (37/60); at 6 months 73% (44/60) vs. 72% (43/60); at 12 months 75% (45/60) vs. 67% (40/60); at 24 months 70% (42/60) vs. 60% (36/60)		51.8 ± 58.6 at baseline (p=0.52); 30.1 ± 31.8 vs. 32.8 ± 31.6 at 3 months (p=0.64); 31.1 ± 37.5 vs. 32.9 ± 31.6 at 6 months P=0.79); 31.1 ± 37.5 vs. 32.8 ± 31.6 at 12 months (p=0.79); 31.1 ± 37.5 vs. 32.8 ± 31.6 at 24 months (p=NR): (p=0.75 for group difference overall) <u>Surgery</u>: NR <u>Other</u>: NR	
Manchikanti 2014	A: Transforaminal epidural injection of betamethasone 0.5	<u>12 months</u> 92% (55/60) vs 88% (53/60)	A vs. B <u>Pain (NRS 0-10):</u> 8.2 ± 0.9 vs. 8.3 ± 0.9 at baseline; 4.0 ± 1.5 vs. 4.1	A vs. B <u>Function (ODI 0-50):</u> 28.0 ± 5.3 vs. 29.9 ±	NR	A vs. B <u>Opioid intake (morphine equivalents in</u>	Not report by group <u>Intravascular infiltration</u>: 4.6%

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	mL plus lidocaine 1.5 mL (1%), with fluoroscopic guidance (n=60) B: Transforaminal epidural injection of lidocaine 1.5 mL (1%) and sodium chloride, with fluoroscopic guidance (n=60)	24 months 83% (50/60) vs 78% (47/60)	± 1.8 at 3 months; 4.1 ± 1.7 vs. 3.9 ± 1.5 at 6 months; 4.1 ± 1.6 vs. 3.9 ± 1.6 at 12 months; 4.2 ± 1.6 vs. 4.0 ± 1.6 at 24 months; overall group difference, p=0.357 Significant pain relief (≥50%) from baseline: 73% (44/60) vs. 77% (46/60) at 3 months; 68% (41/60) vs. 73% (44/60) at 6 months; 63% (38/60) vs. 77% (46/60) at 12 months; 58% (35/60) vs. 67% (40/60) at 24 months Success: Significant pain relief (≥50%) and improvement in ODI (≥50%) from baseline: 67% (40/60) vs. 75% (45/60) at 3 months; 67% (40/60) vs. 73% (44/60) at 6 months; 57% (34/60) vs. 65% (39/60) at 24 months	4.8 at baseline; 14.7 ± 6.4 vs. 16.5 ± 7.2 at 3 months; 14.3 ± 6.6 vs. 15.2 ± 6.7 at 6 months; 14.5 ± 6.6 vs. 14.7 ± 6.9 at 12 months; 14.1 ± 6.5 vs. 14.9 ± 6.9 at 24 months; overall group difference, p=0.278 Significant improvement in ODI (≥50%) from baseline: 68% (41/60) vs. 75% (45/60) at 3 months; 70% (42/60) vs. 77% (46/60) at 6 months; 60% (36/60) vs. 78% (47/60) at 12 months; 65% (39/60) vs. 72% (43/60) at 24 months		mg) 68.9 ± 51.9 vs. 62.9 ± 49.3 at baseline; 40.8 ± 31.8 vs. 48.6 ± 45.1 at 3 months; 39.3 ± 32.2 vs. 45.3 ± 42.4 at 6 months; 38.3 ± 32.2 vs. 45.1 ± 42.4 at 12 months; 36.6 ± 32.4 vs. 42.9 ± 37.5 at 24 months; group difference, p=0.239 Surgery: NR	(28/601 injections) Nerve root irritations: 1.5% (9/601 injections) Post subarachnoid puncture headaches: 0% (0/601 injections)
Manchikanti 2014, 2013, 2010	A: Interlaminar epidural injection with 6 mg betamethasone (1 ml) plus 0.5% lidocaine (5 ml), with	24 months 91% (109/120) at 12 months; 84% (101/120); at	A vs. B: NRS Pain scores (0-10): 8.0 ± 1.0 vs. 8.2 ± 0.8 at baseline; 3.5 ± 1.0 vs. 3.9 ± 1.6 at 3 months; 3.5 ± 1.0 vs.	A vs. B ODI (0-50): 29.6 ± 5.2 vs. 30.3 ± 4.7 at baseline, 14.0 ± 4.2 vs.	NR	A vs B Opioid use (mg med/day): 47.1 ± 27.2 vs. 49.6 ± 39.3 at baseline; 42.4 ± 39.9 vs.	Dural puncture: 1.6% (11/682 procedures); not reported by group

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	fluoroscopic guidance (n=60) B: Interlaminar epidural injection with 0.5% lidocaine (6 ml), with fluoroscopic guidance (n=60)	24 months	4.1 ± 1.6 at 6 months; 3.4 ± 1.2 vs. 4.0 ± 1.6 at 12 months; 3.7 ± 1.4 vs. 4.1 ± 1.7 at 24 months (p>0.05 at all time points) Pain relief ≥50%: 88% (53/60) vs. 78% (47/60) at 3 months; 88% (53/60) vs. 70% (42/60) at 6 months; 85% (51/60) vs. 72% (43/60) at 12 months; 70% (42/60) vs. 63% (38/60) at 24 months Success (significant improvement of ≥50% in pain and ODI from baseline) 6 months f/u: 85% vs. 63% 12 months: 85% vs. 67% 24 months: 70% vs. 60%	15.8 ± 6.3 at 3 months; 13.5 ± 4.2 vs. 16.1 ± 6.6 at 6 months; 13.0 ± 4.2 vs. 15.9 ± 6.9 at 12 months; 13.5 ± 4.8 vs. 16.1 ± 6.8 at 24 months (p>0.05 at all time points) ODI improved ≥50%: 82% (49/60) vs. 73% (44/60) at 3 months; 87% (52/60) vs. 63% (38/60) at 6 months; 87% (52/60) vs. 68% (41/60) at 12 months; 73% (44/60) vs. 63% (38/60) at 24 months		34.3 ± 25.2 at 3 months; 36.5 ± 27.6 vs. 37.3 ± 43.3 at 6 months; 36.5 ± 27.6 vs. 37.3 ± 43.3 at 12 months; 36.6 ± 27.6 vs. 36.2 ± 43.7 at 24 months (p>0.05 at all time points) Surgery: NR Other: NR	Headaches: 0% Nerve root irritations: 0% Other adverse consequences: 0%
Ridley 1988	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) and saline (10 ml) (n=19) B: Interspinous ligament injection	2 weeks 89.7% (35/39)	A vs. B: 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.	NR	NR	NR Note: 14 crossovers in placebo group; timing unclear	A vs. B: Accidental CSF tap: 10.5% (2) vs. 0% Headache: 5.2% (1) (1 of the 2 with accidental CSF

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	with saline (2 ml) (n=16)		0%, (p<0.01)				tap) vs. 0% (0) Hypotension: 0% vs. 0%
Riew 2006, 2000	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)	Mean 23 months, range 13 to 28 months for initial followup (100% f/u (55/55); ≥5 years for second followup (85% f/u (47/55), with differential loss to f/u for A vs. B: 29% (8/28) vs. 0% (0/27) at ≥5 years)	NR	NR	NR	A vs. B: Opioid use: NR 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) OR 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) Other: NR	NR
Rogers 1992	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) plus 2% lignocaine (14 ml) plus saline (4 ml)	1 month for all outcomes except subsequent surgery, which was	A vs. B: Pain "none" at 1 month: 20% (3/15) vs. 6.7% (1/15) Pain "none" or "mild" at 1 month: 47% (7/15) vs. 20% (3/15)	A vs. B: Full ability to work at 1 month: 53% (8/15) vs. 33% (5/15), RR 1.6 (95% CI 0.68 to 3.80)	NR	A vs. B: Reduced analgesic intake: 53% (8/15) vs. 40% Surgery at 20-21	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	(n=15) B: Interlaminar epidural injection with 2% lignocaine (14 ml) + saline (6 ml) (n=15)	evaluated at 20-21 months % f/u NR				months follow-up: 27% (4/15) vs. 27% (4/15) Other: NR	
Sayegh 2009	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)	12 months 89.1% (163/183) at 1 month; 82.5% (151/183) at 12 months	NR	ODI (scale NR): 38.5 ± 2.6 vs. 38.5 ± 2.7 at baseline (p=0.75); 12.1 ± 13.1 vs. 29.9 ± 6.2 at 1 week (p<0.0005); 8.7 ± 11.9 (n=89) vs. 23.5 ± 9.6 (n=85) at 1 month (p<0.0005); 5.8 ± 8.6 (n=83) vs. 13.6 ± 10.5 (n=70) at 6 months (p<0.0005); 4.9 ± 7.1 (n=81) vs. 13.0 ± 10.1 (n=70) at 12 months (p<0.0005)	NR	Opioid use: NR Surgery: 14.0% (13/93) vs. 21.1% (19/90) at 12 months No. who underwent surgery: 1 month: 4 vs. 5 6 months: 6 vs. 15 12 months: 2 vs. 0 Total: 12/93 vs. 20/90	Transient lower extremity numbness: 13% (12/93) vs. 8.9% (8/90); Feeling faint: 5.4% (5/93) vs. 7.8% (7/90); "No patient reported any major immediate or late complications"
Snoek 1977	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) (n=27) B: Interlaminar epidural injection with saline (2 ml) (n=24)	Mean NR, range 8-20 months % f/u NR	*Early results (mean 48 ± 24 hours post-injection)* Relief of radiating pain: 25.9% (7/27) vs. 12.5% (3/24), p=0.37 Relief of low back pain: 33.3% (9/27) vs. 25.0% (6/24), p=0.88	*Early results (mean 48 ± 24 hours post-injection)* Physiotherapist assessment of improvement in ability to perform physical activities: 70.0% (19/27) vs. 42.8% (10/24), p=0.22	NR	A vs. B: Opioid use: discontinuance of analgesic consumption (early results): 40.0% (11/27) vs. 15.8% (4/24), p=0.19 Surgery (over 8 to 20 months	"other than a few patients who felt increased pain of the sciatic distribution shortly after injection, there were no complications or side effects attributable to

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
				Subjective patient assessment of improvement in ability to perform physical activities: 66.7% (18/27) vs. 41.7% (10/24), p=0.13		post-injection): 52% (14/27) vs. 58% (14/24) Other: NR	injection"
Tafazal 2009, Ng 2005	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)	6 weeks 94% (141/150) 12 weeks 83% (124/150) 1 year 86% (129/150)	A vs. B: Leg pain, change from baseline (mean, 0-100 VAS): 26.1 ± 3.3 vs. 18.6 ± 3.4 at 6 weeks (p=0.12), 24.5 ± 3.6 vs. 22.6 ±4.1 at 12 weeks (p=0.74) Back pain, change from baseline (mean, 0-100 VAS): 9.8 ± 3.8 vs. 6.4 ± 3.6 at 6 weeks (p=0.51), 6.9 ± 3.7 vs. 9.9 ± 3.8 at 12 weeks (p=0.57) Leg pain improved ≥20 points (0-100 VAS) (from Ng): at 12 weeks 41.5% (17/40) vs. 47.5% (19/41): RR, 0.90 (95% CI 0.56 to 1.50)	A vs. B: ODI, change from baseline (mean, 0-100 VAS): 8.8 ± 2.1 vs. 8.5 ± 2.1 (p=0.93), 9.3 ± 2.3 vs. 10.7 ± 2.6 at 12 weeks (p=0.69) Low Back Outcome Score, change from baseline (mean, 0-75): 4.4 ± 1.7 vs. 5.4 ± 1.8 at 6 weeks (p=0.70), 9.1 ± 2.0 vs. 9.4 ± 2.3 at 12 weeks (p=0.93) ODI improved ≥10% (from Ng): at 12 weeks 35% (14/40) vs. 55% (23/41); RR 0.63 (95% CI 0.38 to 1.0) Change in walking distance from	A vs. B: QoL: NR Satisfaction excellent or good (from Ng): at 12 weeks 45% (18/40) vs. 49% (20/41) RR, 0.92 (95% CI 0.58 to 1.5)	A vs. B: Opioid use: NR Surgery: at 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); at 1 year: 14% (9/64) vs. 22% (14/65)], RR 0.65 (95% CI 0.30 to 1.40) Other: Subsequent peri-radicular injection: 13% (8/64) vs. 15%	2 deaths; not stratified by treatment group

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
				baseline (yards) (from Ng): at 6 weeks 89 ± 54.9 vs. 219.6 ± 62.5 (p=0.12); 200 ± 82 vs. 240 ± 71 at 12 weeks (p=0.72)		(10/65) at 1 year, RR 0.81 (95% CI 0.34 to 1.93)	
Epidural steroid injection vs. Control injection with other medication							
Burgher 2011	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)	4 weeks for pain, function, and global impression of change; 6 months for surgery 88% f/u (23/26)	A vs. B: Pain difference between groups (clonidine vs. steroid) compared with baseline (0-10 NRS, mean ± SE): at 2 weeks, 0.11 ± 0.97 (95% CI -1.79 to 2.01); at 4 weeks, 1.54 ± 1.05 (95% CI -0.52 to 3.60), p=0.16	A vs. B: Roland Morris Disability Questionnaire, difference between groups compared with baseline (mean ± SE): at 2 weeks, 2.96 ± 2.04 (95% CI -1.04 to 6.96); at 4 weeks, 5.67 ± 2.27 (95% CI 1.22 to 10.1) ODI difference between groups compared with baseline (mean ± SE): at 2 weeks, 5.86 ± 3.28 (95% CI -0.57 to 12.3); at 4 weeks, 7.04 ± 3.17 (95% CI 0.83	A vs. B: Patient Global Impression of Change ≤2 (much improved): at 4 weeks 50% vs. 67% (p=0.669)	A vs. B: Opioid use: NR Surgery: 6.7% (1/15) vs. 27% (3/11) at 6 months, RR = 0.24 (95% CI 0.30 to 2.05), p = 0.158 Other: NR	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% (3/15) vs. 18% (2/11) Dry mouth: 20% (3/15) vs. 18% (2/11) Weakness: 7% (1/15) vs. 36% (4/11)

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
				to 13.2) Multidimensional Pain Inventory, difference between groups compared with baseline (mean ± SE): at 2 weeks, -4.83 ± 3.53 (95% CI -0.57 to 12.3); at 4 weeks, -0.35 ± 3.37 (95% CI -6.96 to 6.26)			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)
Cohen 2012	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	6 months; surgery and remained on active duty assessed through 1 year % f/u: 100% (84/84)	A vs. B. vs. C: *(difference ANCOVA adjusted for study site, sex, duration of pain, opioid use, baseline outcome score)* Leg Pain (0-10 NRS, SD or 95% CI) 5.71 ± 1.93 vs. 6.62 ± 1.66 vs. 6.31 ± 2.02 at baseline; 2.54 1.36 to 3.69) vs. 3.56 (2.35 to 4.72) vs. 3.78 (2.72 to 4.85) at 1 month, difference -1.26 (95% CI -2.79 to 0.27) for A vs. C, -	A vs. B. vs. C: *(difference ANCOVA adjusted for study site, sex, duration of pain, opioid use, baseline outcome score)* ODI (0-100): 42.93 ± 15.57 vs. 41.12 ± 18.29 vs. 40.87 ± 17.50 at baseline, 24.1 (16.64 to 31.55) vs. 40.3 (32.91 to 47.61) vs. 30.0 (23.2 to 36.69)	A vs. B. vs. C: *(difference ANCOVA adjusted for study site, sex, duration of pain, opioid use, baseline outcome score)* 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);	A vs. B. vs. C: *(difference ANCOVA adjusted for study site, sex, duration of pain, opioid use, baseline outcome score)* Medication reduction (cessation of nonopioid analgesic or ≥20% decrease in opioid use): 63%	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.

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	(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)		1.01 (95% CI -2.60 to 0.58) for A vs. B <u>Back pain</u> (0-10 NRS): 5.30 ± 2.50 vs. 6.08 ± 2.51 vs. 4.75 ± 2.49 at baseline, 3.49 (2.48 to 4.50) vs. 4.41 (3.37 to 5.44) vs. 4.01 (3.08 to 4.93) 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>Success (≥50% decrease in leg pain and positive Global Perceived Effect):</u> at 1 month 75% (21/28) vs. 42% (11/26) vs. 50% (15/30), A vs. B adjusted OR 3.63 (95% CI 1.10 to 12.0), A vs. C 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%	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	65% vs. 50% vs. 48% at 3 months, s63% vs. 45% vs. 48% at 6 months	(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) <u>Surgery</u>: 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	0% vs. 0%

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			(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)			4.01) <u>Other:</u> <u>Remained on active duty</u>: 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) <u>Positive categorica outcome</u> 75% (21/28) vs 42% (11/26) vs 50% (15/30) at 1 month (p = 0.09) 50% (14/28) vs 42% (11/26) vs 43% (13/30) at 3 months, 38% (8/28) vs 38% (10/26) vs 40% (12/30) at 6 months.	
Cohen 2015	A: Epidural Spinal Injection, 60 mg	<u>1 month</u> Overall:	**Average leg pain** <u>Baseline:</u> 5.4 ± 2.1 vs 5.4	**Oswestry disability score**	**Global perceived effect positive**	**Reduction in drug treatment‡**	**Related to injection**†**

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	depomethylprednisolone + 1 mL of 0.25% bupivacaine (interlaminar diluted to 4 mL in saline [n=11] or transforaminal diluted to 3 mL in saline [n=62] approach) plus placebo medication; (n=73) B: Sham injection of 3 mL saline (interlaminar [n=12] or transforaminal [n=60]) plus gabapentin 300 mg (n=72)	98.6% (143/145) A vs B: 97.2% (71/73) vs 100% (72/72) 3 months Overall: 50% (73/145) *A vs* B: 56% (41/73) vs 44% (32/72) †	± 1.9 1 month: 3.3 ± 2.6 vs 3.7 ± 2.8 3 months: 3.4 ± 2.7 vs 3.7 ± 2.8 Mean change from baseline 1 month -2.2 ± 2.4 vs -1.7 ± 2.6, p = 0.25 3 months: -2.0 ± 2.6 vs -1.6 ± 2.7, p = 0.43 *Treatment effect at 3 months* - adjusted difference (95% CI): -0.3 (-1.2 to 0.5); p=0.43 **Worst leg pain** Baseline: 7.9 ± 1.7 vs 7.8 ± 2.0 1 month 4.9 ± 3.1 vs 5.8 ± 3.0 3 months: 5.2 ± 3.4 vs 5.5 ± 3.4 Mean change from baseline 1 month -3.0 ± 2.8 vs -2.0 ± 2.9, p = 0.04) 3 months -2.7 ± 3.2 vs -2.3 ± 3.5 at 3 months (p = 0.54) **Composite outcome** >2 point decrease in	Baseline 39.8 ± 15.3 vs 39.8 ± 14.7 1 month 32.6 ± 18.3 vs 29.6 ± 16.0 3 months 33.6 ± 19.4 vs 29.6 ± 16.3 Mean change from baseline 1 month -7.3 ± 12.5 vs -10.2 ± 14.5 (p = 0.18) 3 months -6.2 ± 15.8 vs -10.2 ± 16.7 (p = 0.12)	1 month 67% (49/73) vs 57% (41/72); p = 0.21 3 months 45% (33/73) vs 33% (24/72) p = 0.14	1 month 60% (40/67) vs 49% (32/65) p = 0.23 3 months 58% (23/40) vs 47% (14/30) p = 0.37 **Surgery within year of enrollment** 1 year 13% (9/72) vs 14% (10/69) p = 0.73	3 months ≥1 adverse event: 8% (6/73) vs 10% (7/73) (p = 0.75) Excessive pain: 3% (2/73) vs 6% (4/72) Fever, infection, both: 4% (2/73) vs 0% (0/72) Falls: 1% (1/73) vs 0% (0/74) Vasavagal: 0% (0/73) vs 3% (2/72) "Other": 1% (1/73) vs 4% (3/72) **Related to drug treatment** 3 months ≥ 1 event: 42% (30/72) vs 51% (37/72) (p = 0.24) Sedation/fatigue: 11% (8/73) vs 18% (13/72)

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			average leg pain coupled with positive global perceived effect without additional procedural or non-rescue pharmacological interventions: 1 month: 66% (48/73) vs. 46% (33/72); p=0.02 3 months: 37% (27/73) vs. 29% (21/72); p=0.32 **Average back pain** Mean ± SD <u>Baseline</u> 5.0 ± 2.6 vs 4.7 ± 2.4 <u>1 month</u> 3.5 ± 2.6 vs 3.6 ± 2.6 <u>3 months</u> 3.9 ± 2.7 vs 3.7 ± 2.5 Mean change from baseline <u>1 month</u> -1.5 ± 1.9 vs -1.1 ± 2.3 (p = 0.45) <u>3 months</u> -1.1 ± 2.4 vs -1.0 ± 2.4, p = 0.85 **Worst back pain:** Mean ± SD <u>Baseline</u> 7.0 ± 2.6 vs 7.0 ± 2.9 <u>1 month</u> 5.1 ± 2.9 vs 5.4 ± 3.2 <u>3 months</u>				Cognitive: 7% (5/73) vs 10% (7/72) Weight gain: 6% (4/73) vs 10% (7/72) Headache: 6% (4/73) vs 1% (1/72) GI: 18% (13/73) vs 11% (8/72) Swelling: 0% (0/73) vs 4% (3/72) "Other": 15% (11/73) vs 15% (11/72)

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			5.6 ± 3.2 vs 5.6 ± 3.1 Mean change from baseline 1 month -1.9 ± 2.4 vs -1.6 ± 2.6, p = 0.38 3 months -1.4 ± 2.9 vs -1.4 ± 2.8; p = 0.91				
Epidural steroid injection vs. Disc procedure							
Aronsohn 2010	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)	6 weeks % f/u NR	A vs. B: Mean 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) Mean 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)	NR	A vs. B Patient satisfaction: 42% (10/24) vs. 79% (20/26), p <0.02	Opioid use (tablets/week): Preoperative use: 6 ± 4 vs. 5 ± 3 Postoperative use: 2.2 ± 1 vs. 2.1 ± 2 p for pre- vs. postoperative use < 0.01	A vs. B: Paresthesia and numbness in the lower extremity (resolved spontaneously): 4.2% (1/24) vs. 13% (3/26) Superficial skin infection: 0% vs. 3.8% (1/26) (resolved after antibiotics)
Buttermann 2004	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)	2-3 years 97% (97/100) at 3 years	A vs. B: 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	A vs. B: ODI (0-100, estimated from graph): 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	NR	A vs. B: 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);	Epidural injection (n=50): 2 incidental dural puncture, 3 recurrent disc herniation Discectomy (n=77, including crossovers): 2 incidental durotomies, 1

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			(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, p<0.0001; 2.7 vs. 1.2 at 4-6 months, p<0.03; 1.8 vs. 1.1 at 7-12 months, p=NS; 1.7 vs. 1.2 at 1-2 years, p=NS; 0.8 vs. 1.5 at 2- 3 years, p=NS	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, 72% (36/50) vs. 38% (19/50) at 1-3 months; 30% (8/27) vs. 20% (10/50) at 4-6 months, 20% (5/25) vs. 12% (6/50) at 7-12 months, 12% (3/24) vs. 8.0% (4/50) at 1-2 years, 8.7% (2/23) vs. 4.0% (2/50) at 2-3 years		57% (13/23 vs. 32% (15/47) at 2-3 years Proportion of patients using narcotic pain medication: 1-3 mos. after tx: 24% (12/50) vs. 14% (7/50) 2-3 yrs after tx: 0% (0/23) vs. 2.0% (x/47) Surgery: 46% (23/50) of patients in epidural injection group crossed over to discectomy at 2-3 years	seroma
Gerstzen 2010	A: Transforaminal epidural injection with corticosteroid, medication type (methylprednisolone acetate, betamethasone, methylprednisolone, triamcinolone acetonide) and dose	24 months 6 weeks 92.5% (37/40) vs 97.8% (44/45) 3 months 87.5% (35/40) vs	A vs. B: Leg pain* (mean change ± SE, 0-100 VAS): at 6 weeks -21 ± 4 vs. -42 ± 5 (p=0.002), at 3 months -23 ± 5 vs. -46 ± 4 (p=0.0001), at 6 months -21 ± 5 vs. -47 ± 6 (p=0.0008)	A vs. B: ODI* (mean change, 0-100): at 6 weeks -5 ± 2 vs. -13 ± 3 at 6 weeks (p=0.002); at 3 months -2 ± 2 vs. -11 ± 3 (p=0.002); at 6 months -4 ± 2	A vs. B: 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%	A vs. B: Opioid use: NR Did not undergo secondary procedure through 2 years: 17% vs. 52% (Kaplan Meier estimate)	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%

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	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)	97.8% (44/45) 6 months 90.0% (36/40) vs 95.6% (43/45) 1 year 87.5% (35/40) vs 93.3% (42/45) 2 years 82.5% (33/40) vs 84.4% (38/45) Complete f/u: 2 years 83.5% (71/85)	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) *uses GEE model. See	vs. -14 ± 4 (p=0.002) ODI improved ≥13 points: at 6 months 15% (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	(14/43), RR 0.39 (95% CI 0.16 to 0.99) Patient satisfaction (through 6 months) Extremely satisfied: 15% vs. 38% Very satisfied: 24% vs 18% Somewhat satisfied: 31% vs 26% Somewhat dissatisfied: 3% vs 15% Very dissatisfied: 3% vs 15% Extremely dissatisfied: 0% vs 11% *uses GEE model. See Gerstzen for details	Surgery (not including additional steroid injection or plasma disc decompression): through 2 years: 10% (4/40) vs.15.6% (7/45) (includes radiofrequency ablation, microdiscectomy, and lumbar interbody fusion) Plasma disc decompression: 20 patients in group A received plasma disc decompression Additional steroid injection: 5 pts in group A and 13 in group B received an additional injection Other: NR	(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)

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			Gerstzen for details	0.99) *uses GEE model. See Gerstzen for details			
Wu 2015	A: Transforaminal injection of betamethasone (2.0 mL, dosage NR) plus 1.0% lidocaine (1.0 ml) with 1.0 mL contrast and fluoroscopic guidance (n=40) B: Nucleoplasty plus nerve root injection: nucleoplasty as below (C) immediately followed by nerve root injection of betamethasone (2.0 mL, dosage NR) plus 1.0% lidocaine (1.0 ml) (n=39) C: Nucleoplasty: discography with 0.5 ml contrast to verify annular integrity followed by nucleoplasty using radiofrequency (temperature	12 months 82% f/u (97/118) (5 patients lost to f/u; 8 patients excluded after undergoing surgery; 5 patients excluded after undergoing second injection; 3 patients excluded due to findings on discography)	A (n=29) vs. B (n=35) vs. C (n=33): Pain (NRS 0-10): Baseline: 7.3 ± 1.0 vs. 7.3 ± 1.0 vs. 7.2 ± 1.2; 1 month: 3.2 ± 0.8 vs. 2.5 ± 0.9 vs. 3.4 ± 0.7 (A vs. B p=0.000; A vs. C p=0.432; B vs. C p=0.001) 3 months: 3.3 ± 0.8 vs. 2.3 ± 0.6 vs. 2.3 ± 0.8 (A vs. B p=0.79, A vs. C p=0.000, B vs. C=0.000); 12 months: 3.4 ± 0.6 vs. 2.1 ± 0.7 vs. 2.3 ± 0.6 (A vs. B p=0.401, B vs. C p=0.000, A vs. C p=0.000)	A (n=29) vs. B (n=35) vs. C (n=33): ODI (0-100%): Baseline: 48.1 ± 11.3 vs. 47.7 ± 11.7 vs. 47.7 ± 10.3; 1 month: 32.4 ± 5.9 vs. 27.1 ± 8.5 vs. 32.0 ± 6.7 (A vs. B p=0.007, A vs. C p=0.809, B vs. C p=0.005); 3 months: 30.5 ± 5.6 vs. 24.3 ± 6.3 vs. 25.3 ± 6.5 (A vs. B p=0.498, A vs. C p=0.001, B vs. C p=0.000); 12 months: 27.8 ± 4.9 vs. 22.9 ± 5.3 vs. 22.7 ± 6.3 (A vs. B 0.923, A vs. C p=0.001, B vs. C p=0.001)	NR	A (n=39) vs. B (n=36) vs. C (n=35): Opioid use: NR Surgery: (patients excluded from pain and function outcomes) 12 months: 13% (5/39) vs. 3% (1/36) vs. 6% (2/35) Other: Second injection: (patients excluded from pain and function outcomes) 13% (5/39) vs. 0% (0/36) vs. NR	All procedures were considered technically successful and no neurovascular or infection-related complications were detected during and postoperative course.

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	and length of ablation NR) at six position with fluoroscopic guidance (n=39)						
Epidural steroid injection vs. Conservative Care							
Buchner 2000	A: Interlaminar epidural injection with 100 mg methylprednisolone in 0.25% bupivacaine (10 ml) plus conservative care (see "B" for details) (n=17) B: Conservative care: Bed rest; analgesics; NSAIDS or tramadol; graded rehabilitation including hydrotherapy, electroanalgesia, spinal mobilization physiotherapy (n=19)	6 months 100% f/u (36/36)	A vs. B: Mean pain, type not specified (range) (0-100 VAS): 84.4 (70-100) vs. 81.0 (25-100) at baseline; 30.8 (0-80) vs. 37.1 (0-70) at 2 weeks; 32.9 (0-85) vs. 38.1 (0-100) at 6 weeks; 32.9 (0-85) vs. 39.2 (0-100) at 6 months (p>0.05 at all time points) Mean reduction of Pain (0-100 VAS) 2 weeks: 53.6 ± 22.3 vs. 43.9 ± 24.4, p <0.05	A vs. B: Function Mean Hannover Functional Ability Questionnaire (range): 38.5% (21%-63%) vs. 39.9% (0%-83%) at baseline; 63.7% (range, 33%-88%) vs. 57.5 (21%-88%)% at 2 weeks; 61.5% (25%-88%) vs. 58.3% (13%-100%) at 6 weeks; 61.8% (25%-83%) vs. 57.2% (17%-83%) at 6 months (p>0.05 at all time points)	A vs. B: Overall results "very good" or "good": 88% (15/17) vs. 74% (14/19) at 6 months	A vs. B: Opioid use: NR Surgery: 12% (2/17) vs. 21% (4/19) at 6 months (all occurred within 4 weeks) Other: Return to work: 88% (15/17) vs. 74% (14/19) at 6 months, RR: 1.20 (95% CI 0.87 to 1.65)	"No major side effects were reported after epidural injections"
Murakibhavi 2011	A: Caudal epidural injection with 80 mg triamcinolone acetate (2 ml), 2% lidocaine (2 ml), and normal saline (20 ml), with fluoroscopic guidance (n=50)	6 months % 98.0% (100/102)	A vs. B: Pain (0-10 VAS): 8.1 ± 1.0 vs. 8.1 ± 1.2 at baseline; 2.7 ± 0.8 vs. 6.1 ± 0.5 at 6 months Complete pain relief : 92% (46/50) vs. 32% (16/50) at 3 weeks, RR 2.88 (95 % CI 1.90 to	A vs. B: ODI (0-100): 36.0 ± 2.0 vs. 35.9 ± 2.6 at baseline; 12.3 ± 2.6 vs. 24.9 ± 1.5 at 6 months	NR	Opioid use: NR Surgery: NR Other: Beck Depression Inventory (0-63): 18.0 ± 2.7 vs. 18.9 ± 3.2 at baseline; 8.6 ±	A only (group B N/A): Dural puncture: 0% (0/50) Headache: 18% (9/50) Hypotension during

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	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) (n=50)		4.34); 86% (43/50) vs. 24% (12/50) at 6 months, RR 3.58 (95% CI 2.16 to 5.94)			2.2 vs. 13.3 ± 1.7 at 6 months Surgery required: 2% (1/50)	procedure: 24% (12/50) Bleeding during procedure: 4% (2/50) >1 attempt required for steroid placement: 30% (15/50) Difficulty in approach: 22% (11/50) Repeat injections: 12% (6/50) Surgery required: 2% (1/50) Transient bilateral LE numbness immediately postinjection: 40% (20/50)

Appendix Table F3. Lumbar Radiculopathy Attributed to Disc Pathology Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Epidural steroid injection vs. Control injection				
Arden 2005, Price 2005	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)	12 months 89% (203/228)	No clinical predictors of response to ESIs were found. Variables assessed include: patients with symptoms <4 months; chronic or acute symptoms; anxiety scores; depression scores, SF-36; baseline Oswestry Disability Questionnaire; neurological abnormalities, previous episodes of sciatica, coexistent back pain, work status, gender, and centre.	NR
Bush 1991	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)	12 months 82% (23/28)	None	None
Carette 1997	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)	3 months 99% f/u (156/158)	NR	NR
Cohen 2012	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)	6 months; surgery and remained on active duty assessed through 1 year % f/u: 100% (84/84)	NR	NR
Cuckler 1985	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%	13-30 mos. (mean 20.2 vs. 21.5 months) 100% (73/73)	A vs. B: 24 hours, symptoms improved ≥75%, herniated disc patients: 31.8% (7/22) vs. 35.7% (5/14); RR = 0.8 (95% CI, 0.35 to 2.2), p = 0.8 24 hours, symptoms improved ≥75%, stenosis patients:	None

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
	procaine (5 ml) (n=31)		25% (5/20) vs. 17.6% (3/17); RR = 1.4 (95% CI, 0.39 to 5.0), p = 0.59 24 hours, average symptoms improvement (%), herniated disc patients: 39.8 ± 9 vs. 43.9 ± 11.2, t = NS 24 hours, average symptoms improvement (%), stenosis patients: 43.5 ± 8.7 vs. 43.2 ± 8.0, t = NS Long-term, symptoms 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) Long-term, symptoms improved ≥75%, stenosis patients: 21.7% (5/23) vs. 14.2% (2/14) Surgery, herniated disk: 43% (10/23) vs. 23% (3/13) at mean 20 months, RR 2.56 (95% CI 1.12 to 7.35) Surgery, spinal stenosis: 26% (6/23) vs. 28.5% (4/14) at mean 20 months, RR = 0.91 (95% CI, 0.31 to 2.6), p = 0.87	
Datta 2011	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)	3 months 78.7% (163/207)	None	None
Dilke 1973	A: Interlaminar epidural injection with 80 mg methylprednisolone in saline (10 ml) B: Interspinous ligament injection with saline (1 ml)	3 months 82% (82/100)	NR	NR
el Zahaar 1991	A: Caudal epidural injection with hydrocortisone (5 ml), 4% Carbocaine (4 ml), and saline (21 ml) (n=19 with acute HNP)* B: Caudal epidural injection with 4% Carbocaine (4 ml) plus	Mean 20.9 months (20.2 vs. 21.5 months) (range, 13-36 months) % f/u NR	None	None

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
	saline (26 cc) (n=14 with acute HNP)* *A total of 37 patients were randomized to epidural steroid injection and 26 to placebo; only results for those diagnosed with a herniated disc are reported here.			
Ghahreman 2010	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)	12 months 79% f/u (118/150) Differential loss to f/u for 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	Chronicity did not affect response to treatment (p = NS). No interaction between duration of symptoms, presence of sensory changes or neurologic signs.	NR
Ghai 2015	A: Epidural injection of 6 mL 0.5% lidocaine mixed with 80 mg (2 mL) of methylprednisolone acetate using a parasaggital interlaminar approach B: Epidural injection of 8 mL of 0.5% lidocaine using a parasaggital interlaminar approach	12 months Overall: 81.1% (56/69) A vs B: 88.6% (31/35) vs 73.5% (25/34)	NR	NR
Helliwell 1985	A: Interlaminar epidural injection with 80 mg methylprednisolone in saline (10 ml) (n=20) B: Interspinous ligament injection with saline (5 ml) (n=19)	3 months % f/u NR	NR	NR
Iversen 2011	A: Caudal epidural injection with 40 mg triamcinolone in 0.9% saline (29 ml) (n=37) B: Caudal epidural injection with 0.9% saline (30 ml) (n=39)	12 months 94% (109/116) at 6 weeks; 91% (105/116) at 3 months; 85%	None	None

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
	C: Subcutaneous injection superficial to the sacral hiatus and outside spinal canal with 0.9% saline (2 ml) (n=40)	(99/116) at 12 months		
Karppinen 2001, 2001	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	12 months 94% (75/80) (2 patients lost to f/u; 3 patients excluded because neurogram findings were not typical)	Leg pain (0-100 VAS): by MRI subgroups: bulges no differences at any time point; contained herniation difference -24 (95% CI -8 to -41) at 2 weeks; -19 (95% CI -36 to -3) at 4 weeks; -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): 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 weeks, 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 weeks (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 weeks (p=0.02), otherwise no differences ODI (0-100): by MRI subgroups: bulges no differences at any time point; contained herniation difference -8.0 (-16 to 0.3) at 2 weeks, -2.7 (95% CI -10 to 5) at 4 weeks, 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 weeks, no differences at other time points Surgery: contained herniation subgroup 20% vs. 42% (p=0.10), extrusion subgroup 32% vs. 13% (p=0.05)	NR
Klenerman 1984	A: Epidural injection with 80 mg methylprednisolone plus normal saline (20 ml total)	2 months 85% f/u (63/74) (15%	NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Also included for epidural injection (approach NR) vs. placebo for LBP + radiculopathy	(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)	(11/74) excluded from analysis, including 1 lost to followup)		
Manchikanti 2012, 2011, 2008	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)	24 months 95.0% (114/120) at 3 months; 87.5% (105/120) at 6 months; 82.5% (99/120) at 12 months; 80.0% (96/120) at 24 months	None	None
Manchikanti 2014	A: Transforaminal epidural injection of betamethasone 0.5 mL plus lidocaine 1.5 mL (1%), with fluoroscopic guidance (n=60) B: Transforaminal epidural injection of lidocaine 1.5 mL (1%) and sodium chloride, with fluoroscopic guidance (n=60)	12 months 92% (55/60) vs 88% (53/60) 24 months 83% (50/60) vs 78% (47/60)	NR	NR
Manchikanti 2014, 2013, 2010	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)	24 mos. 84% f/u (101/120)	**NR**	**NR**
Ridley 1988	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)	2 weeks 89.7% (35/39)	There was no association between the patient's age or the duration of the current episode and the likelihood of a particular response at any stage of the study (no data or additional information reported).	NR
Riew 2006, 2000	A: Transforaminal nerve root injection with 6 mg betamethasone (1 ml) plus 0.25% bupivacaine (1 ml), with fluoroscopic guidance	Mean 23 months, range 13 to 28 months for initial	NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
	(n=28) B: Transforaminal nerve root injection with 0.25% bupivacaine (1 ml), with fluoroscopic guidance (n=27)	followup (100% f/u (55/55); ≥5 years for second followup (85% f/u (47/55), with differential loss to f/u for A vs. B: 29% (8/28) vs. 0% (0/27) at ≥5 years)		
Rogers 1992	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)	1 month for all outcomes except subsequent surgery, which was evaluated at 20-21 months % f/u NR	NR	NR
Sayegh 2009	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)	3 months 78.7% (163/207)	Surgery at 1 month: • Disc herniation group: 17% (7/42) vs. 24% (8/33) • Disc degeneration group: 12% (6/51) vs. 33% (11/33) • No formal test for interaction performed	NR
Snoek 1977	A: Interlaminar epidural injection with 80 mg methylprednisolone (2 ml) (n=27) B: Interlaminar epidural injection with saline (2 ml) (n=24)	Mean NR, range 8-20 months % f/u NR	NR	NR
Tafazal 2009, Ng 2005	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)	6 weeks 94% (141/150) 3 months 83% (124/150)	<u>Change in ODI, from Baseline (mean ± SE) at 3 months:</u> Disc prolapse subgroup 13.6 ± 3.1 (n=42) vs. 13.8 ± 3.7 (n=34) Stenosis subgroup 1.5 ± 2.6 vs. 6.5 ± 3.4 overall p=0.042	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
		1 year 86% (129/150)	Change from baseline in VAS Leg Pain (mm; mean ± SE) at 3 months: Disc prolapse subgroup 27.4 ± 4.7 (n=42) vs. 24.3 ± 5.5 (n=34) Stenosis subgroup 19.1 ± 5.4 (n=23) vs. 20.4 ± 6.1 (n=25) overall p= 0.69	
Epidural steroid injection vs. Control injection with other medication				
Burgher 2011	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)	4 weeks for pain, function, and global impression of change; 6 months for surgery 88% f/u (23/26)	NR	NR
Cohen 2012	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)	6 months; surgery and remained on active duty assessed through 1 year % f/u: 100% (84/84)	NR	NR
Cohen 2015	A: Epidural Spinal Injection, 60 mg depomethylprednisolone + 1 mL of 0.25% bupivacaine (interlaminar diluted to 4 mL in saline [n=11] or transforaminal diluted to 3 mL in saline [n=62] approach) plus placebo medication; (n=73) B: Sham injection of 3 mL saline (interlaminar [n=12] or transforaminal [n=60]) plus gabapentin 300 mg (n=72)	3 months Overall: 50% (73/145) *A vs* B: 56% (41/73) vs 44% (32/72) †	Injection at S1 was associated with greater reduction in leg pain than at other levels (-0.7, -0.1, -1.2; p = 0.02), but failed to reach significance when adjusted for multiple comparisons. (no other data reported; it appears that results weren't stratified by treatment group) No associations among the primary or composite outcomes at one month based on etiology, pain duration ≥3 months, injection type, smoking status, presence of	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
			psychiatric disease, obesity, age, sex, or dose of gabapentin. (data NR; it appears that results weren't stratified by treatment group)	
Epidural steroid injection vs. Disc procedure				
Aronsohn 2010	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)	6 weeks % f/u NR	NR	NR
Buttermann 2004	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)	2-3 years 97% (97/100) at 3 years	NR	NR
Gerstzen 2010	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)	24 months, 83.5% (71/85)	Duration of pain was stratified into three categories: <1 year, 1-3 years, >3 years. In group B, the average reduction in pain scores at 6 months for all three strata was approximately 50 points, while for group A, the leg pain score was consistently less, ranging from a mean reduction of 12 points to 38 points. Among patients in the 1-3 years stratum, those in group B did significantly better than those in group A with respect to leg pain at 6 months, p = 0.009.	NR
Wu 2015	A: Transforaminal injection of betamethasone (2.0 mL, dosage NR) plus 1.0% lidocaine (1.0 ml) with 1.0 mL contrast and fluoroscopic guidance (n=40) B: Nucleoplasty plus nerve root injection: nucleoplasty as below (C) immediately followed by nerve root injection of betamethasone (2.0 mL, dosage NR) plus 1.0% lidocaine (1.0 ml) (n=39) C: Nucleoplasty: discography with 0.5 ml contrast to verify annular integrity followed by nucleoplasty using radiofrequency (temperature and length of ablation	12 months 82% f/u (97/118) (5 patients lost to f/u; 8 patients excluded after undergoing surgery; 5 patients excluded after undergoing second injection; 3 patients excluded due to findings on discography)	NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
	NR) at six position with fluoroscopic guidance (n=39)			
Epidural steroid injection vs. Conservative Care				
Buchner 2000	A: Interlaminar epidural injection with 100 mg methylprednisolone in 0.25% bupivacaine (10 ml) plus conservative care (see "B" for details) (n=17) B: Conservative care: Bed rest; analgesics; NSAIDS or tramadol; graded rehabilitation including hydrotherapy, electroanalgesia, spinal mobilization physiotherapy (n=19)	6 months 100% f/u (36/36)	NR	NR
Murakibhavi 2011	A: Caudal epidural injection with 80 mg triamcinolone acetate (2 ml), 2% lidocaine (2 ml), and normal saline (20 ml), with fluoroscopic guidance (n=50) 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) (n=50)	6 months 98.0% (100/102)	None	None

Appendix Table F4. Lumbar Radiculopathy Attributed to Disc Pathology: Baseline Scores for Pain, Function and Opioid Usage

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
Pain on VAS or NRS (0-10)						
Baseline	Datta (2011)	Methylprednisolone 80 mg + bupivacaine 0.125% No imaging	Bupivacaine 0.125%	Caudal	7.4 ± 0.95 (n=50)	7.2 ± 0.79 (n=55)
		Triamcinolone 80 mg + bupivacaine 0.125% No imaging	Bupivacaine 0.125%	Caudal	7.4 ± 0.57 (n=52)	7.2 ± 0.79 (n=55)
		Dexamethasone 15 mg + bupivacaine 0.125% No imaging	Bupivacaine 0.125%	Caudal	7.3 ± 0.65 (n=50)	7.2 ± 0.79 (n=55)
	Manchikanti	Methylprednisolone 40 mg +	Lidocaine 0.5%	Caudal	7.8 ± 0.9	8.1 ± 0.9

Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
(2012,2011,2008)	lidocaine 0.5% Fluoroscopy			(n=60)	(n=60)
Ghai 2015	Methylprednisolone 80 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	8.0 ± 1.6 (n=35)	8.0 ± 1.4 (n=34)
Manchikanti (2014,2013,2010)	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	8.0 ± 1.0 (n=60)	8.2 ± 0.8 (n=60)
Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Bupivacaine 0.5% + water	Trans-foraminal	5.71 ± 1.93 (n=28)	6.31 ± 2.02 (n=30)
Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Bupivacaine 0.5%	Trans-foraminal	7.0 ± 1.7 (n=28)	7.4 ± 2.1 (n=27)
Manchikanti (2014)	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	8.2 ± 0.9 (n=60)	8.3 ± 0.9 (n=60)
Tafazal 2009/Ng 2005	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Bupivacaine 0.25%	Trans-foraminal	7.27 (IQR, 6.0 to 8.0) (n=65)	7.64 (IQR, 7.0 to 9.0) (n=59)
Klenerman 1984	Methylprednisolone 80 mg + saline Imaging NR	Bupivacaine 0.25%	Interlaminar	4.8‡ (n=19)	5.3‡ (n=16)
Bush (1991)	Triamcinolone 80 mg + procaine hydrochloride 0.5% + saline	Saline (25 ml)	Caudal	3.85 (n=12)	4.92 (n=11)
Iversen (2011)	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	5.01 (4.25 to 5.77) (n=37)	5.35 (4.56 to 6.13) (n=39)
Carette 1997	Methylprednisolone 80 mg + saline Imaging NR	Saline	Interlaminar	6.56 ± 2.16 (n=78)	6.15 ± 2.14 (n=80)
Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline	Transforaminal	7.0 ± 1.7 (n=28)	6.6 ± 2.2 (n=37)
Karppinen 2001	Methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline 0.9%	Transforaminal	7.10 ± 1.80 (n=80)	7.52 ± 1.90 (n=80)
Klenerman 1984	Methylprednisolone 80 mg + saline	Saline	Interlaminar	4.8‡	6.5‡

Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
	Imaging NR			(n=19)	(n=16)
Burgher 2011	Triamcinolone 40 or 80 mg + lidocaine 2% Fluoroscopy	Clonidine 200 or 400 mg + lidocaine 2%	Transforaminal	7.0 ± 2.0 (n=15)	7.0 ± 1.9 (n=11)
Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept 4 mg + bupivacaine 0.5% + water	Transforaminal	5.71 ± 1.93 (n=28)	6.62 ± 1.66 (n=26)
Iversen (2011)	Triamcinolone 40 mg + saline 0.9% Ultrasound	Subcutaneous injection of saline 0.9% superficial to the sacral hiatus and outside spinal canal	Caudal	5.01 (4.25 to 5.77) (n=37)	4.83 (3.96 to 5.69) (n=40)
Arden (2005)/Price (2005)	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	Interspinous ligament injection of saline (2 ml)	Interlaminar	5.2 ± 2.3 (n=120)	5.6 ± 2.2 (n=108)
Helliwell 1985	Methylprednisolone 80 mg + saline Imaging NR	Interspinous ligament injection of saline (5 ml)	Interlaminar	NR (n=20)	NR (n=19)
Klenerman 1984	Methylprednisolone 80 mg + saline Imaging NR	Interspinous ligament needling without injection	Interlaminar	4.8‡ (n=19)	6.5‡ (n=12)
Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Intramuscular injection of saline (2 ml)	Transforaminal	7.0 ± 1.7 (n=28)	7.0 ± 1.5 (n=30)
Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Intramuscular injection of triamcinolone 40 mg	Transforaminal	7.0 ± 1.7 (n=28)	7.6 ± 2.0 (n=28)
Cohen 2015	Methylprednisolone 60 mg + bupivacaine 0.25% + saline + oral placebo medication	Posterior ligament injection of saline (3 ml) + oral gabapentin 300 mg	Interlaminar or transforaminal	5.4 ± 2.1 (n=73)	5.4 ± 1.9 (n=72)
Butterman 2004	Betamethasone 10-15 mg Fluoroscopy in 76% of pts	Discectomy Imaging NR	Interlaminar	7.4† (n=50)	7.0† (n=50)
Aronsohn 2010	Methylprednisolone 40 mg + bupivacaine 0.25%	Percutaneous micro-discectomy (single level)	Approach NR	9.3 (n=24)	9.1 (n=26)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
		Fluoroscopy	Fluoroscopy			
	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone Fluoroscopy	Plasma disc decompression with coblation Fluoroscopy	Transforaminal	7.5 ± 1.4 (n=40)	7.2 ± 1.3 (n=45)
	Wu 2015	Betamethasone mg NR + lidocaine 1% Fluoroscopy	Nucleoplasty + nerve root injection of betamethasone and lidocaine Fluoroscopy	Transforaminal	7.3 ± 1.0 (n=40)	7.3 ± 1.0 (n=39)
		Betamethasone mg NR + lidocaine 1% Fluoroscopy	Nucleoplasty only using radiofrequency Fluoroscopy	Transforaminal	7.3 ± 1.0 (n=40)	7.2 ± 1.2 (n=39)
	Murakibhavi 2011	Triamcinolone 80 mg + lidocaine 2% + saline Fluoroscopy	Medication + physiotherapy‡	Caudal	8.1 ± 1.0 (n=50)	8.1 ± 1.2 (n=50)
	Buchner 2000	Methylprednisolone 100 mg + bupivacaine + conservative treatment Imaging not reported	Bed rest + medication + Graded rehabilitation§	Inter-laminar	8.44 (range, 7.0-10.0) (n=17)	8.10 (range, 2.5-10.0) (n=19)
Function on ODI						
	Manchikanti (2012,2011,2008)	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	(ODI 0-50) 27.9 ± 4.8 (n=60)	(ODI 0-50) 29.2 ± 4.6 (n=60)
	Sayegh 2009	Betamethasone 7 mg + xylocaine 2% No imaging used	Xylocaine 2% + water	Caudal	(ODI NR) 38.5 ± 2.6 (n=93)	(ODI NR) 38.5 ± 2.7 (n=90)
	Ghai 2015	Methylprednisolone 80 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Interlaminar	(mODI NR) 46.8 ± 14.3 (n=35)	(mODI NR) 49.6 ± 12.8 (n=34)
	Manchikanti (2014,2013,2010)	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Interlaminar	(ODI 0-50) 29.6 ± 5.2 (n=60)	(ODI 0-50) 30.3 ± 4.7 (n=60)
	Cohen 2012	Methylprednisolone 60 mg +	Bupivacaine 0.5% +	Transforaminal	(ODI 0-100)	(ODI 0-100)

Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
	bupivacaine 0.5% + water Fluoroscopy	water		42.9 ± 15.6 (n=28)	40.9 ± 17.5 (n=30)
Manchikanti (2014)	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Transforaminal	(ODI 0-50) 28.0 ± 5.3 (n=60)	(ODI 0-50) 29.9 ± 4.8 (n=60)
Tafazal 2009/Ng 2005	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Bupivacaine 0.25%	Transforaminal	(ODI 0-100) 43.4 (IQR, 32–54) (n=65)	(ODI 0-100) 46.6 (IQR, 34–58) (n=59)
Iversen (2011)	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	(ODI 0-100) 32.5 (95% CI 28.6 to 36.4) (n=37)	(ODI 0-100) 31.4 (95% CI 26.9 to 35.9) (n=39)
Carette 1997	Methylprednisolone 80 mg + saline Imaging NR	Saline	Interlaminar	ODI (0-100) 59.6 ± 15.7 (n=78)	ODI (0-100) 50.0 ± 15.5 (n=80)
Karppinen 2001	Methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline 0.9%	Transforaminal	ODI (0-100) 42.9 ± 16 (n=80)	ODI (0-100) 43.5 ± 15 (n=80)
Burgher 2011	Triamcinolone 40 or 80 mg + lidocaine 2% Fluoroscopy	Clonidine 200 or 400 mg + lidocaine 2%	Transforaminal	(ODI NR) 28.8 ± 7.2 (n=15)	(ODI NR) 31.3 ± 6.0 (n=11)
Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept 4 mg + bupivacaine 0.5% + water	Transforaminal	(ODI 0-100) 42.9 ± 15.6 (n=28)	(ODI 0-100) 41.1 ± 18.3 (n=26)
Iversen (2011)	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9% subcutaneous injection superficial to the sacral hiatus and outside spinal canal	Caudal	ODI (0-100) 32.5 (95% CI 28.6 to 36.4) (n=37)	ODI (0-100) 26.3 (95% CI 22.0 to 30.6) (n=40)
Arden (2005)/Price (2005)	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	Saline (2 ml) soft tissue injection into interspinous ligament	Inter-laminar	ODI (0-100) 44 ± 15 (n=120)	ODI (0-100) 45 ± 18 (n=108)
Butterman 2004	Betamethasone 10-15 mg Fluoroscopy in 76% of pts	Discectomy Imaging NR	Interlaminar	ODI (0-100) 47† (n=50)	ODI (0-100) 48† (n=50)
Gertzen 2010	Methylprednisolone or	Plasma disc	Transformanial	ODI (0-100)	ODI (0-100)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
		betamethasone or triamcinolone Fluoroscopy	decompression with coblation Fluoroscopy		43 ± 17 (n=40)	42 ± 14 (n=45)
	Wu 2015	Betamethasone mg NR + lidocaine 1% Fluoroscopy	Nucleoplasty + nerve root injection of betamethasone and lidocaine Fluoroscopy	Transformanial	ODI (0-100) 48.1 ± 11.3 (n=40)	ODI (0-100) 47.7 ± 11.7 (n=39)
		Betamethasone mg NR + lidocaine 1% Fluoroscopy	Nucleoplasty only using radiofrequency Fluoroscopy	Trans-formanial	ODI (0-100) 48.1 ± 11.3 (n=40)	ODI (0-100) 47.7 ± 10.3 (n=39)
	Murakibhavi 2011	Triamcinolone 80 mg + lidocaine 2% + saline Fluoroscopy	Medication + physiotherapy†	Caudal	(ODI 0-100) 36.0 ± 2.0 (n=50)	(ODI 0-100) 35.9 ± 2.6 (n=50)
RMDQ (0-24)						
Baseline	Burgher 2011	Triamcinolone 40 or 80 mg + lidocaine 2% Fluoroscopy	Clonidine 200 or 400 mg + lidocaine 2%	Transforaminal	11.0 ± 5.2 (n=15)	14.0 ± 3.8 (n=11)
EQ5D (0.594 to 1)						
Baseline	Iversen (2011)	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	0.54 (95% CI 0.45 to 0.62) (n=37)	0.46 (0.35 to 0.56) (n=39)
Sickness Impact Profile						
Baseline	Carette 1997	Methylprednisolone 80 mg + saline Imaging NR	Saline	Interlaminar	Overall: 21.7 ± 10.5 Physical: 18.6 ± 11.6 Psycho-social: 16.2 ± 11.8 (n=78)	Overall: 21.4 ± 9.7 Physical: 17.8 ± 10.8 Psycho-social: 17.6 ± 12.1 (n=80)
Lifestyle/ function question-naire (scale, 6-18)						
Baseline	Bush (1991)	Triamcinolone 80 mg + procaine hydrochloride 0.5% + saline	Saline (25 ml)	Caudal	13.4 (n=12)	12.9 (n=11)
Opioid usage (morphine equivalents)						
Baseline	Manchikanti (2012,2011,2008) morphine equivalents (mg/day)	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	45.0 ± 57.8 (n=60)	51.8 ± 58.6 (n=60)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
	on the basis of the dosage frequency and schedule of the drug					
	Manchikanti (2014,2013,2010) morphine equivalents (mg/day)	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	47.1 ± 27.2 (n=60)	49.6 ± 39.3 (n=60)
	Manchikanti (2014) morphine equivalents (mg/day)	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	68.9 ± 51.9 (n=60)	62.9 ± 49.3 (n=60)

APPENDIX G. Lumbar Radiculopathy Attributed to Multiple Causes: RCT Study Characteristics and Results

Appendix Table G1. Lumbar Radiculopathy Attributed to Multiple Causes Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Epidural steroid injection vs. Control injection								
Becker 2007	N=84	Inclusion: 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 Exclusion: 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.	A: Perineural epidural injection using oblique interlaminar approach with 10 mg triamcinolone plus unspecified local anesthetic (1 ml), with fluoroscopic guidance (n=25) B: Perineural epidural injection using oblique interlaminar approach with 5 mg triamcinolone plus unspecified local anesthetic (1 ml), with fluoroscopic guidance (n=27) C: Perineural epidural injection using oblique interlaminar approach with autologous conditioned serum (1 ml), with fluoroscopic guidance (n=32)	Levels: Single level Repeat injections: 3 injections at 1 week intervals	Fluoroscopic	No additional medical therapy or physical therapy	A vs. B vs. C: Age (mean): 54 years (p=NS between groups) Male: NR (p=NS between groups) Duration of symptoms: NR (p=NS between groups) Baseline pain (0-100 VAS, estimated from graph): 84 vs. 82 vs. 78 Baseline function (ODI, 0-50): 19 vs. 21 vs. 22	No funding received
Breivik 1976	N=35	Inclusion: Incapacitating chronic (several months to several years) LBP and sciatica	A: Caudal epidural injection with 80 mg methylprednisolone	Levels: Caudal Repeat injections:	NR	All patients received similar	A vs. B: Age (mean): NR, range 30-63 yrs.	Upjohn

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		unresponsive to non-invasive treatments; radiculography with metrizamide showing arachnoiditis, prolapsed disc, no abnormality, or inconclusive findings Exclusion: NR	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)	Mean 2.6 vs. 2.5 injections; repeated at weekly intervals for up to 3 injections; 31.3% (5/16) vs. 57.9% (11/19) patients received other type of injection after no relief from 3 injections		regimens of medical and physical therapy	Male: 50% vs. 47% Duration of symptoms: NR (minimum duration of "several months" required for inclusion) Prior surgery: 25% vs. 37% Baseline pain: NR Baseline function: NR	
Wilson-MacDonald 2005	N=63	Inclusion: Lumbosacral nerve root pain >6 weeks of sufficient intensity to warrant surgery; MRI showing disc prolapse and/or spinal stenosis Exclusion: Not a surgical candidate; cauda equina syndrome; deteriorating neurological function	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)	Levels: Appears to be single Repeat injections: 16% (7/44) vs. 19% (9/48) received a second epidural following the 6 week visit	NR	NR	A vs. B: Age (mean): 49 vs. 49 years Male: 40% (entire cohort) Herniated disc: 52% vs. 40% Spinal stenosis: 41% vs. 29% Both herniated disc and spinal stenosis: 7% vs. 31% Duration of symptoms: NR(>6 weeks for all) Baseline pain: NR Baseline function (ODI 0-100): 44 vs. 40	NR

Appendix Table G2. Lumbar Radiculopathy Attributed to Multiple Causes Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injection vs. Control injection							
Becker 2007	A: Perineural epidural injection using oblique interlaminar approach with 10 mg triamcinolone plus unspecified local anesthetic (1 ml), with fluoroscopic guidance (n=25) B: Perineural epidural injection using oblique interlaminar approach with 5 mg triamcinolone plus unspecified local anesthetic (1 ml), with fluoroscopic guidance (n=27) C: Perineural epidural injection using oblique interlaminar approach with autologous conditioned serum (1 ml), with fluoroscopic guidance (n=32)	22 weeks % f/u NR	A vs. B vs. C: 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	A vs. B vs. C: ODI (mean, 0-50): 19.4 ± 9.9 vs. 20.6 ± 8.1 vs. 22.0 ± 8.3 at baseline; 11 .0 ± 10.2 vs. 12.1 ± 9.0 vs. 13.8 ± 9.8 at 6 weeks; 11.0 ± 10.2 vs. 12.4 ± 9.0 vs. 11.2 ± 10.2 at 10 weeks; 11.4 ± 10.3 vs. 11.1 ± 7.1 vs. 11.7 ± 9.2 at 22 weeks (p>0.05 at all time points)	NR	NR	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"
Breivik 1976	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)	Mean 9.4 months (range, 3-20 months) % f/u NR	A vs. B: Pain relief "considerable" (defined as diminution of pain and/or paresis to enable return to work or rehabilitation for other work): 56.3% (9/16) vs. 26% (5/19); RR, 2.14 (95% CI 0.90 to 5.09) (timing of f/u unclear)	NR	NR	Surgery: NR by group; overall 3 patients underwent disc removal over 2 to 9 months Opioid use: NR	NR
Wilson-MacDonald 2005	A: Interlaminar epidural steroid injection with 80 mg methylprednisolone (2 ml)	At least 2 years % f/u NR	A vs. B: Pain relief: Favored intervention A	NR	NR	A vs. B: Opioid use: NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	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)		(p<0.004), data NR			Surgery: 41% (18/44) vs. 31% (15/48) at ≥2 years, RR: 1.31 (95% CI 0.76 to 2.27), p=0.45 Other: 19% (9/19) in nonepidural injection group received epidural corticosteroid injection due to continued symptoms	

Appendix Table G3. Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Epidural steroid injection vs. Control injection				
Becker 2007	A: Perineural epidural injection using oblique interlaminar approach with 10 mg triamcinolone plus unspecified local anesthetic (1 ml), with fluoroscopic guidance (n=25) B: Perineural epidural injection using oblique interlaminar approach with 5 mg triamcinolone plus unspecified local anesthetic (1 ml), with fluoroscopic guidance (n=27) C: Perineural epidural injection using oblique interlaminar approach with autologous conditioned serum (1 ml), with fluoroscopic guidance (n=32)	22 weeks % f/u NR	NR	NR
Breivik 1976	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)	NR % f/u NR	None	None
Wilson-MacDonald 2005	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)	At least 2 years % f/u NR	NR	NR

Appendix Table G4. Lumbar Facet Joint Pain: Baseline scores of Pain, Function, Quality of Life and Opioid Use

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
Pain on VAS (0-10)						
Baseline	Becker 2007	Triamcinolone 5 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	8.19 ± 0.87 (n=27)	7.78 ± 1.64 (n=32)
		Triamcinolone 10 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	8.48 ± 1.24 (n=25)	7.78 ± 1.64 (n=32)
Function on ODI (0-50) or (0-100)						
Baseline	Becker 2007	Triamcinolone 5 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	20.6 ± 8.1 (n=27)	22.0 ± 8.3 (n=32)
		Triamcinolone 10 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	19.4 ± 9.9 (n=25)	22.0 ± 8.3 (n=32)

APPENDIX H. Lumbar Spinal Stenosis: RCT Study Characteristics and Results

Appendix Table H1. Lumbar Spinal Stenosis: Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
ESI vs Control injection								
Cuckler 1985 Also included under radiculopathy due to disc pathology (HNP)	N=37	Inclusion: Radicular pain in the lower limb; neurogenic claudication; failure to improve with at least two weeks of noninvasive therapy; required to have findings on myelography, CT or epidural venography that were consistent with symptoms and neurological findings; duration of symptoms not specified Exclusion: Lumbar surgery for similar symptoms or any lumbar surgery within 6 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)	Levels: Single level Repeat injections: 43% (18/42) vs. 58% (18/31) received second injection with corticosteroid and local anesthetic after 24 h due to no relief after initial injection	NR	No special exercise program or other physical therapy was employed after injection; all patients advised to take mild analgesics (aspirin or acetaminophen) during the post-injection period	A vs. B: Age (years): 49 vs. 50 Male: 48% vs. 55% Duration of symptoms (months): 17.3 vs. 13.8 Previous surgery: 2% (1/42) vs 7% (2/31) Herniated disc: 52% vs 45% Spinal stenosis: 48% vs. 55% Baseline pain: NR Baseline function: NR	NR
el Zahaar 1991 Note: this study also included in caudal epidural steroid injection versus placebo for radiculopathy due to HNP	N=63	Inclusion: Radicular pain in the lower limb; 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; duration of symptoms not specified Exclusion: Surgery for similar symptoms or within 6 months	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)	Levels: Single injection Repeat injections: NR	NR	Advised to take aspirin; no physical therapy or exercise program	A vs. B: Age (mean): 46 vs. 49 years Male: 54% vs. 65% Duration of symptoms (months):17 vs. 14 Herniated disc: 51% (n=19) vs. 54% (n=14) Spinal stenosis: 49% (n=18) vs. 46% (n=12) Baseline pain: NR Baseline function:	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
							NR	
Friedly 2014	N=400	Inclusion: ≥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 Exclusion: Spondylolisthesis requiring surgery, history of lumbar surgery or epidural injections within past 6 months	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)	Levels: Multilevel and bilateral injections allowed (numbers not reported) Repeat injections: Up to two injections in 1st six weeks	Fluoroscopy	NR	A vs. B: 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% 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 Baseline leg pain (0-10 NS): 7.2 vs. 7.2 Baseline function (RDQ 0-24): 16 vs. 16	Agency for Healthcare Research and Quality
Suri 2015 (secondary analysis of a RCT, Friedly 2014)	N=400	Inclusion: ≥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,	A: Interlaminar (n=NR) or transforaminal (n=NR) injection with 1 to 2 mL triamcinolone (60 to	Levels: Multilevel and bilateral injections allowed (numbers not reported)	Fluoroscopy	NR	A vs. B: Age (mean): 68.1 ± 9.8 vs. 67.8 ± 10.0 Male: 41.7% vs. 48.9% Nonwhite: 32.6%	Agency for Healthcare Research and Quality, award numbers

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		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 Exclusion: Spondylolisthesis requiring surgery, history of lumbar surgery or epidural injections within past 6 months	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=187) B: Interlaminar (n=NR) or transforaminal (n=NR) injection with 0.25% to 1% lidocaine, with fluoroscopic guidance (2 to 6 ml) (n=182)	Repeat injections: Up to two injections in 1st six weeks			vs. 31.9% Duration of symptoms: NR Employed full-time or part-time: NR Smoker: NR Diabetes on insulin: NR Expectation of pain relief (0-10): NR Baseline leg pain (0-10 NS, mean ± SD): 7.2 ± 1.9 vs. 7.3 ± 1.8 Baseline function (RDQ 0-24): NR Back pain intensity (NRS, mean ± SD): 6.7 ± 2.3 vs. 6.7 ± 2.7 Disability (RMDQ, mean ± SD): 16.0 ± 4.5 vs. 15.6 ± 4.3 PHQ-8 depressive symptoms (mean ± SD): 6.9 ± 5.6 vs/ 6.0 ± 5.5 Fatigue (mean ± SD): 1.5 ± 1.0 vs. 1.3 ± 1.0	1R01HS019222-01, 1R01HS022972-01; Patient-Centered Outcomes Research Institute Program Award CE-12-11-4469; VA Puget Sound Health System
Turner 2015 (secondary analysis of an RCT, Friedly 2014)	N=400	Inclusion: ≥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	A: Interlaminar (n=143) or transforaminal (n=57) injection with 1 to 3 ml triamcinolone (60 to 120 mg), betamethasone (6 to	Levels: Multilevel and bilateral injections allowed (numbers not reported) Repeat injections: Up to two injections	Fluoroscopy	NR	A vs. B: NR	Agency for Healthcare Research and Quality

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		the buttock, leg or both than in the back; score ≥7 on RDQ; duration not specified Exclusion: Spondylolisthesis requiring surgery, history of lumbar surgery or epidural injections within past 6 months	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)	in 1st six weeks				
Fukusaki 1998	N=53	Inclusion: Pseudoclaudication and diagnosed by an orthopedist as having lumbar degenerative spinal canal stenosis with CT and MRI correlation; lumbar structural degenerative changes on x-ray; duration not specified. Exclusion: NR	A: Interlaminar epidural injection with 40 mg methylprednisolone and 1% mepivacaine (8 ml) (n=19) B: Interlaminar epidural injection with 1% mepivacaine (8 ml) (n=18) C: Interlaminar epidural injection with normal saline (8 ml) (n=16)	Levels: Not specified (L3/4 or L4/5 interspace) Repeat injections: 2 injections in first week	None	NR	A vs. B vs. C: Mean age (years): 72 vs. 69 vs. 70 Male: 68% vs. 72% vs. 75% Duration of symptoms: NR Baseline pain: NR Baseline function: NR Walking distance (m): 9 vs. 11 vs. 10	NR
Manchikanti 2012, 2015	N=120	Inclusion: >30 years of age, chronic function-limiting low back pain	A: Interlaminar epidural injection with	Levels: appears to be single	Fluoroscopy with contrast	All patients received a structured	A vs. B: Age (mean): 50 vs. 54 years	"no external funding received"

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		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 Exclusion: 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	betamethasone (1 ml, dose not specified) 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)	Repeat injections: mean 3.5 vs. 3.6 per year, Frequency not specified	verification in epidural space	therapeutic exercise program along with medical therapy, and continued employment; the majority of the study participants were taking opioids, non-opioid analgesics, and adjuvant analgesics when enrolled; no specific treatments, including physical therapy, occupational therapy, or other interventions, were provided to the study participants separately in either group	Male: 55% vs. 32%, p=0.02 Duration of pain (months): 105 vs. 125 Baseline pain (0 to 10 NRS): 8.0 ± 1.0 vs. 8.0 ± 0.7 Baseline function (ODI 0 to 50): 30.5 ± 8.4 vs. 31.0 ± 6.3	
Manchikanti 2012, 2012, 2008	N=100	Inclusion: Spinal stenosis with radicular pain, ≥30 years of age; history of function-limiting	A: Caudal epidural injection with betamethasone 6 mg (1	Levels: Caudal Repeat injections: Mean 3.8 vs. 4.2	Fluoroscopy with contrast verification in epidural space	Continuation of conservative management	A vs. B: Age (mean): 56 vs. 57 years Male:50% vs.	Conducted with the internal resources of

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		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 Exclusion: 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	ml)pluslidocaine 0.5% (9 ml) with fluoroscopic guidance B: Caudal epidural injection with lidocaine 0.5% (10 ml) with fluoroscopic guidance	over 2 years, frequency not specified		used prior to intervention (i.e., opioid, nonopioid, and adjuvant analgesics and/or a therapeutic exercise program); medication adjustments were made; exercise and continuation of work were stressed	32% Race: NR Duration of pain (months): 105 vs. 94 Baseline pain (NRS 0 to 10): 7.6 vs. 7.9 Baseline function (ODI, 0 to 50): 28 vs. 40	the practice without any external funding, either from industry or elsewhere
Nam 2011	N=48	Inclusion: ≥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 both CT and MRI; duration not specified Exclusion: Systemic inflammatory disease or diabetes; on anticoagulants; prior side effects from lidocaine or contrast dye; suspected infectious disease; steroid injection within 3 months; degenerative	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)	Levels: Single level (A vs. B: L5-S1 35% vs. 42%; L4-L5 41% vs. 37%) Repeat injections: 2nd injection after 3 weeks for partial improvement (53% vs. 47% received 2 injections)	Fluoroscopic guidance with contrast verification	Physical therapy not allowed	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	Inje University

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		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	N=80	Inclusion: 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 only Exclusion: Cauda equina syndrome; Polyradiculopathy; previous spinal surgery; spinal tumor, infection, or trauma	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)	Levels: Single level (A vs. B. L4: 18% vs. 12%, L5: 60% vs. 60%, S1: 22% vs. 28%) Repeat injections: Single injection	Fluoroscopic guidance with contrast verification of nerve	Patients were allowed NSAIDs to control low back pain and leg pain	A vs. B: Age (mean): 67 vs. 65 years Male: 45% vs. 55% Race: Not reported Mean duration of symptoms (months): 2.3 vs. 2.5 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% Meloxicam use: 85% vs. 88% Oral steroird: 0% vs. 0% Baseline leg pain (0-10 VAS): 7.5 ± 2.0 vs. 7.9 ± 2.0 Baseline back pain	None received

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
							(0-10 VAS): 3.8 ± 0.8 vs. 4.1 ± 0.5 Baseline function (ODI 0-100): 40 ± 7.0 vs. 38 ± 8.2	
Epidural steroid injection vs. Disc procedure								
Brown 2012	N=38	Inclusion: 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 Exclusion: 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	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)	Levels (A vs. B): 7/17 epidural steroid vs. 7/21 had one level treated Repeat injections: One treatment up to 6 weeks, then patient unblinded and given option of additional treatments, including nonallocated treatment	Fluoroscopy with contrast verification in epidural space	Patients continued on conservative medical managment	A vs. B: Age (mean): 74 vs. 79 years Male: 62% vs. 47% Medical management >6 months: 76% vs. 62% Baseline pain (VAS 0-10): 6.4 vs. 6.4 Baseline function (ODI): 40 vs. 39	Vertos Medical
Epidural steroid injection vs Conservative care								
Koc 2009	N=33	Inclusion: Lumbar spinal	A: Interlaminar	Levels: single level	Fluoroscopy	All patients	A vs. B:	"No funds

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		stenosis based on medical history, physical and neurologic exam, and MRI; duration not specified Exclusion: Coronary artery or peripheral artery disease; spinal surgery; recent vertebral fracture; progression neurologic deficit; cauda equina syndrome	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	Repeat injections: none	with contrast verification in epidural space	were trained to pursue a home-based exercise program consisting of stretching and strengthening exercises, to be performed 2x daily for 6 months; oral diclofenac sodium 75 mg given to all patients 2x daily for 2 weeks	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 function (Roland Morris Disability Index, estimated from graph): 18 vs. 19 vs. 15	were received in support of this work"

Appendix Table H2. Lumbar Spinal Stenosis Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injections vs. control injection							
Cuckler 1985	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)	13 to 30 months (mean 20.2 vs. 21.5 months) % f/u: 100% (37/37)	A vs. B in the spinal stenosis subgroup: Patients with pain improving ≥75%: At 24 hours: 25.0% (5/20) vs. 17.6% (3/17) Mean 20 months (range 13-30 months): 22% (5/23) vs. 14% (2/14) Average percent pain improvement at 24 hours: 43.5% ± 8.7% (n=20) vs. 43.2% ± 8.0% (n=17), t = 0.09, p = NS	NR	NR	Opioid use: NR Surgery: 26% (6/23) vs. 29% (4/14) at mean 20 (range 13-30 months) months Other: NR	NR
el Zahaar 1991	A: Caudal epidural injection with hydrocortisone (5 ml), 4% Carbocaine (4 ml), and saline (21 ml) (n=18 with stenosis)* B: Caudal epidural injection with 4% Carbocaine (4 ml) plus saline (26 cc) (n=12 with stenosis)* *A total of 37 patients were randomized to epidural steroid injection and 26 to placebo; only results for those diagnosed	Mean 20.9 months (20.2 vs. 21.5 months) (range, 13-36 months) % f/u NR	A vs. B: Treatment success, short term (≥75% improvement (no formal definition – all patients asked quantitate the % improvement) in pre-injection back, leg, and thigh symptoms after 24 hours): 55.5% (10/18) vs. 50.0 (6/12) Treatment success, long term (≥75% improvement (no formal definition – all patients asked quantitate the % improvement) in pre-injection symptoms at mean 20.9 months, range 13-36 months): 38.9% (7/18) vs. 33.3%	NR	NR	Surgery: 44.4% (8/18) vs. 58.3% (7/12)	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	with stenosis are reported here.		(4/12) Total failures: 61.1% (11/18) vs. 66.6% (8/12)				
Friedly 2014	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)	1.5 months 97% f/u (386/400)	A vs. B Leg pain (0-10) (overall mean ± SD): Baseline: 7.2 ± 1.9 vs. 7.2 ± 1.8 3 weeks: 4.4 ± 2.7 vs. 5.0 ± 2.8; mean change from baseline: -2.9 ± 2.8 vs. -2.2 ± 4.6; adjusted difference -0.6 (95% CI -1.2 to -0.10, p=0.02 6 weeks: 4.4 ± 2.9 vs. 4.6 ± 2.9; mean change from baseline: -2.8 ± 3.1 vs. -2.6 ± 3.0; adjusted difference, -0.2 (95% CI -0.8 to 0.4, p=0.48); post-hoc adjusted difference for duration of pain: -0.3 (95% CI -0.9 to 0.3, p=0.32) Leg pain improved ≥30%: 6 weeks: 49.2% (96/193) vs. 49.7% (96/193), p=0.88; RR 1.0 (95% CI 0.82 to 1.22) Leg pain improved ≥50%: 38.3% (74/193) vs. 38.3% (74/193), p=0.97, RR 1.0 (95% CI 0.78 to 1.29) BPI (mean ± SD): Baseline: 6.0 ± 2.3 vs. 5.6 ± 3.0	A vs. B RMDQ (0-24) (overall mean ± SD): Baseline: 16.1 ± 4.3 vs. 15.7 ± 4.5 3 weeks: 11.7 ± 6.1 vs. 13.1 ± 5.7; mean change from baseline: -4.4 ± 5.7 vs. -2.9 ± 4.4; adjusted difference, -1.8 (95% CI, -2.8 to -0.9, p<0.001) 6 weeks: 11.8 ± 6.3 vs. 12.5 ± 6.4; mean change from baseline: -4.2 ± 5.8 vs. -3.1 vs. 5.3; adjusted difference, -1.0 (95% CI, -2.1 to 0.1, p=0.07); post-hoc adjusted difference for duration of pain: -1.2 (95% CI, -2.3 to 0.1, p=0.03) RMDQ improved ≥30%: 6 weeks: 37.3% (72/193) vs. 31.6% (61/193), p=0.24	A vs. B SSQ satisfaction "very" or "somewhat" satisfied: 67% (129/193) vs. 54% (104/193), p=0.01 EQ-5D (mean ± SD): Baseline: 0.57 ± 0.20 vs. 0.59 ± 0.20 3 weeks: 0.72 ± 0.18 vs. 0.68 ± 0.19; difference from baseline: 0.15 vs. 0.09 6 weeks: 0.70 ± 0.20 vs. 0.68 ± 0.19; ATE, 0.03 (95% CI, -0.01 to 0.07), p=0.11 difference from baseline: 0.13 vs. 0.09	A vs. B PHQ-8 (mean ± SD): Baseline: 7.1 ± 5.7 vs. 6.1 ± 5.5 3 weeks: 5.1 ± 5.4 vs. 4.5 ± 4.6; mean change from baseline: -2.0 vs. -1.6, p=0.28 6 weeks: 4.4 ± 4.3 vs. 4.8 ± 5.1; mean change from baseline: -2.7 vs. -1.3; ATE, -1.0 (95% CI, 1.7 to 0.3, p=0.007) GAD-7 (mean ± SD): Baseline: 4.7 ± 4.7 vs. 4.7 ± 6.1 3 weeks: 5.1 ± 5.4 vs. 4.5 ± 4.6; mean change from baseline: 0.4 vs. -0.2 6 weeks: 4.4 ± 4.3 vs. 4.8 ± 5.1; mean change from baseline: -0.3 vs. 0.1; ATE, -0.3 (95% CI, -1.0 to 0.4, p=0.44)	A vs. B At least 1 adverse event: 22% (43/200) vs. 16% (31/200) Excessive pain: 2.5% (5/200) vs. 3.5% (7/200) Headache: 4% (8/200) vs. 1.5% (3/200) Fever and/or infection: 5% (10/200) vs. 1.0% (2/200) Dizziness/light headedness: 2% (4/200) vs. 2% (4/200) Dural puncture: 0.5% (1/200) vs. 0.5% (1/200) Serious adverse event: 2.5% (5/200) vs. 2.0% (4/200)

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			3 weeks: 3.6 ± 2.9 vs. 3.9 ± 2.7; difference from baseline: -2.4 vs. -1.7 6 weeks: 3.5 ± 2.9 vs. 3.8 ± 3.1; difference from baseline: -2.5 vs. -1.8; average treatment effect (ATE) 0.1 (95% CI, -0.1 to 0.2, p=0.40) <u>SSSQ symptoms (mean ± SD):</u> Baseline: 3.2 ± 0.6 vs. 3.1 ± 0.6 3 weeks: 2.5 ± 0.7 vs. 2.7 ± 0.7 6 weeks: 2.5 ± 0.7 vs. 2.6 ± 0.8; ATE, 0.1 (95% CI, -0.2 to 0.0, p=0.18) <u>Intensity of back pain (mean ± SD):</u> Baseline: 6.7 ± 2.3 vs. 6.6 ± 2.6 3 weeks: 4.0 ± 2.7 vs. 4.6 ± 2.6 6 weeks: 4.3 ± 2.8 vs. 4.4 ± 2.7; ATE, -0.1 (95% CI, -0.7 to 0.5), p=0.58 <u>BPI Interference scale</u> Baseline: 6.0 ± 2.3 vs. 5.6 ± 3.0 3 weeks: 3.6 ± 2.9 vs. 3.9 ± 2.7 6 weeks: 3.5 ± 2.9 vs. 3.8 ± 3.1; ATE, -0.4 (95% CI, -1.0 to 0.2)	<u>RMDQ improved ≥50%:</u> 6 weeks: 23.8% (46/193) vs. 20.2% (39/193), p=0.39 <u>SSSQ physical function (mean ± SD):</u> Baseline: 2.5 ± 0.5 vs. 2.5 ± 0.5 3 weeks: 2.2 ± 0.6 vs. 2.2 ± 0.6 6 weeks: 2.3 ± 0.7 vs. 2.2 ± 0.6; ATE, 0.1 (95% CI, -0.1 to 0.2, p=0.007) *Transforaminal Approach, A vs. B* <u>RMDQ, mean ± SD:</u> Baseline: 14.4 ± 4.4 (n=57) vs. 14.8 ± 4.5 (n=61) 3 weeks: 12.6 ± 5.4 (n=56) vs. 13.0 ± 6.1 (n=54); mean change from baseline: -1.8 ± 4.7 vs. -1.8 ± 3.9; adjusted difference, -0.1 (95% CI, -1.7 to 1.6, p=0.94) 6 weeks: 12.0 ± 5.6 (n=57) vs. 12.1 ± 6.6 (n=57); mean change from baseline: -2.4 ± 4.7 vs. -2.6 ± 5.3; adjusted difference,			

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			Transforaminal Approach, A vs. B Leg pain, mean ± SD: Baseline: 7.0 ± 2.0 (n=57) vs. 7.0 ± 1.8 (n=61) 3 weeks: 5.0 ± 2.5 (n=56) vs. 5.1 ± 2.7 (n=54); mean change from baseline: -1.9 ± 2.1 vs. -2.0 ± 2.6; adjusted difference, -0.0 (95% CI, -0.9 to 0.9, p=0.99) 6 weeks: 4.9 ± 2.6 (n=57) vs. 4.9 ± 2.7 (n=57); mean change from baseline: -2.0 ± 2.6 vs. -2.0 ± 2.8; adjusted difference, 0.1 (95% CI, -0.9 to 1.0, p=0.89) *Interlaminar Approach, A vs. B* Leg pain, mean ± SD: Baseline: 7.3 ± 1.9 (n=143) vs. 7.4 ± 1.8 (n=139) 3 weeks: 4.1 ± 2.7 (n=139) vs. 5.0 ± 2.7 (n=134) ; mean change from baseline: -3.2 ± 2.9 vs. -2.4 ± 3.0; adjusted difference, -0.9 (95% CI, -1.5 to -0.3, p=0.005) 6 weeks: 4.2 ± 3.0 (n=136) vs. 4.5 ± 2.9 (n=136); mean change from baseline: -3.1 ± 3.3 vs. -2.8 ± 3.1; adjusted difference, -0.3 (95% CI, -1.0 to 0.4, p=0.37)	0.3 (95% CI, -1.9 to 1.8, p=0.95) *Interlaminar Approach, A vs. B* RMDQ, mean ± SD: Baseline: 16.7 ± 4.3 (n=143) vs. 16.0 ± 4.1 (n=139) 3 weeks: 11.3 ± 6.3 (n=139) vs. 13.2 ± 5.6 (n=135); mean change from baseline: -5.4 ± 5.8 vs. -2.9 ± 4.6; adjusted difference, -2.5 (95% CI. -3.7 to -1.3, p<0.001) 6 weeks: 11.8 ± 6.5 (n=136) vs. 12.6 ± 6.3 (n=136); mean change from baseline: -4.8 ± 6.0 vs. -3.3 ± 5.3; adjusted difference, -1.4 (95% CI, -2.8 to -0.1, p=0.04)			
Suri 2015	A: Interlaminar (n=NR)	1.5 months	NR	A vs. B:	A vs. B	A vs. B:	A vs. B

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	or transforaminal (n=NR) injection with 1 to 2 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=187) B: Interlaminar (n=NR) or transforaminal (n=NR) injection with 0.25% to 1% lidocaine, with fluoroscopic guidance (2 to 6 ml) (n=182)	92.2% f/u (369/400)		RMDQ disability change from baseline score at 3 weeks: -4.4 vs. -2.6, p=0.0002	Total treatment effect on patient-reported overall satisfaction*: 0.55 (95% CI, 0.12 to 0.97) * Unstandardized regression coefficient for treatment (ESI + lidocaine vs. lidocaine only) effects on 6-week patient satisfaction, unadjusted for mediators but adjusted for recruitment site.	PHQ-8 fatigue change from baseline score at 3 weeks: -0.4 vs. -0.2, p=0.22	Number of adverse event reported through 3 weeks: 0.2 vs. 0.1, p=0.09
Turner 2015	A: Interlaminar (n=NR) or transforaminal (n=NR) injection with 1 to 2 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	1.5 months 92.2% f/u (369/400)	NR	NR	NR	NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	fluoroscopic guidance (n=187) B: Interlaminar (n=NR) or transforaminal (n=NR) injection with 0.25% to 1% lidocaine, with fluoroscopic guidance (2 to 6 ml) (n=182)						
Fukusaki 1998	A: Interlaminar epidural injection with 40 mg methylprednisolone and 1% mepivacaine (8 ml) (n=19) B: Interlaminar epidural injection with 1% mepivacaine (8 ml) (n=18) C: Interlaminar epidural injection with normal saline (8 ml) (n=16) (8 ml)	3 months % f/u NR	NR	A vs. B vs. C: <u>Walking distance (m):</u> 87 ± 58 vs. 92 ± 66 vs. 23 ± 19 at 1 week, 26 ± 23 vs. 28± 24 vs. 18 ± 13 at 1 month, 10 ± 8 vs. 13 ± 7 vs. 11 ± 8 at 3 months (p<0.05 for A and B vs. C at week 1 only) <u>Good or excellent results (walk >20 meters):</u> 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) 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	NR	NR	"No incidence of dural puncture, hypotension, or subarachnoid injection in any group."

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
				2.53 (95% CI 0.29 to 21.98); 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)			
Manchikanti 2012, 2015	A: Interlaminar epidural injection with betamethasone (1 ml, dose not specified) 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)	24 months 92.5% (111/120) at 12 months; 88.3% (106/120) at 24 months	A vs. B <u>Pain (mean NRS, 0 to 10):</u> Baseline 8.0 ± 1.0 vs. 8.0 ± 0.7 3 months: 3.7 ± 1.5 vs. 3.7 ± 1.3; 6 months: 3.8 ± 1.7 vs. 3.6 ± 1.5; 12 months: 3.7 ± 1.8 vs. 3.7 ± 1.6; 24 months: 3.6 ± 1.7 vs. 3.8 ± 1.8 P for group difference = 0.841 <u>Pain relief ≥50% from baseline:</u> 3 months: 83% (50/60) vs. 77% (46/60) 6 months: 80% (48/60) vs. 75% (45/60) 12 months: 77% (46/60) vs. 73% (44/60) 24 months: 73% (44/60) vs. 72% (43/60) <u>Success (≥50% improvement in VAS and ODI)</u> 3 months: 77% (46/60) vs. 75% (45/60)	A vs. B: <u>ODI (0 to 50):</u> Baseline: 30.5 ± 8.4 vs. 31.0 ± 6.3 3 months: 15.2 ± 6.2 vs. 15.3 ± 5.3 6 months: 14.8 ± 6.4 vs. 15.1 ± 5.9 12 months: 14.4 ± 6.4 vs. 15.0 ± 6.4 24 months: 13.7 ± 6.4 vs. 15.1 ± 7.2 P for group difference = 0.781 <u>ODI improved ≥50% from baseline over 2 years</u>: 3 months: 77% (46/60) vs. 78% (47/60) 6 months: 78% (47/60) vs. 73% (44/60) 12 months: 75% (45/60) vs. 75% (45/60)	NR	A vs. B <u>Opioid intake (morphine equivalents in mg)</u> Baseline: 71.0 ± 92.3 vs. 60.5 ± 56.6 3 months: 42.8 ± 40.8 vs. 44.0 ± 40.4 6 months: 40.2 ± 36.2 vs. 40.2 ± 40.6 12 months: 38.2 ± 30.4 vs. 39.4 ± 40.9 24 months: 33.4 ± 29.5 vs. 37.9 ± 38.3 P for group difference = 0.833	Not reported by group <u>Sub-arachnoid entries</u>: 2.2% (14/644 procedures) <u>Nerve root irritation</u>: 0.2% (1/644 procedures) <u>Pain and swelling at the site of injection</u>: 0.2% (1/644 procedures) "There were no major adverse events noted"

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			6 months: 77% (46/60) vs. 72% (43/60) 12 months: 73% (44/60) vs. 73% (44/60) 24 months: 73% (44/60) vs. 72% (43/60)	24 months: 75% (45/60) vs. 75% (45/60)			
Manchikanti 2012, 2012, 2008	A: Caudal epidural injection with betamethasone 6 mg (1 ml) plus lidocaine 0.5% (9 ml) with fluoroscopic guidance (n=50) B: Caudal epidural injection with lidocaine 0.5% (10 ml) with fluoroscopic guidance (n=50)	24 months 97% (97/100) at 3 months; 92% (92/100) at 6 months; 81% (81/100) at 12 months; 71% (71/100) at 24 months	A vs. B Pain (mean NRS, 0 to 10): 7.6 ± 0.8 vs. 7.9 ± 0.9 at baseline; 4.1 ± 1.9 vs. 4.1 ± 1.8 at 3 months; 4.2 ± 1.9 vs. 4.1 ± 1.7 at 6 months; 4.3 ± 2.0 vs. 4.4 ± 1.8 at 12 months; 4.7 ± 2.2 vs. 4.6 ± 1.8 at 24 months, (p=0.80 for group difference) Pain relief ≥50% from baseline: 62% (31/50) vs. 66% (33/50) at 3 months; 56% (28/50) vs. 58% (29/50) at 6 months; 46% (23/50) vs. 48% (24/50) at 12 months; 44% (22/50) vs. 42% (21/50) at 24 months 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;	A vs. B ODI (0 to 50): 28.1 ± 4.6 vs. 29.8 ± 4.2 at baseline; 16.8 ± 7.9 vs. 17.2 ± 6.8 at 3 months; 16.9 ± 8.2 vs. 17.2 ± 7.3 at 6 months; 16.9 ± 7.8 vs. 17.5 ± 7.6 at 12 months; 17.0 ± 7.6 vs. 17.5 ± 7.3 at 24 months, (p=0.60 for group difference) ODI improved ≥50% from baseline: 49% (24/50) vs. 58% (29/50) at 3 months; 50% (25/50) vs. 54% (27/50) at 6 months; 50% (25/50) vs. 50% (25/50) at 12 months; 46% (23/50) vs. 42% (21/50) at 24 months	NR	Opioid use (mg MED/day): 49.2 ± 42.2 vs. 45.7 ± 53.0 at baseline; 33.1 ± 27.5vs. 33.3 ±35.7 at 3 months; 33.7 ± 34.7 vs. 34.4 ± 43.0 at 6 months; 33.3 ± 34.5 vs. 35.9 ± 43.1 at 12 months; 32.5 ± 34.8 vs. 35.7 ± 43.3 at 24 months, (p>0.05 at all time points) Surgery: NR Other: NR	"No major adverse events"

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			44% (22/50) vs. 38% (19/50) at 24 months				
Nam 2011	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)	3 months 75% (36/48)	A vs. B 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 within steroid arm)	A vs. B 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 within steroid arm)	A vs. B: QoL: NR 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*	Surgery by 3 months 12% (2/17) vs 5.3% (1/19)	NR
Ohtori 2012	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 month % f/u NR	A vs. B Leg pain (0-10 VAS): 7.5 ± 2.0 vs. 7.9 ± 2.0 at baseline (p=NS); 5.2 ± 0.7 vs. 3.5 ± 0.8 at 1 month (p=0.03) Back pain (0-10 VAS): 3.8 ± 0.8 vs. 4.1 ± 0.5 at baseline (p=NS); 3.1 ± 0.7 vs. 3.1 ± 0.5 at 1	A vs. B ODI (0-100): 40 ± 7.0 vs. 38 ± 8.2 at baseline (p=NS); 30 ± 6.0 vs. 28 ± 6.2 at 1 month (p=NS);	"Treatment met my expectations": 42.5% (17/40) vs. 55.0% (22/40); p=NR "I did not improvement as much as I had hoped, but I would undergo the same	NR	Deep Infection: 0% vs. 0% Superficial infection: 0% vs. 0% Hematoma: 0% vs. 0% Spinal nerve injury: 0% vs. 0%

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	1% lidocaine (2 ml), with fluoroscopic guidance (n=40)		month (p=NS)		treatment for the same outcome": 30.0% (12/40) vs. 30.0% (12/40); p=NS		Others: 0% vs. 0%
Epidural steroid injections vs. Disc procedures							
Brown 2012	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)	6 weeks f/u NR	A vs. B Pain (mean, 0-10 VAS): 6.4 ± 1.0 vs. 6.3 ± 0.7 at baseline; 6.3 ± 1.4 vs. 3.8 ± 1.3 at 6 weeks; p=0.54 ≥2 point improvement in VAS pain (0-10): 35.3% (6/17) vs. 76.2% (16/21) at 6 weeks; p = 0.03	A vs. B: ODI: 40.5 ± 5.9 vs. 38.8 ± 4.2 at baseline, 34.8 ± 8.2 vs. 27.4 ± 7.0 at 6 weeks; p=0.86	A vs. B: QoL: NR Zurich Claudication Questionnaire patient satisfaction (mean, 1-6): 2.8 ± 0.5 vs. 2.2 ± 0.5 at 6 weeks; p=NS Zurich Claudication Questionnaire patient satisfaction score ≤2.5: 41.2% (7/17) vs. 58.8% (12/21) at 6 weeks, p = NS	NR	Mortality: 0% vs. 0% "No major procedure-related or device- related complications (i.e., dural tear, blood loss requiring transfusion, nerve root damage, hematoma, infection, and re-hospitalization as defined in study protocol) reported in either treatment group"
Epidural steroid injections vs. Conservative care							
Koc 2009	A: Interlaminar epidural injection with 60 mg triamcinolone acetonide (1.5 ml), 15	6 months 88% f/u (29/33): A vs. B vs. C 0% (0/10) vs.	A vs. B vs. C Pain intensity (mean VAS, 0 to 100; estimated from graph): 53 vs. 55 vs. 58 at baseline;	A vs. B vs. C Roland Morris Disability Index (mean, 0-24; estimated from	NR	A vs. B vs. C Opioid use: NR Surgery: NR	2 withdrawals due to adverse events (1 gastric complaint, 1

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	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	23% (3/13) vs. 10% (1/10) at 6 months	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 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	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 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		Other: 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)	angina pectoris), group NR

Appendix Table H3. Lumbar Spinal Stenosis Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Epidural steroid injections vs. Control injection				
Cuckler 1985	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)	13 to 30 months (mean 20 .2 vs. 21.5 months) % f/u: 100.0 (37/37)	NR	NR
el Zahaar 1991	A: Caudal epidural injection with hydrocortisone (5 ml), 4% Carbocaine (4 ml), and saline (21 ml) (n=18 with stenosis)* B: Caudal epidural injection with 4% Carbocaine (4 ml) plus saline (26 cc) (n=12 with stenosis)*	Mean 20-21 months (range, 13-36 months) % f/u NR	None	None
Friedly 2014	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)	1.5 months 97% f/u (386/400)	*Transforaminal Approach, A vs. B* RMDQ, mean ± SD: Baseline: 14.4 ± 4.4 vs. 14.8 ± 4.5 3 weeks: 12.6 ± 5.4 vs. 13.0 ± 6.1; mean change from baseline: -1.8 ± 4.7 vs. -1.8 ± 3.9; adjusted difference, -0.1 (95% CI, -1.7 to 1.6, p=0.94) 6 weeks: 12.0 ± 5.6 vs. 12.1 ± 6.6; mean change from baseline: -2.0 ± 2.6 vs. -2.0 ± 2.8; adjusted difference, 0.3 (95% CI, -1.9 to 1.8, p=0.95) No formal test for interaction conducted *Interlaminar Approach, A vs. B* RMDQ, mean ± SD: Baseline: 16.7 ± 4.3 vs. 16.0 ± 4.1 3 weeks: 4.1 ± 2.7 vs. 5.0 ± 2.7; mean change from baseline: -5.4 ± 5.8 vs. -2.9 ± 3.0; adjusted difference, -2.5 (95% CI. -3.7 to -1.3, p<0.001) 6 weeks:11.8 ± 6.5 vs. 12.6 ± 2.9; mean change from baseline: -3.1 ± 3.3 vs. -2.8 ± 3.1; adjusted difference, -0.3 (95% CI, -1.0 to -0.1, p=0.04) No formal test for interaction conducted *Transforaminal Approach, A vs. B*	*Transforaminal Approach, A vs. B* Adverse event rate: 0.46 (26/57) vs. 0.33 (20/61), p=0.27 *Interlaminar Approach, A vs. B* Adverse event rate: 0.22 (32/143) vs. 0.10

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
			Leg pain, mean ± SD: Baseline: 7.0 ± 2.0 vs. 7.0 ± 1.8 3 weeks: 5.0 ± 2.5 vs. 5.1 ± 2.1; mean change from baseline: -1.9 ± 2.1 vs. -2.0 ± 2.6; adjusted difference, -0.0 (95% CI, -0.9 to 0.9, p=0.99) 6 weeks: 4.9 ± 2.6 vs. 4.9 ± 2.7; mean change from baseline: -2.0 ± 2.6 vs. -2.0 ± 2.8; adjusted difference, 0.1 (95% CI, -0.9 to 1.0, p=0.89) No formal test for interaction conducted *Interlaminar Approach, A vs. B* Leg pain, mean ± SD: Baseline: 7.3 ± 1.9 vs. 14.8 ± 4.5 3 weeks: 4.1 ± 2.7 vs. 5.0 ± 2.7; mean change from baseline: -3.2 ± 2.9 vs. -2.4 ± 3.0; adjusted difference, -0.9 (95% CI, -1.5 to -0.3, p=0.005) 6 weeks: 4.2 ± 3.0 vs. 4.5 ± 2.9; mean change from baseline: -3.1 ± 3.3 vs. -2.8 ± 3.1; adjusted difference, -0.3 (95% CI, -1.9 to 1.8, p=0.37) No formal test for interaction conducted There were no significant interactions between race and treatment in analyses of RMDQ scores (p for interaction = 0.73) or leg pain (p for interaction = 0.99) at 6 weeks.	(14/139), p=0.02 *Race:* NR
Suri 2015	A: Interlaminar (n=NR) or transforaminal (n=NR) injection with 1 to 2 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=187) B: Interlaminar (n=NR) or transforaminal (n=NR) injection with 0.25% to 1% lidocaine, with fluoroscopic guidance (2 to 6 ml) (n=182)	1.5 months 92.2% f/u (369/400)	*Interlaminar Approach, A vs. B* No formal test for interaction conducted for any outcomes. Patient-reported satisfaction with treatment: 67% (n NR) vs. 53% (n NR), p=0.03 Total treatment effect estimate on patient-reported overall satisfaction*: 0.58 (95% CI, 0.08 to 1.09) Primary potential mediator of interest: - Estimate of effect on patient-reported overall satisfaction, Leg pain intensity change at 3 weeks (NRS): 0.20 (95% CI, 0.01 to 0.45) o Percent total effect explained by mediator: 34.4% Secondary potential mediators of interest: - Estimate of effect on patient-reported overall satisfaction, Back pain intensity change at 3 weeks (NRS): 0.13 (95% CI, -0.06 to 0.33) o Percent total effect explained by mediator: 21.8%	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
			- Estimate of effect on patient-reported overall satisfaction, Disability change at 3 weeks (RMDQ): 0.42 (95% CI, 0.18 to 0.72) o Percent total effect explained by mediator: 72.4% - All potential mediators (leg pain, back pain, disability): 0.42 (95% CI, 0.12 to 0.78) o Percent total effect explained by mediator: 72.6% *Transforaminal Approach, A vs. B* No formal test for interaction conducted Patient-reported satisfaction with treatment: 67% (n NR) vs. 56% (n NR), p=0.34 * Unstandardized regression coefficient for treatment (ESI + lidocaine vs. lidocaine only) effects on 6-week patient satisfaction, unadjusted for mediators but adjusted for recruitment site.	
Turner 2015	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)	1.5 months 97% f/u (386/400)	A vs. B Formal test of interaction conducted for all outcomes. **Predictors of treatment effects on RMDQ scores† (Table 1):** No baseline characteristics showed statistically significant treatment effect on RMDQ scores at 3 and 6 weeks follow-up. Characteristics evaluated: gender (male, female); race (Caucasian, non-Caucasian); ethnicity (Hispanic, non-Hispanic); education (HS or less, some college, college, professional/graduate degree); employment (full-/part-time; retired, not disabled; retired, disabled; other), smoking history (never/former smoker, current smoker); diabetes, on insulin (No, yes); Duration of pain (<3 mo; 3-12 mo; 1-5 years; >5 years); and stenosis severity (mild, moderate, severe) **Predictors of treatment interaction coefficient estimates for RMDQ scores† (Table 2)**: The only baseline predictor that showed statistically significant treatment effect on RMDQ scores at 3 weeks follow-up was the EQ-5D index, interaction coefficient (95% CI), 4.77 (-0.04 to 9.59), p=0.05, treatment effect at 25th, 75th percentile: -2.8, -0.9 No baseline predictors showed statistically significant treatment effect on	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
			buttock/hip/leg pain scores at 6 weeks follow-up. Characteristics evaluated: age, BMI, treatment expectations, EQ-5D index, EQ-5D VAS, PHQ-8, GAD-7, PCS total (helplessness, rumination, magnification), FABQ-PA **Predictors of treatment effects on buttock/hip/leg pain† (Table 3):** No baseline characteristics showed statistically significant treatment effect on buttock/hip/leg pain scores at 3 and 6 weeks follow-up. Characteristics evaluated: gender (male, female); race (Caucasian, non-Caucasian); ethnicity (Hispanic, non-Hispanic); education (HS or less, some college, college, professional/graduate degree); employment (full-/part-time; retired, not disabled; retired, disabled; other), smoking history (never/former smoker, current smoker); diabetes, on insulin (No, yes); Duration of pain (<3 mo; 3-12 mo; 1-5 years; >5 years); and stenosis severity (mild, moderate, severe) **Predictors of treatment interaction coefficient estimates for buttock/hip/leg pain† (Table 4)**: No baseline predictors showed statistically significant treatment effect on buttock/hip/leg pain scores at 3 weeks follow-up. The only baseline predictor that showed a statistically significant treatment effect on buttock/hip/leg pain scores at 6 weeks follow-up was the EQ-5D index, interaction coefficient (95% CI): 2.94 (0.11 to 5.76), p=0.04, treatment effect at 25th, 75th percentile: -0.8. 0.4 Characteristics evaluated: age, BMI, treatment expectations, EQ-5D index, EQ-5D VAS, PHQ-8, GAD-7, PCS total (helplessness, rumination, magnification), FABQ-PA **Predictors of treatment effects for Brief Pain Inventory (BPI) interference† (Table 9):** Employment (p=0.03), Smoking history (p=0.01), PCS total (p=0.03), PCS total-helplessness (p=0.02) were the only statistically significant baseline predictors of treatment effect for BPI at 3 weeks follow-up. No baseline predictors showed a statistically significant treatment effect for BPI at 6 weeks follow-up.	

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
			Characteristics evaluated: Gender, race, ethnicity, education, employment, smoking history, diabetes- on insulin, duration of pain, stenosis severity, age, BMI, treatment expectations, EQ-5D index, EQ-5D VAS, PHQ-8, GAD-7, PCS total (helplessness, rumination, magnification), FABQ-PA **Predictors of treatment effects for Swiss Spinal Stenosis Questionnaire (SSSQ) physical function† (Table 9):** No baseline predictors showed a statistically significant treatment effect for SSSQ physical function at 3 weeks follow-up. Only employment (p=0.02) showed a statistically significant treatment effect for SSSQ physical function at 6 weeks follow-up. Characteristics evaluated: Gender, race, ethnicity, education, employment, smoking history, diabetes- on insulin, duration of pain, stenosis severity, age, BMI, treatment expectations, EQ-5D index, EQ-5D VAS, PHQ-8, GAD-7, PCS total (helplessness, rumination, magnification), FABQ-PA **Predictors of treatment effects for Swiss Spinal Stenosis Questionnaire (SSSQ) symptom severity† (Table 9):** No baseline predictors showed a statistically significant treatment effect for SSSQ symptom severity at 3 or 6 weeks follow-up. Characteristics evaluated: Gender, race, ethnicity, education, employment, smoking history, diabetes- on insulin, duration of pain, stenosis severity, age, BMI, treatment expectations, EQ-5D index, EQ-5D VAS, PHQ-8, GAD-7, PCS total (helplessness, rumination, magnification), FABQ-PA **Predictors of treatment effects for Swiss Spinal Stenosis Questionnaire (SSSQ) satisfaction with treatment† (Table 9):** No baseline predictors showed a statistically significant treatment effect for SSSQ satisfaction with treatment at 3 weeks follow-up. Only treatment expectations (p=0.02) showed a statistically significant treatment effect for SSSQ satisfaction with treatment at 6 weeks follow-up. Characteristics evaluated: Gender, race, ethnicity, education, employment, smoking	

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
			history, diabetes- on insulin, duration of pain, stenosis severity, age, BMI, treatment expectations, EQ-5D index, EQ-5D VAS, PHQ-8, GAD-7, PCS total (helplessness, rumination, magnification), FABQ-PA † All coefficients and treatment effect estimates were adjusted for an interaction between the predictor of interest, an indicator of treatment, as well as for recruitment site and baseline value of the outcome measure.	
Manchikanti 2012, 2012, 2008	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	24 months 97% (97/100) at 3 months; 92% (92/100) at 6 months; 81% (81/100) at 12 months; 71% (71/100) at 24 months)	None	None
Manchikanti 2012, 2015	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	12 months 90% f/u (54/60)	NR	NR
Nam 2011	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)	3 months 75% (36/48)	NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Ohtori 2012	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)	1 month % f/u NR	None	None
Epidural steroid injections vs. Disc procedures				
Brown 2012	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)	6 weeks f/u NR	NR	NR
Epidural steroid injections vs. Conservative care				
Koc 2009	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	6 months 88% f/u (29/33): A vs. B vs. C 0% (0/10) vs. 23% (3/13) vs. 10% (1/10) at 6 months	NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
	C: No injection or physical therapy			

Appendix Table H4. Lumbar Spinal Stenosis: Baseline scores for Pain, Function, Quality of Life, and Opioid Usage

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Pain score* Mean ± SD Group A	Group B
Pain on VAS/NRS (0-10)						
Baseline	Manchikanti (2012,2012,2008)	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	7.6 ± 0.8 (n=50)	7.9 ± 0.9 (n=50)
	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1%	Lidocaine 0.25-1%	Interlaminar	7.3 ± 1.9 (n=143)	7.4 ± 1.8 (n=139)
	Manchikanti (2012, 2015)	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Interlaminar	8.0 ± 1.0 (n=60)	8.0 ± 0.7 (n=60)
	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1%	Lidocaine 0.25-1%	Transforaminal	7.0 ± 2.0 (n=57)	7.0 ± 1.8 (n=61)
	Nam (2011)	Triamcinolone 20 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Transforaminal	7.32 (n=17)	7.41 (n=19)
	Tafazal 2009/Ng 2005	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Bupivacaine 0.25%	Transforaminal	NR (n=23 stenosis subgroup)	NR (n=25 stenosis subgroup)
	Ohtori 2012	Dexamethasone 3.3 mg + lidocaine 1% Fluoroscopy	Etanercept + lidocaine 1%	Transforaminal	7.5 ± 2.0 (n=40)	7.9 ± 2.0 (n=40)
	Brown 2012	Triamcinolone 80 mg (40 mg in diabetics) + saline Fluoroscopy	Minimally invasive lumbar decompression Fluoroscopy	Interlaminar	6.4 ± 1.0 (n=17)	6.3 ± 0.7 (n=21)
	Koc 2009	Triamcinolone 60 mg + bupivacaine 0.5% + saline 0.9% (also trained in home exercises and given diclofenac 75 mg) Fluoroscopy	Inpatient physical therapy‡ 5 days/wk for 2 weeks + diclofenac 75 mg	Inter-laminar	5.3 (n=10)	5.5 (n=10)
		Triamcinolone 60 mg +	Home exercises +	Inter-laminar	5.3	5.8

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Pain score* Mean ± SD Group A	Group B
		bupivacaine 0.5% + saline 0.9% (also trained in home exercises and given diclofenac 75 mg) Fluoroscopy	diclofenac 75 mg		(n=10)	(n=9)
Function on ODI						
Baseline	Manchikanti (2012,2012,2008)	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	(ODI 0-50) 28.1 ± 4.6 (n=50)	(ODI 0-50) 29.8 ± 4.2 (n=50)
	Manchikanti (2012, 2015)	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Interlaminar	(ODI 0-50) 30.5 ± 8.4 (n=60)	(ODI 0-50) 31.0 ± 6.3 (n=60)
	Nam (2011)	Triamcinolone 20 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Transforaminal	(ODI 0-100) 63.0 (n=17)	(ODI 0-100) 63.0 (n=19)
	Tafazal 2009/Ng 2005	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Bupivacaine 0.25%	Transforaminal	(ODI 0-100) NR (n=23 stenosis subgroup)	(ODI 0-100) NR (n=25 stenosis subgroup)
	Ohtori 2012	Dexamethasone 3.3 mg + lidocaine 1% Fluoroscopy	Etanercept + lidocaine 1%	Transforaminal	(ODI 0-100) 40 ± 7.0 (n=40)	(ODI 0-100) 38 ± 8.2 (n=40)
	Brown 2012	Triamcinolone 80 mg (40 mg in diabetics) + saline Fluoroscopy	Minimally invasive lumbar decompression Fluoroscopy	Interlaminar	(ODI 0-100) 40.5 ± 5.9 (n=17)	(ODI 0-100) 38.8 ± 4.2 (n=21)
Function on RMDQ (0-24)						
Baseline	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1%	Lidocaine 0.25-1%	Inter-laminar	16.7 ± 4.3 (n=143)	16.0 ± 4.1 (n=139)
		Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1%	Lidocaine 0.25-1%	Transforaminal	14.4 ± 4.4 (n=57)	14.8 ± 4.5 (n=61)
	Koc 2009	Triamcinolone 60 mg + bupivacaine 0.5% + saline 0.9%	Inpatient physical therapy‡ 5 days/wk for 2	Inter-laminar	18 (n=10)	19 (n=10)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Pain score* Mean ± SD Group A	Group B
		(also trained in home exercises and given diclofenac 75 mg) Fluoroscopy	weeks + diclofenac 75 mg			
		Triamcinolone 60 mg + bupivacaine 0.5% + saline 0.9% (also trained in home exercises and given diclofenac 75 mg) Fluoroscopy	Home exercises + diclofenac 75 mg	Inter-laminar	18 (n=10)	15 (n=9)
EQ5D						
Baseline	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1%	Lidocaine 0.25-1%	Interlaminar or Transforaminal	0.57 ± 0.20 (n=200)	0.59 ± 0.20 (n=200)
Opioid usage (morphine equivalents mg/day)						
	Manchikanti (2012,2012,2008)	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	49.2 ± 42.2 (n=50)	45.7 ± 53.0 (n=50)
	Manchikanti (2012, 2015)	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	71.0 ± 92.3 (n=60)	60.5 ± 56.6 (n=60)

APPENDIX I. Low Back Pain Without Radiculopathy: RCT Study Characteristics and Results

Appendix Table I1. LBP Without Radiculopathy Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Epidural steroid injection vs. Control injection								
Manchikanti 2012, 2011, 2008	N=120	Inclusion: 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 Exclusion: 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	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)	Levels: Caudal Repeat injections: Mean 5.5 vs. 4.5 over 2 years, frequency not specified	Fluoroscopy with contrast verification in epidural space	Conservative management with appropriate drug therapy and a therapeutic exercise program were continued as needed, along with work. There was no specific or additional intervention provided other than the study procedure.	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 function (ODI, 0 to 50): 28 vs. 28	Internal resources of the pain management practice without any external funding either from industry or other
Manchikanti 2013, 2012, 2010	N=120	Inclusion: 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 Exclusion: Lumbar facet joint or sacroiliac joint pain based on controlled, comparative	A: Interlaminar epidural injection with 6 mg betamethasone (1 ml) and lidocaine 0.5% (5 ml) with fluoroscopic guidance (n=60) B: Interlaminar	Levels: NR Repeat injections: Mean 3.8 vs. 3.7 per year, frequency not specified	Fluoroscopy with contrast verification in epidural space	Co-interventions were similar in both groups, and included the continuation of previously directed structured	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	"No external resources were utilized in the conduct of this study"

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		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	epidural injection with lidocaine 0.5% (6 ml) with fluoroscopic guidance (n=60)			exercise programs, employment, and medical therapy; there was no one specific type of intervention in any of the patients including physical therapy or other interventions.	Baseline function (ODI 0 to 50): 29 vs. 31	
Intradiscal steroid injection vs. Intradiscal control injection								
Cao 2011	N=120	Inclusion: Chronic low back pain subsiding in supine position and aggravated by sitting or standing, without apparent radicular pain or nerve root compression physical signs. Disc degeneration on MRI, or end plate modic changes in one level only with disc degeneration, positive discography with pain and contrast medium infiltration into annulus. Exclusion: Patients <20 or >60 years. More than one-level end plate modic changes on MRI, negative discography for the focused level, positive discography at level or levels other than the focused level,	A: Lumbar intradiscal injection of betamethasone (n=40) B: Lumbar intradiscal injection of saline (n=40)	Levels: NR Repeat injections: mean injections/year NR	CT guidance	NR	Mean age (±SD) : 42.3 years Male: 61%	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		or positive discography but contrast medium leaking into spinal canal.						
Khot 2004	N=120	Inclusion Discogenic low back pain without radicular pain. MRI findings demonstrating DDD. Failure of at least 6 weeks of conservative treatment Exclusion Medical conditions requiring systemic steroid therapy	A: Lumbar intradiscal injection of methylprednisolone 40 mg (n=60) B: Lumbar intradiscal injection of saline (n=60)	Mean injections/yr: NR	NR	NR	Presumed discogenic back pain. Other: NR	No funds were received in support of this work.
Simmons 1992	N=25	Inclusion Age 18-50 years. Internal disc disruption or nonsequestered nuclear prolapse on MRI and discography. Positive pain response and one-level symptomatic involvement only, verified on discography. Failed at least 6 weeks of conservative treatment Exclusion 2 or more symptomatic levels. Prior lumbar surgery. Stenosis. Medical conditions that required systemic steroids	A: Lumbar intradiscal injection of methylprednisolone 80 mg (n=14) B: Lumbar intradiscal injection of bupivacaine (n=11)	Levels: NR Repeat injections: NR	Fluoroscopic	No nonsteroidal anti-inflammatory drugs were prescribed after injection	Presumed discogenic back pain	NR
Intradiscal non-steroid injection vs. Intradiscal control injection								
Peng 2010	N=72	**Inclusion** Chronic low back pain without radiculopathy. Evidence of lumbar disc degeneration on MRI scan. Failed to have more than 6 months pain free with	Lumbar intradiscal (under fluoroscopy guidance) A: Intradiscal Methylene blue/local anesthetic (n = 36)	Repeat injections: (mean injections/year NR)	Fluoroscopic guidance	Bedrest for 24 hours and patients asked to avoid strenuous	LBP without radiculopathy and lumbar disc degeneration Chronic (mean duration) 3.4 ± 1.7	Work was supported by grant for scientific research from 304th

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		conservative management, including PT and drug therapy. No previous lumbar surgery. Exhibited normal or slight decrease in height of disc space on lateral X-ray. **Exclusion** Lumbar disc herniation*, spinal instability*, lumbar canal stenosis*, spondylolysis*, Spondylolisthesis (isthmic or degenerative)*, disc degeneration with endplate Modic changes*, neurologic disease*, inflammatory arthritis*, tumor*, infection*, psychological problems (depression or taking antidepressants/anxiolytic drugs for treatment of depression) *Based on history, clinical examinations, and imaging	B: saline/local anesthetic (n = 36) (mean scores) Steroids used none Treatment: Methylene blue (10 mg)			exercise for 3 weeks	years Mean age ± SD: 42 ± 13.3 Male: 57%	Hospital and the Foundation of Capital Medical Development, Beijing
Intradiscal steroid injection plus Discography vs. Discography alone								
Buttermann 2004	N=171	Inclusion Symptoms related to DDD as diagnosed by a combination of clinical examination, medical history, and MRI scan. Had undergone a spinal steroid injection as a treatment option after failure of other noninvasive conservative treatment, including physical therapy,	A: Discography + lumbar intradiscal injection of betamethasone (mean 9.7 ± 4.3 mg) (n=86) B: Discography alone (n=85)	Repeat injections: (mean injections/year NR)	Fluoroscopy	NR	Presumed chronic discogenic back pain Chronic (mean duration 7.9 years) Mean age (±SD): 42.6 years % male NR	Nothing of value received from a commercial entity related to this research.

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		chiropractic, medication, nonsteroidal antiinflammatory medication, etc. Exclusion Age <18 or >65 years, Spondylolisthesis, stenosis, disc hernation, deformity, pregnancy, inflammatory joint disease						

Appendix Table I2. LBP Without Radiuclopathy Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injection vs. Control injection							
Manchikanti 2012, 2011, 2008	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)	24 months 94.2% (113/120) at 3 months; 90.8% (109/120) at 6 months; 84.2% (101/120) at 12 months; 81.7% (98/120) at 24 months	A vs. B Pain (mean NRS, 0 to 10): 7.9 ± 1.0 vs. 8.0 ± 0.9 at baseline; 3.6 ± 1.4 vs. 4.2 ± 1.8 at 3 months; 3.7 ± 1.5 vs. 4.1 ± 1.8 at 6 months; 3.8 ± 1.6 vs. 4.3 ± 1.8 at 12 months, 4.0 ± 1.7 vs. 4.4 ± 1.9 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 Success (≥50% improvement in pain and ODI) 72% (43/60) vs. 62% (37/60) at 6 months, 68% (41/60) vs. 56% (34/60) at 12 months, 60% (36/60) vs. 54% (32/60) at 24 month	A vs. B ODI (0 to 50): 28.4 ± 4.7 vs. 28.3 ± 4.9 at baseline; 14.5 ± 5.5 vs. 16.3 ± 7.2 at 3 months; 14.3 ± 5.9 vs. 16.4 ± 7.4 at 6 months; 14.5 ± 6.1 vs. 16.4 ± 7.6 at 12 months; 14.9 ± 6.4 vs. 16.5 ± 7.7 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	NR	Opioid use (mg MED/day): 36.2 ± 19.8 vs. 34.5 ± 33.7 at baseline, 29.9 ± 19.9 vs. 28.7 ± 27.1 at 3 months, 31.0 ± 19.9 vs. 31.5 ± 38.4 at 6 months, 30.0 ± 19.9 vs. 31.5 ± 38.4 at 12 months, 29.8 ± 20.3 vs. 31.0 ± 38.4 at 24 months (p=0.45 for group difference) Surgery: NR	"None of the patients reported significant adverse events"
Manchikanti 2013, 2012, 2010	A: Interlaminar epidural injection with 6 mg betamethasone (1	24 months 78% (94/120)	A vs. B Pain (mean NRS, 0 to 10): 7.7 ± 0.9 vs. 8.0 ± 1.0 at	A vs. B ODI (0 to 50): 29.2 ± 5.2 vs. 30.7	NR	A vs. B Opioid intake (morphine	4 subarachnoid punctures without

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	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)		baseline, 3.5 ± 1.2 vs. 3.6 ± 0.9 at 3 months, 3.6 ± 1.2 vs. 3.9 ± 1.1 at 6 months, 3.7 ± 1.3 vs. 3.7 ± 1.2 at 12 months, 3.6 ± 1.4 vs. 3.9 ± 1.3 at 24 months (p=0.38 for group difference) Pain relief ≥50% from baseline: 83% (50/60) vs. 88% (53/60) at 3 months, 82% (49/60) vs. 77% (46/60) at 6 months, 72% (43/60) vs. 78% (47/60) at 12 months, 72% (43/60) vs. 73% (44/60) at 24 months Success (≥50% improvement in pain and ODI) 77% (46/60) vs. 83% (50/60) at 3 months, 75% (45/60) vs. 72% (43/60) at 6 months, 67% (40/60) vs. 77% (46/60) at 12 months, 67% (40/60) vs. 72% (43/60) at 24 months	± 4.5 at baseline, 14.6 ± 5.1 vs. 14.9 ± 4.3 at 3 months, 14.4 ± 5.2 vs. 15.4 ± 4.8 at 6 months, 15.0 ± 6.4 vs. 14.9 ± 5.0 at 12 months, 14.6 ± 6.1 vs. 14.9 ± 5.1 at 24 months (p=0.29 for group difference) ODI improved ≥50% from baseline: 78% (47/60) vs. 83% (50/60) at 3 months, 77% (46/60) vs. 73% (44/60) at 6 months, 70% (42/60) vs. 77% (46/60) at 12 months, 70% (42/60) vs. 72% (43/60) at 24 months		equivalence mg, mean ± SD) Baseline: 53.4 ± 53.8 vs. 57.2 ± 61.4 3 months: 40.3 ± 35.7 vs. 35.5 ± 24.2 6 months*: 41.8 ± 37.3 vs. 36.1 ± 27.0 12 months: 41.8 ± 37.3 vs. 36.3 ± 27.0 24 months: 41.8 ± 37.3 vs. 36.3 ± 27.0 (p=0.377 for group difference) Surgery: NR	headache and one case of nerve root irritation, not reported by group
Intradiscal steroid injection vs. Intradiscal control injection							
Cao 2011	A: Lumbar intradiscal injection of betamethasone (n=40) B: Lumbar intradiscal injection of saline (n=40)	3, 6 months (100%)	A vs. B **Pain - VAS score** Baseline: 6.7 vs. 6.8 3 months: 1.7 vs. 6.9 6 months: 2.2 vs. 7.0	**Function – ODI score** Baseline: 33.6 vs. 35.2 3 months: 12.9 vs. 37.7 6 months: 14.3 vs. 39.1	NR	NR	**Safety**: NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Khot 2004	A: Lumbar intradiscal injection of methylprednisolone 40 mg (n=60) B: Lumbar intradiscal injection of saline (n=60)	1 year	VAS pain score (0 to 10) median change: 0 vs. 0 (p=0.72)	ODI, mean improvement (percent): 2.28 vs. 3.42 (p=0.71)	NR	Surgery: 10% (6/60) vs 6.7% (4/60)	NR
Simmons 1992	A: Lumbar intradiscal injection of methylprednisolone 80 mg (n=14) B: Lumbar intradiscal injection of bupivacaine (n=11)	10-14 days	Proportion improved on VAS pain scale: 43% vs. 36% (NS) Proportion improved on OPQ: 36% vs. 27% (NS) Pain decrease based on Pain grid: 36% vs 65% (NS)	NR	Proportion improved overall: 3/14 (21%) vs. 1/11 (9%) (NS)	NR	NR
Intradiscal non-steroid injection vs. Intradiscal control injection							
Peng 2010	A: Intradiscal Methylene blue/local anesthetic (n = 36) B: saline/local anesthetic (n = 36) (mean scores)	6, 12, 24 months (98.6% f/u; 71/72)	**Pain** **Pain scores (NRS, 0 to 100 cm) (mean ±SD):** • Baseline: 72.33 ±12.35 versus 67.28 ±11.45 (ns) • 6 months: 24.94 ±17.38 versus 63.51 ±11.66 (*P* < .001) • 12 months: 21.58 ±17.93 versus 62.40 ±12.05 (*P* < .001) • 24 months: 19.83 ±16.03 versus 60.37 ±14.10 (*P* < .001) **Pain relief†** • 6 months, complete relief: 19% (7/36) versus NR (*P* = NR) • 6 months, dramatic improvement: 28%	**Function** **ODI (0-100 scale) (mean ±SD):** • Baseline: 48.47 ±5.12 versus 49.37 ±6.79 (ns) • 6 months: 16.00 ±11.91 versus 48.40 ±7.77 (*P* < .001) • 12 months: 14.39 ±12.87 versus 49.09 ±10.20 (*P* < .001) • 24 months: 12.89 ±11.95 versus 47.69 ±10.92 (*P* < .001)	**Patient Satisfaction (% patients)‡** •24 months, completely satisfied: 19.4% (7/36) versus 0% (0/35) (*P* < .001) •24 months, satisfied: 72.2% (26/36) versus 14.3% (5/35) (*P* < .001) •24 months, unsatisfied: 8.4% (3/36) versus 85.7% (30/35) (*P* < .001) ‡Patient satisfaction defined as: Completely satisfied = no back pain at all time and no restriction of activities; Satisfied = slight pain that requires no medication and mild restriction of activities; Unsatisfied = moderate to severe pain that requires	**Medication usage§** • 24 months, none: 83.3% (30/36) versus 5.7% (2/35) (*P* < .001) • 24 months, occasional: 8.3% (3/36) versus 51.4% (18/35) (*P* < .001) • 24 months, regular: 8.3% (3/36) versus 42.9% (15/35) (*P* < .001) §Medication usage includes	**Safety:** nerve root injury: 0/36 patients back pain aggravation: 0/36 patients disc space infection: 0/72 patients nerve root stab injury: 0/72 patients major adverse events (not specified): NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			(10/36) versus NR (*P* = NR) • 6 months, obvious improvement: 42% (15/36) versus NR (*P* = NR) †Pain relief defined as: complete relief (NRS = 0 – 10); Dramatic improvement (NRS < 20 points); Obvious improvement (reduction in NRS score ≤ 20 points)		medication and moderate to severe restriction of activities	nonsteroidal anti-inflammatory drugs or opioid medications; dosages not specified and categories not defined. Patients advised to avoid taking medication at least 24 hours before outcome assessment at all follow-ups	
Intradiscal steroid injection plus Discography vs. Discography alone							
Buttermann 2004	A: Discography + lumbar intradiscal injection of betamethasone (mean 9.7 ± 4.3 mg) (n=86) B: Discography alone (n=85)	1-2 years	Pain, mean improvement in VAS (0 to 10): -0.8 vs 0.6	ODI (0 to 100), mean improvement: -8.9 vs 3.5	"Success" (not defined): 17% (15/86) vs 1.1% (1/85)	Less/much less use of medication: 20% (17/86) vs 3.1% (~3/85) Underwent fusion: 65% (56/86) vs 83% (71/85)	NR

Appendix Table I3. LBP Without Radiuclopathy Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Epidural steroid injection vs. Control injection				
Manchikanti 2012, 2011, 2008	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)	24 months 94.2% (113/120) at 3 months; 90.8% (109/120) at 6 months; 84.2% (101/120) at 12 months; 81.7% (98/120) at 24 months	None	None
Manchikanti 2013, 2012, 2010	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)	24 months 78% (94/120)	NR	NR
Intradiscal steroid injection vs. Intradiscal control injection				
Cao 2011	A: Lumbar intradiscal injection of betamethasone (n=40) B: Lumbar intradiscal injection of saline (n=40)	3, 6 months (100%)	NR	NR
Khot 2004	A: Lumbar intradiscal injection of methylprednisolone 40 mg (n=60) B: Lumbar intradiscal injection of saline (n=60)	1 year	NR	NR
Simmons 1992	A: Lumbar intradiscal injection of methylprednisolone 80 mg (n=14) B: Lumbar intradiscal injection of bupivacaine (n=11)	10-14 days	NR	NR
Intradiscal non-steroid injection vs. Intradiscal control injection				
Peng 2010	A: Intradiscal Methylene blue/local anesthetic (n = 36) B: saline/local anesthetic (n = 36) (mean scores)	6, 12, 24 months (98.6% f/u; 71/72)	NR	NR
Intradiscal steroid injection plus Discography vs. Discography alone				
Buttermann 2004	A: Discography + lumbar intradiscal injection of betamethasone (mean 9.7 ± 4.3 mg) (n=86) B: Discography alone (n=85)	1-2 years	*Inflammatory end-plate modic changes present:* Pain (VAS 0-10): -0.3 vs 0.6 ODI (0-100), mean improvement: -18 vs 9 Success (not defined): 25% (10/40) vs 0% (0/38)	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
			Less/much less use of medication: 43% (17/40) vs 0% (0/38) Underwent fusion: 50% (20/40) vs 76% (29/38) *No inflammatory end-plate modic changes present:* Pain (VAS 0-10): -1.2 vs 0.6 ODI (0-100), mean improvement: -1 vs -1 Success (not defined): 11% (5/46) vs 2% (1/47) Less/much less use of medication: 4.3% (2/46) vs 2.1% (1/47) Underwent fusion: 78% (36/46) vs 89% (42/47)	

Appendix Table I4. LBP Without Radiculopathy, ESI vs. control injection: Baseline scores for pain, function, and opioid use

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Pain score Mean ± SD Group A	Group B
Pain on VAS (0-10)						
Baseline	Manchikanti (2012, 2011, 2008)	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	7.9 ± 1.0 (n=60)	8.0 ± 0.9 (n=60)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	7.7 ± 0.9 (n=60)	8.0 ± 1.0 (n=60)
Function on ODI (0-50)						
Baseline	Manchikanti (2012, 2011, 2008)	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	28.4 ± 4.7 (n=60)	28.3 ± 4.9 (n=60)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Interlaminar	29.2 ± 5.2	30.7 ± 4.5
Opioid use (morphine equivalents, mg/day)						
Baseline	Manchikanti (2012, 2011, 2008)	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	36.2 ± 19.8	34.5 ± 33.7
	Manchikanti (2013, 2012, 2010)	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Interlaminar	53.4 ± 53.8	57.2 ± 61.4

Appendix Table I5. LBP Without Radiculopathy, Intradiscal steroid injection vs. control injection: Baseline scores for pain, function, and opioid use

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
Pain on VAS (0-10)						
Baseline	Cao (2011)	Betamethasone (dose NR) Guidance NR	Saline	Intradiscal	6.65 ± 1.15 (n=40)	6.8 ± 1.25 (n=40)
	Khot 2004	Methylprednisolone 40 mg Fluoroscopic guidance	Saline	Intradiscal	Median (IQR) 3 (3-4) (n=60)	Median (IQR) 3.5 (2-4) (n=60)
	Peng (2010)	Methylene blue (10 mg) + lidocaine 2% Fluoroscopic guidance	Isotonic saline + lidocaine 2%	Intradiscal	7.23 ± 1.24 (n=36)	6.73 ± 1.15 (n=36)
Function on ODI (0-100)						
Baseline	Cao (2011)	Betamethasone (dose NR) Guidance NR	Saline	Intradiscal	33.6 ± 8.5 (n=40)	35.15 ± 12.15 (n=40)
	Khot 2004	Methylprednisolone 40 mg Fluoroscopic guidance	Saline	Intradiscal	50.8 ± 14.4 (n=60)	49.8 ± 16.6 (n=60)
	Peng (2010)	Methylene blue (10 mg) + lidocaine 2% Fluoroscopic guidance	Isotonic saline + lidocaine 2%	Intradiscal	48.47 ± 5.12 (n=36)	49.37 ± 6.79 (n=36)

APPENDIX J. Lumbar Failed Back Syndrome: RCT Study Characteristics and Results

Appendix Table J1. Lumbar Failed Back Syndrome Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Epidural steroid injection vs Epidural non-steroid injection								
Manchikanti 2012, 2010, 2008	140	Inclusion: >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 Exclusion: positive response to local anesthetic blocks; un-controllable or unstable opioid use; uncontrolled psychiatric disorder or acute/chronic medical illness; pregnant or lactating; history or potential for adverse reaction to study medications	A: Caudal epidural injection with 6 mg betamethasone (1 ml), 0.5% lidocaine (9 ml), 0.9% normal saline (2 ml), with fluoroscopic guidance (n=70) B: Caudal epidural injection with 0.5% lidocaine (10 ml), 0.9% normal saline (2 ml), with fluoroscopic guidance (n=70)	Levels: single injection Repeat injection: average no. of procedures over 24 months, 5.3 ± 2.7 vs. 4.6 ± 2.8	Fluoroscopic guidance with contrast verification in epidural space	Previous drug therapy, therapeutic exercise program, and work were all continued; however, there were no specific additional interventions given to any of the patients.	A vs. B: Age (mean): 48 vs. 52 years Male: 51% vs. 39% Duration of symptoms (months): 161 vs.152 Baseline pain (0-10 NRS): 7.8 vs. 7.8 Baseline function (ODI, 0-50): 29.1 vs. 30.3	Internal resources of the pain management practice without external funding from industry or other
Epidural steroid injection vs. Control injection with other medication								
Devulder 1999	N=60	Inclusion: 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	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	Levels: Appears to be single level Repeat injections: Two injections 1 week apart	Fluoroscopic guidance with contrast verification in nerve root sleeve	NR	A vs. B vs. C: Age (mean ± SD): 48.3 ± 11.3 vs. 47 ± 14.3 vs. 44.1 ± 7.1, p = 0.68 Male: 50% (10/20) vs. 40% (8/20) vs. 30% (6/20), p = 0.5 Number of injected nerves: 1.35 ± 0.4 vs 1.2 ± 0.4 vs 1.45 ± 0.5, p = 0.32 Race: Not reported	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		specified Exclusion: Lumbar instability; recurrent lumbar disc herniation; spinal stenosis	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)				Duration of symptoms: NR Baseline pain: NR Baseline function: NR	
Meadab 2001	N=58	Inclusion: 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 Exclusion: Clotting disorders; skin lesion at injection site; hypersensitivity to iodine	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)	Levels: Single injection Repeat injections: None	Fluoroscopic guidance with contrast verification in epidural space	NR	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 Discectomy, time since surgery 38 vs. 43 vs. 34 months Prior epidural steroid injection: 80% vs. 80% vs. 86% Baseline pain (0-100 VAS): 55 vs. 70 vs. 60 Baseline function (Dallas ADL, 0-100): 66 vs. 71 vs. 61	French Society for Rheumatology

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
							Level 2 or 3 analgesic: 44% (7/16) vs. 82% (13/16) vs. 73% (11/15), p=0.06 Psychotropic agent: 50.0% (8/16) vs. 13.0% (2/16) vs. 40.0% (6/15), p=0.06	
Rocco 1989	N=24	Inclusion: Prior laminectomy, still symptomatic; duration not specified; imaging findings not specified Exclusion: NR	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)	Levels: NR Repeat injections: Up to 3 injections at 1 month intervals; 62% vs. 67% vs. 86% received 3 blocks	NR	NR	A vs. B vs. C: Age (mean): 49 vs. 50 vs. 52 years Male: 50% vs. 29% vs. 57% Duration of symptoms: NR Prior laminectomies 2.1 vs. 2.4 vs. 2.1; Prior epidural steroid injections: 4 vs. 4 vs. 4 Baseline pain: NR Baseline function: NR	NR

Appendix Table J2. Lumbar Failed Back Syndrome Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injection vs Epidural non-steroid injection							
Manchikanti 2012, 2010, 2008	A: Caudal epidural injection with 6 mg betamethasone (1 ml), 0.5% lidocaine (9 ml), 0.9% normal saline (2 ml), with fluoroscopic guidance (n=70) B: Caudal epidural injection with 0.5% lidocaine (10 ml), 0.9% normal saline (2 ml), with fluoroscopic guidance (n=70)	24 months 94.3% (132/140) at 3 months; 80% (112/140) at 6 months; 70.7% (99/140) at 12 months; 80.7% (113/140) at 24 months	A vs. B Pain (NRS 0-10): 7.8 ± 0.9 vs. 7.8 ± 1.0 at baseline (p=NS); 4.1 ± 1.7 vs. 4.2 ± 1.8 at 3 months (p=NS); 4.1 ± 1.7 vs. 4.3 ± 1.9 at 6 months (p=NS); 4.2 ± 1.7 vs. 4.5 ± 1.9 at 12 months (p=NS); 4.2 ± 1.8 vs. 4.4 ± 1.9 at 24 months (p=NS) Pain relief ≥50%: 69% (48/70) vs. 66% (46/70) at 3 months; 66% (46/70) vs. 60% (42/70) at 6 months; 61% (43/70) vs. 56% (39/70) at 12 months; 56% (39/70) vs. 49% (34/70) at 24 months Success (pain relief ≥50% and ODI improved ≥50%): 61% (43/70) vs. 56% (39/70) at 6 months; 59% (41/70) vs. 53% (37/70) at 12 months; 58% (41/70) vs. 47% (33/70) at 24 months	A vs. B ODI (0-50): 29.1 ± 4.5 vs. 30.3 ± 4.5 at baseline (p=NS); 16.8 ± 6.8 vs. 17.6 ± 6.3 at 3 months (p=NS); 16.3 ± 7.0 vs. 17.6 ± 6.9 at 6 months (p=NS); 16.5 ± 7.0 vs. 17.7 ± 6.9 at 12 months (p=NS); 16.6 ± 7.0 vs. 17.8 ± 7.2 at 24 months (p=NS) ODI improvement ≥50%: 57% (40/70) vs. 56% (39/70) at 3 months; 63% (44/70) vs. 56% (39/70) at 6 months; 61% (43/70) vs. 54% (38/70) at 12 months; 56% (39/70) vs. 49% (34/70) at 24 months	NR	Opioid intake (mg MED/day): 47 ± 41.7 vs. 49 ± 53.7 at baseline (p=0.80); 39 ± 35.8 vs. 40 ± 47.5 at 3 months (p=0.84); 39 ± 35.6 vs. 38 ± 43.4 at 6 months (p=0.83); 40 ± 35.5 vs. 38 ± 43.2 at 12 months (p=0.85) Surgery: NR Other outcomes: NR	"No major adverse events"
Epidural steroid injection vs. Control injection with other medication							
Devulder 1999	A: Transforaminal epidural injection to nerve root sleeve with 40 mg	Complete f/u: 6 months % f/u 100% (60/60)	A vs. B vs. C Pain improved >50% (verbal pain rating scale): 40% (8/20) vs. 35% (7/20) vs. 35%	NR	NR	NR	"No side effects or complications were

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	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)	All f/u: 1 month: 100% (60/60) 3 months: 100% (60/60) 6 months: 100% (60/60)	(7/20) at 1 month, 40% (8/20) vs. 25% (5/20) vs. 25% (5/20) at 3 months, 35% (7/20) vs. 20% (4/20) vs. 25% (5/20) at 6 months Any temporary pain relief (Verbal pain rating scale): 60% (12/20) vs 45% (9/20) vs 50% (10/20) at 1 month, 40% (8/20) vs 30% (6/20) vs 25% (7/20) at 3 months, 35% (7/20) vs 25% (5/20) vs 25% (5/20) at 6 months P = 0.02 at 3 and 6 months for A and B vs baseline for pain scores, while for group C, p = 0.07. The effect of the three treatments was not significant after 1, 3, and 6 months, (p = 0.71, 0.69, 0.66 respectively).				reported"
Meadeb 2001	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	4 months 81% (47/58)	A vs. B vs. C Pain (mean, 0-100 VAS): 55.4 ± 13.9 vs. 70.2 ± 23.5 vs. 59.5 ± 19.9 at baseline p=0.09); 47.6 ± 20.4 vs. 65.6 ± 22.4 vs. 57.5 ± 17.8 at 1 month (p=0.02); 53.0 ± 24.7 vs. 61.6 ± 24.4 vs. 52.5 ± 22.5 at 2 months (p=NS); 45.3 ± 24.0 vs. 59.5 ± 24.2 vs. 57.6 ± 24.7 at 4 months (p=NS)	A vs. B vs. C Dallas ADL (mean ± SD): 65.6 ± 14.1 vs. 71 ± 12.6 vs. 60.8 ± 16.4 at baseline (p=NS); 58.2 ± 18.7 vs. 68.8 ± 17.2 vs. 61.6 ± 11.8 at 1 month; 60.3 ± 23.4 vs. 68.0 ± 14.6 vs. 59.6 ± 16.5 at 2 months; 58.4 ± 22.8 vs. 67.3 ± 18.9 vs. 65.3 ± 18.5	NR	NR	A vs. B vs. C: Pain induced by injection: 76.4% (12/16) vs. 73.3% (12/16) vs. 70.0% (11/15), p=NS

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	saline (20 ml) plus 125 mg prednisolone acetate, with fluoroscopic guidance (n=15)		Pain improved ≥15% by 4 months: 25.0% (4/16) vs. 43.8% (7/16) vs. 20.0% (3/15), p=0.3	at 4 months			
Rocco 1989	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)	6 months 92% (22/24) (1 lost to f/u; 1 inadvertant subarachnoid injection)	A vs. B vs. C: 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 at long-term*: 12% (1/8) vs. 0% (0/7) vs. 0% (0/7) at 6 months (p=NR) * Long-term pain relief was defined as improvement lasting longer than 1 month.	NR	NR	NR	A vs. B vs. C: Required naloxone for reversal of respiratory depression: 0% (0/8) vs. 0% (0/7) vs. 43% (3/7); p<0.05 Urinary retention: 0% (0/8) vs. (1/7) vs. (5/7); p<0.05 Nausea and vomiting: 12.5% (1/8) vs. 71.4% (5/7) vs. 57.1% (4/7); p=NR Pruiritus: 12.5% (1/8) vs. 57.1% (4/7) vs. 57.1% (4/7); p=NR

Appendix Table J3. Lumbar Failed Back Syndrome Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Epidural steroid injection vs Epidural non-steroid injection				
Manchikanti 2012, 2010, 2008	A: Caudal epidural injection with 6 mg betamethasone (1 ml), 0.5% lidocaine (9 ml), 0.9% normal saline (2 ml), with fluoroscopic guidance (n=70) B: Caudal epidural injection with 0.5% lidocaine (10 ml), 0.9% normal saline (2 ml), with fluoroscopic guidance (n=70)	24 months 70.7% (99/140) at 12 months; 80.7% (113/140) at 24 months	None	None
Epidural steroid injection vs. Control injection with other medication				
Devulder 1999	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)	6 months % f/u: 100% (60/60)	NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Meadab 2001	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)	4 mos. 81% (47/58)	None	None
Rocco 1989	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)	6 months 92% (22/24) (1 lost to f/u; 1 inadvertant subarachnoid injection)	NR	NR

Appendix Table J4. Lumbar Failed Back Syndrome: Baseline scores for pain, function, and opioid use

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Pain score Mean ± SD Group A	Group B
Pain on VAS or NRS (0-10)						
Baseline	Manchikanti (2012, 2010, 2008)	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	7.8 ± 0.9 (n=70)	7.8 ± 1.0 (n=70)
	Meadeb (2001)	Predisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	5.54 ± 1.39 (n=16)	7.02 ± 2.35 (n=16)
		Forceful injection, prednisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	5.95 ± 1.99 (n=15)	7.02 ± 2.35 (n=16)
	Rocco (1989)	Triamcinolone diacetate 75 mg + lidocaine 5% + saline Imaging NR	Morphine 8 mg + lidocaine 5%	NR	6.4 (n=8)	4.0 (n=7)
		Triamcinolone diacetate 75 mg + morphine 8 mg + lidocaine 5% Imaging NR	Morphine 8 mg + lidocaine 5%	NR	5.0 (n=7)	4.0 (n=7)
Function on ODI (0-50)						
Baseline	Manchikanti (2012, 2010, 2008)	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	29.1 ± 4.5 (n=70)	30.3 ± 4.5 (n=70)
Function on Dallas ADLs domain						
Baseline	Meadeb (2001)	Predisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	65.6 ± 14.1 (n=16)	71 ± 12.6 (n=16)
		Forceful injection, prednisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	60.8 ± 16.4 (n=15)	71 ± 12.6 (n=16)
Opioid use (morphine equivalents, mg/day)						
Baseline	Manchikanti (2012, 2010, 2008)	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	47 ± 41.7 (n=70)	49 ± 53.7 (n=70)

APPENDIX K. Lumbar Facet Joint Pain: RCT Study Characteristics and Results

Appendix Table K1. Lumbar Facet Joint Pain Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Intra-articular steroid injection vs. Intra-articular control injection								
Carette 1991	N=101	Inclusion: 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 single 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) Exclusion: 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.	A: Intra-articular facet joint injection with 20 mg methylprednisolone acetate (1 ml) plus isotonic saline (1 ml), with fluoroscopic guidance (n=51) B: Intra-articular facet joint injection with isotonic saline (2 ml), with fluoroscopic guidance (n=50)	Levels: (A vs. B) 2 vs. 2 (L4/L5 and L5/S1), bilateral 80% vs. 79% Repeat injections: Mean 3.6 vs. 3.6 injections, frequency not specified. No patient in saline injection group received methylprednisolone injection	Fluoroscopic guidance	Treatments prior to intervention: Restricted to acetaminophen Physicians asked to limit concurrent treatments to acetaminophen; 22% (11/51) vs. 12% (6/50) (p=0.20) patients received other treatments (antidepressant, physical therapy, additional injection) through 6 months	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 Baseline McGill pain questionnaire, pain rating index (scale NR): 22.6 vs. 21.3 Baseline McGill pain questionnaire, present pain intensity (0 to 5): 2.7 vs. 2.8 Baseline mean finger-to-floor distance with maximum flexion (cm): 9.7 vs. 8.0	NR
Fuchs 2005	N=60	Inclusion: Low back pain for at least 3 months; radiologic evidence (CT) of facet joint osteoarthritis with osteophyte formation	A: Intraarticular facet joint injection with 10 mg triamcinolone acetonide (1 ml),	Levels: 3 levels total, with one level injected bilaterally per week over the first 3	CT fluoroscopic guidance	NR	A vs. B: Age (mean): 66 vs. 65 years Male: 20% vs. 40% (p=0.094)	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		(Kellgren grade 2/3); facet joint block not required Exclusion: Hypersensitivity or contraindication to study medications; contraindication to intraarticular treatment; anticoagulation, radicular pain, or other specific conditions on clinical examination or CT scan	with CT fluoroscopic guidance (n=30) B: Intraarticular facet joint injection with 10 mg sodium hyaluronate (1 ml), with CT fluoroscopic guidance (n=30)	weeks (S1-L5, L5-L4, and L4-L3) Repeat injections: see above			Duration of symptoms: NR (minimum 3 mos.) Baseline pain (0-100 VAS): 68.7 ± 11.5 vs. 69.2 ± 14.2 vs. 31.9 ± 11.4 Baseline function (RDQ 0-24): 12.5 ± 4.4 vs. 12.5 ± 4.9 Baseline function (ODI 0-50): 18.4 ± 6.2 vs. 20.7 ± 8.5 Baseline function (0-75 LBOS) 32.7 ± 11.4	
Lilius 1989 Also includes comparison of IASI vs EASI	N=109	Inclusion: 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) Exclusion: Not described	A: Intraarticular facet joint injection with 80 mg methylprednisolone acetate (2 ml) plus 30 mg bupivacaine (6 ml), with fluoroscopic guidance (n=28) B: Extra-articular (pericapsular) facet joint injection with 80 mg of methylprednisolone (2 ml) + 30 mg bupivacaine (6 ml), with fluoroscopic guidance (n=39) C: Intra-articular	Levels: Unilateral, 2 levels per patient (L3/4 and L4/5 in15 patients and L4/5 and L5/S1 in 94 patients) Repeat injections: Appears to be single injection	Fluoroscopic guidance	NR	A vs. B vs. C: Age (mean): 44 years overall (NR by group) Male: 44% overall (NR by group) Duration of symptoms: NR (>3 months required for inclusion) Baseline pain (0 to 100 VAS): 49 overall (estimated from graph: 45 vs. 52 vs. 52) Baseline function: NR "No important differences between groups for	None

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
			facet join injection with 8 ml saline, with fluoroscopic guidance (n=42)				age, sex, duration of symptoms, previous operations"; data NR by group	
Intra-articular steroid injection vs. Extra-articular steroid injection								
Ribeiro 2013	N=60	Inclusion: 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 Exclusion: 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	A: Intra-articular facet joint injection with 20 mg triamcinolone hexacetonide (1 ml) and lidocaine (dose not reported, 1 ml), with fluoroscopic guidance (n=31) B: Intramuscular injections in the lumbar paravertebral musculature with 20 mg triamcinolone hexacetonide (1 ml) and lidocaine (dose not reported, 1 ml) (n=29)	Levels: 6 injections performed bilaterally at L3 to S1, each level injected bilaterally (the control group received injections at 6 surface points) Repeat injections: unclear	Fluoroscopic guidance	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	A vs. B: Age (mean): 63 vs. 64 years Male: 19% vs. 17% Duration of pain (mean, months): 50 vs. 53 Diabetes: 13% vs. 17% Systemic arterial hypertension: 20% vs. 21% Baseline pain (0-10 VAS): 7.0 ± 1.2 vs. 6.8 ± 1.4 (p=0.8) Baseline pain on extension (0-10 VAS): 6.8 vs. 6.5 (p=0.53) Baseline function (RDQ 0-24): 15 vs. 16 (p=0.31)	Grant funding (from Fundacao de Amparo a Pesquisa do Estado de Sao Paulo)

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		months; allergy to the contrast medium; pregnancy or suspected pregnancy; current involvement in litigation						
Intra-articular steroid injection vs. Medial branch radiofrequency denervation								
Lakemeier 2013	N=56	Inclusion: 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 Exclusion: 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.	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) (n=29) 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 (n=27)	Levels: Unclear Repeat injections: Unclear	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	Analgestics (opioid and NSAID) given to most patients; drug dosage adjusted as needed; all previously-directed exercise programs & work were to be continued; no specific program was offered	A vs. B: Age (mean): 56 vs. 58 years Male: 62% vs. 65% Duration of symptoms: NR (≥24 months required for inclusion) Baseline pain (0-10 VAS): 7.0 ± 1.7 vs. 6.6 ± 1.8 Baseline function (ODI 0-100): 38.7 ± 18.4 vs. 40.8 ± 16.4 Baseline function (RDQ 0-24): 13.2 ± 5.9 vs. 12.8 ± 5.4	No funding
Extra-articular steroid injection vs. Extra-articular control injection								
Manchikanti 2001	N=84	Inclusion: Low back pain for >6 months with or without lower extremity pain; positive response to two comparative facet joint blocks	A: Extra-articular facet joint injection of the medial branch with 0.5-1 ml of 1 mg/ml	Levels: 4 per patient (L1/2 to L4/5) (bilateral for bilateral pain and ipsilateral for unilateral pain)	Fluoroscopic guidance	NR	A vs. B: Age (mean): 47 vs. 46 years Male: 44% vs. 36% Duration of	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		(criteria for positive response not reported); imaging findings not required Exclusion: <18 or >90 years, neurological deficits, response to conservative treatment, previous nerve block	methylprednisolone and 0.5% lidocaine or 0.25% bupivacaine plus equal volume of Sarapin, with fluoroscopic guidance (n=42) B: Extra-articular facet joint injection of the medial branch with 0.5-1 ml of 0.5% lidocaine or 0.25% bupivacaine plus equal volume of Sarapin, with fluoroscopic guidance (n=42)	Repeat injections: Mean 7.3 vs. 6.6 over 2.5 years, frequency not specified *One procedure:* 0% (0/41) vs. 0% (0/32) *Two procedures*: 2% (1/41) vs. 13% (4/32) *Three procedures*: 2% (1/41) vs. 9% (3/32) *Four procedures:* 5% (2/41) vs. 9% (3/32) *Five procedures:* 7% (3/41) vs. 3% (1/32) *Six procedures:* 17% (7/41) vs. 13% (4/32) *Seven procedures:* 20% (8/41) vs. 22% (7/32) *Eight procedures:* 17% (7/41) vs. 3% (1/32) *Nine procedures:* 10% (4/41) vs. 6% (2/32) *Ten procedures:* 20% (8/41) vs. 22% (7/32)			symptoms (years): 1.7 vs. 1.8 Prior laminectomy 17% vs. 31% Occupational: 12% vs. 16% Depression: 73% vs. 81% Generalized anxiety disorder: 76% vs. 72% Somatization disorder: 56% vs. 41% Disabled: 47% vs. 34% Baseline pain (0-10 NRS): 7.7 vs. 7.6 Functional status (scale not reported): 3.7 vs. 3.6	
Manchikanti 2010, 2008	N=120	Inclusion: History of chronic function-	A: Extra-articular facet joint nerve	Levels: Unclear (blocks	Fluoroscopic guidance	All patients received any	A vs. B: Age (mean): 46 vs.	None

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		limiting low back pain for >6 months; >18 years of age; positive results on two controlled diagnostic lumbar facet joint nerve blocks (≥80% concordant pain relief and ability to perform previously painful movements); Imaging findings not required Exclusion: 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	blocks 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 (n=60) B: Extra-articular facet joint nerve blocks with 0.5-1.5 ml solution of 0.25% bupivacaine or bupivacaine and Sarapin in equal amounts, with fluoroscopic guidance (n=60)	performed on minimum of 2 nerves) Repeat 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) *One procedure:* 7% (4/60) vs. 12% (7/60) *Two procedures*: 10% (6/60) vs. 7% (4/60) *Three procedures*: 7% (4/60) vs. 13% (8/60) *Four procedures:* 13% (8/60) vs. 3% (2/60) *Five procedures:* 8% (5/60) vs. 5% (3/60) *Six procedures:* 8% (5/60) vs. 8% (5/60) *Seven procedures:* 10% (6/60) vs. 17% (10/60) *Eight procedures:* 33% (20/60) vs. 30% (18/60)		of the following as needed: opioid and non-opioid analgesics, adjuvant analgesics, exercise programs as previously directed (no specific programs were used) Injections repeated as needed and based on previous responses; patients who did not respond and received other treatments were withdrawn from the study	48 years Male: 45% vs. 35% Duration of symptoms (months): 108 vs. 108 Prior lumbar surgery: 13% vs. 20% Baseline pain (0-10 NRS): 7.9 ± 1.0 vs. 8.2 ± 0.8 (p=0.085) Baseline function (ODI 0-50): 25.9 ± 5.0 vs. 26.6 ± 4.6	

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
				Nine procedures: 3% (2/60) vs. 5% (3/60)				
Extra-articular steroid injection cs. Medial branch radiofrequency denervation								
Civelek 2012	N=100	Inclusion: 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) Exclusion: Radicular pain; neurogenic claudication; neurologic deficits; acute or uncontrolled medical illness; history of adverse reaction to local anesthetics; pregnant or lactating	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 (n=50) 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 (n=50)	Levels: 1-level: 54% vs. 52% 2-level: 26% vs. 28% 3-level: 16% vs. 16% 4-level: 4% vs. 4% Repeat injections: Appears to be single	A: Fluoroscopic guidance B: Fluoroscopic guidance with electrostimulation confirmation	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	A vs. B: Age (mean): 56 vs. 52 years Male: 29% vs. 30% Duration of symptoms (mean months): 19 vs. 19 Baseline pain (0-10 NRS): 8.5 vs. 8..2 Baseline function: NR	NR

Appendix Table K2. Lumbar Facet Joint Pain Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Intra-articular steroid injection vs. Intra-articular control injection							
Carette 1991	A: Intra-articular facet joint injection with 20 mg methylprednisolone acetate (1 ml) plus isotonic saline (1 ml), with fluoroscopic guidance (n=51) B: Intra-articular facet joint injection with isotonic saline (2 ml), with fluoroscopic guidance (n=50)	6 months 94% f/u (95/101) 1 month 95% f/u (96/101)	A vs. B Pain (0-10 VAS): 6.3 vs. 6.2 at baseline, 4.5 vs. 4.7 at 1 m (reported MD -0.2, 95% CI -1.1 to 0.8, p>0.05), 4.0 vs. 5.0 at 6 m, (reported MD -1.0, 95% CI -2.0 to -0.1, p<0.05) McGill pain questionnaire, pain rating index (scale NR): 19.0 vs. 22.8 at 1 m (reported MD -3.8, 95% CI-9.4 to 1.9, p>0.05); 17.1 vs. 21.6 at 6 m (reported MD -4.5, 95% CI -9.7 to 0.7, p>0.05) McGill pain questionnaire, present pain intensity (0 to 5): 2.3 vs. 2.6 at 1 m (reported MD -0.3, 95% CI -0.8 to 0.2, p>0.05); 2.1 vs. 2.9 at 6 m (reported MD -0.8, 95% CI -1.3 to -0.4, p>0.05)	A vs. B Sickness Impact Profile, overall (0-100): 9.3 vs. 9.8 at 1 m (reported MD -0.5, 95% CI -2.8 to 1.7, p>0.05), 7.8 vs. 10.8 at 6 m (reported MD -3.0, 95% CI -6.2 to 0.2, p>0.05) Sickness Impact Profile, physical dimension (0-100): 5.2 vs. 6.3 at 1 m (reported MD -0.5, 95% CI -2.8 to 1.7, p>0.05), 4.3 vs. 7.9 at 6 m (reported MD -3.5, 95% CI -6.2 to -0.9, p<0.05) Complete restriction in main activity in past 2 weeks (days): 3.2 vs. 2.2 at 1 m (reported MD 1.0, 95% CI NR, p=0.22); 1.3 vs. 2.9 at 6 m (reported MD -1.6, 95% CI NR, p=0.07) Mean finger-to-floor distance (cm): 9.4 vs. 7.9 at 1 m (reported MD 1.5,	A vs. B Overall effect of "very marked" or "marked improvement) (on a 7 category scale): 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)	A vs. B Opioid use: NR Surgery: NR Other outcomes: Other treatments received (physical therapy, antidepressant medication, peridural injections): 22% (11/51) vs. 12% (6/50) (p=0.20) at 6 m Sickness Impact Profile, psychosocial dimension: 8.2 vs. 9.0 at 1 m (reported MD -0.8, 95% CI -4.0 to 2.4, p>0.05); 7.7 vs. 9.0 at 6 m (reported MD -1.3, 95% CI -5.3 to 2.6, p>0.05) Bed rest in past 2 weeks (days): 0.3 vs. 0.1 at 1 m (reported MD 0.2, 95% NR, p=0.85), 0.2 vs. 0.4 at 6 m (reported MD -0.2, 95% NR, p=0.95),	"No adverse events reported, other than transient local pain at the injection sites."

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
				95% CI -2.5 to 5.6, p>0.05); 9.1 vs. 11.4 at 6 m (reported MD -2.3, 95% CI -5.1 to 0.6, p>0.05)			
Lilius 1989 Also includes comparison of IASI vs EASI and EASI vs IANSI	A: Intraarticular facet joint injection with 80 mg methylprednisolone acetate (2 ml) plus 30 mg bupivacaine (6 ml), with fluoroscopic guidance (n=28) B: Extra-articular (pericapsular) facet joint injection with 80 mg of methylprednisolone (2 ml) + 30 mg bupivacaine (6 ml), with fluoroscopic guidance (n=39) C: Intra-articular facet join injection with 8 ml saline, with fluoroscopic guidance (n=42)	3 months 97% f/u (106/109) (A vs. B vs. C: 3.6% (1/28) vs. 0% (0/39) vs. 4.8% (2/42))	A vs. B vs. C Pain (VAS, 0-100, estimated from graph): 45 vs. 52 vs. 52 at baseline, 31 vs. 35 vs. 41 at 0.5 m; 40 vs. 40 vs. 42 at 1.5 m; 44 vs. 42 vs. 43 at 3 m (p>0.05 between all groups at all timepoints) Symptom improvement: No difference between groups (data NR) Pain during flexion, extension and rotation of the back: No difference between groups (data NR)	A vs. B vs. C Disability score: Data NR (p=0.89 for A + B vs. C)	NR	A vs. B vs. C Opioid use: NR Surgery: NR Other: Return to work: No difference between groups (data NR)	Not reported by intervention group; unspecified "side effects" reported in 7/106 overall; no difference between groups (data NR)
Fuchs 2005	A: Intraarticular	6 months	A vs. B	A vs. B	SF-36 physical	NR	"No

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	facet joint injection with 10 mg triamcinolone acetonide (1 ml), with CT fluoroscopic guidance (n=30) B: Intraarticular facet joint injection with 10 mg sodium hyaluronate (1 ml), with CT fluoroscopic guidance (n=30)	% f/u NR	Pain (0-100 VAS): 68.7 ± 11.5 vs. 69.2 ± 14.2 at baseline, 30.1 ± 23.3 vs. 40.8 ± 25.6 at 1 m, 33.4 ± 20.7 vs. 38.0 ± 26.5 at 6 m (p>0.05)	Roland Morris (0-24): 12.5 ± 4.4 vs. 12.5 ± 4.9 at baseline, 7.2 ± 5.1 vs. 8.4 ± 5.4 at 1 m, 8.3 ± 4.8 vs. 7.1 ±5.4 at 6 m (p>0.05) ODI (0-50): 18.4 ± 6.2 vs. 20.7 ± 8.5 at baseline, 12.3 ± 7.5 vs. 14.2 ± 10.7 at 1 m, 13.0 ± 7.1 vs. 12.6 ± 9.7 at 6 m (p>0.05) Low Back Outcome Score (0-75): 32.7 ± 11.4 vs. 31.9 ± 11.4 at baseline, 43.7 ± 11.3 vs. 43.3 ± 15.5 at 1 m, 44.1 ± 14.0 vs. 46.0 ± 16.5 at 6 m (p>0.05)	function (estimated from graph): 40 vs. 39 at baseline; 55 vs. 55 at 1 m; 55 vs. 58 at 6 m SF-36 functional limitation caused by physical problems (estimated from graph): 12 vs. 6 at baseline; 35 vs. 33 at 1 m; 36 vs. 43 at 6 m SF-36 physical pain (estimated from graph): 26 vs. 25 at baseline; 47 vs. 48 at 1 m; 50 vs. 52 at 6 m SF-36 functional limitation caused by emotional problems (estimated from graph): 51 vs. 51 at baseline; 60 vs. 50 at 1 m; 75 vs. 70 at 6 m Patient satisfaction: NR		significant adverse events"
Intra-articular steroid injection vs Extra-articular steroid injection							
Ribeiro 2013	A: Intra-articular facet joint injection with 20	6 months 93% f/u (56/60) (but all	A vs. B Pain (0-10 VAS): 7.0 (95% CI 6.5, 7.4) vs. 6.8 (95% CI	A vs. B RDQ (0-24): 15 (95% CI 13.1,	A vs. B Global Improvement (5-	A vs. B Diclofenac daily intake	A vs. B Gastrointestinal bleeding

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	mg triamcinolone hexacetonide (1 ml) and lidocaine (dose not reported, 1 ml), with fluoroscopic guidance (n=31) B: Intramuscular injections in the lumbar paravertebral musculature with 20 mg triamcinolone hexacetonide (1 ml) and lidocaine (dose not reported, 1 ml) (n=29)	60 patients included in the intention to treat analysis)	6.2, 7.3) at baseline (p=0.54), 4.0 (95% CI 3.0, 5.0) vs. 4.0 (95% CI 3.0, 4.9) at 1 week (p=0.92), 4.0 (95% CI 3.0, 5.0) vs. 3.6 (95% CI 2.3 4.7) at 1 m (p=0.53), 4.7 (95% CI 3.5, 5.7) vs. 6.1 (95% CI 5.0, 7.0) at 3 m (p=0.06), 5.3 (95% CI 4.4, 6.4) vs. 5.8 (95% CI 4.5, 6.9) at 6 m (p=0.54) Pain improvement (0-100%): 65.2% (95% CI 55.3%, 74.9%) vs. 49.7% (95% CI 38.4%, 60.9%) at 1 week (p=0.03), 57.5% (95% CI 47.2%, 68.2%) vs. 50.6% (95% CI 38.0%, 63.0%) at 1 m (p=0.37), 51.9% (95% CI 39.8%, 64.0%) vs. 45.2% (95% CI 33.3%, 57.0%) at 3 m (p=0.41), 55.2% (95% CI 43.2%, 67.0%) vs. 38.3% (95% CI 50.3%, 62.2%) at 6 m (p=0.04) Pain on extension (0-10 VAS): 6.8 (95% CI 5.7, 7.2) vs. 6.5 (95% CI 6.1, 7.4) at baseline (p=0.53), 3.6 (95% CI 3.1, 5.6) vs. 4.4 (95% CI 2.5, 4.6) at 1 week (p=0.30), 4.0 (95% CI 2.8, 5.0) vs. 5.1 (95% CI 3.8, 6.3) at 1 m (p=0.17), 5.1 (95% CI 3.9, 6.2) vs. 6.4 (95% CI 5.2, 7.5) at 3 m (p=0.10), 5.3 (95% CI 4.2, 6.3) vs. 6.1 (95% CI 4.8, 7.4) at 6 m (p=0.32)	16.8) vs. 16.4 (95% CI 14.2, 18.6) at baseline (p=0.31), 11.5 (95% CI 9.1, 13.7) vs. 13.4 (95% CI 10.6, 16.2) at 1 week (p=0.24), 10.2 (95% CI 7.8, 12.4) vs. 12.2 (95% CI 9.7, 14.6) at 1 m (p=0.21), 10.6 (95% CI 8.2, 12.9) vs. 14.7 (95% CI 12.3, 16.9) at 3 m (p=0.01), 10.9 (95% CI 8.2, 13.5) vs. 13.4 (95% CI 10.8, 15.9) at 6 m (p=0.17)	point Likert scale, "much worse/ a little worse/ unchanged/ a little better/ much better), percentage of patients who were "better: OR "much better": 90.3% (28/31) vs. 86.2% (25/29) at 1 week; 87.1% (27/31) vs. 75.9% (22/29) at 1 m; 77.4% (24/31) vs. 72.4% (21/29) at 3 m; 77.4% (24/31) vs. 69/0% (20/29) at 6 m QoL: SF-36 Physical Functioning: p=0.21 between the groups over time SF-36 Role Physical: p=0.023 between the groups over time (favors group A) SF-36 Body Pain: p=0.15 between the groups over time SF-36 General	(number of tablets): 1.5 vs. 1.4 at 1 week (p=0.99), 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) Acetaminophen daily intake (number of tablets): 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) No differences between groups in terms of the number of patients between groups who used other pharmacological treatments (data NR) Surgery: p=NS No differences between groups in terms of the number of patients between	(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 (heart failure): 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]

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
					Health: p=0.52 between the groups over time SF-36 Vitality: p=0.45 between the groups over time SF-36 Social Functioning: p=0.16 between the groups over time SF-36 Role Emotional: p=0.35 between the groups over time SF-36 Mental Health: p=0.68 between the groups over time	groups who used physical therapy.	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
Intra-articular steroid injection vs. Medial branch radiofrequency denervation							
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) (n=29)	6 months 93% f/u (52/56)	A vs. B Pain (0-10 VAS): 7.0 ± 1.7 vs. 6.6 ± 1.8 at baseline, 5.4 ± 2.1 vs. 4.7 ± 2.4 at 6 m; improvement from baseline to 6 m: 1.6 ± 2.5 vs. 1.9 ± 3.0 (p=0.60)	A vs. B Roland Morris Disability Questionnaire (0-24): 13.2 ± 5.9 vs. 12.8 ± 5.4 at baseline, 9.0 ± 6.4 vs. 9.1 ± 6.0 at 6 m; improvement from baseline to 6 m: 4.2 ± 7.0 vs. 3.7 ± 6.9 (p=0.51) ODI (0-100): 38.7 ± 18.4 vs. 40.8 ±	NR	A vs. B Analgesic intake: "No measurable differences between the 2 groups in absolute terms," data NR Surgery: NR Other 10% (3/29) vs. 3.7% (1/27) did not undergo allocated	"No major adverse events reported during the observation period of 6 months"

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	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 (n=27)			16.4 at baseline, 33.0 ± 17.4 vs. 28.0 ± 20.0 at 6 m, improvement from baseline to 6 m: 5.7 ± 20.9 vs. 12.8 ± 24.8 (p=0.46)		procedure or underwent additional procedure (nucleotomy)	
Extra-articular steroid injection vs. Extra-articular control injection							
Manchikanti 2001	A: Extra-articular facet joint injection of the medial branch of the medial branch 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 (n=42)	Unclear (up to 2.5 years) 87% f/u (73/84) at 2.5 yrs. (A vs. B: 2.3% (1/42) vs. 23.8% (10/42) excluded from all analyses and after random-ization (due to decision by a third party carrier (n=3 in group B),	A vs. B <u>Pain</u> (0-10 NRS, mean ± SEM): 7.7 ± 0.1 vs. 7.6 ± 0.1 at baseline, 3.3 ± 0.2 vs. 3.5 ± 0.3 post-treatment (duration unclear) (p>0.05) <u>Pain relief >50% (cumulative):</u> 100% (41/41) vs. 100% (32/32) <3 m, 88% (36/41) vs. 75% (24/32) 4-6 m, 17% (7/41) vs. 25% (8/32) 7-12 m, 5% (2/41) vs. 16% (5/32) >12 m <u>Length of >50% pain relief per procedure (weeks (mean ± SEM)):</u>	A vs. B <u>Functional status</u> (0-10 NRS, mean ± SEM): 3.7 ± 0.2 vs. 3.6 ± 0.2 at baseline, 5.7 ± 0.2 vs. 5.3 ± 0.2 post-treatment (duration unclear) (P>0.05)	NR	A vs. B <u>Use of schedule II opioids</u>: 15% (6/41) vs. 19% (6/32) post-treatment (duration unclear) <u>Narcotic intake*:</u> *None:* 15% (6/41) vs. 9% (3/32) at baseline; 19% (8/41) vs. 25% (8/32) post-treatment (duration unclear) *Mild*:* 15% (6/41) vs. 13% (4/32) at baseline; 32% (13/41) vs. 22% (7/32)	A vs. B <u>Infection</u>: 0% (0/41) vs. 0% (0/32) <u>Rash</u>: 0% (0/41) vs. 0% (0/32) <u>Reaction to drugs, epidural or subarachnoid blockade</u>: 0% (0/41) vs. 0% (0/32) <u>Postlumbar</u>

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	B: Extra-articular facet joint injection of the medial branch of the medial branch with 0.5-1 ml of 0.5% lidocaine or 0.25% bupivacaine plus equal volume of Sarapin, with fluoroscopic guidance (n=42)	unrelated medical problems and hospitalizations (n=1 in group B), and decision to undergo RF thermo-nucrolysis (n=1 in group A and n=6 in group B)	*Procedure #1:* 5.2 ± 0.4 (n=41) vs. 7.2 ± 2.1 (n=32) *Procedure #2:* 9.1 ± 1.8 (n=41) vs. 11.9 ± 3.1 (n=32) *Procedure #3:* 10.4 ± 1.8 (n=40) vs. 15.1 ± 4.2 (n=28) *Procedure #4:* 9.6 ± 0.5 (n=39) vs. 9.7 ± 1.9 (n=25) *Procedure #5:* 14.6 ± 3.1 (n=37) vs. 8.6 ± 0.7 (n=22) *Procedure #6:* 10.5 ± 0.8 (n=34) vs. 14.5 ± 3.4 (n=21) (p<0.05) *Procedure #7:* 10.7 ± 0.6 (n=27) vs. 21.0 ± 5.6 (n=17) (p<0.05) *Procedure #8:* 15.6 ± 3.7 (n=19) vs. 8.8 ± 1.5 (n=10) *Procedure #9:* 12.2 ± 2.15 (n=12) vs. 9.4 ± 1.5 (n=9) *Procedure #10:* 10.0 ± 1.0 (n=8) vs. 14.4 ± 2.6 (n=7) (p<0.05)			post-treatment (duration unclear) *Moderate*:* 39% (16/41) vs. 50% (16/32) at baseline; 34% (14/41) vs. 34% (11/32) post-treatment (duration unclear) *Heavy*:* 32% (13/41) vs. 28% (9/32) at baseline; 15% (6/41) vs. 19% (6/32) post-treatment (duration unclear) Surgery: NR Other: Physical health (0-10 NRS, mean ± SEM): 5.1 ± 0.2 vs. 4.6 ± 0.2 at baseline, 7.1 ± 0.2 vs. 6.7 ± 0.3 post-treatment (duration unclear) (p>0.05) Mental health (0-10 NRS, mean ± SEM): 4.7 ± 0.2 vs. 4.2 ± 0.2 at baseline; 6.7 ± 0.1 vs. 6.3 ± 0.3 post-treatment (duration unclear)	puncture headache: 0% (0/41) vs. 0% (0/32) Weight gain: 0% (0/41) vs. 0% (0/32)

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
						(p>0.05) <u>Depression</u> (criteria not reported): 73% (30/41) vs. 81% (26/32) (baseline); 58% (24/41) vs. 72% (23/32) (follow-up unclear) (p>0.05) <u>Generalized anxiety disorder</u> (criteria not reported): 76% (31/41) vs. 72% (23/32) (baseline); 61% (25/41) vs. 63% (20/32) (follow-up unclear) (p>0.05) <u>Somatization disorder</u> (criteria not reported): 56% (23/41) vs. 41% (13/32) (baseline); 32% (13/41) vs. 18% (9/32) (p<0.05) <u>Symptom magnification</u> (criteria not reported): 34% (14/41) vs. 28% (9/32) (baseline); 22% (9/41) vs. 19% (6/32) (p>0.05) *Narcotic intake classified as follows: "intake of class IV narcotics… up to a	

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
						maximum of four times, or hydrocodone twice or less per day, was considered as mild; intake of class III narcotics… up to four times as moderate; and intake of class II narcotics in any dosage was considered as heavy."	
Manchikanti 2010, 2008	A: Extra-articular facet joint nerve blocks 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 (n=60) B: Extra-articular facet joint inerve blocks with 0.5-1.5 ml solution of 0.25% bupivacaine or bupivacaine and Sarapin in equal amounts, with fluoroscopic guidance (n=60)	24 months 80% f/u (96/120) (A vs. B: 20.0% (12/60 vs. 20.0% (12/60))	A vs. B Pain (mean NRS, 0 to 10): 7.9 ± 1.0 vs. 8.2 ± 0.8 at baseline, 3.5 ± 1.1 vs. 3.8 ± 1.3 at 3 m; 3.3 ± 0.8 vs. 3.6 ± 1.5 at 6 m; 3.5 ± 1.1 vs. 3.7 ± 1.7 at 12 m; 3.3 ± 1.0 vs. 3.5 ± 1.5 at 18 m; 3.2 ± 0.9 vs. 3.5 ± 1.5 at 24 m 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 18 m; 90% (54/60) vs. 85% (51/60) at 24 m Length of pain relief per procedure (weeks): *One procedure:* 59 ± 51.7 (n=4) vs. 42 ± 47.1 (n=7)	A vs. B ODI (0 to 50): 25.9 ± 5.0 vs. 26.6 ± 4.6 at baseline, 13.5 ± 5.6 vs. 12.7 ± 4.7 at 3 m, 12.2 ± 5.0 vs. 12.7 ± 4.7 at 6 m, 12.0 ± 5.4 vs. 12.3 ± 4.8 at 12 m, 11.2 ± 4.9 vs. 12.1 ± 5.0 at 18 m, 11.0 ± 4.8 vs. 12.0 ± 4.9 at 24 m 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, 87% (52/60) vs. 83% (50/60) at 18 m	NR	A vs. B Opioid use (mg MED/day): 37 ± 40.4 vs. 31 ± 25.2 at baseline (p=0.29), 33 ± 31.1 vs. 29 ± 25.6 at 12 m (p=0.41), 30 ± 27.1 vs. 27 ± 23.8 at 24 m (p=0.55) Surgery: NR Other: 4/60 vs. 5/60 unblinded prematurely due to lack of treatment response Employed: 28% (17/60) vs. 17% (10/60) at baseline; 37% (22/60) vs. 27% (16/60) at 12 m; 37% (22/60) vs. 27%	"No adverse events reported"

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			Two procedures: 29 ± 21.3 (n=6) vs. 39 ± 25.5 (n=4) *Three procedures*: 21 ± 10.9 (n=4) vs. 21 ± 12.6 (n=8) *Four procedures:* 18 ± 6.9 (n=8) vs. 18 ± 11.8 (n=2) *Five procedures:* 18 ± 2.9 (n=5) vs. 16.5 ± 5.8 (n=3) *Six procedures:* 15 ± 2.9 (n=5) vs. 13 ± 3.8 (n=5) *Seven procedures:* 13 ± 2.1 (n=6) vs. 13 ± 0.7 (n=10) *Eight procedures:* 12 ± 0.6 (n=20) vs. 13 ± 0.6 (n=18) *Nine procedures:* 11 ± 0.1 (n=2) vs. 11 ± 0.4 (n=3) *Average relief per procedure:* 19 ± 18.2 (n=60) vs. 19 ± 19.9 (n=60) <u>Total length of pain relief (weeks):</u> *One procedure:* 59 ± 51.7 (n=4) vs. 42 ± 47.1 (n=7) *Two procedures*: 58 ± 42.6 (n=6) vs. 79 ± 51.0 (n=4) *Three procedures:* 63 ± 32.6 (n=4) vs. 63 ± 37.8 (n=8) *Four procedures:* 71 ± 27.7 (n=8) vs. 71 ± 47.4 (n=2) *Five procedures:* 89 ± 14.4 (n=5) vs. 81 ± 28.5 (n=3) *Six procedures:* 88 ± 17.6 (n=5) vs. 80 ± 20.3 (n=5) *Seven procedures:* 91 ± 14.5 (n=6) vs. 93 ± 4.8 (n=10) *Eight procedures:* 99 ± 4.8 (n=20) vs. 100 ± 5.1 (n=18)	88% (53/60) vs. 87% (52/60) at 24 m		(16/60) at 24 m <u>Disabled</u> (i.e., and unemployed): 42% (25/60) vs. 48% (29/60) at baseline; 40% (24/60) vs. 50% (30/60) at 12 m; 42% (25/60) vs. 50% (30/60) at 24 m	

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			Nine procedures: 103 ± 0.7 (n=2) vs. 99 ± 3.8 (n=3) *Average length of pain relief:* 84 ± 27.5 (n=60) vs. 82 ± 31.8 (n=60)				
Extra-articular steroid injection vs Medial branch radiofrequency denervation							
Civelek 2012	A: Extra-articular facet joint injection to site of medial branch of the dorsal spinal ramus with 40 mg methyl-prednisolone (1 ml) and 1% lidocaine (8 ml), with fluoroscopic guidance (n=50) 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 (n=50)	12 months 100% f/u (100/100)	A vs. B 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	NR	A vs. B 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 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	NR	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)

Appendix Table K3. Lumbar Facet Joint Pain Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Intra-articular steroid injection vs. Intra-articular control injection				
Carette 1991	A: Intra-articular facet joint injection with 20 mg methylprednisolone acetate (1 ml) plus isotonic saline (1 ml), with fluoroscopic guidance (n=51) B: Intra-articular facet joint injection with isotonic saline (2 ml), with fluoroscopic guidance (n=50)	6 months 94% f/u (95/101) 1 month 95% f/u (96/101)	NR	NR
Lilius 1989 Also includes comparison of IASI vs EASI and EASI vs IANSI	A: Intraarticular facet joint injection with 80 mg methylprednisolone acetate (2 ml) plus 30 mg bupivacaine (6 ml), with fluoroscopic guidance (n=28) B: Extra-articular (pericapsular) facet joint injection with 80 mg of methylprednisolone (2 ml) + 30 mg bupivacaine (6 ml), with fluoroscopic guidance (n=39) C: Intra-articular facet join injection with 8 ml saline, with fluoroscopic guidance (n=42)	3 months 97% f/u (106/109) (A vs. B vs. C: 3.6% (1/28) vs. 0% (0/39) vs. 4.8% (2/42))	NR	NR
Fuchs 2005	A: Intraarticular facet joint injection with 10 mg triamcinolone acetonide (1 ml), with CT fluoroscopic guidance (n=30) B: Intraarticular facet joint injection with 10 mg sodium hyaluronate (1 ml), with CT fluoroscopic guidance (n=30)	6 months % f/u NR	NR	NR
Intra-articular steroid injection vs. Extra-articular steroid injection				
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 (n=31) B: Intramuscular injections in the lumbar paravertebral musculature with 20 mg triamcinolone hexacetonide (1 ml) and lidocaine (dose not reported, 1 ml) (n=29)	6 months 93% f/u (56/60) (but all 60 patients included in the intention to treat analysis)	NR	NR
Intra-articular steroid injection vs. Medial branch radiofrequency denervation				
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) (n=29) 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 (n=27)	6 months 93% f/u (52/56)	NR	NR
Extra-articular steroid injection vs. Extra-articular control injection				
Manchikanti 2001	A: Extra-articular facet joint injection of the medial branch of the medial branch with 0.5-1 ml of 1 mg/ml methylprednisolone and 0.5%	Unclear (up to 2.5 years) 87% f/u (73/84) at 2.5 yrs. (A vs.	NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
	lidocaine or 0.25% bupivacaine plus equal volume of Sarapin, with fluoroscopic guidance (n=42) B: Extra-articular facet joint injection of the medial branch of the medial branch with 0.5-1 ml of 0.5% lidocaine or 0.25% bupivacaine plus equal volume of Sarapin, with fluoroscopic guidance (n=42)	B: 2.3% (1/42) vs. 23.8% (10/42) at 2.5y		
Manchikanti 2010, 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 (n=60) 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 (n=60)	24 months 80% f/u (96/120) (A vs. B: 20.0% (12/60 vs. 20.0% (12/60))	NR	NR
Extra-articular steroid injection vs. Medial branch radiofrequency denervation				
Civelek 2012	A: Extra-articular facet joint injection to site of medial branch of the dorsal spinal ramus with 40 mg methyl-prednisolone (1 ml) and 1% lidocaine (8 ml), with fluoroscopic guidance (n=50) 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 (n=50)	12 months 100% f/u (100/100)	NR	NR

Appendix Table K4. Lumbar Facet Joint Pain: Baseline scores of Pain, Function, Quality of Life and Opioid Use

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
Pain on VAS or NRS (0-10)						
Baseline	Civelek 2012	Extra-articular injection of Methylprednisolone 40 mg + lidocaine 1% Fluoroscopy	Radio-frequency denervation	Extra-articular, Medial branch	8.5 ± 0.7 (n=50)	8.2 ± 0.6 (n=50)
	Manchikanti 2010, 2008	Extra-articular injection of Betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Bupivacaine 0.25% or bupivacaine + Sarapin	Extra-articular, Medial branch	7.9 ± 1.0 (n=60)	8.2 ± 0.8 (n=60)
	Manchikanti 2001	Extra-articular injection of Methylprednisolone 40 and bupivacaine 0.25% or lidocaine 0.5% + Sarapin Fluoroscopy	Bupivacaine 0.25% or lidocaine 0.5% + Sarapin	Extra-articular, Medial branch	7.7 ± 0.1 (n=42)	7.6 ± 0.1 (n=42)
	Lilius 1989	Intra-articular injection of methylprednisolone acetate 80 mg + bupivacaine 30 mg Fluoroscopy	Extra-articular (pericapsular) injection of methylprednisolone acetate 80 mg + bupivacaine 30 mg	Intra-articular	4.5± 1.2‡ (n=28)	5.2± 1.4‡ (n=39)
	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg and lidocaine Fluoroscopy	Extra-articular (intramuscular,paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	Intra-articular	7.0 ± 1.28 (n=31)	6.8 ± 1.51 (n=29)
	Carette 1991	Intra-articular injection of methylprednisolone acetate 20 mg + isotonic saline Fluoroscopy	Intra-articular injection of isotonic saline	Intra-articular	6.3 ± 1.2 (n=49)	6.2 ± 1.4 (n=48)
	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg CT fluoroscopy	Intra-articular injection of sodium hyaluronate 10 mg	Intra-articular	6.87 ± 1.15 (n=30)	6.92 ± 1.42 (n=30)
	Lilius 1989	Intra-articular injection of methylprednisolone acetate 80 mg + bupivacaine 30 mg Fluoroscopy	Intra-articular injection of saline	Intra-articular	4.5 ± 1.2‡ (n=28)	5.2 ± 1.4‡ (n=42)
	Lakemeier 2013	Intra-articular injection of betamethasone 3 mg + bupivacaine 0.5% + sham denervation Fluoroscopy	Radiofrequency denervation of the medial branch + bupivacaine 0.5%	Intra-articular	7.0 ± 1.7 (n=26)	6.6 ± 1.8 (n=26)
Function on ODI (0-50) or (0-100)						
Baseline	Manchikanti 2010,	Extra-articular injection of Betamethasone +	Bupivacaine 0.25% or	Extra-articular,	25.9 ± 5.0	26.6 ± 4.6

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
	2008	bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	bupivacaine + Sarapin	Medial branch	(n=60)	(n=60)
	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg CT fluoroscopy	Intra-articular injection of sodium hyaluronate 10 mg	Intra-articular	18.4 ± 6.2 (n=30)	20.7 ± 8.5 (n=30)
	Lakemeier 2013	Intra-articular injection of betamethasone 3 mg + bupivacaine 0.5% + sham denervation Fluoroscopy	Radiofrequency denervation of the medial branch + bupivacaine 0.5%	Intra-articular	38.7 ± 18.4 (n=26)	40.8 ± 16.4 (n=26)
RMDQ (0-24)						
Baseline	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg and lidocaine Fluoroscopy	Extra-articular (intramuscular,paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	Intra-articular	15 ± 5.26 (n=31)	16.4 ± 6.04 (n=29)
	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg CT fluoroscopy	Intra-articular injection of sodium hyaluronate 10 mg	Intra-articular	12.5 ± 4.4 (n=30)	12.5 ± 4.9 (n=30)
	Lakemeier 2013	Intra-articular injection of betamethasone 3 mg + bupivacaine 0.5% + sham denervation Fluoroscopy	Radiofrequency denervation of the medial branch + bupivacaine 0.5%	Intra-articular	13.2 ± 5.9 (n=26)	12.8 ± 5.4 (n=26)
Sickness Impact Profile (0-100)						
Baseline	Carette 1991	Intra-articular injection of methylprednisolone acetate 20 mg + isotonic saline Fluoroscopy	Intra-articular injection of isotonic saline	Intra-articular	Overall: 11.4 Physical: 4.2 Psychosocial: 10.7 (n=49)	Overall: 13.4 Physical: 6.9 Psychosocial: 12.3 (n=48)
SF-36 physical function						
Baseline	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg and lidocaine Fluoroscopy	Extra-articular (intramuscular,paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	Intra-articular	32‡ (n=31)	32‡ (n=29)
	Fuchs 2005	Intra-articular injection of triamcinolone	Intra-articular injection of	Intra-articular	40‡	39‡

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Score Mean ± SD Group A	Group B
		acetonide 10 mg CT fluoroscopy	sodium hyaluronate 10 mg		(n=30)	(n=30)
Opioid usage (morphine equivalents)						
Baseline	Manchikanti 2010, 2008	Extra-articular injection of Betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Bupivacaine 0.25% or bupivacaine + Sarapin	Extra-articular, Medial branch	37 ± 40.4 (n=60)	31 ± 25.2 (n=60)

‡ Estimated from graphs in article.

APPENDIX L. Sacroiliac pain: RCT Study Characteristics and Results

Appendix Table L1. Sacroiliac Pain Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Intra-articular steroid injection vs. Conservative Care								
Visser 2013	N=51	Inclusion: SIJ-related pain (defined as radiating pain below the buttocks, pain in the region of SIJ, ≥3 positive provocation sacroiliac tests at first visit and confirmed at second visit, exclusion of other causes of leg pain [e.g., HNP, stenosis, tumor, Lyme disease], and exclusion of sacroiliits in inflammatory spondylo-arthropathies); leg pain for >4 weeks but <1 year Exclusion: pregnancy; previous back surgery; and inability to perform follow-up investigations	A: Intraarticular sacroiliac joint injection with 20 mg kenacort and 30 mg lidocaine (mean 1.1 ml, range 0.6 to 2.0 ml) (n=18) B: Physiotherapy: fixed exercise schedule aimed at improving flexibility of the sacroiliac joint and strengthening back and pelvic floor muscles; guided by a physiotherapist 1x week with a max period of 6 weeks; exercises to be performed 5-6x day during week 1, then 3x day in subsequent weeks (n=15) C: Manual therapy: high-velocity thrust manipulation techniques to mobilize the sacroiliac joint; 2 sessions with an interval of 2 weeks (n=18)	Levels: Sacroiliac Repeat injections: 22.2% (4/18), administered 2 weeks after initial injection if pain returned	Fluoroscopic guidance	NR	A vs. B vs. C Age (mean): 46.2 ± 13.9 (range, 20-73) years (NR by group) Male: 11% vs. 27% vs. 44% Race: NR Duration of symptoms (weeks): 27 ± 24.1 vs. 24 ± 16.5 vs. 25 ± 14.4 Baseline pain: (VAS 0-10): 5.7 ± 1.7 vs. 4.3 ± 1.2 vs. 5.2 ± 1.4 (p=NS) Baseline QOL: NR	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Extra-articular steroid injection vs. Extra-articular non-steroid injection								
Luukkainen 2002	N=24	Inclusion: 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 Exclusion: NR	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)	Levels: Sacroiliac Repeat injections: Single injection	No use of imaging guidance reported	If a patient was receiving NSAIDs, the mediation was kept stable during the followup.	A vs. B: Age (mean): 50 vs. 49 years Male: 23% vs. 36% Race: NR Duration of symptoms (years): 5.4 vs. 4.4 Baseline pain (median, 0-100 VAS): 53 vs. 53 Baseline function: NR	NR

Appendix Table L2. Sacroiliac Pain Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Intra-articular steroid injection vs. Conservative Care							
Visser 2013	A: Intraarticular sacroiliac joint injection with 20 mg kenacort and 30 mg lidocaine (mean 1.1 ml, range 0.6 to 2.0 ml) (n=18) B: Physiotherapy: fixed exercise schedule aimed at improving flexibility of the sacroiliac joint and strengthening back and pelvic floor muscles; guided by a physiotherapist 1x week with a max period of 6 weeks; exercises to be performed 5-6x day during week 1, then 3x day in subsequent weeks (n=15) C: Manual therapy: high-velocity thrust manipulation techniques to mobilize the sacroiliac joint; 2 sessions with an interval of 2 weeks (n=18)	3 months 82.4% (42/51) at 6 weeks; 58.8% (30/51) at 3 months	A vs. B vs. C Pain (VAS 0-10): 5.7 ± 1.7 vs. 4.3 ± 1.2 vs. 5.2 ± 1.4 at baseline; 4.8 ± 1.8 vs. 4.5 ± 0.7 vs. 3.5 ± 2.3 at 6 weeks; 5.0 ± 1.9 vs. 3.9 ± 1.4 vs. 3.3 ± 2.3 at 3 months; Difference at 3 months: -0.7 vs. -0.4 vs. -1.9 p=NR for all for b/w group differences Improvement of ≥2 points in VAS: 28% (5/18) vs. 20% (3/15) vs. 56% (10/18) at 3 months; p=NR for all for b/w group differences Treatment success (complete relief of complaints at 6 weeks or 3 months, or 3 month average VAS pain score < baseline VAS score): 50% (9/18) vs. 20% (3/15) vs. 72% (13/18); A vs. B, p=0.07 A vs. C, p=0.17 Treatment failure (drop out before 3 months due to worsening	RAND 36 questionnaire: Physical functioning 45.3 ± 16.8 vs. 27.5 ± 6.5 vs. 30.0 ± 18.6 at baseline; 45.8 ± 20.7 vs. 50.0 ± 24.8 vs. 49.1 ± 23.5 at 6 weeks; 37.9 ± 15.4 vs. 51.25 ± 28.7 vs. 60.5 ± 24.3 at 3 months Difference at 3 months: -7.4 vs. 23.75 vs. 30.5	A vs. B vs. C RAND 36 questionnaire: Social functioning 48.0 ± 24.3 vs. 40.8 ± 18.9 vs. 40.3 ± 21.9 at baseline; 55.7 ± 21.3 vs. 47.3 ± 11.9 vs. 69.0 ± 24.4 at 6 weeks; 55.8 ± 25.3 vs. 47.0 ± 21.3 vs. 70.2 ± 28.5 at 3 months Role limitations (physical) 15.0 ± 24.2 vs. 12.5 ± 25.0 vs. 2.5 ± 8.0 at baseline; 32.5 ± 42.6 vs. 12.5 ± 14.4 vs. 35.0 ± 42.8 at 6 weeks; 25.0 ± 42.5 vs. 25.0 ± 20.4 vs. 45.0 ± 49.7 at 3 months Role limitations (emotional) 53.3 ± 50.2 vs. 83.3 ± 33.5 vs. 18.6 ± 37.7 at baseline; 60.0 ± 46.6 vs. 83.3 ± 33.5 vs. 51.9 ± 50.3 at 6 weeks; 60.0 ± 51.6 vs. 58.3 ± 50.1 vs. 63.0 ± 48.4 at 3 months Mental health 63.2 ± 24.2 vs. 65.0 ± 21.5 vs. 50.7 ± 20.9 at baseline; 66.0 ± 24.8 vs. 66.0 ± 8.3 vs. 68.0 ± 18.1 at 6 weeks; 65.2 ± 23.7 vs. 69.0 ± 22.9 vs. 73.3 ± 17.6 at 3 months Vitality 43.5 ± 21.0 vs. 55.0 ± 18.6 vs. 33.3 ± 12.0 at baseline; 51.2 ± 16.1 vs. 55.0 ± 18.7 vs.	NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			symptoms, or 3 month average VAS pain score ≥ baseline VAS score): 50% (9/18) vs. 80% (12/15) vs. 28% (5/18)		47.4 ± 21.9 at 6 weeks; 49.5 ± 17.7 vs. 61.3 ± 15.5 vs. 55.8 ± 18.5 at 3 months <u>Pain</u> 32.5 ± 13.9 vs. 27.5 ± 15.0 vs. 23.7 ± 16.1 at baseline; 45.9 ± 15.4 vs. 47.5 ± 6.4 vs. 53.7 ± 19.3 at 6 weeks; 43.8 ± 20.6 vs. 44.5 ± 9.0 vs. 57.0 ± 23.7 at 3 months <u>Health perception</u> 51.3 ± 23.0 vs. 48.8 ± 26.6 vs. 59.0 ± 19.7 at baseline; 57.1 ± 18.9 vs. 53.8 ± 21.0 vs. 56.5 ± 21.9 at 6 weeks; 57.3 ± 17.8 vs. 51.3 ± 14.9 vs. 59.5 ± 26.2 at 3 months <u>Health change</u> 40.9 ± 12.6 vs. 50.0 ± 20.4 vs. 27.8 ± 26.4 at baseline; 47.7 ± 26.1 vs. 43.8 ± 12.5 vs. 50.0 ± 21.7 at 6 weeks; 45.5 ± 21.8 vs. 56.3 ± 31.5 vs. 44.4 ± 27.3 at 3 months p=NR for all for b/w group differences		
Extra-articular steroid injection vs. Extra-articular non-steroid injection							
Luukkainen 2002	A: Periarticular sacroiliac joint injection with 60 mg methylprednisolone (1.5 ml) and 20 mg/ml lidocaine (1.5 ml) (n=13) B: Periarticular	1 month % f/u NR	A vs. B: <u>Improvement in pain from baseline</u> (median, 0-100 VAS): -40 vs. -13 at 1 m (p=0.046)	NR	NR	NR	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
	sacroiliac joint injection with 20 mg/ml lidocaine (1.5 ml) (n=11)						

Appendix Table L3. Sacroiliac Pain Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Intra-articular steroid injection vs. Conservative Care				
Visser 2013	A: Intraarticular sacroiliac joint injection with 20 mg kenacort and 30 mg lidocaine (mean 1.1 ml, range 0.6 to 2.0 ml) (n=18) B: Physiotherapy: fixed exercise schedule aimed at improving flexibility of the sacroiliac joint and strengthening back and pelvic floor muscles; guided by a physiotherapist 1x week with a max period of 6 weeks; exercises to be performed 5-6x day during week 1, then 3x day in subsequent weeks (n=15) C: Manual therapy: high-velocity thrust manipulation techniques to mobilize the sacroiliac joint; 2 sessions with an interval of 2 weeks (n=18)	3 months 82.4% (42/51) at 6 weeks; 58.8% (30/51) at 3 months	None	None
Extra-articular steroid injection vs. Extra-articular non-steroid injection				
Luukkainen 2002	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)	1 month % f/u NR	None	None

Appendix Table L4. Sacroiliac Joint Pain: Baseline Scores for pain, function, and quality of life

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Pain score Mean ± SD Group A	Group B
Pain on VAS or NRS (0-10)						
Baseline	Luukkainen 2002	Methylprednisolone 60 mg + lidocaine 20 mg	lidocaine 20 mg	Peri-articular	median 5.3 (range, 2.7 to 8.4) (n=13)	median 5.3 (range, 2.0 to 8.3) (n=11)
	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	5.7 ± 1.7 (n=18)	4.3 ± 1.2 (n=15)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	5.7 ± 1.7 (n=18)	5.2 ± 1.4 (n=18)
RAND-36 physical function						
Baseline	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	45.3 ± 16.8 (n=18)	27.5 ± 6.5 (n=15)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	45.3 ± 16.8 (n=18)	30.0 ± 18.6 (n=18)
RAND-36 social functioning						
Baseline	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	48.0 ± 24.3 (n=18)	40.8 ± 18.9 (n=15)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	48.0 ± 24.3 (n=18)	40.3 ± 21.9 (n=18)
RAND-36 role limitations (physical)						
Baseline	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	15.0 ± 24.2 (n=18)	12.5 ± 25.0 (n=15)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	15.0 ± 24.2 (n=18)	2.5 ± 8.0* (n=18)
RAND-36 Role limitations (emotional)						
Baseline	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	53.3 ± 50.2 (n=18)	83.3 ± 33.5 (n=15)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	53.3 ± 50.2 (n=18)	18.6 ± 37.7 (n=18)
RAND-36 Mental health						
Baseline	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	63.2 ± 24.2 (n=18)	65.0 ± 21.5 (n=15)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	63.2 ± 24.2 (n=18)	50.7 ± 20.9 (n=18)
RAND-36 Vitality						
Baseline	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	43.5 ± 21.0	55.0 ± 18.6

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Pain score Mean ± SD Group A	Group B
					(n=18)	(n=15)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	43.5 ± 21.0 (n=18)	33.3 ± 12.0 (n=18)
RAND-36 Pain						
Baseline	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	32.5 ± 13.9 (n=18)	27.5 ± 15.0 (n=15)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	32.5 ± 13.9 (n=18)	23.7 ± 16.1 (n=18)
RAND-36 Health perception						
Baseline	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	51.3 ± 23.0 (n=18)	48.8 ± 26.6 (n=15)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	51.3 ± 23.0 (n=18)	59.0 ± 19.7 (n=18)
RAND-36 Health change						
Baseline	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	40.9 ± 12.6 (n=18)	50.0 ± 20.4 (n=15)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	40.9 ± 12.6 (n=18)	27.8 ± 26.4 (n=18)

*Typo in table in the article.

APPENDIX M. Cervical Radiculopathy Attributed to Disc Pathology: RCT Study Characteristics and Results

Appendix Table M1. Cervical Radiculopathy Attributed to Disc Pathology Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Epidural steroid injection vs Conservative care								
Cohen 2014	N=169	Inclusion: Adults with cervical radicular pain extending into the arm(s) based on history and physical; arm pain NRS score ≥4/10 or equivalent in intensity to neck pain; MRI correlation of symptoms with pathology. Exclusion: Patients with pain <1 month or >4 years; signs or symptoms of myelopathy; surgical referral for a diagnostic injection; previous spine surgery; previous trials with gabapentin or pregabalin and amitriptyline or nortriptyline; serious medical or psychiatric disorders that might preclude an optimal response to treatment; ongoing litigation and previous cervical ESI; allergy to steroids or contrast	A: Interlaminar ESI of 3 mL solution consisting of 60 mg depo-methylprednisolone and normal saline. (injected ipsilateral to midline if symptoms were unilateral, or with the midline approach if symptoms were bilateral) (n = 55) B: Conservative care: pharmacotherapy with gabapentin and/or nortriptyline plus PT geared toward alleviation of radicular symptoms that began within 1 week of enrollment. (n = 59) C: Combination of both A and B (n = 55)	Number of levels: C6-7 or C7-T1 Repeat injections: Allowed after the 1 and 3 month follow-ups at the discretion of the physician for those patients who had pain recurrence or only partial benefit. Number of injections (among those in groups A and C) (mean ± SD): 1.3 ± 0.6	Fluoro-scopic guidance with contrast	Medica-tions used: B: Nortriptyline: 42.5% (25/59) Gabapentin: 23.7% (14/59), Both nortriptyline and gabapentin: 33.9% (20/59) C: Nortriptyline: 41.8% (23/55) Gabapentin: 41.8% (23/55) Both nortriptyline and gabapentin: 16.4% (9/55)	A vs. B vs. C: Age (median, IQR): 44.0 (39.0-51.0) vs. 45.0 (41.0-54.0) vs. 49.0 (41.0-59.0), p = 0.10 Female (%, n/n): 50.9% (28/55), 55.9% (33/59), 45.5% (25/55), p = 0.54 Duration of pain in years (median, IQR): 0.8 (0.3-2.0) vs. 1.0 (0.5-2.0) vs. 0.7 (0.3-2.5), p = 0.61 Opioid therapy (%, n/n): 37% (20/55) vs. 31% (18/59) vs. 44.4% (24/55), p = 0.42 Smoker (%, n/n): 16.4% (9/55) vs. 22.0% (13/59)† vs. 23.6% (13/55), p = 0.61 Obese: (%, n/n): 25.5% (14/55) vs. 35.6% (21/59) vs. 21.8% (12/55), p = 0.23 Psychiatric comorbidity none (%, n/n): 69.1% (38/55) vs. 59.3% (35/59) vs. 65.5% (36/55) Baseline arm pain (mean ± SD): 6.2 ± 1.7 vs. 5.9 ± 2.1 vs. 5.6 ± 2.4, p = 0.76 Baseline neck pain (mean ± SD): 5.8 ± 2.3 vs. 5.9 ± 2.1 vs. 5.6 ± 2.4, p = 0.81	Congress-ional Grant from the Center for Rehabilita-tion Sciences Research, Uniformed services University of Health Sciences, Bethesda, Maryland The role of funding source was only to provisions to pay research personnel.

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
							Baseline NDI (median, IQR): 38.0 (30.0-50.0) vs. 34.0 (28.0-52.0) vs. 38.0 (28.0-48.0), p = 0.60 † Reported as "23.6% (13/59)". Assumed that the n was correct, and the percent was not	

Appendix Table M2. Cervical Radiculopathy Attributed to Disc Pathology. Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injection vs Conservative care							
Cohen 2014	A: Interlaminar ESI of 3 mL solution consisting of 60 mg depo-methylprednisolone and normal saline. (injected ipsilateral to midline if symptoms were unilateral, or with the midline approach if symptoms were bilateral) (n = 55) B: Conservative care: pharmacotherapy with gabapentin and/or nortriptyline plus PT geared toward alleviation of radicular symptoms that began within 1 week of enrollment. (n = 59) C: Combination of both A and B (n = 55)	1 month: 96.4% (163/169) 3 months: 6 months: A vs. B. vs. C: 1 month: 98% (54/55) vs. 98% (58/59) vs. 93% (51/55) 3 months: 89% (49/55) vs. 95% (56/59) vs. 93% (51/55) 6 months: 85% (47/55) vs. 93% (55/59) vs. 91% (50/55) NOTE. Per study protocol, patients who failed treatment at any time point (pain worsened, not satisfied, and >2-point reduction in arm pain) could exit the study. Once a patient exited the study, data at later time points were used by carrying	*A vs. B vs. C* **NRS arm pain** Baseline 6.2 ± 1.7 (n = 55) vs. 6.1 ± 2.2 (n = 59) vs. 6.4 ± 1.9 (n = 55), p = 0.76 1 month Adjusted† mean (95% CI) 4.2 (3.5-4.9) (n = 54) vs. 4.3 (3.6-5.0) (n = 58) vs. 3.5 (2.8-4.2) (n = 51), p = 0.26 Mean change from baseline (95% CI): -2.0 (-2.7—1.3) vs. -1.8 (-2.5 to -1.2) vs. -3.1 (-3.8 to -2.3), p = 0.035 Mean change from baseline intergroup differences: B vs. A: 0.2 (-0.7 to 1.1) p = 0.722; B vs. C: -1.2 (-2.3 to -0.1) p = 0.027; A vs. C: -1.1 (-2.2 to 0) p = 0.045) **NRS arm pain- last observation carried forward** (for patients who failed and exited study per protocol) 3 months 2.96 ± 0.56 (n = 49) vs. 3.29 ± 0.51 (n = 56) vs. 2.30 ± 0.47 (n = 51), p = 0.33	*A vs. B vs. C* **NDI** Baseline Median IQR: 38.0 (30.0 to 50.0) (n = 55) vs. 34.0 (28.0 to 52.0) (n = 59) vs. 38.0 (28.0 to 48.0) (n = 55), p = 0.6 1 month Adjusted† mean (95% CI): 33.4 (29.8 to 36.9) (n = 54 vs. 32.0 (28.7 to 35.4) (n = 598 vs. 28.4 (24.8 to 32.1) (n = 51), p = 0.15 Mean change from baseline (95% CI): -6.8 (-10.3 to -3.4) vs. -8.2 (-11.6 vs. -4.9) vs. -11.8 (-15.5 to -8.2), p = 0.15 Mean change from baseline intergroup differences: B vs. A: -1.2 (-6.1 to 3.6) p = 0.61; B vs. C: -3.6 (-8.3 to 1.1) p = 0.13; A	*A vs. B vs. C* **Positive Global Perceived Effect** (pain improved since last visit; satisfied with treatment and would recommend to others) 1 month 61.1% (33/54) vs. 60.3% (35/58) vs. 72.6% (37/51); p = 0.23 OR (95% CI)— B vs. A: 1.0 (0.4 to 2.2) p = 0.98; B vs. C: 1.8 (0.7 to 4.3) p = 0.21; A vs. C: 1.8 (0.7 to 4.5) p = 0.19 **Positive categorical outcome** (≥50% decrease in arm pain coupled with a positive global perceived effect) 1 month: 53.7% (29/54) vs. 51.7% (30/58) vs. 64.7% (33/51); OR (95% CI): B vs. A: 1.0 (0.5 to 2.1) p = 0.94; B vs. C: 1.7 (0.7 to 3.9) p = 0.20; A vs. C: 1.6 (0.7 to 3.6) p = 0.29 **Successful treatment** (Positive GPE, ≥2-point decrease in NRS arm pain score, without additional procedural interventions)	*A vs. B vs. C* **Medication reduction** (≥20% reduction in opioid use or cessation of nonopioid analgesics) 1 month† 34.9% (15/43) vs. 35.6% (16/45) vs. 54.8% (23/42); OR (95% CI): B vs. A: 1.0 (0.4 to 2.7) p = 0.97; B vs. C: 1.9 (0.7 to 4.9) p = 0.18; A vs. C: 2.3 (0.9-5.8) p = 0.08 **Proceeded to surgery within 1 year of treatment** 12 months 5.5% (3/55) vs. 6.8% (4/59) vs. 5.5% (3/55) OR (95% CI): B vs. A: 2.1 (0.4 to 12.8) p = 0.41; B vs. C: 0.4 (0.1 to 2.5) p = 0.41; A vs. C: 0.8 (0.1 to	**Adverse effects stratified by medication type** *(nortriptyline only vs. gabapentin only vs. nortriptyline + gabapentin)* 1 month None: 20.8% (10/48) vs. 70.3% (26/37) vs. 41.4% (12/29) Sleepiness/fatigue:29.2% (14/48) vs. 21.6% (8/37) vs. 31.0% (9/29) Cognitive: 12.5% (6/48) vs. 13.5% (5/37) vs. 13.8% (4/29) Weight gain: (4.2% (2/48) vs. 0% (0/37) vs. 0% (0/29) Dry mouth: 18.8% (9/48) vs. 0% (0/37) vs. 17.2% (5/29) Gastrointestinal: 2.1% (1/48) vs. 5.4% (2/37) vs. 6.9% (2/29) Bowel/Bladder: 4.2% (2/48) vs.

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
		forward the last available data. (Patients who dropped out were excluded from outcomes data.) Patients exited study per protocol *at* the following time points: A vs. B. vs. C: Exited after 1 month f/u: 45% (25/55) vs. 47% (28/59) vs. 33% (18/55) Exited after 3 month f/u: 11% (6/55) vs. 7% (4/59) vs. 24% (13/55) Exited after 6 month f/u: 0% (0/55) vs. 0% (0/59) vs. 0% (0/55) Cumulative- patients who exited the study: 56% (31/55) vs. 54% (32/59) vs. 56% (31/55) **Patients included in**	6 months 2.38 ± 0.48 (n = 49) vs. 1.16 ± 0.50 (n = 55) vs. 2.02 ± 0.37 (n = 50), p = 0.20 **NRS Neck Pain:** Baseline 5.8 ± 2.3 (n = 55) vs. 5.9 ± 2.1 (n = 59) vs. 5.6 ± 2.4 (n = 55), p = 0.81 1 month†: Mean (95% CI): 4.6 (3.9 to 5.3) (n = 54) vs. 4.7 (4.1 to 5.4) (n = 58) vs. 3.5 (2.8 to 4.3) (n = 51) Mean change from baseline (95% CI): -1.1 (-1.8 to -0.4) vs. -1.2 (-1.9 to -0.5) vs. -2.2 (-3.0 to -1.5), p = 0.06 Mean change from baseline intergroup differences: B vs. A: -0.1 (-1.0 to 0.8) p = 0.89; B vs. C: -1.1 (-2.2 to 0) p = 0.056; A vs. C: -1.1 (-2.2 to 0) p = 0.054 **NRS neck pain- last observation carried forward** (for patients who failed and exited study per protocol) 1 month 4.66 ± 0.37 (n = 54) vs. 4.72 ± 0.35 (n = 58) vs.	vs. C: -5.5 (-11.0 to 0.1) p = 0.055 **NDI- last observation carried forward** (for patients who failed and exited study per protocol) 1 month 34.61 ± 2.39 (n = 54) vs. 31.81 ± 2.31 (n = 58) vs. 27.57 ± 2.46 (n = 51), p = 0.12 3 months 15.82 ± 2.85 (n = 49) vs. 14.10 ± 2.73 (n = 56) vs. 18.10 ± 2.96 (n = 51), p = 0.61 6 months 11.02 ± 2.43 (n = 49) vs. 5.37 ± 2.43 (n = 55) vs. 15.02 ± 2.49 (n = 50), p = 0.023	1 month 53.7% (29/54) vs. 51.7% (30/58) vs. 64.7% (33/51); p = 0.35 3 months 36.7% (18/49) vs. 26.8% (15/56) vs. 56.9% (29/51); p = 0.006 6 months 25.5% (12/47) vs. 23.6 % (13/55) vs. 44.0% (22/50); p = 0.06 †Means adjusted for sex, duration of symptoms, baseline NDI, opiate use, and type of hospital	6.6) p = 0.82 †Means adjusted for sex, duration of symptoms, baseline NDI, opiate use, and type of hospital	0% (0/37) vs. 3.5% (1/29) Other§: 10.4% (5/48) vs. 10.8% (4/37) vs. 17.2% (5/29) Multiple: 16.7% (8/48) vs. 18.9% (7/37) vs. 17.6% (8/29) **Adverse events associated with ESI** Headache: 1.4% (2/147) Wet-tap not associated with neurological sequelae: 0.7% (1/147) Prolonged post-procedure pain requiring prescription: 0.7% (1/147) Temporary worsening neurological symptoms not accompanied by MRI progression: 1.4% (2/147) Rash: 0.7% (1/147) Vasovagal episodes: 1.4%

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
		the analysis: 1 month: 98% (54/55) vs. 98% (58/59) vs. 93% (51/55) 3 months: 11% (24/55) vs. 44% (28/59) vs. 60% (33/55) 6 months: 29% (16/55) vs. 24% (14/59) vs. 51% (28/55)	3.48 ± 0.38 (n = 51), p = 0.38 <u>3 months</u> 3.04 ± 0.51 (n = 49) vs. 3.98 ± 0.49 (n = 56) vs. 2.83 ± 0.45 (n = 51), p = 0.20 <u>6 months</u> 3.32 ± 0.54 (n = 47) vs. 1.80 ± 0.61 (n = 55) vs. 2.83 ± 0.43 (n = 50), p = 0.18 †Means adjusted for sex, duration of symptoms, baseline NDI, opiate use, and type of hospital				(2/147) Tachycardia: 0.7% (1/147) § includes nightmares, hair loss, tremors, rash, headache, visual changes, wheezing, paresthesias, cramping, and decreased libido

Appendix Table M3. Cervical Radiculopathy Attributed to Disc Pathology Differential efficacy and safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Epidural steroid injection vs Conservative care				
Cohen 2014	A: Interlaminar ESI of 3 mL solution consisting of 60 mg depo-methylprednisolone and normal saline. (injected ipsilateral to midline if symptoms were unilateral, or with the midline approach if symptoms were bilateral) (n = 55) B: Conservative care: pharmacotherapy with gabapentin and/or nortriptyline plus PT geared toward alleviation of radicular symptoms that began within 1 week of enrollment. (n = 59) C: Combination of both A and B (n = 55)	1 month: 96.4% (163/169) 6 months: A vs. B. vs. C: 1 month: 98% (54/55) vs. 98% (58/59) vs. 93% (51/55) 3 months: 89% (49/55) vs. 95% (56/59) vs. 93% (51/55) 6 months: 85% (47/55) vs. 93% (55/59) vs. 91% (50/55)	NR	NR

APPENDIX N. Cervicobrachialgia: RCT Study Characteristics and Results

Appendix Table N1. Cervicobrachialgia Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Epidural steroid injection vs. Control injection								
Stav 1993	N = 50	Inclusion: Chronic (≥6 months) refractory cervicobrachialgia due to chronic DDD and/or osteoarthritis of cervical spine with or without radiculopathy; all patients had received prior treatment with NSAIDs and PT with or without antidepressants or sedative agents and experienced at best partial, temporary relief; all patients had clinical and radiological signs of pathology in C4-C7 region with or without signs of mechanical pressure on the dura mater and/or nerve root (imaging by CT or MRI, x-ray) Exclusion: History of cervical spinal surgery or cervical epidural injections; psychiatric disorders; in process of litigation of insurance claims	A: Cervical epidural injection with 80 mg methylprednisolone sodium acetate and 1% lidocaine (5 ml) (1-3 injections/patient) (n = 25) B: Posterior neck muscle injection with 80 mg methylprednisolone and 1% lidocaine (5 ml) (same as group A) (1-3 injections/patient) (n = 25)	Levels: Cervical epidural injection into C5-C6 or C6-C7 interspace Repeat injections: for both groups, 1-3 injections total as needed with increasing pain at 2 week intervals; treatment discontinued if there was complete failure (not defined) of first injection Number of injections* (mean ± SE) (A vs. B): 2.5 ± 0.1 (n=25) vs. 2.5 ± 0.2 (n=17) (p=0.42) Total dose of steroid injected* (mean ± SE) (A vs. B): 201.6 ± 11.4 mg (n=25) vs. 197.7 ± 15.5 mg (n=17) (p=0.43)	NR	Patients continued pre-injection treatments with non-narcotic analgesics and/or NSAIDs	A vs. B: Age* (mean ± SE years): 52.3 ± 2.4 (n=25) vs. 49.3 ± 3.0 (n=17) (p=0.22) Male*: 36% (9/25) vs. 47% (8/17) (p=0.41) Duration of symptoms* (mean ± SE months): 16.2 ± 2.1 (n=25) vs. 14.2 ± 2.0 (n=17) (p=0.27) History of cervical epidural injections: 0% vs. 0% History of cervical surgery: 0% vs. 0% Visible narrowing (any) of intervertebral foramina on CT or MRI: 76% (19/25) vs. 71% (12/17) (p=0.35) Spinal canal narrowing ≥30% on CT or MRI: 16% (4/25) vs. 18% (3/17) (p=0.44) Baseline pain: NR **Baseline function: NR**	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding

Appendix Table N2. Cervicobrachialgia Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injection vs. Control injection							
Stav 1993	A: Cervical epidural injection with 80 mg methylprednisolone sodium acetate and 1% lidocaine (5 ml) (1-3 injections/patient) (n = 25) B: Posterior neck muscle injection with 80 mg methylprednisolone and 1% lidocaine (5 ml) (same as group A) (1-3 injections/patient) (n = 25)	1 week, 12 months: (84% f/u; 42/50) A vs. B: 100% (25/25) vs. 68% (17/25) (NOTE: 8 patients excluded from group B after beginning litigation of insurance claims during the f/u period)	A vs. B: <u>Pain (improvement from baseline based on VAS) (% patients):</u> *1 week:* Very good or good (≥50% improvement): 76% (19/25) vs. 35% (6/17) (*P* = .004) Very good (≥75% improvement): 44% (11/25) vs. 18% (3/17) (*P* =0.0377) Good (50-74% improvement): 32% (8/25) vs. 18% (3/17) (*P* = NR) Satisfactory (31-49% improvement): 8% (2/25) vs. 24% (4/17) (*P* = NR) Poor (≤30% improvement): 8% (2/25) vs. 29% (5/17) (*P* = NR) Worse: 8% (2/25) vs. 12% (2/17) (*P* = NR) *12 months:* (≥50% improvement): 68% (17/25) vs. 12% (2/17) (*P* = .0002) Very good (≥75% improvement): 56% (14/25) vs. 6% (1/17) (*P* = .0004) Good (50-74% improvement): 12% (3/25) vs. 6% (1/17) (*P* = NR) Satisfactory (31-49% improvement): 20% (5/25) vs. 18% (3/17) (*P* = NR) Poor (≤30% improvement): 4% (1/25) vs. 59% (10/17) (*P* = NR) Worse: 8% vs. 12% (2/17) (*P* = NR)	NR	NR	A vs. B: Analgesic use, decrease in daily dose (% patients taking analgesics, n=NR) 1 week: 81.7% (n=NR) vs. 8.6% (n=NR) (p<0.05) 1 year: 63.9% (NR) vs. 9.4% (NR) (p<0.05)	Complications of ESI (not specified) in group A: 0/25 patients

Appendix Table N3. Cervicobrachialgia Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Epidural steroid injection vs. Control injection				
Stav 1993	A: Cervical epidural injection with 80 mg methylprednisolone sodium acetate and 1% lidocaine (5 ml) (1-3 injections/patient) (n = 25) B: Posterior neck muscle injection with 80 mg methylprednisolone and 1% lidocaine (5 ml) (same as group A) (1-3 injections/patient) (n = 25)	1 week, 12 months: (84% f/u; 42/50) A vs. B: 100% (25/25) vs. 68% (17/25) (NOTE: 8 patients excluded from group B after beginning litigation of insurance claims during the f/u period)	NR	NR

APPENDIX O. Cervical Disc Herniation With or Without Radiculopathy: RCT Study Characteristics and Results

Appendix Table O1. Disc Herniation With or Without Radiculopathy Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Epidural steroid injection vs. Control injection								
Manchikanti 2013 (A Randomized, Double-Blind) Manchikanti 2012 (Management of Chronic)	N = 120	Inclusion: Patients ≥18 years with chronic cervical disc herniation with or without radiculitis: chronic (≥6 months) function-limiting neck and upper extremity pain duration; previous use of conservative medical management including drug therapy, physical therapy and structured exercise programs. Radiologic investigations (CT and/or MRI) were performed prior to enrollment; it is implied but not explicitly stated that evidence of disc herniation was required on imaging for inclusion. Exclusion: patients with cervical spine surgery, radiculitis secondary to spinal stenosis, discogenic pain without disc herniation, uncontrollable or unstable opioid use, uncontrolled psychiatric disorders, and uncontrolled medical illness, any condition that could interfere with the	A: Cervical interlaminar epidural injection with 6 mg (1 mL) nonparticulate betamethasone plus 4 mL 0.5% lidocaine (n=60) B: Cervical interlaminar epidural injections with 5 mL 0.5% lidocaine (n=60)	Levels: C5-C6: 12% C6-C7: 60% C7-T1: 28% Repeat injections provided based on response to prior injections, based on increased levels of pain with deterioration of functional status and pain relief to below 50% Average number of procedures: ≤1 year: 3.4 ± 1.3 (n=60) vs. 3.6 ± 1.2 (n=60) ≤2 years: 5.3 ± 2.7 (n=60) vs. 5.6 ± 2.7 (n=60)	Fluoroscopic guidance with contrast	Continuation of drug therapy with opioids or nonopioid analgesics, therapeutic exercise program, normal activities, and work.	A vs. B: Male: 42% (25/60) vs. 47% (28/60) (p=0.51) Age (mean ± SD): 45.6 ± 10.4 vs. 46.2 ± 10.3, p = 0.738 Weight (mean ± SD), units NR: 168.1 ± 35.2 vs. 208.9 ± 53.3, p < 0.001 Disc herniation:: C3/4: 13% (8/60) vs. 13% (8/60) C4/5: 20% (12/60) vs. 30% (18/60) C5/6: 60% (36/60) vs. 50% (30/60) C6/7: 47% (28/60) vs. 40% (24/60) C7/T1: 12% (7/60) vs. 10% (6/60) Duration of Pain (mean months ± SD): 91.9 ± 94.5 vs. 118.3 ± 98.6, p = 0.137 Onset of pain Gradual: 52% (31/60) vs. 53% (32/60) Injury: 48% (29/60) vs. 47% (28/60), p = 0.855 Neck pain distribution: Neck pain only: 17% (10/60) vs. 15% (9/60) Neck pain worse than upper extremity: 55% (33/60) vs. 57% (34/60) Upper extremity worse than neck pain: 7% (4/60) vs. 8% (5/60) Both equal: 21% (23/60) vs. 20%	No external funding

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		interpretation of the outcome assessment (pregnancy, lactation, history of adverse reactions to local anesthetic or steroids)					(12/60) Baseline NRS (mean ± SD): 7.9 ± 0.9 vs. 7.9 ± 1.0, P = 1.000 Baseline NDI (mean ± SD): 29.2 ± 6.1 vs. 29.6 ± 5.3, p = 0.678	

Appendix Table O2. Disc Herniation With or Without Radiculopathy Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injection vs. Control injection							
Manchikanti 2013 (A Randomized, Double-Blind) Manchikanti 2012 (Management of Chronic)	A: Cervical interlaminar epidural injection with 6 mg (1 mL) nonparticulate betamethasone plus 4 mL 0.5% lidocaine (n=60) B: Cervical interlaminar epidural injections with 5 mL 0.5% lidocaine (n=60)	3, 6 months: NR but no less than that reported for 24 months 24 months: 90% (54/60) vs. 92% (55/60)	A vs. B Pain NRS (mean ± SD) Baseline: 7.9 ± 0.9 (n = 60) vs. 7.9 ± 1.0 (n = 60) 3 months: 3.8 ± 1.4 (n = 60) vs. 3.7 ± 1.4 (n = 60) 6 months: 3.9 ± 1.5 (n = 60) vs. 3.5 ± 1.4 (n = 60) 24 months: 3.8 ± 1.7 (n = 60) vs. 3.8 ± 1.6 (n = 60) Significant pain relief (≥50% NRS) from baseline (% patients) 3 months: 75% (45/60) vs. 85% (51/60) 6 months: 73% (44/60) vs. 83% (50/60) 24 months: 68% (41/60) vs. 72% (43/60) Average time per procedure with ≥50% pain relief (mean weeks ± SD) For initial 2 procedures: 6.8 ± 7.9 (n=NR) vs. 8.8 ± 8.0 (n=NR) After initial 2 procedures: 12.3 ± 3.5 (n=NR) vs. 13.1 ± 6.6 (n=NR) Overall: 11.8 ± 10.6 (n=60) vs. 12.6 ± 10.9 (n=60) Total time with ≥50% pain relief (mean weeks ± SD)	A vs. B NDI (mean ± SD) Baseline: 29.2 ± 6.1 (n = 60) vs. 29.6 ± 5.3 (n = 60) 3 months: 15.6 ± 6.3 (n = 60) vs. 14.7 ± 5.5 (n = 60) 6 months: 15.3 ± 7.0 (n = 60) vs. 13.8 ± 5.4 (n = 60) 24 months: 14.3 ± 6.9 (n = 60) vs. 13.7 ± 5.7 (n = 60) Significant reduction (≥50%) in NDI (% patients) 3 months: 70% (42/60) vs. 85% (51/60) 6 months: 73% (44/60) vs. 83% (50/60) 24 months: 70% (42/60) vs. 73% (44/60) "Success" (≥50% improvement in both NRS and NDI) (% patients) 3 months: NR 6 months: 73% (44/60) vs. 82% (49/60) 24 months: 68% (48/60) vs. 72% (43/60)	NR	A vs. B Opioid intake (time period NR), morphine equivalence mg (mean ± SD) Baseline: 36.1 (n = 60) vs. 57.0 ± 46 (n = 60) 3 months: 35.2 ± 16.3 (n = 60) vs. 34.4 ± 21.7 (n = 60) (MD 0.8, 95% CI -6.1 to 7.7, p=0.820) 6 months: 35.5 ± 16.3 (n = 60) vs. 33.0 ± 22.3 (n = 60) (MD 2.5, 95% CI -4.6 to 9.6, p=0.485) 24 months: 31.3 ± 19.1 (n = 60) vs. 35.8 ± 24.9 (n = 60) (MD -4.5, 95% CI -12.5 to 3.5, p=0.269)	Adverse events not stratified by group Subarachnoid punctures: 0.3% (2/654) Intravascular penetrations: 0.6% (4/654) Nerve root irritations: 0.8% (5/654) Postoperative headache following subarachnoid punctures: 0% (0/654) Soreness lasting 1 week 0.2% (1/654) No long-term sequelae reported for any of the above events.

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			24 months 62.1 ± 38.4 vs. 69.6 ± 35.0				

Appendix Table O3. Disc Herniation With or Without Radiculopathy Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Intra-articular steroid injection vs. Conservative Care				
Manchikanti 2013 (A Randomized, Double-Blind) Manchikanti 2012 (Management of Chronic)	A: Cervical interlaminar epidural injection with 6 mg (1 mL) nonparticulate betamethasone plus 4 mL 0.5% lidocaine (n=60) B: Cervical interlaminar epidural injections with 5 mL 0.5% lidocaine (n=60)	3, 6 months: NR 12 months: 93% (56/60) vs. 98% (58/60) 18 months: NR 24 months: 90% (54/60) vs. 92% (55/60)	NR	NR

APPENDIX P. Cervical Nonradicular Neck Pain: RCT Study Characteristics and Results

Appendix Table P1. Nonradicular Neck Pain Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Epidural steroid injection vs. Control injection								
Manchikanti 2014 (Two-year) Manchikanti 2012 (Fluoroscopic cervical)	N = 120	Inclusion: Patients over age 18 with chronic function-limiting neck pain with or without upper extremity pain of ≥6 months; without disc herniation, radiculitis, spinal stenosis, spondylosis, and those judged to have negative cervical facet joint pain by means of controlled, comparative anesthetic blocks; failure of conservative medical management including drug therapy, physical therapy and structured exercise programs. Radiologic investigations performed prior to enrollment but no specific pathology required for inclusion. Exclusion: Patients with cervical disc herniation, radiculitis, spinal stenosis, significant spondylosis, uncontrollable or unstable opioid use, uncontrolled psychiatric disorders, uncontrolled medical illness (acute or chronic), medical conditions that could interfere with outcome assessment,	A: Cervical interlaminar epidural injection with 6 mg (1 mL) nonparticulate betamethasone plus 4 mL 0.5% lidocaine (n=60) B: Cervical interlaminar epidural injections with 5 mL 0.5% lidocaine (n=60)	Levels: C5-C6: 9% C6-C7: 58% C7-T1: 33% Repeat injections were provided when increased levels of pain were reported along with the deterioration of pain relief, along with the deterioration of functional status to below 50%. Number of injections (mean ± SD) (A vs. B): ≤1 year: 3.6 ± 1.0 vs. 3.6 ± 1.1 ≤2 years: 5.8 ± 2.3 vs. 5.7 ± 2.4	Fluoroscopic guidance with contrast	All patients provided with structured exercise program along with continuation of conservative management with drug therapy plus continuation of work (if they were already working).	A vs. B: Male: 32% (19/60) vs. 25% (15/60), p = 0.544 Age (mean years ± SD): 41.8 ± 11.6 vs. 44.5 ± 12.6, p = 0.235 Weight (units NR, mean ± SD): 164.7 ± 39.3 vs 183.6 ± 57.5, p = 0.038 Duration of Pain (mean months ± SD): 95.8 ± 95.7 vs. 100.3 ± 94.3, p = 0.794 Onset of Pain Gradual: 47% (28/60) vs. 58% (35/60) Injury: 53% (32/60) vs. 42% (25/60), p = 0.273 Neck pain distribution: Neck pain only: 43% (26/60) vs. 33% (20/60) Neck pain worse than upper extremity: 37% (22/60) vs. 45% (27/60) Upper extremity worse than neck pain: 2% (1/60) vs. 3% (2/60) Both equal: 18% (11/60) vs. 18% (11/60) Baseline NRS (mean ± SD): 7.6 ± 0.8 vs. 7.9 ± 0.9, p = 0.074 Baseline NDI (mean ± SD): 28.6 ± 7.2 vs. 30.2	No external funding

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		pregnant or lactating women, history of or potential for adverse reaction(s) to injectates.					± 4.7, p = 0.164	

Appendix Table P2. Nonradicular Neck Pain Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injection vs. Control injection							
Manchikanti 2014 (Two-year) Manchikanti 2012 (Fluoroscopic cervical)	A: Cervical interlaminar epidural injection with 6 mg (1 mL) nonparticulate betamethasone plus 4 mL 0.5% lidocaine (n=60) B: Cervical interlaminar epidural injections with 5 mL 0.5% lidocaine (n=60)	3, 6 months: NR but no less than that reported for 24 months 24 months: 88% (53/60) vs 83% (50/60)	A vs. B: Numeric Pain Rating Score (mean ± SD): Baseline: 7.6 ± 0.8 (n=60) vs. 7.9 ± 0.9 (n=60) (p=0.074) 3 months: 3.3 ± 1.0 (n=60) vs. 3.7 ± 1.4 (n=60) (p=0.055) 6 months: 3.5 ± 1.3 (n=60) vs. 3.6 ± 1.4 (n=60) (p=0.679) 24 months: 3.5 ± 1.4 (n=60) vs. 3.7 ± 1.6 (n=60) (p=NR) Significant (≥50%) relief from baseline based on NRS (% patients): 3 months: 85% (51/60) vs. 73% (44/60) 6 months: 77% (46/60) vs. 78% (47/60) 24 months: 75% (45/60) vs. 75% (45/60) Average time with ≥50% pain relief (in weeks) (mean ± SD): Per procedure for initial two procedures: 8.2 ± 7.0 (117 procedures) vs. 8.6 ± 5.7 (118 procedures) (MD -0.4 (95% CI -2.0 to 1.2), p=0.63)† Per procedure after initial two procedures:	A vs. B: Neck Disability Index (mean ± SD): Baseline: 28.6 ± 7.2 (n=60) vs. 30.2 ± 4.7 (n=60) (p=0.164) 3 months: 13.7 ± 5.4 (n=60) vs. 15.5 ± 6.0 (n=60) (p=0.082) 6 months: 14.2 ± 6.1 (n=60) vs. 15.0 ± 5.6 (n=60) (p=0.464) 24 months: 13.8 ± 6.5 (n=60) vs. 14.1 ± 5.7 (n=60) Significant (≥50%) relief from baseline based on NDI (% patients): 3 months: 78% (47/60) vs. 70% (42/60) 6 months: 73% (44/60) vs. 68% (41/60) 24 months: 70% (42/60) vs. 75% (45/60) "Success" (≥50% improvement in both NRS and NDI) (% patients) 3 months: 77% (46/60) vs. 68% (41/60)	NR	A vs. B: Opioid intake (time period NR), morphine equivalence mg (mean ± SD) Baseline: 39.1 ± 27.1 (n=60) vs. 47.0 ± 35.0 (n=60) (p=0.171) 3 months: 33.7 ± 22.0 (n=60) vs. 37.1 vs. 21.2 (p=0.386) 6 months: 33.8 ± 22.0 (n=60) vs. 36.8 ± 21.0 (n=60) (p=0.451) 24 months: 34.5 ± 23.5 (n=60) vs. 36.9 ± 20.9 (n=60) (p=0.556)†	Adverse events not stratified by group Subarachnoid puncture: 0.9% (6/688) injections Intravascular penetrations: 1.5% (10/688) injections Nerve root irritation: 0.4% (3/688) injections Postoperative headache following subarachnoid puntures: 0% No long-term sequelae observed for any of the above events

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			11.5 ± 4.5 (100 procedures) vs. 13.1 ± 7.0 (99 procedures) (MD -1.6 (95% CI -3.2 to 0.04), p=0.0563)† Per procedure: 11.7 ± 9.1 (n=60) vs. 12.2 ± 8.8 (n=60) (MD -0.5 (95% CI -3.7 to 2.7), p=0.760)† Total time with ≥50% pain relief (in weeks) (mean ± SD): ≥24 months: 68.3 ± 33.6 (n=60) vs. 66.5 ± 35.0 (n=60) (MD 1.8 (95% CI -10.6 to 14.2), p=0.774)† †calculated	6 months: 73% (44/60) vs. 67% (40/60) 24 months: 70% (42/60) vs. 73% (44/60)			

Appendix Table P3. Nonradicular Neck Pain Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Epidural steroid injection vs. Control injection				
Manchikanti 2014 (Two-year) Manchikanti 2012 (Fluoroscopic cervical)	**A: Cervical interlaminar epidural injection with 6 mg (1 mL) nonparticulate betamethasone plus 4 mL 0.5% lidocaine (n=60)** **B: Cervical interlaminar epidural injections with 5 mL 0.5% lidocaine (n=60)**	3, 6 months: NR but no less than that for 24 months 24 months: 88% (53/60) vs 83% (50/60)	NR	NR

APPENDIX Q. Cervical Spinal Stenosis: RCT Study Characteristics and Results

Appendix Table Q1. Cervical Spinal Stenosis Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Epidural steroid injection vs. Control injection								
Manchikanti 2012 (Fluoroscopic epidural injections)	N = 98	Inclusion: Patients >30 years with a diagnosis of cervical central spinal stenosis with or without foraminal stenosis, history of chronic function-limiting neck and upper extremity pain of at least 6 on a 0-10 pain scale, pain ≥6 months in duration, and failure to improve substantially with conservative management such but not limited to physical therapy, chiropractic manipulation, exercises, drug therapy, and bed rest. Exclusion: Patients with a history of cervical spinal surgery, foraminal stenosis without central stenosis, uncontrollable or unstable opioid use, uncontrolled psychiatric disorders, uncontrolled medical illness (acute or chronic), or conditions that could interfere with the interpretation of the outcome assessments (pregnant or lactating, history of potential for	A: Cervical interlaminar epidural injection with 6 mg nonparticulate betamethasone (1 mL) and 0.5% lidocaine (4 mL) (n randomized = NR; n reported=30) B: Cervical interlaminar epidural injection with 0.5% lidocaine (5 mL) (n randomized = NR; n reported=30)	Epidural entry levels: C5-C6: 10% C6-C7: 52% C7-T1: 38% Repeat injections: when there was increased pain and deteriorating relief below 50%, repeat injections were given. Procedures per year: 3.6 ± 1.2 (n=30) vs. 3.7 ± 1.2 (n=30)	Fluoro-scopic	Patients did not receive bracing, specific PT or OT, or any intervention other than the assigned study intervention. Patients continued exercise programs and their occupation, as well as analgesics (opioid and nonopioid); upon improvement, adjuvants were either stopped or dosages decreased. In some instances, dosages increased.	A vs. B Male: 43% (13/30) vs. 30% (9/30), p = 0.284 Age (mean years ± SD): 49.7 ± 8.9 vs. 49.9 ± 8.5, p = 0.918 Weight (mean units NR ± SD): 170.7 ± 32.7 vs. 196.0 ± 54.2, p = 0.032 Duration or pain (mean months ± SD): 94.3 ± 77.4 vs. 115.2 ± 89.9, p = 0.338 Onset of pain Gradual: 53% (16/30) vs. 60% (18/30) Injury: 47% (14/30) vs. 40% (12/30), p = 0.531 Number of stenosis levels: One Level: 63% (19/30) vs. 53% (16/30) Two Levels: 37% (11/30) vs. 37% (11/30) Three Levels: 0% (0/30) vs. 3.3% (1/30) Four Levels: 0% (0/30) vs. 6.6% (2/30) Pain Ratio Neck pain only: 11% (3/30) vs. 18% (5/30) Neck worse than upper extremity: 54% (15/30) vs. 68% (19/30) Upper extremity worse than neck: 3% (1/30) vs. 7% (2/30), Both equal: 32% (9/30) vs. 7%	No external funding

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		adverse reactions to local anesthetics or steroids).					(2/30), p = 0.531 Neck pain distribution Right: 17% (5/30) vs. 10% (3/30) Left: 10% (3/30) vs. 20% (6/30) Bilateral: 73% (22/30) vs. 70% (21/30), p = 0.467 NRS Score (mean ± SD) 8.0 ± 0.9 vs. 7.9 ± 0.8, p = 0.762 NDI (mean ±SD) 29.2 ± 5.8 vs. 29.2 ± 5.2, p = 0.981 Stenosis Severity per level affected Mild: 44% (18/41) vs. 51% (25/49) Moderate: 37% (15/41) vs. 39% (19/49) Severe: 20% (8/41) vs. 10% (5/49)	

Appendix Table Q2. Cervical Spinal Stenosis Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injection vs. Control injection							
Manchikanti 2012 (Fluoroscopic epidural injections)	A: Cervical interlaminar epidural injection with 6 mg nonparticulate betamethasone (1 mL) and 0.5% lidocaine (4 mL) (n randomized = NR; n reported=30) B: Cervical interlaminar epidural injection with 0.5% lidocaine (5 mL) (n randomized = NR; n reported=30)	3, 6 months: NR but ≥ than that at 12 months 12 months: 56% (55/98) (NR by treatment group)	NRS Score (mean ± SD) Baseline 8.0 ± 0.9 (n = 30) vs. 7.9 ± 0.8 (n = 30), p = 0.862 3 months 3.5 ± 0.9 (n = 30) vs. 3.7 ± 1.2 (n = 30), p = 0.625 6 months 3.7 ± 1.0 (n = 30) vs. 3.4 ± 0.9 (n = 30), p = 0.353 12 months 3.8 ± 1.2 (n = 30) vs. 3.6 ± 1.1 (n = 30), p = 0.434 Significant Relief (≤50% NRS of baseline) 3 months 87% (26/30) vs. 87% (26/30) 6 months 80% (24/30) vs. 90% (27/30) 12 months 70% (21/30) vs. 73% (22/30) Average Relief per procedure in weeks (mean ± SD) Overall 8.6 ± 3.6 (n = 30) vs. 11.3 ± 5.8 (n = 30) After initial 2 procedures 13.6 ± 4.7 (n = 30) vs. 13.7 ± 8.7 (n = 30) Total relief in weeks (mean ± SD)	NDI Score (mean ± SD) Baseline 29.2 ± 5.8 (n = 30) vs. 29.2 ± 5.2 (n = 30), p = 0.981 3 months 13.6 ± 3.8 (n = 30) vs. 15.1 ± 5.8 (n = 30), p = 0.219 6 months 13.5 ± 4.6 (n = 30) vs. 13.2 ± 4.8 (n = 30), p = 0.826 12 months 13.9 ± 4.5 (n = 30) vs. 13.2 ± 5.4 (n = 30), p = 0.824 Significant improvement (NDI score ≤50% of baseline) 3 months 87% (26/30) vs. 77% (23/30) 6 months 83% (25/30) vs. 87% (26/30) 12 months 70% (21/30) vs. 77% (23/30) Composite: Reduction (≥50%) in average NRS and NDI from baseline 3 months 87% (26/30) vs. 77% (23/30) 6 months 80% (24/30) vs. 87% (26/30) 12 months 70% (21/30) vs. 73% (22/30)	NR	Opioid intake, morphine equivalence mg (mean ± SD) Baseline 66.07 ± 72.62 (n = 30) vs. 51.37 ± 31.30 (n = 30), p = 0.313 3 months 49.03 ± 70.40 (n = 30) vs. 45.63 ± 38.29 (n = 30), p = 0.817 6 months 48.70 ± 70.52 (n = 30) vs. 45.13 ± 38.40 (n = 30), p = 0.809 12 months 48.70 ± 70.52 (n = 30) vs. 46.13 ± 37.56 (n = 30), p = 0.861	Subarachnoid punctures 0.9% (2/214) Intravascular entry 0.5% (1/214) Soreness lasting one week or more 0.5% (1/214) Postoperative headache 0% (0/2 patients after subarachnoid puncture)

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			12 months 30.4 ± 16.1 (n = 30) vs. 40.8 ± 16.36 (n = 30)				

Appendix Table Q3. Cervical Spinal Stenosis Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Epidural steroid injection vs. Control injection				
Manchikanti 2012 (Fluoroscopic epidural injections)	A: Cervical interlaminar epidural injection with 6 mg nonparticulate betamethasone (1 mL) and 0.5% lidocaine (4 mL) (n randomized = NR; n reported=30) B: Cervical interlaminar epidural injection with 0.5% lidocaine (5 mL) (n randomized = NR; n reported=30)	3, 6 months: NR but ≥ than that at 12 months 12 months: 56% (55/98) (NR by treatment group)	NR	NR

APPENDIX R. Cervical Failed Surgery Syndrome: RCT Study Characteristics and Results

Appendix Table R1. Cervical Failed Surgery Syndrome Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Epidural steroid injection vs. Control injection								
Manchikanti 2012 (Fluoroscopic Cervical…)	N=102	Inclusion: Patients ≥18 years with cervical postsurgery syndrome with surgery performed ≥1 year before enrollment; a history of chronic function-limiting neck and upper extremity pain ≥6 months duration Exclusion: Patients without previous cervical spine surgery, uncontrollable or unstable opioid use, uncontrolled psychiatric disorders, uncontrolled medical illness either acute or chronic, any conditions that could interfere with the interpretation of the outcome assessments, pregnant and	A: Cervical interlaminar epidural injection with 6 mg nonparticulate betamethasone (1 mL) and 0.5% lidocaine (4 mL) (n randomized = NR; n reported=28) B: Cervical interlaminar epidural injection with 0.5% lidocaine (5 mL) (n randomized = NR; n reported=28)	Levels C5-C6: 11% C6-C7: 57% C7-T1: 32% Repeat injections provided based on response to prior injections, based on increased levels of pain with deterioration of functional status and pain relief to below 50% Average number of procedures (mean, SD): 12 months: 4.0 ± 1.1 (n = 28) vs. 3.7 ± 0.9 (n = 28)	Fluoroscopic guidance with contrast	Continuation of drug therapy with opioids or nonopioid analgesics, some involved in a therapeutic exercise program. If patients improved significantly, medications were stopped or dosages were decreased. Some dosages increased based on necessity. Previously prescribed exercise programs and work were continued. No additional PT, OT, bracing, or other interventions were offered other than the study intervention.	A vs. B Male: 68% (19/28) vs. 36% (10/28), p = 0.016 Age (mean ± SD): 49.0 ± 10.3 vs. 48.3 ± 9.9 p = 0.782 Weight (mean units NR ± SD): 179.2 ± 39.9 vs. 200.0 ± 50.6, p = 0.093 Height (mean units NR ± SD): 68.2 ± 5.0 vs. 65.6 ± 4.2, p = 0.03 Duration of Pain (mean months ± SD): 111.2 ± 73.9 vs. 122.3 ± 77.7, p = 0.585 Onset of pain Gradual: 36% (10/28) vs. 50% (14/28) Injury: 64% (18/28) vs. 50% (14/28), p = 0.280 Neck pain distribution Neck pain only: 14% (4/28) vs. 14% (4.28) Neck pain worse: 53% (15/28) vs. 50% (14/28) Upper extremity worse: 4% (1/28) vs. 4% (1/28) Both equal: 29% (8/28) vs. 32% (9/29), p = 0.993 Surgical interventions Anterior: 89% (25/28) vs. 86% (24/28), p =	No external funding

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		lactating women, and patients with a history or potential for adverse reaction(s) to local anesthetics or steroid					1.000 Posterior: 4% (1/28) vs. 14% (4/28), p = 0.352 Anterior and posterior: 7% (2/28) vs. 7% (2/28), p = 0.570 Number of surgeries 1: 79% (22/28) vs. 86% (24/28) 2: 18% (5/28) vs. 11% (3/28) >2: 3% (1/28) vs. 3% (1/28), p = 0.485 Baseline NRS (mean ± SD): 7.8 ± 0.9 vs. 8.0 ± 1.23, p = 0.534 Baseline NDI (mean ± SD): 28.8 ± 4.0 vs. 30.0 ± 5.0, p = 0.289	

Appendix Table R2. Cervical Failed Surgery Syndrome Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Epidural steroid injection vs. Control injection							
Manchikanti 2012 (Fluoroscopic Cervical Interlminar…)	A: Cervical interlaminar epidural injection with 6 mg nonparticulate betamethasone (1 mL) and 0.5% lidocaine (4 mL) (n randomized = NR; n reported=28) B: Cervical interlaminar epidural injection with 0.5% lidocaine (5 mL) (n randomized = NR; n reported=28)	3,6 months: NR but not less than that at 12 months 12 months: 48% (49/102) (NR by treatment group)	NRS Score (mean ± SD) Baseline 7.8 ± 0.9 (n = 28) vs. 8.0 ± 1.23 (n = 28), p = 0.534 3 months 4.0 ± 1.2 (n = 28) vs. 3.7 ± 1.2 (n = 28), p = 0.369 6 months 3.8 ± 1.1 (n = 28) vs. 3.7 ± 1.1 (n = 28), p = 0.714 12 months 3.9 ± 1.4 (n = 28) vs. 3.6 ± 1.1 (n = 28), p = 0.465 Pain relief (≥50% NRS reduction) 3 months 71% (20/28) vs. 79% (22/28) 6 months 75% (21/28) vs. 71% (20/28) 12 months 68% (19/28) vs. 71% (20/28) Average pain relief (≥50% NRS) (mean weeks ± SD) Per procedure 9.4 ± 4.9 (n = 28) vs. 8.4 ± 3.8 (n = 28) (MD 1.0, 95% CI -1.3 to 3.3, p=0.397) Per procedure ≥3rd procedure 14.8 ± 11.8 (n = 25) vs. 11.8 ± 4.4 (n = 24) (MD 3.0, 95% CI -2.2 to 8.2, p=0.248) Total time of relief (mean weeks ± SD)	Neck Disability Index (mean ± SD) Baseline 28.8 ± 4.0 (n = 28) vs. 30.0 ± 5.0 (n = 28), p = 0.289 3 months 14.8 ± 5.7 (n = 28) vs. 15.9 ± 5.3 (n = 28), p = 0.451 6 months 14.6 ± 5.8 (n = 28) vs. 15.3 ± 5.0 (n = 28), p = 0.656 12 months 15.0 ± 5.6 (n = 28) vs. 15.0 ± 4.7 (n = 28), p = 0.998 NDI Improvement ≥50% 3 months 75% (21/28) vs. 71% (20/28) 6 months 75% (21/28) vs. 68% (19/28) 12 months 64% (18/28) vs. 71% (20/28) Reduction (≥50%) in average NRS and NDI from baseline 3 months 68% (19/28) vs. 68%	NR	Opioid Intake, morphine equivalence in mg (mean ± SD) Baseline 90.32 ± 104.54 (n = 28) vs. 52.21 (n = 28) ± 42.34, p = 0.079 3 months 64.25 ± 56.01 (n = 28) vs. 44.68 ± 42.91 (n = 28), p = 0.148 6 months 63.54 ± 56.20 (n = 28) vs. 44.68 ± 42.91 (n = 28), p = 0.164 12 months 63.54 ± 56.20 (n = 28) vs. 53.74 ± 51.00 (n = 28), p = 0.502	Adverse events not stratified by treatment arm Subarachnoid puncture: 0.9% (2/215) Intravascular entry: 0.9% (2/215) Headaches: 0.0% (0/215) No other complications

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			12 months 37.8 ± 18.2 (n = 28) vs. 33.2 ± 17.4 (n = 28) (MD 4.6, 95% CI -4.9 to 14.1, p=0.338)	(19/28) 6 months 71% (20/28) vs. 64% (18/28) 12 months 64% (18/28) vs. 71% (20/28)			

Appendix Table R3. Cervical Failed Surgery Syndrome Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Epidural steroid injection vs. Control injection				
Manchikanti 2012 (Fluoroscopic Cervical Interlminar…)	A: Cervical interlaminar epidural injection with 6 mg nonparticulate betamethasone (1 mL) and 0.5% lidocaine (4 mL) (n randomized = NR; n reported=28) B: Cervical interlaminar epidural injection with 0.5% lidocaine (5 mL) (n randomized = NR; n reported=28)	3,6 months: NR but no less than 12 months 12 months: 93% (26/28) vs. 82% (23/28)	NR	NR

APPENDIX S. Cervical Facet Joint Pain: RCT Study Characteristics and Results

Appendix Table S1. Cervical Facet Joint Pain Study and Patient Characteristics

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
Intra-articular steroid injection vs. control injection								
Barnsley 1994	N = 42	Inclusion: Patients ≥18 years with chronic (≥ 3 months) neck pain attributed to a motor vehicle accident, "complete" or "definite" relief of pain on two separate diagnostic blocks, longer period of pain relief with bupivacaine than lidocaine block; OR an inordinately prolonged response to diagnostic block(s) (n = 6 patients) Exclusion: NR	A: Intra-articular (medial branch) injection with betamethasone (5.7 mg in 1.0 ml) (n randomized NR; n reported = 21) B: Intra-articular (medial branch) injection with bupivacaine (0.5% in 1.0 ml) (n randomized NR; n reported = 20)	Number of levels: NR Repeat injections: none (patients received 1 injection only)	Fluoroscopic guidance with contrast	No co-interventions were required; continuation of medical and physical therapies; surgical and neurolytic treatments were prohibited	A vs. B: Age (mean ± SD): 44.4 ± 11.4 vs. 41.5 ± Male: 38% (8/21) vs. 40% (8/20) Duration of pain in months (median (IQR)): 52 (33 to 60.5) vs. 46.5 (30.5 to 72) Baseline VAS (mean ± SD): 49 ± 21 (n=21) vs. 49 ± 25 (n=20) Baseline McGill Pain (pain intensity) (median (IQR)): 30.7 (19.9 to 40.6) (n=21) vs. 28.3 (20.9 to 43.1) (n=20) Onset of pain: Motor vehicle injury: 100% (21/21) vs. 100% (20/20)	Grant received from Motor Accidents Authority of New South Wales, Australia
Manchikanti 2010 (Comparative outcomes) Manchikanti 2008 (Cervical medial)	N = 120	Inclusion: Patients ≥18 years with a history of chronic function-limiting neck pain of at least 6 months duration; positive results with controlled diagnostic cervical facet joint nerve blocks with at least 80% concordant pain relief and the ability to perform previously	A: Intra-articular (medial branch) injection of 0.15 mg non-particulate betamethasone and 0.25% bupivacaine with or without Sarapin (total volume 0.5-1 mL)	Levels injected: NR Repeat injections offered when reported pain levels deteriorated below 50%, with initial report of significant pain relief of 50%, or	Fluoroscopic	Continuations of opioid and nonopioid analgesics, adjuvant analgesics, and exercise programs. Adjustments	A vs. B: Age (mean ± SD): 43 ± 14 vs. 46 ± 13 Male: 20% (12/60) vs. 32% (19/60) Weight (mean ± SD: 169 ± 42 vs. 180 ± 55 Height in inches (mean ± SD): 65 ± 3.7	No external funding

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		painful movements. (Diagnostic cervical medial branch blocks consisted of an injection with 0.5 mL of 1% lidocaine, and a second injection of 0.5 mL of 0.25% bupivacaine on a separate occasion- usually 3 to 4 weeks after the first injection if positive results with lidocaine block. All performed with fluoroscopic guidance.) Exclusion: Disc herniation with radicular pain, symptomatic spinal stenosis, surgical interventions of the cervical spine within the last 3 months, uncontrolled major depression or psychiatric disorders, heavy opioid usage (morphine equivalent of 300 mg), acute or uncontrolled medical illness, chronic severe conditions that could interfere with the interpretations of the outcome assessments, women who were pregnant or lactating, patients unable to be positioned in a prone position, patients with a history of adverse reactions to local anesthetics, Sarapin, or steroids.	(n=60) B: Intra-articular (medial branch) injection 0.25% bupivacaine with or without Sarapin (total volume 0.5-1 mL) (n=60)	more after the previous block. Number of injections (mean ± SD): 5.7 ± 2.1 (n=60) vs. 5.7 ± 2.4 (n=60)		in medical therapy were carried out based on response, and physical and functional needs.	vs. 66 ± 3.9 Duration of pain in months (mean ± SD): 87 ± 104 vs. 120 ± 122 Baseline NRS (mean ± SD): 8.2 ± 1.1 (n = 60) vs. 8.2 ± 0.8 (n = 60) Baseline NDI (mean ± SD): 25.1 ± 5.0 (n = 60) vs. 25.4 ± 5.7 (n = 60) Onset of pain: Gradual: 57% (34/60) vs. 57% (34/60) Sudden: 11% (7/60) vs. 11% (7/60) Worker's comp or motor vehicle injury: 32% (19/60) vs. 32% (19/60) Joints involved*: 2 joints: 48% (58/120) 3 joints: 52% (62/120) 4 joints: 2% (2/120) Bilateral involvement: 73% (88/120) *unclear why the percentage of patients with 2, 3, or 4 joints involved adds up to more than 100%.	
Intra-articular steroid injection vs. Conservative Care								
Park 2012	N= 400	Inclusion: Patients with chronic (>6 months) cervical MPS with referral pain patterns of CFJ syndrome, and positive response (≥80% pain relief for ≥2 hours	A: Cervical bilateral intra-articular injections with triamcinolone (5 mg) + hyaluronidase	A vs. B Number of Levels: 2 (C5/C6 and C6/C7) vs. 0	Anteroposterior and lateral fluoroscopic guidance	Conservative care: exercise regimen and a mixture of 10 mg	A vs. B (after loss to f/u)*: Age (mean): 55.2 ± 20.6 vs. 53.5 ± 19.5 yrs.	NR

RCT	N*	Inclusion & Exclusion Criteria	Interventions	Number of levels Repeat injections	Imaging Guidance	Co-interventions	Patient Characteristics	Funding
		with lidocaine and ≥5 hours with bupivacaine) to controlled comparative diagnostic local anesthetic blocks performed on separate occasions. By definition, MPS patients had at least 3 of the following: trigger points in at least one trapezius muscle, splenius capitis or cervicis, levator scapulae, anterior and medial scalen, intraspinatus muscles; taut bands; referred pain; sensory changes; or local twitch response. Exclusion: History of radiating pain in the shoulder and upper extremities, cervical radiculopathy on electrodiagnostic examination, herniated nucleus pulposus and spinal stenosis on magnetic resonance imaging and computed tomography, and previous neck trauma from traffic accident or fall to exclude herniated nucleus pulposus, spinal stenosis, and whiplash-associated disorders.	(187.5 IU) + 1% lidocaine (0.5 ml) (n=200) B: No injections (n=200)	Repeat injections: No additional steroid injections offered.		codeine-containing weak opioid, 250 mg actetaminophen, 200 mg ibuprofen, and 1 mg tizanidine Additional non-steroidal injections were offered to group A only: injection of 1 mL 1% lidocaine to remaining trigger points on first two post-treatment visit; injection of Botox (50 IU) to remaining trigger points on each trapezius muscle.	Male: 30.0% (46/155) vs. 35.8% (54/151) Duration of symptoms: Mean NR; 6 mos to 1 yr: 16.7% vs. 21.2% 1 yr to 2 yrs: 12.3% vs. 12.6% >2 yrs: 70.9% vs. 66.2% Comorbid tension-type headache: 61.2% (95/155) vs. 59.6% (90/151) Baseline pain: NR Baseline function: NR *Reported out of patients who completed f/u (306), NOT total patients enlisted (400)	

Appendix Table S2. Cervical Facet Joint Pain Efficacy and Safety Outcomes

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
Intra-articular steroid injection vs. control injection							
Barnsley 1994	A: Intra-articular (medial branch) injection with betamethasone (5.7 mg in 1.0 ml) (n=21) B: Intra-articular (medial branch) injection with bupivacaine (0.5% in 1.0 ml) (n=20)	2.7 months (98% (41/42)) (NR by treatment group)	A vs. B: Significant pain relief (≥50% reduction from baseline VAS) 2.7 months (80 days) ~10% vs. ~11% (data approximated from graph) Time to return to ≤50% baseline pain (days) (median) 3 vs. 3.5 (p=0.42)	NR	NR	NR	Transient facial flushing (2/41), temporary exacerbation of usual when analgesic effect worn off (NR), major adverse events (not specified): NR
Manchikanti 2010 (Comparative outcomes) Manchikanti 2008 (Cervical medial)	A: Medial branch injection of 0.15 mg non-particulate betamethasone and 0.25% bupivacaine with or without Sarapin (total volume 0.5-1 mL) (n=60) B: Medial branch injection 0.25% bupivacaine with or without Sarapin (total volume 0.5-1 mL) (n=60)	3 months: 98% (59/60) vs. 93% (56/60) 6 months: 95% (57/60) vs. 90% (54/60) 24 months: NR	A vs. B: NRS Score (mean ± SD) Baseline 8.2 ± 1.1 (n = 60) vs. 8.2 ± 0.8 (n = 60) 3 months 3.7 ± 0.9 (n = 60) vs. 3.8 ± 1.0 (n = 60) 6 months 3.4 ± 0.7 (n = 60) vs. 3.6 ± 1.1 (n = 60) 24 months 3.2 ± 1.0 (n = 60) vs. 3.5 ± 1.1 (n = 60) Significant pain relief (≥50% reduction from baseline NRS) 6 months 95% (57/60) vs. 87% (52/60) 24 months 93% (56/60) vs. 85% (51/60) Total pain relief (≥50% reduction from baseline NRS) in weeks (mean ± SD) 24 months 89 ± 21.1 (n=60) vs. 83 ± 27.5 (n=60) (MD 6.0, 95% CI -2.9 to 14.9, p=0.183)	A vs. B: Score (mean ± SD) Baseline 25.1 ± 5.0 (n = 60) vs. 25.4 ± 5.7 (n = 60) 3 months 12.2 ± 4.6 (n = 60) vs. 12.0 ± 5.2 (n = 60) 6 months 11.6 ± 4.2 (n = 60) vs. 12.0 ± 5.6 (n = 60) 24 months 11.0 ± 4.7 (n = 60) vs. 11.6 ± 4.4 (n = 60) Significant functional status	NR	A vs. B: Intake in morphine equivalence mg (mean ± SD) Baseline 44 ± 48.2 (n = 60) vs. 45 ± 43.3 (n = 60), p = 0.852 24 months 35 ± 38.1 (n = 60) vs. 39 ± 43.1 (n = 60), p = 0.619	No adverse events reported, including: Infection 0% (0/120) Nerve Root or Spinal Trauma 0% (0/120)

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Pain	Function	QoL Patient satisfaction	Opioid use Surgery Other outcomes	Adverse events
			Average pain relief (≥50% reduction from baseline NRS) per procedure in weeks (mean ± SD) <u>24 months</u> 19 ± 14.8 (n=60) vs. 17 ± 9.0 (n=60) (MD 2.0, 95% CI -2.4 to 6.4, p=0.373)	improvement (≥50% from baseline NDI) <u>6 months</u> 65% (39/60) vs. 60% (36/60) <u>24 months</u> 75% (45/60) vs. 70% (42/60)			
Intra-articular steroid injection vs. Conservative Care							
Park 2012	A: Cervical bilateral intra-articular injections with triamcinolone (5 mg) + hyaluronidase (187.5 IU) + 1% lidocaine (0.5 ml) (n=200) B: No injections (n=200)	12 months 76.5% (306/400) A vs. B: 75.5% (155/200) vs. 77.5% (151/200)	A vs. B: NRS (0 to 10) (data estimated from graph) <u>Baseline</u> ~6.6 (n=155) vs. ~6.4 (n=151) <u>3 months</u> ~2.9 (n=155) vs. ~5.0 (n=151), p<0.05 <u>6 months</u> ~2.7 (n=155) vs. ~4.8 (n=151), p<0.05 <u>12 months</u> ~2.6 (n=155) vs. ~4.8 (n=151), p<0.05 Tension headache (estimated % of patients; n=NR because data estimated from graph) <u>Baseline</u> ~35% vs. ~30% <u>3 months</u> ~16% vs. ~24 % <u>6 months</u> ~9% vs. ~21% <u>12 months</u> ~3% vs. ~19% Symptom-free period after treatment until end of study (months): 7.2 (n=155) vs. 4.2 (n=151) months (p=NR)	NR	NR	NR	"There were no adverse events reported during the study."

Appendix Table S3. Cervical Facet Joint Pain Differential Efficacy and Safety

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
Intra-articular steroid injection vs. control injection				
Manchikanti 2010 (Comparative outcomes) Manchikanti 2008 (Cervical medial)	A: Medial branch injection of 0.15 mg non-particulate betamethasone and 0.25% bupivacaine with or without Sarapin (total volume 0.5-1 mL) (n=60) B: Medial branch injection 0.25% bupivacaine with or without Sarapin (total volume 0.5-1 mL) (n=60)	3 months: 98% (59/60) vs. 93% (56/60) 6 months: 95% (57/60) vs. 90% (54/60) 24 months: NR	NR	NR
Barnsley 1994	A: Intra-articular (medial branch) injection with betamethasone (5.7 mg in 1.0 ml) (n=21) B: Intra-articular (medial branch) injection with bupivacaine (0.5% in 1.0 ml) (n=20)	2.7 months (98% (41/42)) (NR by treatment group)	NR	NR
Intra-articular steroid injection vs. Conservative Care				
Park 2012	A: Cervical bilateral intra-articular injections with triamcinolone (5 mg) + hyaluronidase (187.5 IU) + 1% lidocaine (0.5 ml) (n=200) B: No injections (n=200)	12 months 76.5% (306/400) A vs. B: 75.5% (155/200) vs. 77.5% (151/200)	A vs. B: Symptom-free period after treatment until end of study (months): No formal test for interaction reported. • Young age group (<45 yrs): 10.2 ± 1.1 (n=35) vs. 5.5 ± 2.1 (n=37) (p=0.0) • Middle age group (45-64 yrs): 6.5 ± 2.8 (n=77) vs. 4.2 ± 1.3 (n=76) (p=0.04) • Elderly age group (>65 yrs): 5.9 ± 2.9 (n=43) vs. 3.1 ± 2.5 (n=38) (p=0.04) NRS (0-10) No formal test for interaction reported. <u>Baseline</u> Young group: 6.5 (n=35) vs. 6.4 (n=37) Middle age group: 2.8 (n=77) vs. 5.7 (n=76) Old group: 6.4 (n=43) vs. 6.2 (n=38)	NR

RCT	Type of Intervention	Length f/u Complete f/u (% (n/N))	Differential efficacy	Differential safety
			3 months Young group: 2.5 (n=35) vs. 5.0 (n=37) Middle age group: 3.0 (n=77) vs. 5.0 (n=76) Old group: 3.2 (n=43) vs. 5.7 (n=38) 6 months Young group: 2.3 (n=35) vs. 4.8 (n=37) Middle age group: 2.8 (n=77) vs. 4.8 (n=76) Old group: 2.7 (n=43) vs. 5.6 (n=38) 12 months Young group: 2.3 (n=35) vs. 4.7 (n=37) Middle age group: 2.8 (n=77) vs. 4.7 (n=76) Old group: 2.7 (n=43) vs. 5.6 (n=38) Tension headache No formal test for interaction reported. Baseline Young group: 21 (n=35) vs. 18 (n=37) Middle age group: 52 (n=77) vs. 41 (n=76) Old group: 22 (n=43) vs. 19 (n=38) 3 months Young group: 9 (n=35) vs. 14 (n=37) Middle age group: 23 (n=77) vs. 34 (n=76) Old group: 11 (n=43) vs. 14 (n=38) 6 months Young group: 3 (n=35) vs. 11 (n=37) Middle age group: 13 (n=77) vs. 31 (n=76) Old group: 4 (n=43) vs. 12 (n=38) 12 months Young group: 1 (n=35) vs. 10 (n=37) Middle age group: 2 (n=77) vs. 27 (n=76) Old group: 2 (n=43) vs. 11 (n=38)	

APPENDIX T. Lumbar spinal injections: Adverse events from RCTs

Appendix Table T1. Lumbar epidural steroid injections (ESI) vs. non-steroidal epidural injections (ENSI): Adverse events from RCTs

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
Catastrophic									
Meningitis	Datta (2011)	DEX 15 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/40)	0% (0/42)	NC	NS
Meningitis	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/39)	0% (0/42)	NC	NS
Meningitis	Datta (2011)	TAC 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/42)	0% (0/42)	NC	NS
Serious									
Epidural hematoma	Datta (2011)	DEX 15 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/40)	0% (0/42)	NC	NS
Epidural hematoma	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/39)	0% (0/42)	NC	NS
Epidural hematoma	Datta (2011)	TAC 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/42)	0% (0/42)	NC	NS
Hematoma	Ohtori (2012)	DEX 3.3 mg + LA Fluoroscopic	Etanercept + LA Fluoroscopic	TF	1 mo.	0% (0/40)	0% (0/40)	NC	NS
Infection (deep)	Ohtori (2012)	DEX 3.3 mg + LA Fluoroscopic	Etanercept + LA Fluoroscopic	TF	1 mo.	0% (0/40)	0% (0/40)	NC	NS
Nerve root injury	Datta (2011)	DEX 15 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/40)	0% (0/42)	NC	NS
Nerve root injury	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/39)	0% (0/42)	NC	NS
Nerve root injury	Datta (2011)	TAC 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/42)	0% (0/42)	NC	NS
Retro-peritoneal hematoma	Karppinen (2001, 2001)	MPS 40 mg + LA Fluoroscopic	Saline Fluoroscopic	TF	12 mos.	1.25% (1/80)	0% (0/80)	infinity (NC to NC)	0.317
Spinal nerve injury	Ohtori (2012)	DEX 3.3 mg + LA Fluoroscopic	Etanercept + LA Fluoroscopic	TF	1 mo.	0% (0/40)	0% (0/40)	NC	NS
Subarachnoid	Manchikanti	BET (dosage NR)	LA	IL	24	2.2% (14/644 procedures)		NA	NA

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
entries (details NR)	(2012, 2015)	+ LA Fluoroscopic	Fluoroscopic		mos.				
Subarachnoid injection	Datta (2011)	DEX 15 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/40)	0% (0/42)	NC	NS
Subarachnoid injection	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/39)	0% (0/42)	NC	NS
Subarachnoid injection	Datta (2011)	TAC 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/42)	0% (0/42)	NC	NS
Subarachnoid injection	Fukusaki (1998)	MPS 40 mg + LA Imaging NR	LA Imaging NR	IL	3 mos.	0% (0/19)	0% (0/18)	NC	NS
Subarachnoid injection	Fukusaki (1998)	MPS 40 mg + LA Imaging NR	Saline Imaging NR	IL	3 mos.	0% (0/19)	0% (0/16)	NC	NS
Subarachnoid puncture w/o headache (details NR)	Manchikanti (2013, 2012, 2010)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	3% (4/120)		NA	NA
"Major adverse events" (specifics NR)	Manchikanti (2012, 2010, 2008)	BET 6 mg + LA + saline Fluoroscopic	LA + saline Fluoroscopic	Caudal	24 mos.	0% (0/70)	0% (0/70)	NC	NS
"Major adverse events" (specifics NR)	Manchikanti (2012, 2010, 2008)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	Caudal	24 mos.	0% (0/70)	0% (0/70)	NC	NS
"Major adverse events" (specifics NR)	Manchikanti (2012, 2011, 2008)	BET 6 mg OR MPS 40 mg + LA Fluoroscopic	LA Fluoroscopic	Caudal	24 mos.	0% (0/60)	0% (0/60)	NC	NS
"Serious adverse event" (hospitalization and or surgery)	Friedly (2014)	TAC 1-3 mL, BET 6-12 mg, DEX 8-10 mg, or MPS 60-120 mg + LA Fluoroscopic	LA Fluoroscopic	IL or TF	1.5 mos.	2.5% (5/200)	2% (4/200)	1.250 (0.34 to 4.58)	0.736
Non-serious (or insufficient detail to categorize as serious)									
"Cognitive"	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill	Sham injection + gabapentin 300	IL (n = 11 vs. 12) or TF (n =	3 mos.	7% (5/73)	10% (7/72)	NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
			mg	62 vs. 60)					
Bladder incontinence	Ghahreman (2011, 2010)	TAC 40 mg/ml + LA Fluoroscopic	LA Fluoroscopic	TF	12 mos.	0% (0/28)	3.7% (1/27)	NR	NR
Bladder incontinence	Ghahreman (2011, 2010)	TAC 40 mg/ml + LA Fluoroscopic	Saline Fluoroscopic	TF	12 mos.	0% (0/28)	0% (0/37)	NR	NR
Constipation	Burgher (2011)	TAC 40 or 80 mg + LA Fluoroscopic	Clonidine 200 or 400 µg + LA Fluoroscopic	TF	1 mos.	7% (1/15)	18% (2/11)	NR	NR
Death (details NR, not attributed to procedure)	Tafazal (2009, 2005)	MPS 40 mg + LA Fluoroscopic	LA Fluoroscopic	TF	1 yr.	1.33% (2/150)		NR	NR
Discomfort at injection site	Burgher (2011)	TAC 40 or 80 mg + LA Fluoroscopic	Clonidine 200 or 400 µg + LA Fluoroscopic	TF	1 mos.	27% (4/15)	18% (2/11)	NR	NR
Dizziness/ lightheaded-ness	Friedly (2014)	TAC 1-3 mL, BET 6-12 mg, DEX 8-10 mg, or MPS 60-120 mg + LA Fluoroscopic	LA Fluoroscopic	IL or TF	1.5 mos.	2% (4/200)	2% (4/200)	NR	NR
Drowsiness	Burgher (2011)	TAC 40 or 80 mg + LA Fluoroscopic	Clonidine 200 or 400 µg + LA Fluoroscopic	TF	1 mos.	20% (3/15)	18% (2/11)	NR	NR
Dry mouth	Burgher (2011)	TAC 40 or 80 mg + LA Fluoroscopic	Clonidine 200 or 400 µg + LA Fluoroscopic	TF	1 mos.	20% (3/15)	18% (2/11)	NR	NR
Dural puncture*	Carette (1997)	MPS 80 mg + saline Imaging NR	Saline Imaging NR	IL	3 mos.	1.3% (1/78)	1.2% (1/80)	NR	NR
Dural puncture (details NR)	Friedly (2014)	TAC 1-3 mL, BET 6-12 mg, DEX 8-	LA Fluoroscopic	IL or TF	1.5 mos.	0.5% (1/200)	0.5% (1/200)	NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
		10 mg, or MPS 60-120 mg + LA Fluoroscopic							
Dural puncture	Fukusaki (1998)	MPS 40 mg + LA Imaging NR	LA Imaging NR	IL	3 mos.	0% (0/19)	0% (0/18)	NR	NR
Dural puncture	Fukusaki (1998)	MPS 40 mg + LA Imaging NR	Saline Imaging NR	IL	3 mos.	0% (0/19)	0% (0/16)	NR	NR
Dural puncture (details NR)	Manchikanti (2014, 2013, 2010)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	1.6% (11/682)		NR	NR
Excessive pain	Cohen (2015)	Depo-MPS 60 mgL + LA + placebo med	Sham injection + gabapentin 300 mg	IL (n = 11 vs 12) or TF (n = 62 vs 60)	3 mos.	3% (2/73)	6% (4/72)	0.49 (0.09 to 2.61)	0.396
Faintness	Sayegh (2009)	BET + LA Imaging NR	LA + water Imaging NR	Caudal	12 mos.	5.4% (5/93)	7.8% (7/90)	NR	NR
Falls	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill	Sham injection + gabapentin 300 mg	IL (n = 11 vs. 12) or TF (n = 62 vs. 60)	3 mos.	1% (1/73)	0% (0/74)	NR	NR
Fever and/ or infection (details NR)	Friedly (2014)	TAC 1-3 mL, BET 6-12 mg, DEX 8-10 mg, or MPS 60-120 mg + LA Fluoroscopic	LA Fluoroscopic	IL or TF	1.5 mos.	5% (10/200)	1% (2/200)	NR	NR
Fever and/or infection (details NR)	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill.	Sham injection + gabapentin 300 mg	IL (n = 11 vs. 12) or TF (n = 62 vs. 60)	3 mos.	4% (2/73)	0% (0/72)	NR	NR
Gastro-intestinal	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill	Sham injection + gabapentin 300 mg	IL (n = 11 vs. 12) or TF (n = 62 vs. 60)	3 mos.	18% (13/73)	11% (8/72)	NR	NR
Headache	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill	Sham injection + gabapentin 300 mg	IL (n = 11 vs. 12) or TF (n = 62 vs. 60)	3 mos.	6% (4/73)	1% (1/72)	NR	NR
Headache	Datta (2011)	DEX 15 mg + LA	LA	Caudal	3	22%	31% (31/42)	NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
		Imaging NR	Imaging NR		mos.	(9/40)			
Headache	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	38% (15/39)	31% (31/42)	NR	NR
Headache	Datta (2011)	TAC 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	38% (16/42)	31% (31/42)	NR	NR
Headache	Friedly (2014)	TAC 1-3 mL, BET 6-12 mg, DEX 8-10 mg, or MPS 60-120 mg + LA Fluoroscopic	LA Fluoroscopic	IL or TF	1.5 mos.	4% (8/200)	1.5% (7/200)	NR	NR
Headache	Manchikanti (2014, 2013, 2010)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0% (0/60)	0% (0/60)	NR	NR
Headache (post-subarachnoid puncture)	Manchikanti (2014)	BET 0.5 mL + LA Fluoroscopic	LA + NaCl Fluoroscopic	TF	24 mos.	0% (0/60)	0% (0/60)	NR	NR
Headache (severe, attributed to injection)	Becker (2007)	TAC 10 mg + LA Fluoroscopic	Autologous conditioned serum Fluoroscopic	IL	5.5 mos.	4.0% (1/25)	3.1% (1/32)	NR	NR
Headache (severe, attributed to injection)	Becker (2007)	TAC 5 mg + LA Fluoroscopic	Autologous conditioned serum Fluoroscopic	IL	5.5 mos.	3.7% (1/27)	3.1% (1/32)	NR	NR
Headache (transient)	Carette (1997)	MPS 80 mg + saline Imaging NR	Saline Imaging NR	IL	3 mos.	27% (21/78)	20% (16/80)	NR	NR
Hypotension	Fukusaki (1998)	MPS 40 mg + LA Imaging NR	LA Imaging NR	IL	3 mos.	0% (0/19)	0% (0/18)	NR	NR
Hypotension	Fukusaki (1998)	MPS 40 mg + LA Imaging NR	Saline Imaging NR	IL	3 mos.	0% (0/19)	0% (0/16)	NR	NR
Infection (sinusitis,	Cohen (2012)	MPS acetate 60 mg + LA + water	Etanercept + LA + water	TF	6 mos.	0% (0/28)	4% (1/26)	NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
unrelated to procedure)		Fluoroscopic	Fluoroscopic						
Infection (sinusitis, unrelated to procedure)	Cohen (2012)	MPS acetate 60 mg + LA + water Fluoroscopic	LA + water Fluoroscopic	TF	6 mos.	0% (0/28)	10% (3/30)	NR	NR
Infection (superficial)	Ohtori (2012)	DEX 3.3 mg + LA Fluoroscopic	Etanercept + LA Fluoroscopic	TF	1 mos.	0% (0/40)	0% (0/40)	NR	NR
Intravascular infiltration (contents of infiltrate NR)	Manchikanti (2014)	BET 0.5 mL + LA Fluoroscopic	LA + NaCl Fluoroscopic	TF	24 mos.	4.6% (28/601 injections)		NR	NR
Intravascular injection	Datta (2011)	DEX 15 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/40)	0% (0/42)	NR	NR
Intravascular injection	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/39)	0% (0/42)	NR	NR
Intravascular injection	Datta (2011)	TAC 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/42)	0% (0/42)	NR	NR
Irregular menses	Bush (1991)	TAC acetonide 80 mg + LA + saline Imaging NR	Saline Imaging NR	Caudal	12 mos.	8% (1/12)	0% (0/11)	NR	NR
Lightheaded-ness	Burgher (2011)	TAC 40 or 80 mg + LA Fluoroscopic	Clonidine 200 or 400 µg + LA Fluoroscopic	TF	1 mos.	7% (1/15)	45% (5/11)	NR	NR
Local pain	Iversen (2011)	TAC 40 mg + saline Imaging NR	Saline Imaging NR	Caudal	12 mos.	5.2% (6/116)†		NR	NR
Local pain (>24 hours)	Datta (2011)	DEX 15 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	10% (4/40)	7.1% (3/42)	NR	NR
Local pain (>24 hours)	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	21% (8/39)	7.1% (3/42)	NR	NR
Local pain (>24	Datta (2011)	TAC 80 mg + LA	LA	Caudal	3	17%	7.1% (3/42)	NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
hours)		Imaging NR	Imaging NR		mos.	(7/42)			
Low cortisol noted on lab tests after injection in patient also receiving oral steroids with no symptoms, bruising, temporary inability to lift legs, GI bleed after three days in patient receiving low molecular weight heparin	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill	Sham injection + gabapentin 300 mg	IL (n = 11 vs. 12) or TF (n = 62 vs. 60)	3 mos.	1% (1/73)	4% (3/72)	NR	NR
Nausea	Burgher (2011)	TAC 40 or 80 mg + LA Fluoroscopic	Clonidine 200 or 400 µg + LA Fluoroscopic	TF	1 mos.	13% (2/15)	9% (1/11)	NR	NR
Nausea	Datta (2011)	DEX 15 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	20% (8/40)	17% (7/42)	NR	NR
Nausea	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	15% (6/39)	17% (7/42)	NR	NR
Nausea	Datta (2011)	TAC 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	17% (7/42)	17% (7/42)	NR	NR
Nerve root irritation	Manchikanti (2012, 2015)	BET (dosage NR) + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0.2% (1/644 procedures)		NR	NR
Nerve root irritation	Manchikanti (2013, 2012, 2010)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	1% (1/120)		NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
Nerve root irritation	Manchikanti (2014)	BET 0.5 mL + LA Fluoroscopic	LA + sodium chloride Fluoroscopic	TF	24 mos.	1.5% (9/601 injections)		NR	NR
Nerve root irritation	Manchikanti (2014, 2013, 2010)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0% (0/60)	0% (0/60)	NR	NR
New neurological symptom (details NR)	Cohen (2012)	MPS acetate 60 mg + LA + water Fluoroscopic	Etanercept + LA + water Fluoroscopic	TF	6 mos.	0% (0/28)	4% (1/26)	NR	NR
New neurological symptom (details NR)	Cohen (2012)	MPS acetate 60 mg + LA + water Fluoroscopic	LA + water Fluoroscopic	TF	6 mos.	0% (0/28)	3% (1/30)	NR	NR
Numbness (transient, lower extremity)	Sayegh (2009)	BET + LA Imaging NR	LA + water Imaging NR	Caudal	12 mos.	13% (12/93)	8.9% (8/90)	NR	NR
Pain (excessive) (details NR)	Friedly (2014)	TAC 1-3 mL, BET 6-12 mg, DEX 8-10 mg, or MPS 60-120 mg + LA Fluoroscopic	LA Fluoroscopic	IL or TF	1.5 mos.	2.5% (5/200)	3.5% (7/200)	NR	NR
Pain and swelling at injection site	Manchikanti (2012, 2015)	BET (dosage NR) + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0.2% (1/644 procedures)		NR	NR
Rash (nonlocal)	Cohen (2012)	MPS acetate 60 mg + LA + water Fluoroscopic	Etanercept + LA + water Fluoroscopic	TF	6 mos.	4% (1/28)	0% (0/26)	NR	NR
Rash (nonlocal)	Cohen (2012)	MPS acetate 60 mg + LA + water Fluoroscopic	LA + water Fluoroscopic	TF	6 mos.	4% (1/28)	0% (0/30)	NR	NR
Required naloxone for reversal of	Rocco (1989)	TAC diacetate 75 mg + LA + morphine	Morphine + LA Imaging NR	NR	6mos.	43% (3/7)‡	0% (0/7)	infinity (NC to NC)	0.06

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
respiratory depression (attributed to combination of steroid and morphine)		Imaging NR							
Required naloxone for reversal of respiratory depression (attributed to combination of steroid and morphine)	Rocco (1989)	TAC diacetate 75 mg + LA + saline Imaging NR	Morphine + LA Imaging NR	NR	6 mos.	0% (0/8)	0% (0/7)	NC	NC
Sedation/ fatigue	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill	Sham injection + gabapentin 300 mg	IL (n = 11 vs. 12) or TF (n = 62 vs. 60)	3 mos.	11% (8/73)	18% (13/72)	NR	NR
Sensory deficits (details NR)	Datta (2011)	DEX 15 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	28% (11/40)	48% (20/42)	NR	NR
Sensory deficits (details NR)	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	13% (5/39)	48% (20/42)	NR	NR
Sensory deficits (details NR)	Datta (2011)	TAC 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	21% (9/42)	48% (20/42)	NR	NR
Swelling	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill	Sham injection + gabapentin 300 mg	IL (n = 11 vs. 12) or TF (n = 62 vs. 60)	3 mos.	0% (0/73)	4% (3/72)	NR	NR
Tinnitus	Datta (2011)	DEX 15 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	2.5% (1/40)	7.1% (3/42)	NR	NR
Tinnitus	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	2.6% (1/39)	7.1% (3/42)	NR	NR
Tinnitus	Datta (2011)	TAC 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	9.5% (4/42)	7.1% (3/42)	NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
Vasovagal	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill	Sham injection + gabapentin 300 mg	IL (n = 11 vs. 12) or TF (n = 62 vs. 60)	3 mos.	0% (0/73)	0% (0/74)	NR	NR
Weakness	Burgher (2011)	TAC 40 or 80 mg + LA Fluoroscopic	Clonidine 200 or 400 µg + LA Fluoroscopic	TF	1 mos.	7% (1/15)	36% (4/11)	NR	NR
Weight gain	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill	Sham injection + gabapentin 300 mg	IL (n = 11 vs. 12) or TF (n = 62 vs. 60)	3 mos.	6% (4/73)	10% (7/72)	NR	NR
Weight gain	Datta (2011)	DEX 15 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/40)	0% (0/42)	NR	NR
Weight gain	Datta (2011)	MPS 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	0% (0/39)	0% (0/42)	NR	NR
Weight gain	Datta (2011)	TAC 80 mg + LA Imaging NR	LA Imaging NR	Caudal	3 mos.	2.4% (1/42)	0% (0/42)	NR	NR
Worsening pain	Cohen (2012)	MPS acetate 60 mg + LA + water Fluoroscopic	Etanercept + LA + water Fluoroscopic	TF	6 mos.	4% (1/28)	19% (5/26)	NR	NR
Worsening pain	Cohen (2012)	MPS acetate 60 mg + LA + water Fluoroscopic	LA + water Fluoroscopic	TF	6 mos.	4% (1/28)	20% (6/30)	NR	NR
"Complications attributable to injection"§	Snoek (1977)	MPS 80 mg Imaging NR	Saline Imaging NR	IL	8-20 mos.	0% (0/27)	0% (0/24)	NR	NR
"Complications from administered treatment"	Klenerman (1984)	MPS 80 mg + saline Imaging NR	LA Imaging NR	NR	2 mos.	0% (0/19)	0% (0/16)	NR	NR
"Complications from administered treatment"	Klenerman (1984)	MPS 80 mg + saline Imaging NR	Saline Imaging NR	NR	2 mos.	0% (0/19)	0% (0/16)	NR	NR
"Other adverse	Manchikanti	BET 6 mg + LA	LA	IL	24	0% (0/60)	0% (0/60)	NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
consequence"	(2014, 2013, 2010)	Fluoroscopic	Fluoroscopic		mos.				
"Other"	Ohtori (2012)	DEX 3.3 mg + LA Fluoroscopic	Etanercept + LA Fluoroscopic	TF	1 mos.	0% (0/40)	0% (0/40)	NR	NR
"Side effects or complications"	Devulder (1999)	MPS 40 mg + hyaluronidase + LA Imaging NR	Hyaluronidase + LA Imaging NR	TF	6 mos.	0% (0/20)	0% (0/20)	NR	NR
"Side effects or complications"	Devulder (1999)	MPS 40 mg + LA Imaging NR	Hyaluronidase + LA Imaging NR	TF	6 mos.	0% (0/20)	0% (0/20)	NR	NR
Number of adverse events per patient	Suri (2015)	TAC 60-120 mg, BET 6-12 mg, DEX 8-10 mg, or MPS 60-120 mg + LA Fluoroscopic	LA Fluoroscopic	IL or TF	1.5 mos.	0.2 events	0.1 events	NR	NR
Other adverse events (Ataxia, balance problems, depression, emotionality, kidney stones, muscle twitching, hot flashes, restlessness, rhinorrhea with congestion, sexual, vivid dreams)	Cohen (2015)	Depo-MPS 60 mg + LA + placebo pill	Sham injection + gabapentin 300 mg	IL (n = 11 vs. 12) or TF (n = 62 vs. 60)	3 mos.	15% (11/73)	15% (11/72)	NR	NR
Worsening of symptoms	Burgher (2011)	TAC 40 or 80 mg + LA	Clonidine 200 or 400 µg + LA	TF	1 mos.	13% (2/15)	36% (4/11)	NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	ENSI Injectate Guidance	Approach	F/U	ESI % (n/N)	ENSI % (n/N)	RR (95% CI)	p-value
		Fluoroscopic	Fluoroscopic						

BET: betamethasone; DEX: dexamethasone; IL: Interlaminar; LA: local anesthetic; mos.: months; MPS: methylprednisolone; NC: not calculable; NR: not reported; TAC: triamcinolone; TF: transforaminal

* given an epidural injection of 10 mL of blood drawn from the antecubital vein, no other details reported

† Includes data from a third treatment group (Subcutaneous injection superficial to the sacral hiatus and outside spinal canal with 0.9% saline)

‡ Post injection, all patients were somnolent, with a p_aCO_2 of 44 or above, with p_aO_2 of 73 or less, and respiratory rates between 0 and 12 at the time noxalone was administered.

§ "other than a few patients who felt increased pain of the sciatic distribution shortly after injection, there were no complications or side effects attributable to injection"

Appendix Table T2. Lumbar epidural steroid injections (ESI) vs. non-epidural injections (NEI): Adverse events from RCTs

Adverse event	Author (year)	ESI Injectate Guidance	NEI Injectate Guidance	Approach	F/U	ESI % (n/N)	NEI % (n/N)	RR (95% CI)	p-value
Catastrophic									
(none reported)									
Serious									
(none reported)									
Non-serious (or insufficient detail to categorize as serious)									
CSF tap (accidental) (headache in one, additional details NR)	Ridley (1988)	MPS 80 mg + saline Imaging NR	Interspinous ligament saline injection Imaging NR	IL	0.5 mos.	10.5% (2/19)	0% (0/16)	NR	NR
CSF tap (accidental)*	Dilke (1973)	MPS 80 mg + saline Imaging NR	Interspinous ligament saline injection Imaging NR	IL	3 mos.	6% (6/100)		NC	NC
Headache (post-dural puncture, details NR)	Arden (2005), Price (2005)	TAC acetonide 80 mg + LA Imaging NR	Interspinous ligament saline injection Imaging NR	IL	12 mos.	0.8% (1/120)	0% (0/108)	NR	NR
Headache	Ridley (1988)	MPS 80 mg + saline Imaging NR	Interspinous ligament saline injection Imaging NR	IL	0.5 mos.	1.2% (1/19)	0% (0/16)	NR	NR
Headache (non-specific)	Arden (2005), Price (2005)	TAC acetonide 80 mg + LA Imaging NR	Interspinous ligament saline injection Imaging NR	IL	12 mos.	3% (4/120)	4% (4/108)	NR	NR
Hypotension	Ridley (1988)	MPS 80 mg + saline Imaging NR	Interspinous ligament saline injection Imaging NR	IL	0.5 mos.	0% (0/19)	0% (0/16)	NR	NR
Local pain	Iversen (2011)	TAC 40 mg + saline Imaging NR	Subcutaneous Injections with saline	Caudal	12 mos.	5.2% (6/116)†		NC	NC

Adverse event	Author (year)	ESI Injectate Guidance	NEI Injectate Guidance	Approach	F/U	ESI % (n/N)	NEI % (n/N)	RR (95% CI)	p-value
Nausea	Arden (2005), Price (2005)	TAC acetonide 80 mg + LA Imaging NR	Interspinous ligament saline injection Imaging NR	IL	12 mos.	1.6% (2/120)	1.8% (2/108)	NR	NR
Transient side-effects (details NR)	Arden (2005), Price (2005)	TAC acetonide 80 mg + LA Imaging NR	Interspinous ligament saline injection Imaging NR	IL	12 mos.	4.1% (5/120)	4.6% (5/120)	NR	NR
Complications attributable to treatment	Ghahreman (2011, 2010)	TAC 40 mg/ml + LA Fluoroscopic	IM saline injection Fluoroscopic	TF	12 mos.	0% (0/28)	0% (0/30)	NR	NR
Complications attributable to treatment (details NR)	Ghahreman (2011, 2010)	TAC 40 mg/ml + LA Fluoroscopic	IM injection TAC 40 mg/ml Fluoroscopic	TF	12 mos.	0% (0/28)	0% (0/28)	NR	NR
Complications during injection procedures	Helliwell (1985)	MPS + saline Imaging NR	Interspinous ligament saline injection Imaging NR	IL	3 mos.	0% (0/20)	NC	NC	NC
Complications from administered treatment	Klenerman (1984)	MPS 80 mg + saline Imaging NR	Interspinous ligament needling Imaging NR	NR	2 mos.	0% (0/19)	0% (0/12)	NR	NR

IL: Interlaminar; LA: local anesthetic; mos.: months; MPS: methylprednisolone; NC: not calculable; NR: not reported; TAC: triamcinolone; TF: transforaminal

* needle was withdrawn and an extradural injection was immediately performed through an adjacent interspinous space.

† Includes data from a third treatment group "Triamcinolone 40 mg + saline"

Appendix Table T3. Lumbar epidural steroid injections (ESI) vs. disc procedure: Adverse events from RCTs

Adverse event	Author (year)	ESI Injectate Guidance	Disc procedure	Approach	F/U	ESI % (n/N)	Disc procedure % (n/N)	RR (95% CI)	p-value
Catastrophic									
(none)									
Serious									
Hematoma	Brown (2012)	TAC acetate 80 mg + saline	Lumbar decompression	IL	1.5 mos.	0% (0/17)	0% (0/21)	NC	NC

Adverse event	Author (year)	ESI Injectate Guidance	Disc procedure	Approach	F/U	ESI % (n/N)	Disc procedure % (n/N)	RR (95% CI)	p-value
		Fluoroscopic	Fluoroscopic						
Infection	Brown (2012)	TAC acetate 80 mg + saline Fluoroscopic	Lumbar decompression Fluoroscopic	IL	1.5 mos.	0% (0/17)	0% (0/21)	NC	NC
Nerve root damage	Brown (2012)	TAC acetate 80 mg + saline Fluoroscopic	Lumbar decompression Fluoroscopic	IL	1.5 mos.	0% (0/17)	0% (0/21)	NC	NC
Neurovascular complications	Wu (2015)	BET (dosage NR) + LA Fluoroscopic	Nucleoplasty	TF	12 mos.	0% (0/40)	0% (0/39)	NC	NC
Paresthesia and numbness in the lower extremity (resolved spontaneously after 3-4 days)	Aronsohn (2010)	MPS 40 mg + LA Fluoroscopic	Lumbar discectomy	NR	1.5 mos.	4.2% (1/24)	13% (3/26)	0.36 (0.04 to 3.24)	0.34
Seroma (details NR)	Buttermann (2004)	BET 10-15 mg Fluoroscopic	Discectomy	IL	24-36 mos.	0% (0/50)	1.3% (1/77)	0.00 (NC to NC)	0.420
Transfusion due to blood loss	Brown (2012)	TAC acetate 80 mg + saline Fluoroscopic	Lumbar decompression Fluoroscopic	IL	1.5 mos.	0% (0/17)	0% (0/21)	NC	NC
Re-hospitalization following injection due to adverse event(s)	Brown (2012)	TAC acetate 80 mg + saline Fluoroscopic	Lumbar decompression Fluoroscopic	IL	1.5 mos.	0% (0/17)	0% (0/21)	NC	NC
Non-serious (or insufficient detail to categorize as serious)									
Disc herniation (recurrent)	Buttermann (2004)	BET 10-15 mg Fluoroscopic	Discectomy	IL	24-36 mos.	6% (3/50)	0% (0/77)	NR	NR
Dural puncture (details NR)	Buttermann (2004)	BET 10-15 mg Fluoroscopic	Discectomy	IL	24-36 mos.	4% (2/50)	0% (0/77)	NR	NR
Dural tear	Brown (2012)	TAC acetate 80 mg + saline	Lumbar decompression	IL	1.5 mos.	0% (0/17)	0% (0/21)	NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	Disc procedure	Approach	F/U	ESI % (n/N)	Disc procedure % (n/N)	RR (95% CI)	p-value
		Fluoroscopic	Fluoroscopic						
Durotomy (details NR)	Buttermann (2004)	BET 10-15 mg Fluoroscopic	Discectomy	IL	24-36 mos.	0% (0/50)	2.6% (2/77)	NR	NR
Lightheaded-ness	Gerstzen (2010)	Corticosteroid* Fluoroscopic	Plasma disc decompression Fluoroscopic	TF	27 mos.	0% (0/40)	2.2% (1/45)	NR	NR
Muscle tightness or spasms	Gerstzen (2010)	Corticosteroid* Fluoroscopic	Plasma disc decompression Fluoroscopic	TF	27 mos.	5% (2/40)	2.2% (1/45)	NR	NR
Pain (increased back pain)	Gerstzen (2010)	Corticosteroid* Fluoroscopic	Plasma disc decompression Fluoroscopic	TF	27 mos.	2.5% (1/40)	8.9% (4/45)	NR	NR
Pain (increased radicular pain)	Gerstzen (2010)	Corticosteroid* Fluoroscopic	Plasma disc decompression Fluoroscopic	TF	27 mos.	2.5% (1/40)	11% (5/45)	NR	NR
Pain (injection site pain)	Gerstzen (2010)	Corticosteroid* Fluoroscopic	Plasma disc decompression Fluoroscopic	TF	27 mos.	5% (2/40)	4.4% (2/45)	NR	NR
Superficial skin infection	Aronsohn (2010)	MPS 40 mg + LA Fluoroscopic	Lumbar discectomy	NR	1.5 mos.	0% (0/24)	3.8% (1/26)	NR	NR
Weakness	Gerstzen (2010)	Corticosteroid* Fluoroscopic	Plasma disc decompression Fluoroscopic	TF	27 mos.	2.5% (1/40)	0% (0/45)	NR	NR
"Infection-related complications"	Wu (2015)	BET (dosage NR) + LA Fluoroscopic	Nucleoplasty + nerve root injection with BET + LA	TF	12 mos.	0% (0/40)	0% (0/39)	NR	NR
"Infection-related complications"	Wu (2015)	BET (dosage NR) + LA Fluoroscopic	Nucleoplasty	TF	12 mos.	0% (0/40)	0% (0/39)	NR	NR
"Procedure related adverse events"	Gerstzen (2010)	Corticosteroid* Fluoroscopic	Plasma disc decompression Fluoroscopic	TF	27 mos.	18% (7/40)	11% (5/45)	NR	NR

BET: betamethasone; IL: Interlaminar; LA: local anesthetic; mos.: months; MPS: methylprednisolone; NC: not calculable; NR: not reported; TAC: triamcinolone; TF: transforaminal
* dosage and type at physician's discretion

Appendix Table T4. Lumbar epidural steroid injections (ESI) vs. conservative care (CC): Adverse events from RCTs

Adverse event	Author (year)	ESI Injectate Guidance	CC	Approach	F/U	ESI % (n/N)	CC % (n/N)	RR (95% CI)	p-value
Catastrophic									
(none)									
Serious									
"Major side effects" (details NR)	Buchner (2000)	MPS 100 mg + LA + conservative care (as described in group B)	Bed rest, medical therapy, physical therapy, physiotherapy	IL	6 mos.	0% (0/17)	0% (0/19)	NC	NC
Non-serious (or insufficient detail to categorize as serious)									
>1 attempt required for steroid placement	Murakibh avi (2011)	TAC acetate 80 mg + LA + saline Fluoroscopic	MT + bilateral skin traction + physiotherapy + short-wave diathermy + PT	Caudal	6 mos.	30% (15/50)	NR	NR	NR
Angina Pectoris (details NR)	Koc 2009	TAC acetonide 60 mg + LA + saline Fluoroscopic	PT	IL	6 mos.	3% (1/33)		NR	NR
Angina Pectoris (details NR)	Koc 2009	TAC acetonide 60 mg + LA + saline Fluoroscopic	No treatment	IL	6 mos.	3% (1/33)		NR	NR
Bleeding during procedure (details NR)	Murakibh avi (2011)	TAC acetate 80 mg + LA + saline Fluoroscopic	MT + bilateral skin traction + physiotherapy + short-wave diathermy + PT	Caudal	6 mos.	4% (2/50)	NR	NR	
Difficulty in approach	Murakibh avi (2011)	TAC acetate 80 mg + LA + saline Fluoroscopic	MT + bilateral skin traction + physiotherapy + short-wave	Caudal	6 mos.	22% (11/50)	Group B N/A	NR	NR

Adverse event	Author (year)	ESI Injectate Guidance	CC	Approach	F/U	ESI % (n/N)	CC % (n/N)	RR (95% CI)	p-value
			diathermy + PT						
Dural puncture	Murakibhavi (2011)	TAC acetate 80 mg + LA + saline Fluoroscopic	MT + bilateral skin traction + physiotherapy + short-wave diathermy + PT	Caudal	6 mos.	0% (0/50)	NR	NR	NR
Gastric complaint	Koc 2009	TAC acetonide 60 mg + LA + saline Fluoroscopic	PT	IL	6 mos.	3% (1/33)		NR	NR
Gastric complaint	Koc 2009	TAC acetonide 60 mg + LA + saline Fluoroscopic	No treatment	IL	6 mos.	3% (1/33)		NR	NR
Headache	Murakibhavi (2011)	TAC acetate 80 mg + LA + saline Fluoroscopic	MT + bilateral skin traction + physiotherapy + short-wave diathermy + PT	Caudal	6 mos.	18% (9/50)	NR	NR	NR
Hypotension during procedure leading to vasovagal response (managed immediately)	Murakibhavi (2011)	TAC acetate 80 mg + LA + saline Fluoroscopic	MT + bilateral skin traction + physiotherapy + short-wave diathermy + PT	Caudal	6 mos.	24% (12/50)	N/A	NR	NR
Transient bilateral LE numbness immediately postinjection	Murakibhavi (2011)	TAC acetate 80 mg + LA + saline Fluoroscopic	MT + bilateral skin traction + physiotherapy + short-wave diathermy + PT	Caudal	6 mos.	40% (20/50)	N/A	NR	NR

CC: conservative care; IL: Interlaminar; LA: local anesthetic; mos.: months; MPS: methylprednisolone; MT: medical therapy; NC: not calculable; NR: not reported; PT: physical therapy; TAC: triamcinolone; TF: transforaminal

Appendix Table T5. Lumbar Intra-articular steroid injections (IASI) vs. intra-articular non-steroidal injections (IANSI): Adverse events from RCTs

Adverse event	Author (year)	IASI Injectate Guidance	IANSI Injectate Guidance	F/U	IASI % (n/N)	IANSI % (n/N)	RR (95% CI)	p-value
Catastrophic								
(none)								
Serious								
"Significant adverse events"	Fuchs (2005)	TAC acetonide 10 mg Fluoroscopic	Sodium hyaluronate Fluoroscopic	6 mos.	0% (0/30)	0% (0/30)	NC	NC
Non-serious (or insufficient detail to categorize as serious)								
"Adverse events"	Carette (1991)	MPS acetate 20 mg + saline Fluoroscopic	Saline Fluoroscopic	6 mos.	0% (0/51)	0% (0/50)	NR	NR
"Side-effects"	Lilius (1989)	MPS acetate 80 mg + LA Fluoroscopic	Saline Fluoroscopic	3 mos.	6.6% (7/106)		NR	NR

LA: local anesthetic; mos.: months; MPS: methylprednisolone; NC: not calculable; NR: not reported
*Includes data from a third treatment group (Extra-articular MPS 80 mg), reported in both tables

Appendix Table T6. Lumbar intra-articular steroid injections (IASI) vs. non-intra-articular injections (NIAI): Adverse events from RCTs

Adverse event	Author (year)	IASI Injectate Guidance	NIAI Injectate Guidance	F/U	IASI % (n/N)	NIAI % (n/N)	RR (95% CI)	p-value
Catastrophic								
(none)								
Serious								
(none)								
Non-serious (or insufficient detail to categorize as serious)								
Cutaneous hypochromia	Ribeiro (2013)	TAC hexacetonide 20 mg + LA Fluoroscopic	IM injection TAC hexacetonide 20 mg + LA Fluoroscopic	6 mos.	1.66% (1/60)*		NC	NC
Death (heart failure; (not attributed to procedure)†	Ribeiro (2013)	TAC hexacetonide 20 mg + LA Fluoroscopic	IM injection TAC hexacetonide 20 mg + LA Fluoroscopic	3-6 mos.	3% (1/31)	0% (0/29)	NR	NR
Dizziness	Ribeiro (2013)	TAC hexacetonide 20 mg + LA Fluoroscopic	IM injection TAC hexacetonide 20 mg + LA Fluoroscopic	6 mos.	5% (3/60)*		NC	NC
Gastrointestinal bleeding and endoscopic surgery between 12-24 weeks (additional details NR)	Ribeiro (2013)	TAC hexacetonide 20 m + LA Fluoroscopic	IM injection TAC hexacetonide 20 mg + LA Fluoroscopic	3-6 mos.	0% (0/31)	3% (1/29)	NR	NR
Increased blood glucose	Ribeiro (2013)	TAC hexacetonide 20 mg + LA Fluoroscopic	IM injection TAC hexacetonide 20 mg + LA Fluoroscopic	6 mos.	8.33% (5/60)*		NC	NC
Nausea	Ribeiro (2013)	TAC hexacetonide 20 mg + LA Fluoroscopic	IM injection TAC hexacetonide 20 mg + LA Fluoroscopic	6 mos.	5% (3/60)*		NC	NC
Pain (post procedure)	Ribeiro (2013)	TAC hexacetonide 20 mg + LA Fluoroscopic	IM injection TAC hexacetonide 20 mg + LA Fluoroscopic	6 mos.	15% (9/60)*		NC	NC
Spinal arthrodesis for aggravation of back pain after a fall	Ribeiro (2013)	TAC hexacetonide 20 mg + LA Fluoroscopic	IM injection TAC hexacetonide 20 mg + LA Fluoroscopic	6 mos.	3% (1/31)	0% (0/29)	NR	NR

Adverse event	Author (year)	IASI Injectate Guidance	NIAI Injectate Guidance	F/U	IASI % (n/N)	NIAI % (n/N)	RR (95% CI)	p-value
Vaginal bleeding	Ribeiro (2013)	TAC hexacetonide 20 mg + LA Fluoroscopic	IM injection TAC hexacetonide 20 mg + LA Fluoroscopic	6 mos.	5% (3/60)*		NC	NC

IM: intramuscular; LA: local anesthetic; mos.: months; NC: not calculable; NR: not reported; TAC: Triamcinolone

* "No significant differences were found between the groups regarding the number of adverse [local and systemic] events."

† Patient had no history of heart disease and did not report any adverse events during follow-up that might be related to heart disease.

Appendix Table T7. Lumbar intra-articular steroid injections (IASI) vs. radiofrequency denervation: Adverse events from RCTs

Adverse event	Author (year)	IASI Steroid used Imaging guidance	RFN	F/U	IASI % (n/N)	RFN % (n/N)	RR (95% CI)	p-value
Catastrophic								
(none)								
Serious								
"Major adverse events" (details NR)	Lakemeier (2013)	BET 3 mg + sham denervation Fluoroscopic	RF denervation + LA Fluoroscopic + electro stimulation confirmation	6 mos.	0% (0/29)	0% (0/27)	NC	NC
Non-serious (or insufficient detail to categorize as serious)								
(none)								

BET: betamethasone; LA: local anesthetic; mos.: months; NC: not calculable; RF: radiofrequency

Appendix Table T8. Lumbar Extra-articular steroid injections (EASI) vs. extra-articular non-steroidal injections (EANSI): Adverse events from RCTs

Adverse event	Author (year)	EASI Injectate Guidance	EANSI Injectate Guidance	F/U	EASI % (n/N)	EANSI % (n/N)	RR (95% CI)	p-value
Catastrophic								
(none)								
Serious								
(none)								
Non-serious (or insufficient detail to categorize as serious)								
Headache (post lumbar puncture)	Manchikanti (2001)	MPS + LA or LA with Sarapin Fluoroscopic	LA or LA with Sarapin Fluoroscopic	<30 mos.	0% (0/41)	0% (0/32)	NR	NR
Infection	Manchikanti (2001)	MPS + LA or LA with Sarapin Fluoroscopic	LA or LA with Sarapin Fluoroscopic	<30 mos.	0% (0/41)	0% (0/32)	NR	NR
Rash	Manchikanti (2001)	MPS + LA or LA with Sarapin Fluoroscopic	LA or LA with Sarapin Fluoroscopic	<30 mos.	0% (0/41)	0% (0/32)	NR	NR
Reaction to drugs, epidural, or subarachnoid block	Manchikanti (2001)	MPS + LA or LA with Sarapin Fluoroscopic	LA or LA with Sarapin Fluoroscopic	<30 mos.	0% (0/41)	0% (0/32)	NC	NC
Weight gain	Manchikanti (2001)	MPS + LA or LA with Sarapin Fluoroscopic	LA or LA with Sarapin Fluoroscopic	<30 mos.	0% (0/41)	0% (0/32)	NR	NR
"Adverse events"	Manchikanti (2010, 2008)	BET + LA or LA with Sarapin Fluoroscopic	LA or LA with Sarapin Fluoroscopic	24 mos.	0% (0/60)	0% (0/60)	NR	NR

mos.: months; NC: not calculable; BET: betamethasone; LA: local anesthetic; mos.: months; MPS: methylprednisolone; NR: not reported

Appendix Table T9. Lumbar Extra-articular steroid injections (EASI) vs. non-extra-articular injections (NEAI): Adverse events from RCTs

Adverse event	Author (year)	EASI Injectate Guidance	NEAI Injectate Guidance	F/U	EASI % (n/N)	NEAI % (n/N)	RR (95% CI)	p-value
Catastrophic								
(none)								
Serious								
(none)								
Non-serious (or insufficient detail to categorize as serious)								
"Side-effects"	Lilius (1989)	MPS 80 mg + LA Fluoroscopic	Intra-articular saline injection Fluoroscopic	3 mos.	6.6% (7/106)*		NC	NC

LA: local anesthetic; mos.: months; MPS: methylprednisolone; NC: not calculable; NR: not reported

*Includes data from a third treatment group (Intra-articular MPS 80 mg), reported in both tables.

Appendix Table T10. Lumbar Extra-articular steroid injections (EASI) vs. disc procedure: Adverse events from RCTs

Adverse event	Author (year)	EASI Injectate Guidance	Disc procedure	F/U	EASI % (n/N)	Disc procedure % (n/N)	RR (95% CI)	p-value
Catastrophic								
(none)								
Serious								
Infection	Civelek (2012)	MPS 40 mg + LA Fluoroscopic	RFN Fluoroscopic + electro stimulation confirmation	12 mos.	0% (0/50)	0% (0/50)	NR	NR
Non-serious (or insufficient detail to categorize as serious)								
Increase in severity of low back pain	Civelek (2012)	MPS 40 mg + LA Fluoroscopic	RFN Fluoroscopic + electro stimulation confirmation	12 mos.	0% (0/50)	4% (2/50)	NR	NR
New motor deficit	Civelek (2012)	MPS 40 mg + LA Fluoroscopic	RFN Fluoroscopic + electro stimulation confirmation	12 mos.	0% (0/50)	0% (0/50)	NR	NR
New sensory deficit	Civelek (2012)	MPS 40 mg + LA Fluoroscopic	RFN Fluoroscopic + electro stimulation confirmation	12 mos.	0% (0/50)	0% (0/50)	NR	NR

LA: local anesthetic; mos.: months; MPS: methylprednisolone; NR: not reported; RFN: radiofrequency facet neurotomy

APPENDIX U. Lumbar spinal injections: Adverse events from cohort studies

Appendix Table U1. Lumbar epidural steroid injections vs. conservative care: Adverse events from cohort studies

Adverse event	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	F/U	Group A % (n/N)	Group B % (n/N)	Effect Estimate (95% CI)	p-value
Catastrophic									
(none)									
Serious									
(none)									
Non-serious (or insufficient detail to categorize as serious)									
Disc degeneration	Mandel 2013	NR Epidural spinal injection	No injection	NR (likely varies)	5 years	7.3%	7.4%	NR	0.547
Intervertebral disc disorder with myelopathy	Mandel 2013	NR Epidural spinal injection	No injection	NR (likely varies)	5 years	5.2%	4.5%	NR	0.597
Lumbago	Mandel 2013	NR Epidural spinal injection	No injection	NR (likely varies)	5 years	90.0%	91.9%	NR	0.011
Lumbar disc degeneration	Mandel 2013	NR Epidural spinal injection	No injection	NR (likely varies)	5 years	38.8%	34.8%	NR	0.012
Lumbar disc disorder with myelopathy	Mandel 2013	NR Epidural spinal injection	No injection	NR (likely varies)	5 years	19.8%	17.6%	NR	0.383
Lumbar disc displacement	Mandel 2013	NR Epidural spinal injection	No injection	NR (likely varies)	5 years	37.0%	35.0%	NR	0.605
Lumbar spinal stenosis	Mandel 2013	NR Epidural spinal injection	No injection	NR (likely varies)	5 years	54.7%	51.9%	NR	0.082
Post laminectomy	Mandel	NR	No injection	NR (likely	5	12.2%	11.8%	NR	0.389

Adverse event	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	F/U	Group A % (n/N)	Group B % (n/N)	Effect Estimate (95% CI)	p-value
surgery	2013	Epidural spinal injection		varies)	years				
Radiculopathy	Mandel 2013	NR Epidural spinal injection	No injection	NR (likely varies)	5 years	59.3%	62.0%	NR	0.194
Sciatica	Mandel 2013	NR Epidural spinal injection	No injection	NR (likely varies)	5 years	44.9%	40.7%	NR	0.021

Appendix Table U2. Lumbar extra-articular steroid injections vs. non-steroid extra articular injections: Adverse events from cohort studies

Adverse event	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	F/U	Group A % (n/N)	Group B % (n/N)	Effect Estimate (95% CI)	p-value
Any complication (undefined)	Fotiadou 2012	Triamcinolone 40 mg/mL + LA	Nerve root block (injectate NR)	NR	3 mos.	0% (0/55) patients	0% (0/31)	NR	NR

APPENDIX V. Lumbar spinal injections: Adverse events from case series

Appendix Table V1. Lumbar epidural steroid injections: Adverse events from case series

Adverse event	% (n/N) Mean (range)	F/U	Approach	Steroid used Imaging guidance	Author (year)
Catastrophic					
Serious					
Epidural lipomatosis	6.1% (52/856)	NR	NR	MPS 120 mg Guidance NR	Jaimes III (2014)
Fever	0% patients (0/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Infection	0% injections (0/2412)	Procedural	TF	NR Fluoroscopic imaging	Candido (2010)
Infection	0% injections (0/4723)	Procedural	IL	NR Fluoroscopic imaging	Candido (2010)
Paraplegia (transient, recovery within 90 minutes)	5.8% (1/17)	14 mos.	IL epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Respiratory depression	0% (0/152)	14 mos.	TF epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Respiratory depression	0% (0/17)	14 mos.	IL epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Respiratory Failure	0% (0/152)	14 mos.	TF epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Respiratory Failure	0% (0/17)	14 mos.	IL epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Non-serious (or insufficient detail to categorize as serious)					
Blood pressure elevation (24 hours)	0.5% patients (1/207); 0.3% injections (1/322)	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	Botwin (2000)
Blood sugar elevation	0.5% patients (1/207);	24 hours;	TF	BET acetate (9-12 mg) OR	Botwin (2000)

Adverse event	% (n/N) Mean (range)	F/U	Approach	Steroid used Imaging guidance	Author (year)
(24 hours)	0.3% injections (1/322) (patient had insulin-dependent diabetes)	1-3 weeks		methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	
Chest discomfort	0% (0/152)	14 mos.	TF epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Chest discomfort	0% (0/17)	14 mos.	IL epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Chest pain	0% (0/152)	14 mos.	TF epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Chest pain	0% (0/17)	14 mos.	IL epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Dizziness	0% patients (0/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Dizziness	1.6% (4/251) injections	Periprocedural	TF	TAC 40 mg + LA Fluoroscopic guidance	Hong (2013)
Dizziness (24 hours)	0.5% patients (1/207); 0.3% injections (1/322)	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	Botwin (2000)
Dural puncture	0% injections and patients	24 hours; 1-3 weeks	Caudal	BET acetate (12 mg) OR TAC acetate (80 mg) Fluoroscopic imaging	Botwin (2001)
Dural puncture	0% injections and patients	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	Botwin (2000)
Dural puncture + postdural puncture headache	0.3% (1/251) injections	Periprocedural	TF	TAC 40 mg + LA Fluoroscopic guidance	Hong (2013)
Dural puncture with	1.1% (1/90)	Periproced	IL	Steroid NR	McGrath (2011)

Adverse event	% (n/N) Mean (range)	F/U	Approach	Steroid used Imaging guidance	Author (year)
ensuing spinal headache		ural		Fluoroscopic guidance	
Facial flushing	2.4% injections (6/246); (% patients NR)	24 hours; 1-3 weeks	Caudal	BET acetate (12 mg) OR TAC acetate (80 mg) Fluoroscopic imaging	Botwin (2001)
Facial flushing (transient, resolved in several days without treatment)	1.4% patients (3/207); 1.2% injections (4/322)	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	Botwin (2000)
Flushing (defined as redness or warmth without rash)	11.3% patients (27/240); 11.3% injections (27/240)	2 days	TF	BET acetate/ BET sodium phosphate (6 mg) OR methlyprednisolone (80 mg) Fluoroscopic imaging	Everett (2004)
Groin pain	0.05% (1/1667)	Periproced ural	TF	Steroid Fluoroscopic guidance	McGrath (2011)
Headache	1% patients (1/100)	Procedural , post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Headache (nonpositional, 24 hours)	3.7% injections (9/246; (% patients NR)	24 hours; 1-3 weeks	Caudal	BET acetate (12 mg) OR TAC acetate (80 mg) Fluoroscopic imaging	Botwin (2001)
Headache (nonpositional, 24 hours)	4.8% patients (10/207); 3.1% injections (10/322)	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	Botwin (2000)
Inadvertent intra-articular lumbar facet joint injection	1.2% (8/685) injections	Periproced ural	IL	TAC dose NR + LA Fluoroscopic guidance	Huang (2012)
Increased leg pain (24 hours)	0.8% patients (1/128); 0.4% injections (1/246)	24 hours; 1-3 weeks	Caudal	BET acetate (12 mg) OR TAC acetate (80 mg) Fluoroscopic imaging	Botwin (2001)
Increased leg pain	1.0% patients (2/207);	24 hours;	TF	BET acetate (9-12 mg) OR	Botwin (2000)

Adverse event	% (n/N) Mean (range)	F/U	Approach	Steroid used Imaging guidance	Author (year)
(with radicular symptoms, persistent until 2nd injection two weeks later)	0.6% injections (2/322) (Transient in one patient)	1-3 weeks		methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	
Increased pain	1% patients (1/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Increased pain	1.1% (42/3964) injections	Periprocedural	TF	Steroid Fluoroscopic guidance	McGrath (2011)
Insomnia	0% patients (0/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Insomnia (night of procedure)	4.9% injections (12/246); (% patients NR)	24 hours; 1-3 weeks	Caudal	BET acetate (12 mg) OR TAC acetate (80 mg) Fluoroscopic imaging	Botwin (2001)
Intravascular injection of steroid	0% (0/249)	Perioprocedural	TF	DEX 5 mg + LA	Hong (2014)
Intravascular uptake of injectate (steroid + LA)	14.3% (40/280) injections	Periprocedural	NR	TAC ≤3 mL (40 mg/mL) + LA Fluoroscopic guidance	Goodman 2005
Kerma Area Product	101.7 (3.02 to 1048.2), n = 181	Periprocedural	TF	TAC acetonide 40 mg + LA Fluoroscopic guidance	Kim (2014)
Kerma Area Product	101.8 (16.0-604.5), n = 47	Periprocedural	Caudal	TAC acetonide 40 mg + LA Fluoroscopic guidance	Kim (2014)
Leg weakness	0% (0/152)	14 mos.	TF epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Leg weakness	1.3% (2/152)	14 mos.	TF epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Leg weakness (24 hours)	0.5% patients (1/207); 0.3% injections	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate	Botwin (2000)

Adverse event	% (n/N) Mean (range)	F/U	Approach	Steroid used Imaging guidance	Author (year)
	(1/322)			(80 mg) Fluoroscopic imaging	
Minor bleeding	0% patients (0/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Motor weakness	0% patients (0/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Muscle spasms	1% patients (1/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Nausea	0% (0/152)	14 mos.	TF epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Nausea	0% (0/17)	14 mos.	IL epidural block	TAC acetonide 40 mg + LA Fluoroscopic guidance	Lee (2012)
Nausea (24 hours)	0.5% patients (1/207); 0.3% injections (1/322)	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	Botwin (2000)
Nausea (transient)	0.8% injections (2/246) (% patients NR)	24 hours; 1-3 weeks	Caudal	BET acetate (12 mg) OR TAC acetate (80 mg) Fluoroscopic imaging	Botwin (2001)
Nausea/ vomiting	1% patients (1/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Numbness	0% patients (0/100)	Procedural	TF	BET acetate/ BET sodium phosphate	Manchikanti (2004)

Adverse event	% (n/N) Mean (range)	F/U	Approach	Steroid used Imaging guidance	Author (year)
		, post-procedure, 24 hours, 72 hours		(3-6 mg) Fluoroscopic imaging	
Numbness	0.15% (6/3964) injections	Periprocedural	TF	Steroid Fluoroscopic guidance	McGrath (2011)
Pain at injection site	0.23% (9/3964) injections	Periprocedural	TF	Steroid Fluoroscopic guidance	McGrath (2011)
Pain at injection site (defined as increased back pain, 24 hours)	3.9% patients (8/207); 2.4% injections (8/322)	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	Botwin (2000)
Pain at injection site (increased back pain)	3.3% injections (8/246), (% patients NR)	24 hours; 1-3 weeks	Caudal	BET acetate (12 mg) OR TAC acetate (80 mg) Fluoroscopic imaging	Botwin (2001)
Paresthesia during procedure	2.0% (5/251) injections	Periprocedural	TF	TAC 40 mg + LA Fluoroscopic guidance	Hong (2013)
Postinjection back soreness	3.2% (8/251) injections	Periprocedural	TF	TAC 40 mg + LA Fluoroscopic guidance	Hong (2013)
Rash (two weeks)	0.5% patients (1/207); 0.3% injections (1/322)	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	Botwin (2000)
Soreness at injection site	6% patients (6/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Swelling	0% patients (0/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Transient leg	0.8% (2/251)	Periproced	TF	TAC 40 mg + LA	Hong (2013)

Adverse event	% (n/N) Mean (range)	F/U	Approach	Steroid used Imaging guidance	Author (year)
weakness	injections	ural		Fluoroscopic guidance	
Vasovagal reaction	0% patients (0/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Vasovagal reaction (relieved with Trendelenburg positioning)	0.5% patients (1/207); 0.3% injections (1/322)	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	Botwin (2000)
Vasovagal reaction (relieved with Trendelenburg positioning)	0.8% injections (2/246); (% patients NR)	24 hours; 1-3 weeks	Caudal	BET acetate (12 mg) OR TAC acetate (80 mg) Fluoroscopic imaging	Botwin (2001)
Voiding difficulty	0% patients (0/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Wrong (intradiscal) injection	0.021% injections (1/4723)	Procedural	IL	NR Fluoroscopic imaging	Candido (2010)
Wrong (intradiscal) injection	0.249% injections (6/2412)	Procedural	TF	NR Fluoroscopic imaging	Candido (2010)
Wrong (intradiscal) injection	2.3% (6/251) injections	Periproced ural	TF	TAC 40 mg + LA Fluoroscopic guidance	Hong (2013)
Other complications (not further specified)	0.68% (27/3964) injections	Periproced ural	TF	Steroid Fluoroscopic guidance	McGrath (2011)
Overall complication rate	9.6% (31 complications/322 injections)	24 hours; 1-3 weeks	TF	BET acetate (9-12 mg) OR methylprednisone sodium succinate (80 mg) Fluoroscopic imaging	Botwin (2000)
Overall complication rate	16.3% (40 complications/246 injections)	24 hours; 1-3 weeks	Caudal	BET acetate (12 mg) OR TAC acetate (80 mg) Fluoroscopic imaging	Botwin (2001)

Adverse event	% (n/N) Mean (range)	F/U	Approach	Steroid used Imaging guidance	Author (year)
Overall complication rate (per injection)	#1: 15.1% (21/139 injections) #2: 16.9% (14/83 injections) #3: 14.3% (5/35)	24 hours; 1-3 weeks	Caudal	BET acetate (12 mg) OR TAC acetate (80 mg) Fluoroscopic imaging	Botwin (2001)
Any complication (not including vascular puncture)	7% patients (7/100)	Procedural, post-procedure, 24 hours, 72 hours	TF	BET acetate/ BET sodium phosphate (3-6 mg) Fluoroscopic imaging	Manchikanti (2004)
Any minor complications (not further specified)	2.1% (83/3964) injections	Periprocedural	TF	Steroid NR Fluoroscopic guidance	McGrath (2011)

BET: betamethasone; DEX: dexamethasone; IL: interlaminar; mos.: months; MPS: methylprednisolone; NR: not reported; TAC: triamcinolone; TF: transforaminal

Appendix Table V2. Lumbar intra-articular injections: Adverse events from case series

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
Catastrophic					
(none)					
Serious					
Medication entered into subarachnoid space (no adverse sequelae)	0.06% (1/1777)	Procedural, immediate post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Stalcup (2006)
Non-serious (or insufficient detail to categorize as serious)					
Increased pain or new pain	2.3% procedures (41/1777)	Procedural, immediate post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Stalcup (2006)
Puncture of dural sac	0.06% procedures (1/1777)	Procedural, immediate post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Stalcup (2006)
Inability to localize needle tip properly (injection could not be given)	0.4% procedures (7/1777)	Procedural, immediate post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Stalcup (2006)
Injection given at wrong vertebral level (resulting in no adverse events)	0.06% procedures (1/1777)	Procedural, immediate post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Stalcup (2006)
Leg weakness or lightheadedness	3.0% procedures (54/1777)	Procedural, immediate post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Stalcup (2006)
Any complication (all resolved with no prolonged damage or harm)	5.5% procedures (98/1777)	Procedural, immediate post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Stalcup (2006)

BET: betamethasone; DEX: dexamethasone; IL: interlaminar; mos.: months; MPS: methylprednisolone; NR: not reported; TAC: triamcinolone; TF: transforaminal

Appendix Table V3. Lumbar extra-articular (medial branch) injections: Adverse events from case series

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
Catastrophic					
Quadriparesis	0% (0/291)	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Serious					
Paraplegia (transient, patients recovered within 1.3-8 hours; 5 events in 3 patients)	1.7% (5/291)	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Respiratory depression or failure	0% (0/291)	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Non-serious (or insufficient detail to categorize as serious)					
Chest pain or discomfort	0% (0/291)	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Leg weakness	0% (0/291)	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Nausea	0% (0/291)	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)

BET: betamethasone; DEX: dexamethasone; IL: interlaminar; mos.: months; MPS: methylprednisolone; NR: not reported; TAC: triamcinolone; TF: transforaminal

APPENDIX W. Cervical spinal injections: Adverse events from RCTs

Appendix Table W1. Cervical epidural steroid injections (ESI) vs. non-steroidal epidural injections (ENSI): Adverse events from RCTs

Adverse event	Author (year)	ESI Steroid used Imaging guidance	ENSI Substance used	Approach	F/U	ESI % (n/N)	ENSI % (n/N)
Catastrophic							
(none)							
Serious							
Subarachnoid puncture*	Manchikanti (2012) (FBSS)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	12 mos.	0.9% (2/215 injections)	
Subarachnoid puncture*	Manchikanti (2012) (Stenosis)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	12 mos.	0.9% (2/214 injections)	
Subarachnoid puncture*	Manchikanti (2013, 2012)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0.3% (2/654 injections)	
Subarachnoid puncture*	Manchikanti (2014, 2012)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0.9% (6/688 injections)	
Non-serious (or insufficient detail to categorize as serious)							
Headache (postoperative following subarachnoid puncture)	Manchikanti (2012) (Stenosis)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	12 mos.	0% (0/214)	
Headache (postoperative following subarachnoid puncture)	Manchikanti (2013, 2012) (disc herniation)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0% (0/654)	
Headache (postoperative following subarachnoid puncture)	Manchikanti (2014, 2012) (pain only)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0% (0/688)	
Headache	Manchikanti (2012) (FBSS)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	12 mos.	0% (0/215 injections)	
Intravascular entry*	Manchikanti (2012) (FBSS)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	12 mos.	0.9% (2/215 injections)	

Adverse event	Author (year)	ESI Steroid used Imaging guidance	ENSI Substance used	Approach	F/U	ESI % (n/N)	ENSI % (n/N)
Intravascular entry*	Manchikanti (2012) (Stenosis)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	12 mos.	0.5% (1/214 injections)	
Intravascular penetration*	Manchikanti (2013, 2012)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0.6% (4/654 injections)	
Intravascular penetration*	Manchikanti (2014, 2012)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	1.5% (10/688 injections)	
Nerve root irritation	Manchikanti (2013, 2012)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0.8% (5/654 injections)	
Nerve root irritation (no long term sequelae)	Manchikanti (2014, 2012)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0.4% (3/688 injections)	
Soreness lasting 1 week	Manchikanti (2013, 2012)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0.2% (1/654 injections)	
Soreness lasting ≥ 1 week	Manchikanti (2012) (Stenosis)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	12 mos.	0.5% (1/214 injections)	
Long-term sequelae	Manchikanti (2014, 2012)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0% (0/120)	
Long-term sequelae	Manchikanti (2013, 2012)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	24 mos.	0% (0/654 injections)	
"Other complications"	Manchikanti (2012) (FBSS)	BET 6 mg + LA Fluoroscopic	LA Fluoroscopic	IL	12 mos.	0% (0/215 injections)	

BET: betamethasone; DEX: dexamethasone; IL: Interlaminar; LA: local anesthetic; mos.: months; MPS: methylprednisolone; NR: not reported; TAC: triamcinolone
*whether there was an intravascular injection of steroid or local anesthetic was not reported

Appendix Table W2. Cervical epidural steroid injections (ESI) vs. non-epidural (NEI): Adverse events from RCTs

Adverse event	Author (year)	ESI Steroid used Imaging guidance	NEI Substance used	Approach	F/U	ESI % (n/N)	NEI % (n/N)
"Complications of ESI"	Stav (1993)	MPS 80 mg + sodium acetate + LA Imaging NR	Posterior neck muscle injection MPS 80 mg + LA Imaging NR	NR	12 mos.	0% (0/25)	NA

NA: not applicable; LA: local anesthetic; mos.: months; MPS: methylprednisolone

Appendix Table W3. Cervical epidural steroid injections (ESI) vs. conservative care (CC): Adverse events from RCTs

Adverse event	Author (year)	ESI Steroid used Imaging guidance	CC	Approach	F/U	ESI % (n/N)	CC % (n/N)
Catastrophic							
(none)							
Serious							
(none)							
Non-serious (or insufficient detail to categorize as serious)							
Headache (details NR, not considered serious)	Cohen (2014)	Depo-MPS 60 mg + saline Fluoroscopic	Pharmacotherapy + PT	IL	6 mos.	1.4% (2/147)	NR
Prolonged post-procedure pain requiring prescription (details NR, not considered serious)	Cohen (2014)	Depo-MPS 60 mg + saline Fluoroscopic	Pharmacotherapy + PT	IL	6 mos.	0.7% (1/147)	NR
Rash	Cohen (2014)	Depo-MPS 60 mg + saline Fluoroscopic	Pharmacotherapy + PT	IL	6 mos.	0.7% (1/147)	NR
Tachycardia*	Cohen (2014)	Depo-MPS 60 mg + saline Fluoroscopic	Pharmacotherapy + PT	IL	6 mos.	0.7% (1/147)	NR
Temporary worsening neurological symptoms not accompanied by MRI progression	Cohen (2014)	Depo-MPS 60 mg + saline Fluoroscopic	Pharmacotherapy + PT	IL	6 mos.	1.4% (2/147)	NR
Vasovagal episodes (details NR)	Cohen (2014)	Depo-MPS 60 mg + saline Fluoroscopic	Pharmacotherapy + PT	IL	6 mos.	1.4% (2/147)	NR
Wet-tap associated with neurological sequelae (details NR)	Cohen (2014)	Depo-MPS 60 mg + saline Fluoroscopic	Pharmacotherapy + PT	IL	6 mos.	0.7% (1/147)	NR
"Adverse events"	Park (2012)	TAC 5 mg + hyaluronidase + LA Fluoroscopic	No injection	IL	12 mos.	0% (0/200)	0% (0/200)

IL: Interlaminar; LA: local anesthetic; mos.: months; MPS: methylprednisolone; NR: not reported; PT: physical therapy; TAC: triamcinolone;

* postanesthesia,"resolved with assurance"

Appendix Table W4. Cervical intra-articular steroid injections (IASI) vs. intra-articular non-steroidal injections (IANSI): Adverse events from RCTs

Adverse event	Author (year)	IASI Steroid used Imaging guidance	IANSI Substance used	F/U	IASI % (n/N)	IANSI % (n/N)
Catastrophic						
(none)						
Serious						
Infection	Manchikanti (2010, 2008)	BET 0.15 mg + LA with or without Sarapin Fluoroscopic	LA with or without Sarapin Fluoroscopic	24 mos.	0% (0/120)	
Nerve root or spinal trauma	Manchikanti (2010, 2008)	BET 0.15 mg + LA with or without Sarapin Fluoroscopic	LA with or without Sarapin Fluoroscopic	24 mos.	0% (0/120)	
Non-serious (or insufficient detail to categorize as serious)						
Facial flushing (transient)	Barnsley (1994)	BET 5.7 mg Fluoroscopic	LA Fluoroscopic	2.7 mos.	4.9% (2/41)	

BET: betamethasone; LA: local anesthetic; mos.: months;

APPENDIX X. Cervical spinal injections: Adverse events from case series

Appendix Table X1. Cervical epidural steroid injections: Adverse events from case series

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
Catastrophic					
Paraplegia	0% (0/47)	14 mos.	TF	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Quadriparesis	0% (0/47)	14 mos.	TF	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Respiratory depression or failure	0% (0/47)	14 mos.	TF	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Serious					
Superficial infection/abscess at injection site (requiring incision/drainage and antibiotics)	0.5% patients (1/192)	Immediate post-procedure, 3 and 6 weeks	Steroid nerve block	MPS (80 mg for first injection; 40 mg for subsequent injections; 20 mg after first injection if multiple injections performed simultaneously) No fluoroscopic imaging	Waldman (1989)
Serious/significant complications (not further specified)	0% (0/247)	2 mos.	TF	DEX 10 mg + LA CT guidance	Wald (2012)
Non-serious (or insufficient detail to categorize as serious)					
Chest pain or discomfort	0% (0/47)	14 mos.	TF	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Device malfunction	0.7% (3/409)	Periprocedural	TF	DEX 4 mg/mL + LA Fluoroscopic guidance	Kloth (2011)
Dural puncture and associated headache (24-72 hours)	1.0% patients (2/192)	Immediate post-procedure, 3 and 6 weeks	Steroid nerve block	MPS (80 mg for first injection; 40 mg for subsequent injections; 20 mg after first injection if multiple injections performed simultaneously) No fluoroscopic imaging	Waldman (1989)
Inadequate epi-radicular flow	4.1% (17/410)	Periprocedural	TF	DEX 4 mg/mL + LA Fluoroscopic guidance	Kloth (2011)
Intra-arterial injection	1.7% (7/411)	Periprocedural	TF	DEX 4 mg/mL + LA Fluoroscopic guidance	Kloth (2011)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
Leg weakness	0% (0/47)	14 mos.	TF	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Nausea	0% (0/47)	14 mos.	TF	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Operative nerve pain or paresthesia	15.6% (64/410)	Periprocedural	TF	DEX 4 mg/mL + LA Fluoroscopic guidance	Kloth (2011)
Vascular trespass (per level)	19.7% (81/411)	Periprocedural	TF	DEX 4 mg/mL + LA Fluoroscopic guidance	Kloth (2011)
Vasovagal reaction (occurred during first block)	1.6% patients (3/192)	Immediate post-procedure, 3 and 6 weeks	Steroid nerve block	MPS (80 mg for first injection; 40 mg for subsequent injections; 20 mg after first injection if multiple injections performed simultaneously) No fluoroscopic imaging	Waldman (1989)
Vasovagal reactions	1.6% (4/247)	2 mos.	TF	DEX 10 mg + LA CT guidance	Wald (2012)

BET: betamethasone; DEX: dexamethasone; IL: interlaminar; mos.: months; MPS: methylprednisolone; NR: not reported; TAC: triamcinolone; TF: transforaminal

Appendix Table X2. Cervical intra-articular injections: Adverse events from case series

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
No studies					

BET: betamethasone; DEX: dexamethasone; IL: interlaminar; mos.: months; MPS: methylprednisolone; NR: not reported; TAC: triamcinolone; TF: transforaminal

Appendix Table X3. Cervical extra-articular (medial branch) injections: Adverse events from case series

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
Catastrophic					
Brain stem injury/infarct	0% patients (0/4612)	Immediate post-procedure	Selective cervical nerve root blockade (anterolateral oblique approach)	BET acetate suspension (dose NR) OR generic/formulated sodium phosphate or MPS phosphate or acetate (dose NR) Fluoroscopic imaging	Schellhas (2007)
Cerebellar/cerebral injury/infarct	0% patients (0/4612)	Immediate post-procedure	Selective cervical nerve root blockade (anterolateral oblique approach)	BET acetate suspension (dose NR) OR generic/formulated sodium phosphate or MPS phosphate or acetate (dose NR) Fluoroscopic imaging	Schellhas (2007)
Death	0% patients (0/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Paralysis	0% patients (0/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Paraplegia	0% (0/197)	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Spinal cord injury	0% patients (0/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Spinal cord injury/infarct	0% patients (0/4612)	Immediate post-procedure	Selective cervical nerve root blockade (anterolateral oblique approach)	BET acetate suspension (dose NR) OR generic/formulated sodium phosphate or MPS phosphate or acetate (dose NR) Fluoroscopic imaging	Schellhas (2007)
Stroke	0% patients	Immediate	Extraforaminal nerve	BET acetate/ BET sodium phosphate (6 mg) OR	Ma (2005)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
	(0/844)	post-procedure	block	MPS acetate suspension (40 mg) Fluoroscopic imaging	
Serious					
Grand mal seizure (occurred within 10 seconds of injection, lasted 3-4 minutes)	0.02% patients (1/4612)	Immediate post-procedure	Selective cervical nerve root blockade (anterolateral oblique approach)	BET acetate suspension (dose NR) OR generic/formulated sodium phosphate or MPS phosphate or acetate (dose NR) Fluoroscopic imaging	Schellhas (2007)
Haematoma (suspected, resolved without sequelae)	0.2% patients (1/659)	30 minutes post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (dose NR) OR DEX sodium phosphate (dose NR) Fluoroscopic imaging	Pobiel (2009)
Increased clinical pain (≥ 10 days)	10% of patients (~461/4612)	Immediate post-procedure	Selective cervical nerve root blockade (anterolateral oblique approach)	BET acetate suspension (dose NR) OR generic/formulated sodium phosphate or MPS phosphate or acetate (dose NR) Fluoroscopic imaging	Schellhas (2007)
Infection	0% patients (0/4612)	Immediate post-procedure	Selective cervical nerve root blockade (anterolateral oblique approach)	BET acetate suspension (dose NR) OR generic/formulated sodium phosphate or MPS phosphate or acetate (dose NR) Fluoroscopic imaging	Schellhas (2007)
Infection	0% patients (0/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Life-threatening generalized analphylactic reaction (occurred within minutes of procedure completion)	0.02% patients (1/4612)	Immediate post-procedure	Selective cervical nerve root blockade (anterolateral oblique approach)	BET acetate suspension (dose NR) OR generic/formulated sodium phosphate or MPS phosphate or acetate (dose NR) Fluoroscopic imaging	Schellhas (2007)
Nerve root injury/infarct	0% patients (0/4612)	Immediate post-procedure	Selective cervical nerve root blockade (anterolateral oblique approach)	BET acetate suspension (dose NR) OR generic/formulated sodium phosphate or MPS phosphate or acetate (dose NR) Fluoroscopic imaging	Schellhas (2007)
Quadriparesis (transient, patient recovered within 60 minutes, attributed to	0.5% (1/197) injections	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
intravascular injection)					
Quadriparesis (attributed to conversion disorder, patient recovered within 2 months)	05% (1/197) injections	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Respiratory depression	0.5% (1/197) injections	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Respiratory failure	0.5% (1/197) injections	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Vertebral artery injury	0% patients (0/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Any major complication	0% patients (0/659)	Postprocedurally and up to 30 days postop	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (dose NR) OR DEX sodium phosphate (dose NR) Fluoroscopic imaging	Pobiel (2009)
Non-serious (or insufficient detail to categorize as serious)					
Chest discomfort	1.0% (2/197) injections	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Chest pain	0.5% (1/197) injections	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Contralateral paresthesias (considered unrelated)	0.3% patients (1/345)	3 weeks	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (dose NR) OR DEX sodium phosphate (dose NR) Fluoroscopic imaging	Pobiel (2009)
Headache or dizziness	0.6% patients (5/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Hypersensitivity reaction	0.1% patients (1/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Increase in usual pain (30 days)	2.0% patients (7/345)	30 days	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR	Pobiel (2009)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
				MPS acetate suspension (dose NR) OR DEX sodium phosphate (dose NR) Fluoroscopic imaging	
Increase in usual pain (immediate post-procedure)	0.5% patients (3/659)	Immediate post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (dose NR) OR DEX sodium phosphate (dose NR) Fluoroscopic imaging	Pobiel (2009)
Leg weakness	0% (0/197)	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Localized skin discoloration (≥ 14 days)	"Small number of patients" (n NR)	Immediate post-procedure	Selective cervical nerve root blockade (anterolateral oblique approach)	BET acetate suspension (dose NR) OR generic/formulated sodium phosphate or MPS phosphate or acetate (dose NR) Fluoroscopic imaging	Schellhas (2007)
Minor allergic reaction	0.2% patients (1/659)	30 minutes post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (dose NR) OR DEX sodium phosphate (dose NR) Fluoroscopic imaging	Pobiel (2009)
Nausea	0.2% patients (1/659)	1 day	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (dose NR) OR DEX sodium phosphate (dose NR) Fluoroscopic imaging	Pobiel (2009)
Nausea	0.5% (1/197) injections	14 mos.	Medial branch block	TAC acetonide 8 mg + LA Fluoroscopic guidance	Lee (2012)
Sensation of transient incomplete lung expansion (resolved without sequelae)	0.2% patients (1/659)	30 minutes post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (dose NR) OR DEX sodium phosphate (dose NR) Fluoroscopic imaging	Pobiel (2009)
Sympathetic blockade	0.9% patients (6/659)	30 minutes post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (dose NR) OR DEX	Pobiel (2009)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
				sodium phosphate (dose NR) Fluoroscopic imaging	
Transient global amnesia	0.1% patients (1/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Transient neurological deficits (pain or weakness)	0.7% patients (6/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Vasovagal reaction	0.1% patients (1/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Vasovagal reaction (responded to conservative treatments)	2.9% patients (19/659)	30 minutes post-procedure	Selective nerve root block	BET acetate/ BET sodium phosphate (dose NR) OR MPS acetate suspension (dose NR) OR DEX sodium phosphate (dose NR) Fluoroscopic imaging	Pobiel (2009)
Wrong injection site (vertebral level)	0.2% patients (2/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Wrong injection type (facet block instead of nerve block)	0.1% patients (1/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Wrong site injection	0.4% patients (3/844)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)
Any complication	1.7% patients (14/844), 1.64% injections (17/1036)	Immediate post-procedure	Extraforaminal nerve block	BET acetate/ BET sodium phosphate (6 mg) OR MPS acetate suspension (40 mg) Fluoroscopic imaging	Ma (2005)

BET: betamethasone; DEX: dexamethasone; IL: interlaminar; mos.: months; MPS: methylprednisolone; NR: not reported; TAC: triamcinolone; TF: transforaminal

APPENDIX Y. Mixed population: Lumbar or Cervical spinal injections: Adverse events from cohort studies

Appendix Table Y1. Mixed Cervical and Lumbar steroid injections vs. no injection: Adverse events from cohort studies

Adverse event	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	F/U	Group A % (n/N)	Group B % (n/N)	Effect Estimate (95% CI)	p-value
Catastrophic									
(none)									
Serious									
(none)									
Non-serious (or insufficient detail to categorize as serious)									
Agitation	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	17% (25/151)	53% (32/60)	NR	.001
Dural puncture (1 week)	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	0% (0/151)	n/a	NR	NR
Dural puncture (procedural, cervical)	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	0.7% (1/151)	n/a	NR	NR
Esophagitis/gastritis-heartburn	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	24% (36/151)	28% (17/60)	NR	NS
Facial or chest flushing	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	19% (29/151)	13% (8/60)	NR	NS
Fatigue/malaise	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	19% (28/151)	43% (26/60)	NR	.001
Fluid retention	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	8% (12/151)	23% (14/60)	NR	.002
Headache (increased	Huston	BET	No	Selective nerve	1 wk	5% (8/151)	2% (1/60)	NR	NR

Adverse event	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	F/U	Group A % (n/N)	Group B % (n/N)	Effect Estimate (95% CI)	p-value
with standing)	(2005)*	(mg NR) Fluoroscopic imaging	injection	root injection					
Headache (nonspecific, not spinal)	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	8% (12/151)	2% (1/60)	NR	NS
Headache (not increased with standing)	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	18% (27/151)	12% (7/60)	NR	NS
Hearing loss	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	1% (2/151)	7% (4/60)	NR	NR
Increased pain	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	15% (22/151)	22% (13/60)	NR	NS
Increased pain at injection site	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	30% (46/151)	8% (5/60) †	NR	.001
Increased radicular pain	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	37% (56/151)	36% (21/60)	NR	NS
Increased spine pain	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	37% (56/151)	33% (20/60)	NR	NS
Insomnia (not pain related)	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	9% (14/151)	40% (24/60)	NR	NR
Insomnia (pain related)	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	11% (17/151)	38% (23/60)	NR	.001
Lightheadedness	Huston (2005)*	BET (mg NR)	No injection	Selective nerve root injection	1 wk	19% (29/151)	27% (16/60)	NR	NS

Adverse event	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	F/U	Group A % (n/N)	Group B % (n/N)	Effect Estimate (95% CI)	p-value
		Fluoroscopic imaging							
Nausea	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	17% (26/151)	10% (6/60)	NR	NS
Numbness (distribution of nerve block)	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	6% (9/151)	n/a	NR	NR
Numbness (lower extremity)	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	11% (17/151)	32% (19/60)	NR	ns
Numbness (upper extremity)	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	2% (3/151)	8% (19/60)	NR	.024
Vasovagal	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	0% (0/151)	0% (0/60)	NR	NR
Weight gain	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	7% (11/151)	0% (0/60)	NR	NR
Overall rate of any complaints	Huston (2005)*	BET (mg NR) Fluoroscopic imaging	No injection	Selective nerve root injection	1 wk	80% patients (121/151)	97% patients (58/60)	NR	.003

BET: Betamethasone; NR: Not reported; NS: not significant; wk: week

* Huston 2005: 75% lumbar (114/151), 25% cervical (37/151)

† Huston 2005: increased pain at injection site reported for control group even though no injection was received

APPENDIX Z. Mixed population: Lumbar or Cervical spinal injections: Adverse events from case series

Appendix Table Z1. Mixed Cervical and Lumbar epidural steroid injections: Adverse events from case series

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
Catastrophic					
(none)					
Serious					
Epidural hematoma (18 hours)	0.019% patients/injections (1/5334)	Immediate post-procedure, 2 weeks	Variable	Steroid NR Fluoroscopic imaging	Johnson (1999)
Fever and pain at the injection site	0.05% (1/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Infection	0% patients/ injections (0/5334)	Immediate post-procedure, 2 weeks	Variable	Steroid NR Fluoroscopic imaging	Johnson (1999)
Presented to ED and admitted to hospital with leg weakness	0.05% (1/1857)	9 days	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Presented to ED on day of injection for chest pain with subsequent overnight admission	0.05% (1/1857)	Same day as injection	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Major complications (not further specified)	0% (0/4265) injections	Periprocedural	IL, TF, and Caudal	Steroid Fluoroscopic guidance	McGrath (2011)
Non-serious (or insufficient detail to categorize as serious)					
"Significant" transient hypotensive episode	0.019% patients/injections (1/5334)	Immediate post-procedure, 2 weeks	Variable	Steroid NR Fluoroscopic imaging	Johnson (1999)
"Transient increase in pain for which the injection was performed"	1.1% (49/4265) injections	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Back stiffness extending from shoulders to buttocks	0.05% (1/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Chest pain	0.16% (3/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Chest and back pain	0.05% (1/1857)	1 week	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Cold sensation on the limb	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Cold sensation on the limb	0.7% (1/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
Decrease of heart rate	0% (0/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Decrease of heart rate	0.7% (1/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Delayed complications/ infections	0% (0/150 consecutive patients)	2 years	Variable	Steroid NR Fluoroscopic imaging	Johnson (1999)
Elevation in blood sugar	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Elevation in blood sugar	0.7% (1/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Elevation of heart rate	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Elevation of heart rate	1.3% (2/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Flushing	0.16% (7/4265) injections	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
General Discomfort	0% (0/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
General discomfort	0.7% (1/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Headache	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Headache	13.3% (20/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Headaches, no clear etiology	0.16% (3/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Heart burn	6% (9/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Heartburn	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Hiccups	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Hiccups	3.3% (5/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA	El Abd (2015)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
				Fluoroscopic guidance	
Hyperactivity/euphoria/ anxiety	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Hyperactivity/euphoria/ anxiety	5.3 % (8/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Imbalance	2% (3/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Increased Pain	2.1% (6/284) injections	Periprocedural	IL	Steroid Fluoroscopic guidance	McGrath (2011)
Increased pain and chest pain	0.05% (1/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Increased pain and headache	0.05% (1/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Increased pain and pain at injection site	0.05% (1/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Increased pain at injection site	14.6% (22/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Increased radicular pain	12% (18/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Increased spine pain	6% (9/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Insomnia	13.3% (20/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Leg cramping	0.16% (3/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Lightheadedness	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Lightheadedness	1.3% (2/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Local injection-site infections	0% (0/4265) injections	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Local irritation of soft tissues	0.16% (3/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Localized pain at injection site	0.33% (13/4265)	Periprocedural	IL, TF, and Caudal	Steroid NR	McGrath (2011)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
	injections			Fluoroscopic guidance	
Muscle spasms/cramps	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Muscle spasms/cramps	2% (3/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Nausea	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Nausea	5.3% (8/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Night sweats or chills	0.16% (3/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Nonpainful neurological complaints	0.16% (3/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Numbness	0% (0/284) injections	Periprocedural	IL	Steroid Fluoroscopic guidance	McGrath (2011)
Numbness	10% (15/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Numbness	4% (6/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Numbness and weakness	0.05% (1/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Pain at injection site	1.8% (5/284) injections	Periprocedural	IL	Steroid Fluoroscopic guidance	McGrath (2011)
Pain on the other limb	0% (0/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Pain on the other limb	0.7% (1/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Presented to ED for chest pain	0.05% (1/1857)	4 days	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Presented to ED for headache	0.05% (1/1857)	3 days	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Pruritus (genital, perineal, groin area)	0% (0/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Pruritus (genital, perineal, groin	4.7% (7/150)	Periprocedural	TF	DEX 10 mg/mL + LA	El Abd (2015)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
area)				Fluoroscopic guidance	
Rash/flush	0.7% (1/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Rash/flush	3.3% (5/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Sensation of numbness	0.14% (6/4265) injections	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Shaking	0% (0/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Shaking	0.7% (1/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Subjective fever	0.02% (1/4265) injections	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Swelling in area of injection	0.16% (3/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Symptoms suggestive of cardiovascular involvement, including heart palpitations and "feeling described as a 'rush'"	0.1% (2/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Tachycardia + hypertension (3 days)	0.019% patients/injections (1/5334)	Immediate post-procedure, 2 weeks	Variable	Steroid NR Fluoroscopic imaging	Johnson (1999)
Temporary bowel function impairment	0.1% (2/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Tingling	2.7% (4/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Tingling	4.7% (7/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Vasovagal reaction	3.50% (158/4512) injections	Periprocedural	TF	Steroid NR Fluoroscopic guidance	Kennedy 2013
Vasovagal response (severe)	0.019% patients/injections (1/5334)	Immediate post-procedure, 2 weeks	Variable	Steroid NR Fluoroscopic imaging	Johnson (1999)
Warm sensation on the limb	0.7% (1/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA	El Abd (2015)

Adverse event	% (n/N)	F/U	Approach	Steroid used Imaging guidance	Author (year)
				Fluoroscopic guidance	
Weakness	0% (0/150)	1 day to 2 weeks	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Weakness	0.16% (3/1857)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Weakness	0.7% (1/150)	Periprocedural	TF	DEX 10 mg/mL + LA Fluoroscopic guidance	El Abd (2015)
Any minor complications (not further specified)	6.0% (17/284) injections	Periprocedural	IL	Steroid Fluoroscopic guidance	McGrath (2011)
Any minor complications (not further specified)	2.4% (103/4265) injections	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Other minor complications (not further specified)	2.1% (6/284) injections	Periprocedural	IL	Steroid Fluoroscopic guidance	McGrath (2011)
Other minor complications (not further specified)	0.8% (34/4265 injections)	Periprocedural	IL, TF, and Caudal	Steroid NR Fluoroscopic guidance	McGrath (2011)
Overall complication rate	0.075% patients/injections (4/5334)	Immediate post-procedure, 2 weeks	Variable	Steroid NR Fluoroscopic imaging	Johnson (1999)

BET: betamethasone; DEX: dexamethasone; IL: interlaminar; mos.: months; MPS: methylprednisolone; NR: not reported; TAC: triamcinolone; TF: transforaminal

El Abd (2015) (2015):

- 81.3% (122/150) lumbar injections, 18.6% (28/150) cervical injections.

Kennedy 2013:

- Vasovagal reaction: decrement in heart rate and blood pressure as well as symptoms consistent with vv reaction including: lightheadedness, dizziness, palpitations, weakness, dimming or blurred vision, nausea and epigastric distress, feeling warm or cold, facial pallor, excessive sweating and syncope.
- Other injections of interest not included as the use of steroid could not be extrapolated from the information in the text.

McGrath 2011

- Approach by patients: TF: 89.7% (1667/1857), IL: 9.3% (173/1857), Caudal 1.0% (17/1857)
- Approach by injections: TF: 93% (3964/4265), IL: 6.6% (284/4265), Caudal: 0.4% (17/4265)
- Flushing: some cases were suspected allergic reactions
- Nonpainful neurological complaints: characterized as jerking of the hand after a cervical injection and pressure and tingling after a lumbar injection
- Temporary bowel function impairment: includes diarrhea and incontinence
- Chest and back pain: Authors indicated that because symptoms were at 1 week post-injection, they felt this was not related to the procedure. Have included for completeness.

Johnson 1999

- ~87.1% lumbar, ~12.2% cervical, ~0.7% thoracic

APPENDIX AA. Differential efficacy and safety assessment in studies that did not perform a formal test for interaction

Appendix Table AA1. ESI versus ENSI: Differential efficacy and safety- dichotomous outcomes from studies that did not perform a formal test for interaction

		Outcome	Subgroup	ESI % (n/N)	ENSI % (n/N)	Risk difference (95% CI)	p-value	Interaction p-value
TF ESI versus ENSI (LA group) for radiculopathy due to HNP	Ghahreman 2010	**Pain improved ≥50% (1 mos.)**	Symptoms <3 mos.	47% (9/19)†	0% (0/13)†	47% (NC)	0.01	NS*
			Symptoms ≥3 mos.	55% (5/9)†	13% (2/14)†	41% (4% to 79%)	0.04	
TF ESI versus ENSI (saline group) for radiculopathy due to HNP	Ghahreman 2010	**Pain improved ≥50% (1 mos.)**	Symptoms <3 mos.	47% (9/19)†	24% (5/21)†	24% (-5% to 52%)	0.12	NS*
			Symptoms ≥3 mos.	55% (5/9)†	13% (2/16)†	43% (7% to 79%)	0.02	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**Leg pain improved ≥75% (3 mos.)**	Herniations on baseline MRI	24% (6/25)	29% (7/24)	-5% (-30% to 20%)	0.69	NS*
			Extrusions on baseline MRI	47% (20/43)	57% (21/37)	-10% (-32% to 12%)	0.36	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**Leg pain improved ≥75% (6 mos.)**	Herniations on baseline MRI	24% (6/25)	33% (8/24)	-9% (-35% to 16%)	0.47	NS*
			Extrusions on baseline MRI	36% (15/42)	58% (22/38)	-22% (-44% to -1%)	0.05	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**Leg pain improved ≥75% (12 mos.)**	Herniations on baseline MRI	44% (11/25)	21% (5/24)	23% (-2% to 49%)	0.09	<0.05*
			Extrusions on baseline MRI	36% (15/42)	59% (22/37)	-24% (-45% to -2%)	0.04	
IL ESI versus NEI for radiculopathy due to HNP	Arden 2005	**ODI improved ≥75% (3 mos.)**	Symptoms <4 mos.	~19%	~28%	~-9% (NC)	0.32	NS*
			Symptoms ≥4 mos.	~16%	~20%	~-4% (NC)	0.56	
IL ESI versus NEI for radiculopathy due to HNP	Arden 2005	**ODI improved ≥75% (12 mos.)**	Symptoms <4 mos.	~35%	~34%	~1% (NC)	0.96	NS*
			Symptoms ≥4 mos.	~31%	~27%	~-4% (NC)	0.60	
Caudal ESI versus ENSI for radiculopathy due to HNP	Sayegh 2009	**Surgery (1 month)**	Disc herniation	17% (7/42)	24% (8/33)	-8% (-23% to 8%)	0.42	NS*
			Disc degeneration	12% (6/51)	33% (11/33)	-22% (-40% to -3%)	0.02	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**Surgery (12 mos.)**	Herniations on baseline MRI	20% (5/24)†	42% (11/26)†	-21% (-46% to 4%)	0.11	<0.05*
			Extrusions on baseline MRI	32% (12/38)†	13% (6/43)†	18% (-0.4% to 36%)	0.06	
TF or IL ESI versus ENSI for	Suri 2015	**Satisfaction**	Transforaminal	67%	53%	NC	0.34**	NS*

		Outcome	Subgroup	ESI % (n/N)	ENSI % (n/N)	Risk difference (95% CI)	p-value	Interaction p-value
radiculopathy due to HNP	(Friedly trial)	**with treatment (1.5 mos.)**		(NR)§	(NR)§			
			Interlaminar	67% (NR)§	56% (NR)§	NC	0.03**	
TF or IL ESI versus ENSI for radiculopathy due to HNP	Friedly 2014	**Adverse events‡ (1.5 mos.)**	Transforaminal	46% (26/57)	33% (20/61)	13% (-5% to 30%)	0.16	NS*
			Interlaminar	22% (32/143)	10% (14/139)	12% (4% to 21%)	0.01	

~ indicates data were estimated from graph; IL: interlaminar; NC: not calculable; NS: not statistically significant; TF: transforaminal

*NR by the study; statistical significance estimated based on evaluation of effect estimates between the subgroups

†Percentages reported; patient numbers calculated

‡Adverse events reported by study included hospitalization, surgery (due to complication), excessive pain, headache, fever, infection, dizziness, light-headedness, numbness, tingling, cardiovascular problems, lung problems, falls, facial flushing, skin irritation, leg swelling, dural puncture, and other.

§Patient satisfaction data were available for a subset of patients in the trial (TF: 106 of 118 randomized; IL: 263 of 282 randomized), however the study did not report the number of patients with data available in each treatment group for these subgroups.

**p-values reported by study

Appendix Table AA2. ESI versus ENSI: Differential efficacy and safety- continuous outcomes from studies that did not perform a formal test for interaction

		Outcome	Subgroup	ESI (mean ± SD (n))	ENSI (mean ± SD (n))	Mean difference (95% CI)	p-value	Interaction p-value
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**Leg pain VAS (0-100) (3 mos.)**	Herniations on baseline MRI	NR	NR	1.4 (-20 to 23)†	NS‡	NS*
			Extrusions on baseline MRI	NR	NR	-3.3 (-19 to 12)†	NS‡	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**Leg pain VAS (0-100) (6 mos.)**	Herniations on baseline MRI	NR	NR	-22.5 (-40 to -5)†	0.01‡	NS*
			Extrusions on baseline MRI	NR	NR	-16.6 (-32 to -1)†	0.03‡	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**Leg pain VAS (0-100) (12 mos.)**	Herniations on baseline MRI	NR	NR	-0.3 (-16 to 16)†	NS‡	NS*
			Extrusions on baseline MRI	NR	NR	-7.5 (-22 to 7)†	NS‡	
TF or IL ESI versus ENSI for radiculopathy due to HNP	Friedly 2014	**Change in leg pain VAS (0-10) (1.5 mos.)**	Transforaminal	-2.0 ± 2.6 (n=57)	-2.0 ± 2.8 (n=61)	0.1 (-0.9 to 1.0)§	0.89‡	NS*
			Interlaminar	-3.1 ± 3.3 (n=143)	-2.8 ± 3.1 (n=139)	-0.3 (-1.9 to 1.8)§	0.37‡	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**ODI (0-100) (3 mos.)**	Herniations on baseline MRI	NR	NR	-2.3 (-13 to 9)†	NS‡	NS*
			Extrusions on baseline MRI	NR	NR	2.7 (-8 to 14)†	NS‡	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**ODI (0-100) (6 mos.)**	Herniations on baseline MRI	NR	NR	-13.5 (-24 to -3)†	0.01‡	NS*
			Extrusions on baseline MRI	NR	NR	-1.0 (-11 to 9)†	NS‡	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**ODI (0-100) (12 mos.)**	Herniations on baseline MRI	NR	NR	-1.2 (-12 to 9)†	NS‡	NS*
			Extrusions on baseline MRI	NR	NR	3.7 (-6 to 13)†	NS‡	
TF or IL ESI versus ENSI for radiculopathy due to HNP	Friedly 2014	**Change in RMDQ (1.5 mos.)**	Transforaminal	-2.0 ± 2.6 (n=57)	-2.0 ± 2.8 (n=61)	0.3 (-1.9 to 1.8)§	0.95	NS*
			Interlaminar	-3.1 ± 3.3 (n=143)	-2.8 ± 3.1 (n=139)	-2.5 (-3.7 to -1.3)§	0.04	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**NHP pain (QoL) (3 mos.)**	Herniations on baseline MRI	NR	NR	-5.1 (-27 to 17)†	NS‡	NS*
			Extrusions on	NR	NR	-0.4 (-18 to 17)†	NS‡	

		Outcome	Subgroup	ESI (mean ± SD (n))	ENSI (mean ± SD (n))	Mean difference (95% CI)	p-value	Interaction p-value
			baseline MRI					
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**NHP pain (QoL) (6 mos.)**	Herniations on baseline MRI	NR	NR	-21.6 (-43 to -0.3)†	0.05‡	NS*
			Extrusions on baseline MRI	NR	NR	-8.2 (-25 to 9)†	NS‡	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**NHP pain (QoL) (12 mos.)**	Herniations on baseline MRI	NR	NR	0.1 (-22 to 22)†	NS‡	NS*
			Extrusions on baseline MRI	NR	NR	-4.7 (-21 to 11)†	NS‡	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**NHP emotional (QoL) (3 mos.)**	Herniations on baseline MRI	NR	NR	13.3 (4 to 23)†	0.01‡	<0.05*
			Extrusions on baseline MRI	NR	NR	-2.2 (-9 to 5)†	NS‡	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**NHP emotional (QoL) (6 mos.)**	Herniations on baseline MRI	NR	NR	-3.2 (-13 to 7)†	NS‡	NS*
			Extrusions on baseline MRI	NR	NR	2.7 (-5 to 10)†	NS‡	
TF ESI versus ENSI for radiculopathy due to HNP	Karppinen 2001	**NHP emotional (QoL) (12 mos.)**	Herniations on baseline MRI	NR	NR	-3.2 (-13 to 7)†	NS‡	NS*
			Extrusions on baseline MRI	NR	NR	2.7 (-5 to 10)†	NS‡	

~ indicates data were estimated from graph; IL: interlaminar; NC: not calculable; NHP: Nottingham Health Profile; NS: not statistically significant; TF: transforaminal
*Interaction p-value NR by the study; statistical significance estimated based on evaluation of effect estimates between the subgroups
†Study reported that positive treatment difference values indicate better results in the ESI group compared with the ENSI group (and vice versa).
‡p-values reported by study
§adjusted for baseline values and recruitment site

Appendix Table AA3. ESI versus NEI: Differential efficacy and safety- dichotomous outcomes from studies that did not perform a formal test for interaction

		Outcome	Subgroup	ESI % (n/N)	NEI % (n/N)	Risk difference (95% CI)	p-value	Interaction p-value
TF ESI versus NEI (IM steroid group) for radiculopathy due to HNP	Ghahreman 2010	**Pain improved ≥50% (1 mos.)**	Symptoms <3 mos.	47% (9/19)†	25% (3/12)†	22% (-11% to 56%)	0.22	NS*
			Symptoms ≥3 mos.	55% (5/9)†	19% (3/16)†	37% (-1% to 74%)	0.06	
TF ESI versus NEI (IM saline group) for radiculopathy due to HNP	Ghahreman 2010	**Pain improved ≥50% (1 mos.)**	Symptoms <3 mos.	47% (9/19)†	7% (1/15)†	41% (15% to 66%)	0.01	NS*
			Symptoms ≥3 mos.	55% (5/9)†	20% (3/15)†	36% (-3% to 74%)	0.08	

~ indicates data were estimated from graph; IM: intramuscular; NC: not calculable; NS: not statistically significant; TF: transforaminal
*NR by the study; statistical significance estimated based on evaluation of effect estimates between the subgroups
†Percentages reported; patient numbers calculated

Appendix Table AA4. ESI versus disc procedures: Differential efficacy and safety- continuous outcomes from studies that did not perform a formal test for interaction

		Outcome	Subgroup	ESI (mean ± SD (n))	Disc (mean ± SD (n))	Mean difference (95% CI)	p-value	Interaction p-value
TF ESI versus disc decompression for radiculopathy due to HNP	Gerstzen 2010	**Reduction in leg pain VAS (0-100) scores from baseline (6 months)**	Leg pain <1 yr.	~-38 (n=6)	~-50 (n=13)	~12 (NC)	0.5	NR
			Leg pain 1-3 yrs.	~-12 (n=15)	~-50 (n=10)	~38 (NC)	0.01	
			Leg pain >3 yrs.	~-36 (n=6)	~-50 (n=4)	~14 (NC)	0.40	

~ indicates data were estimated from graph; NC: not calculable; NS: not statistically significant; TF: transforaminal
*NR by the study; statistical significance estimated based on evaluation of effect estimates between the subgroups

APPENDIX BB. Sensitivity Analyses

Figure 3. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED PAIN, SHORT-TERM FOLLOW-UP

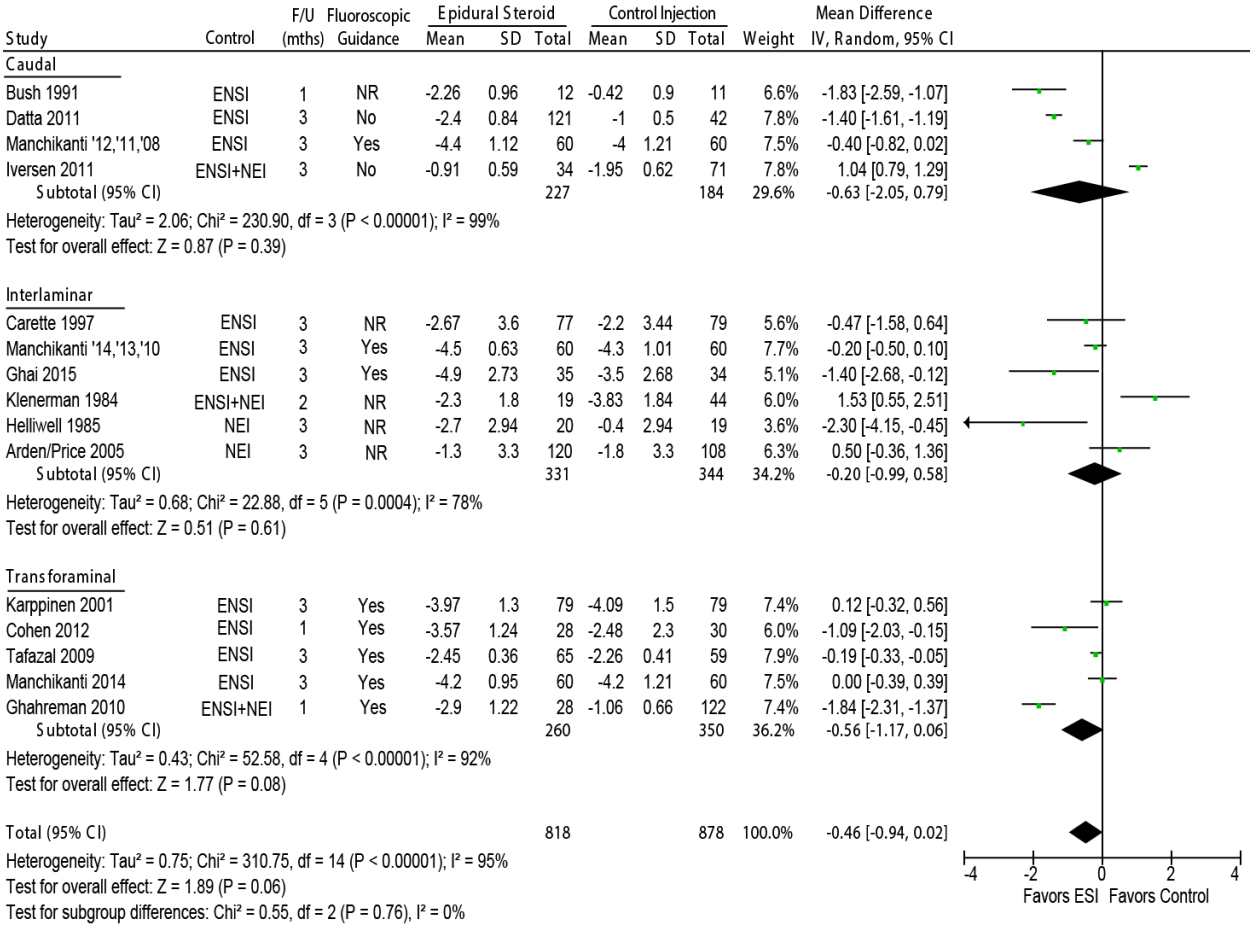


Figure 3. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED PAIN, SHORT-TERM FOLLOW-UP

DROPPED HIGH BIAS RISK

	Epidural Steroid			ENSI				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
1.3.1 Caudal								
Manchikanti '12,'11,'08	-4.4	1.12	60	-4	1.21	60	10.1%	-0.40 [-0.82, 0.02]
Iversen 2011	-0.91	0.59	34	-1.95	0.62	71	10.7%	1.04 [0.79, 1.29]
Subtotal (95% CI)			**94**			**131**	**20.7%**	**0.33 [-1.08, 1.74]**
Heterogeneity: Tau² = 1.01; Chi² = 34.02, df = 1 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 0.46 (P = 0.65)								
1.3.2 Interlaminar								
Carette 1997	-2.67	3.6	77	-2.2	3.44	79	6.7%	-0.47 [-1.58, 0.64]
Manchikanti '14,'13,'10	-4.5	0.63	60	-4.3	1.01	60	10.5%	-0.20 [-0.50, 0.10]
Ghai 2015	-4.9	2.73	35	-3.5	2.68	34	5.9%	-1.40 [-2.68, -0.12]
Arden/Price 2005	-1.3	3.3	120	-1.8	3.3	108	7.9%	0.50 [-0.36, 1.36]
Subtotal (95% CI)			**292**			**281**	**30.9%**	**-0.26 [-0.83, 0.32]**
Heterogeneity: Tau² = 0.17; Chi² = 6.18, df = 3 (P = 0.10); I² = 51%								
Test for overall effect: Z = 0.87 (P = 0.39)								
1.3.3 Transforaminal								
Karppinen 2001	-3.97	1.3	79	-4.09	1.5	79	10.0%	0.12 [-0.32, 0.56]
Cohen 2012	-3.57	1.24	28	-2.48	2.3	30	7.5%	-1.09 [-2.03, -0.15]
Tafazal 2009	-2.45	0.36	65	-2.26	0.41	59	10.9%	-0.19 [-0.33, -0.05]
Manchikanti 2014	-4.2	0.95	60	-4.2	1.21	60	10.2%	0.00 [-0.39, 0.39]
Ghahreman 2010	-2.9	1.22	28	-1.06	0.66	122	9.9%	-1.84 [-2.31, -1.37]
Subtotal (95% CI)			**260**			**350**	**48.4%**	**-0.56 [-1.17, 0.06]**
Heterogeneity: Tau² = 0.43; Chi² = 52.58, df = 4 (P < 0.00001); I² = 92%								
Test for overall effect: Z = 1.77 (P = 0.08)								
Total (95% CI)			**646**			**762**	**100.0%**	**-0.30 [-0.75, 0.16]**
Heterogeneity: Tau² = 0.49; Chi² = 151.74, df = 10 (P < 0.00001); I² = 93%								
Test for overall effect: Z = 1.28 (P = 0.20)								
Test for subgroup differences: Chi² = 1.43, df = 2 (P = 0.49), I² = 0%								

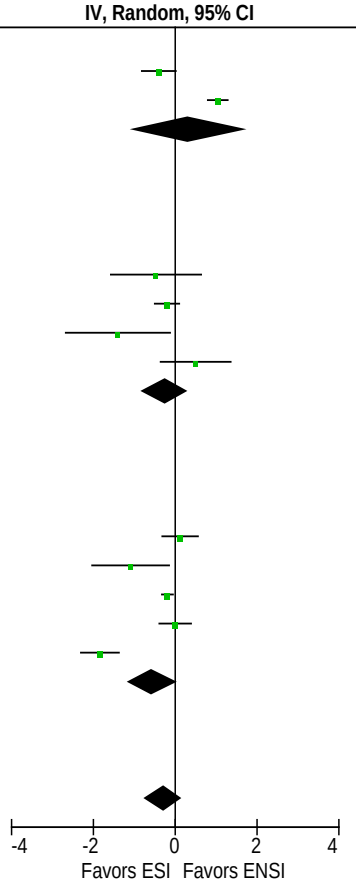


Figure 5. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED PAIN, LONG-TERM FOLLOW-UP

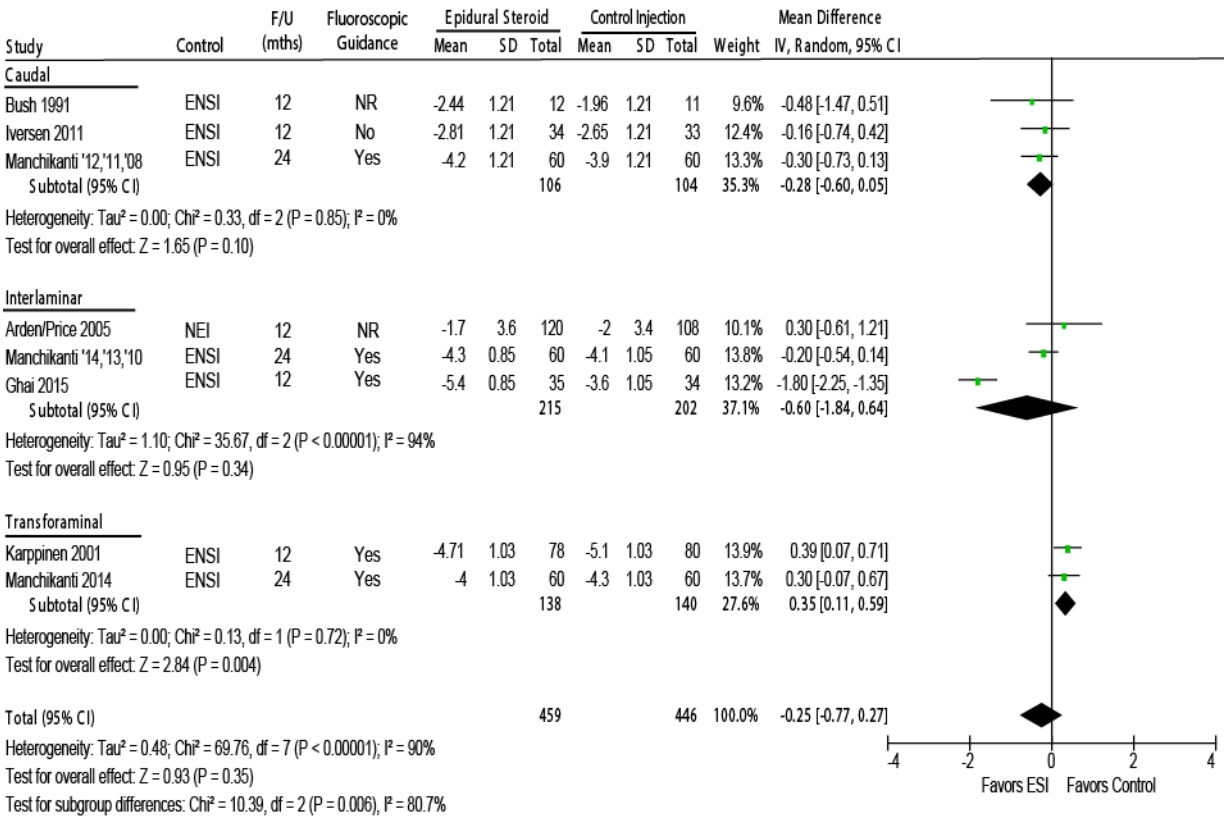


Figure 5. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED PAIN, LONG-TERM FOLLOW-UP

DROPPED OUTLIER

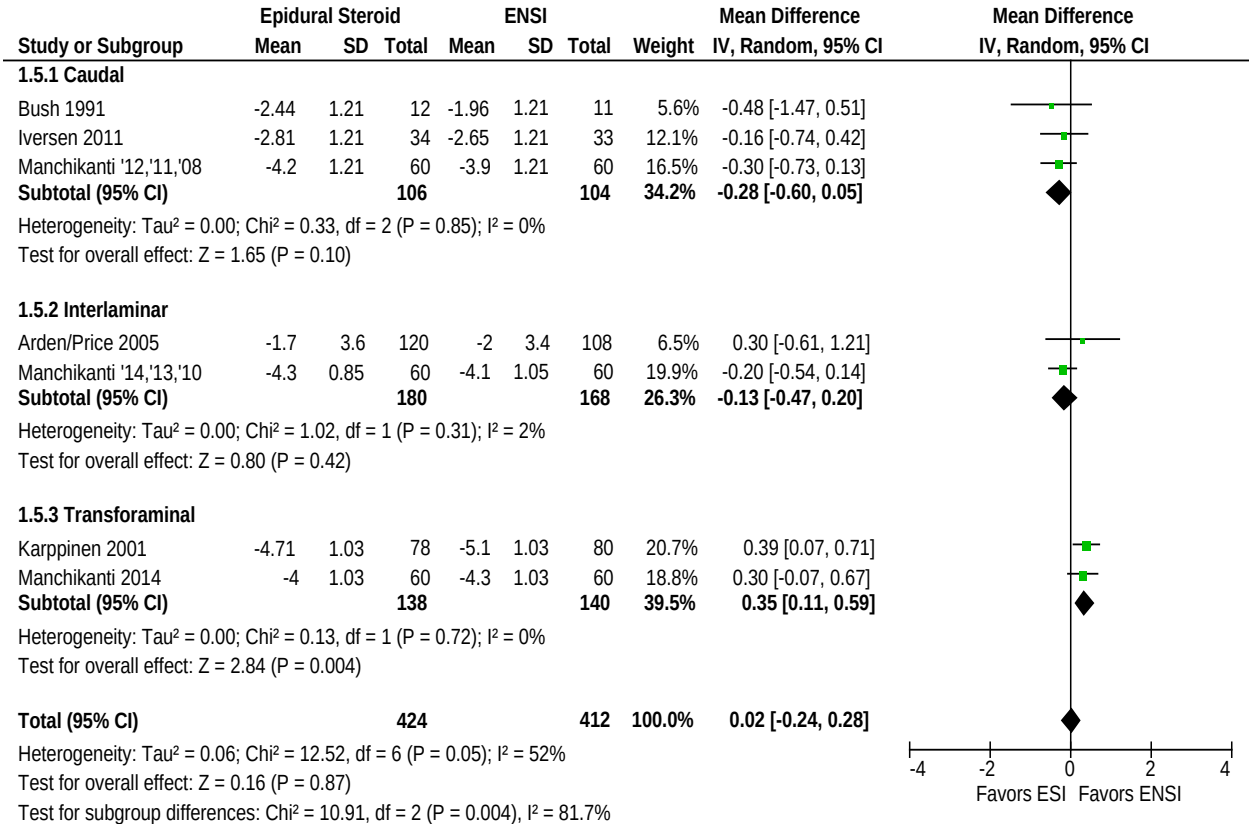


Figure 5. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED PAIN, LONG-TERM FOLLOW-UP

DROPPED HIGH BIAS RISK

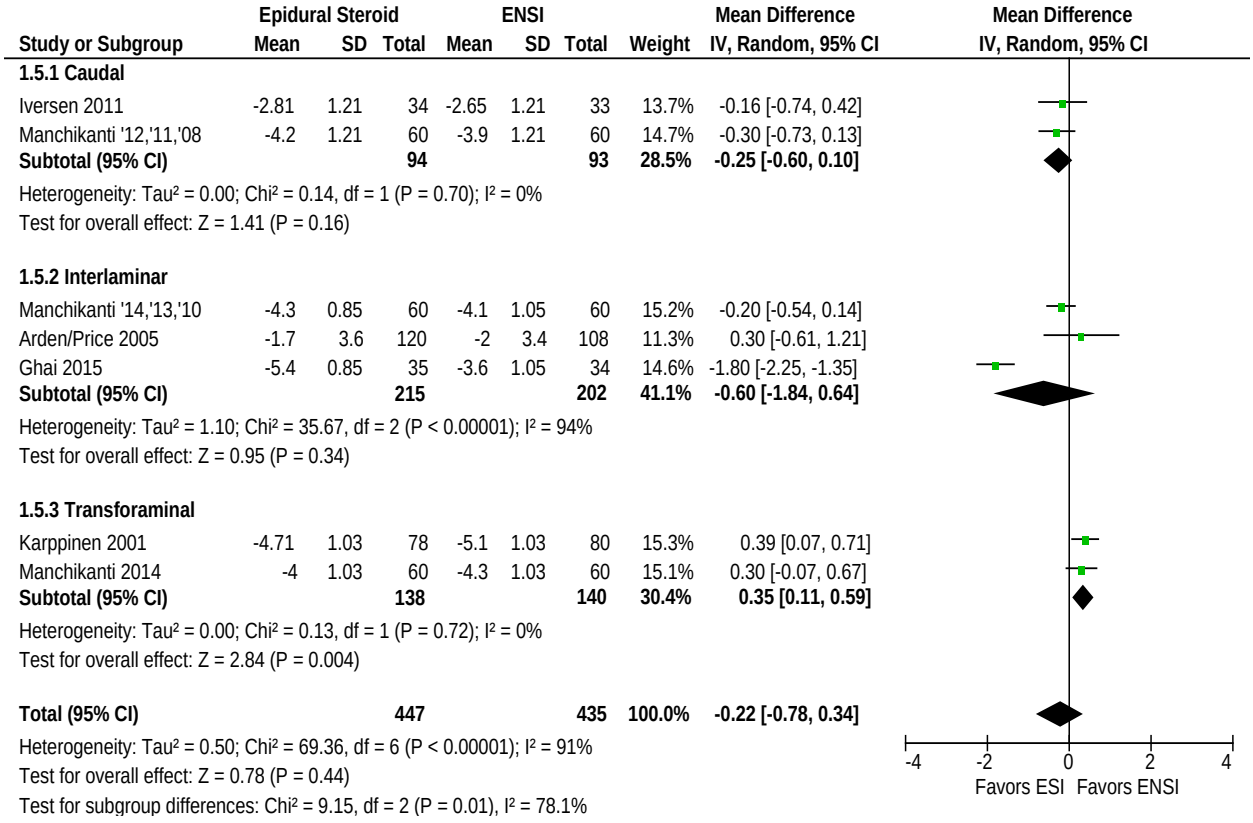


Figure 6. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH PAIN SUCCESS, SHORT-TERM FOLLOW-UP

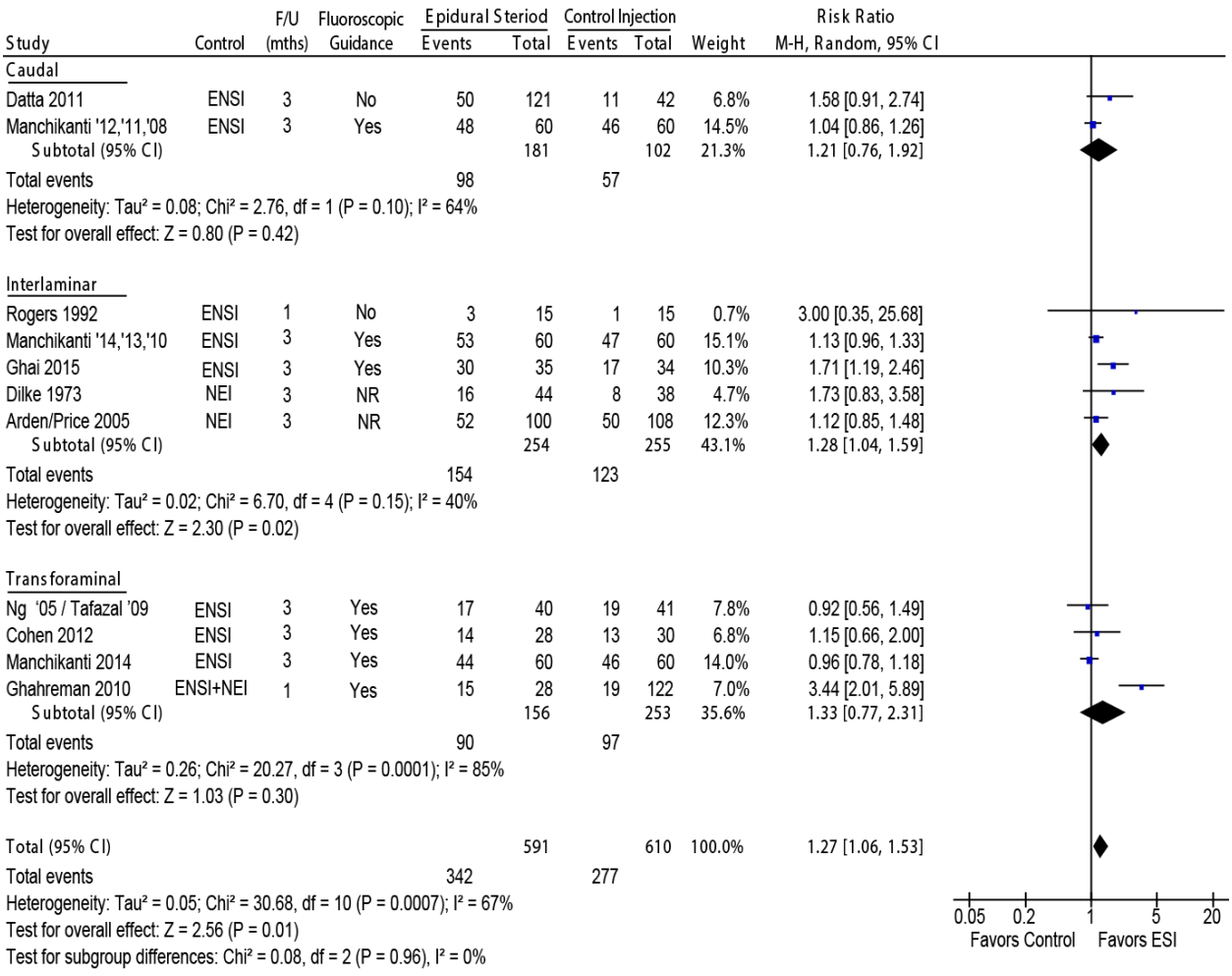


Figure 6. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH PAIN SUCCESS, SHORT-TERM FOLLOW-UP

DROPPED HIGH BIAS RISK

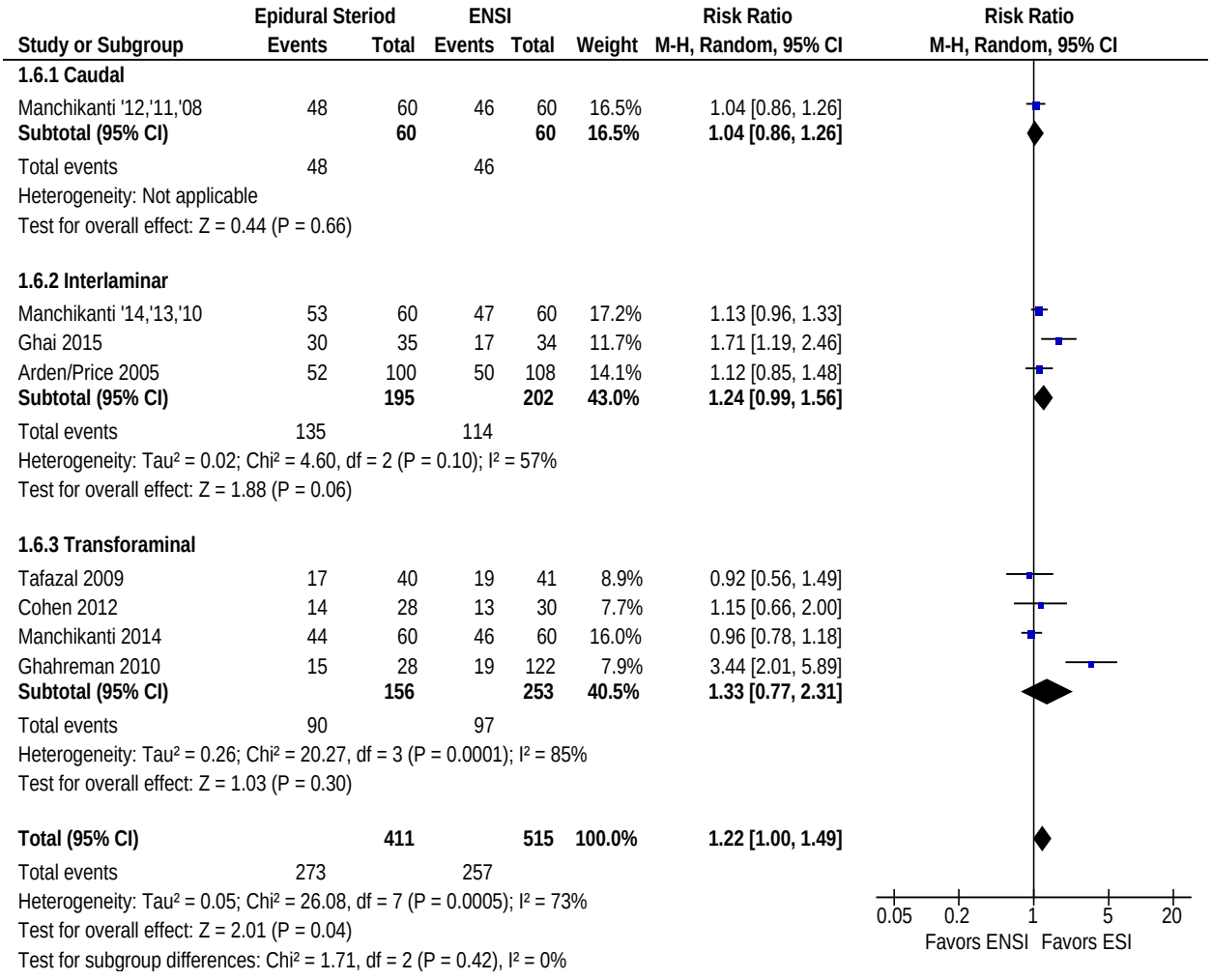


Figure 8. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH PAIN SUCCESS, LONG-TERM FOLLOW-UP

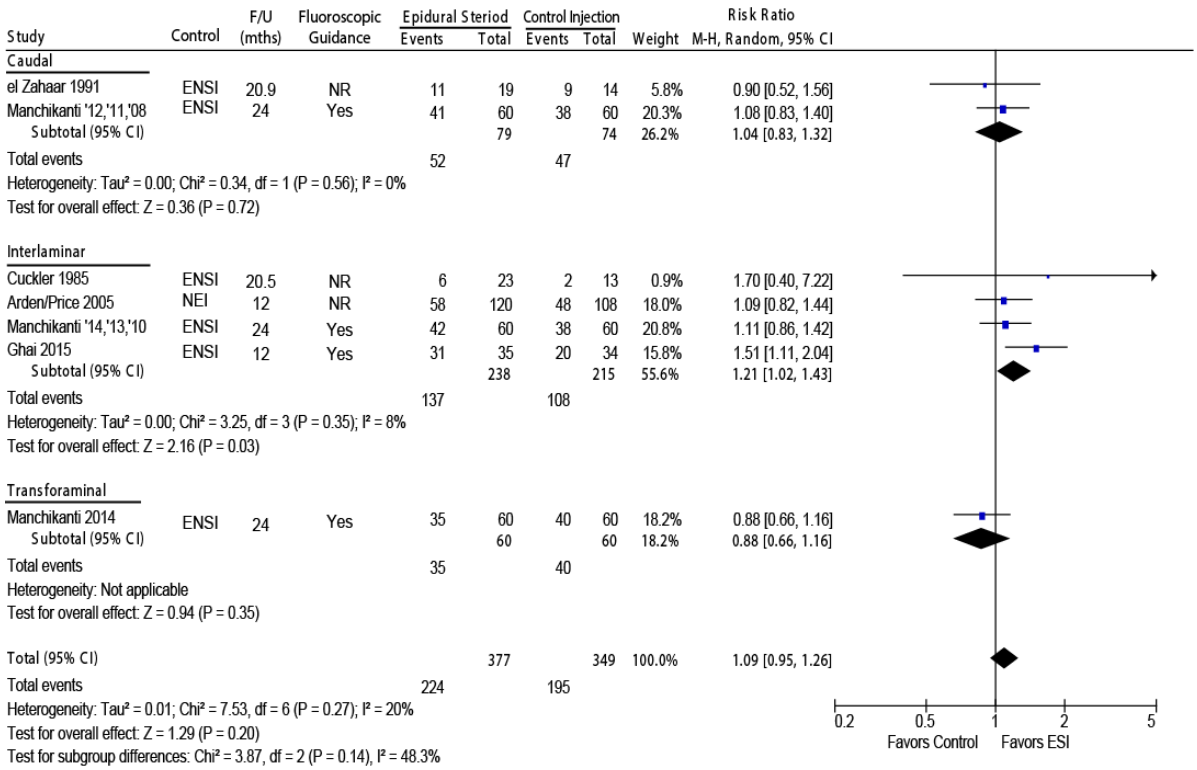


Figure 8. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH PAIN SUCCESS, LONG-TERM FOLLOW-UP

DROPPED HIGH BIAS RISK

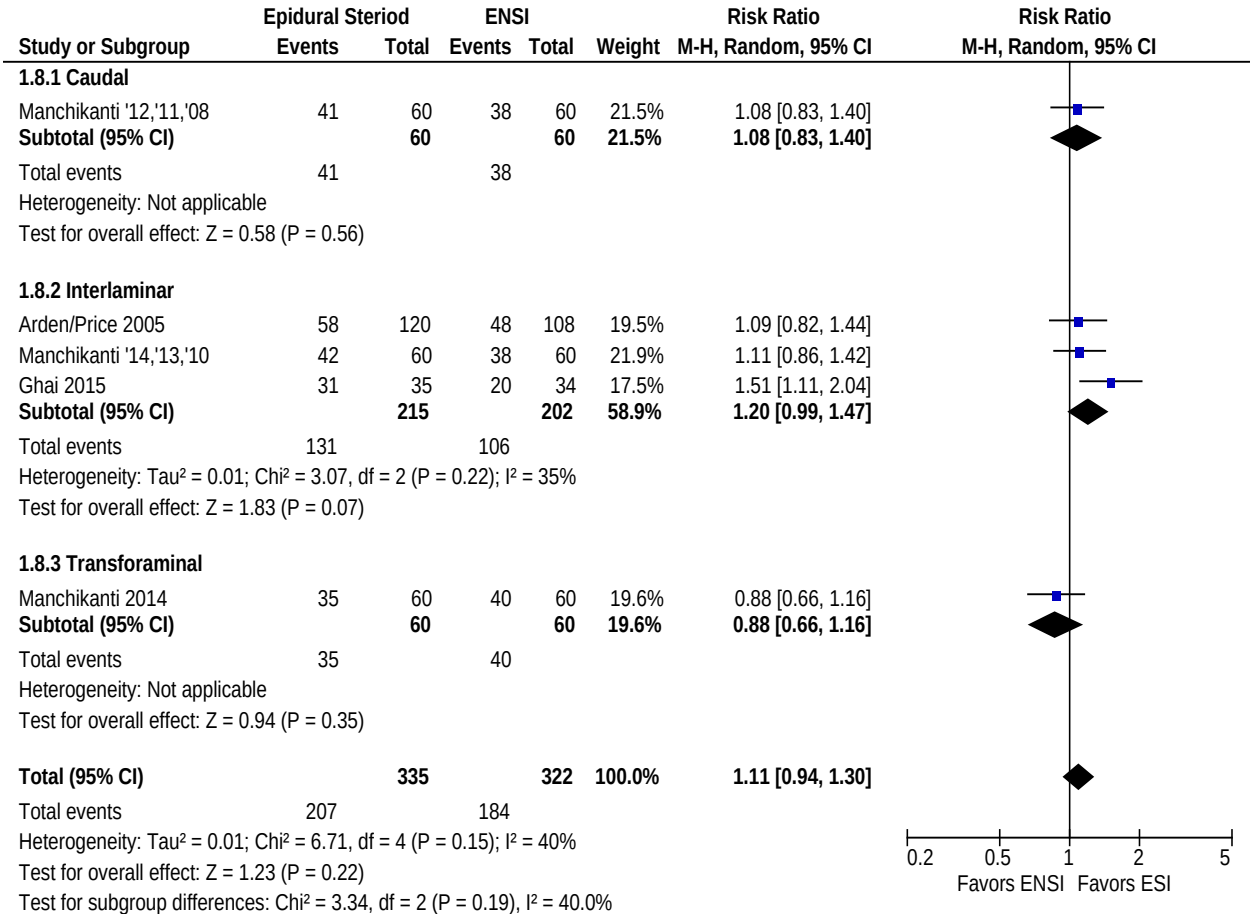


Figure 9. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED FUNCTION, SHORT-TERM FOLLOW-UP

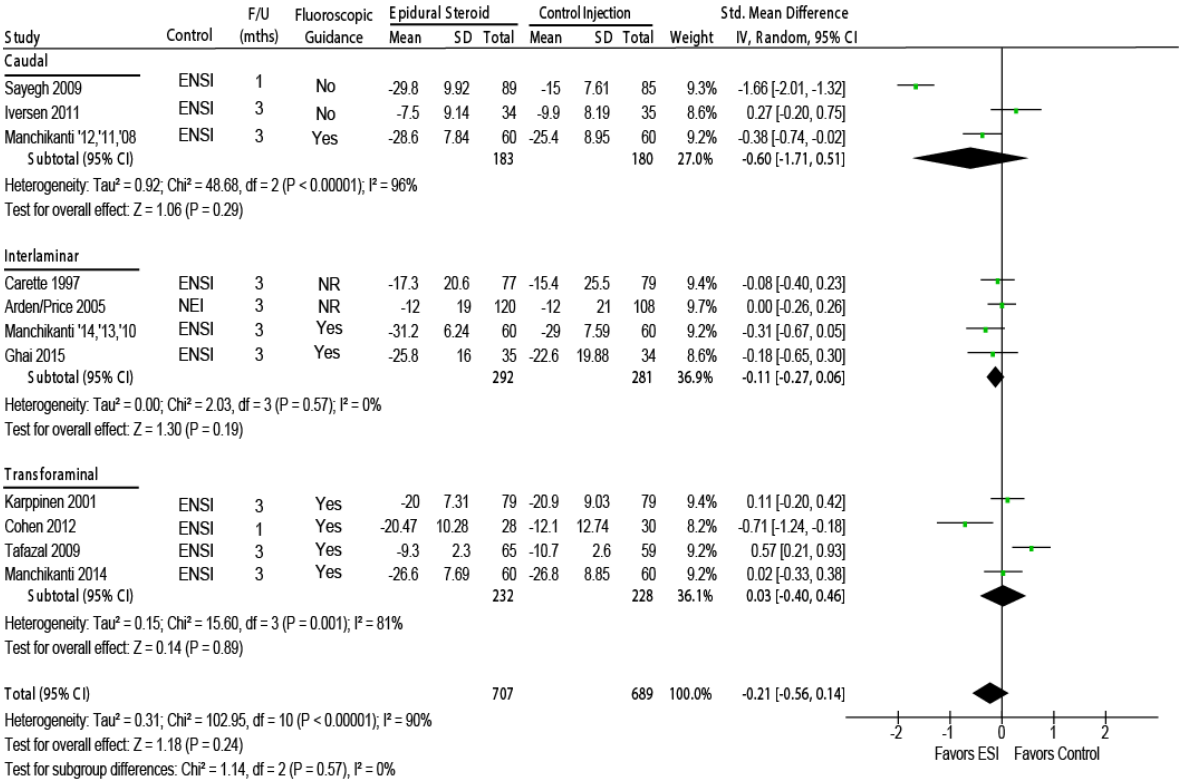


Figure 9. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED FUNCTION, SHORT-TERM FOLLOW-UP

DROPPED HIGH BIAS RISK AND OUTLIER

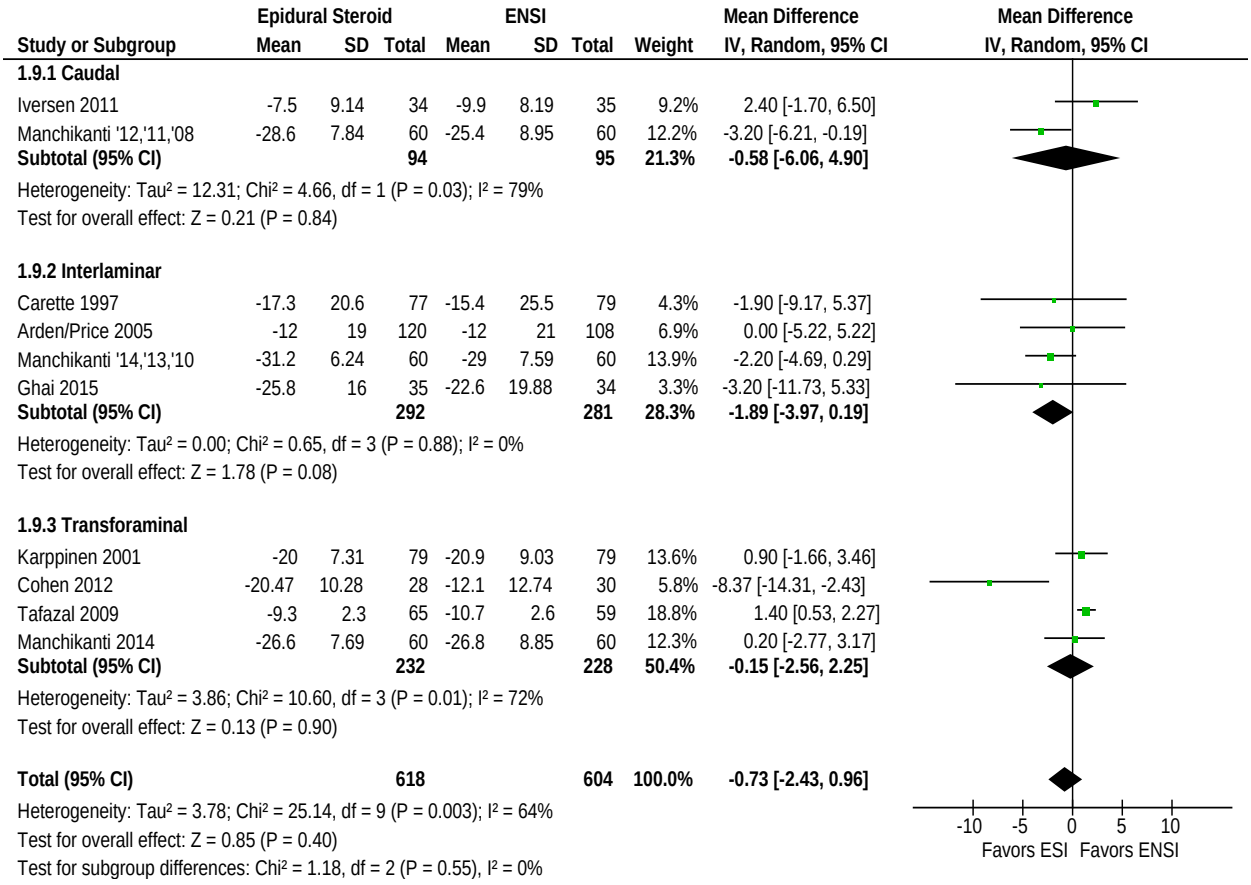


Figure 10. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED FUNCTION, INTERMEDIATE FOLLOW-UP

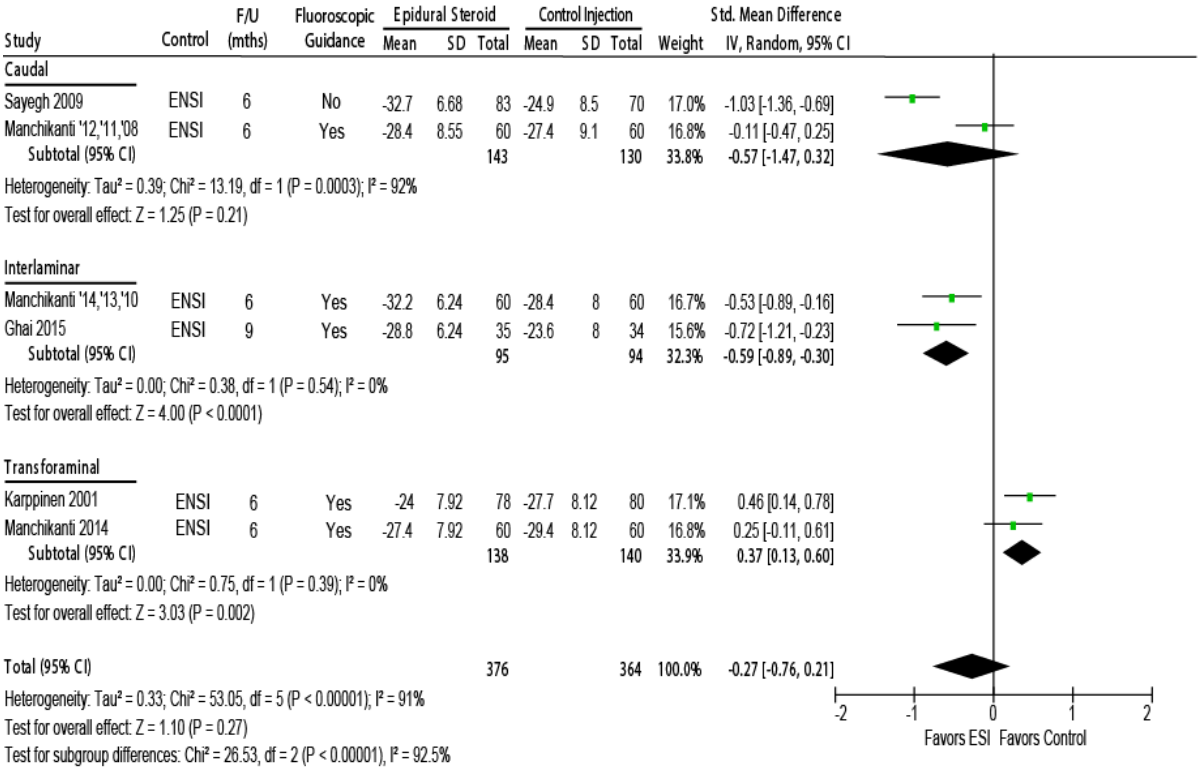


Figure 10. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED FUNCTION, INTERMEDIATE FOLLOW-UP

DROPPED HIGH BIAS RISK

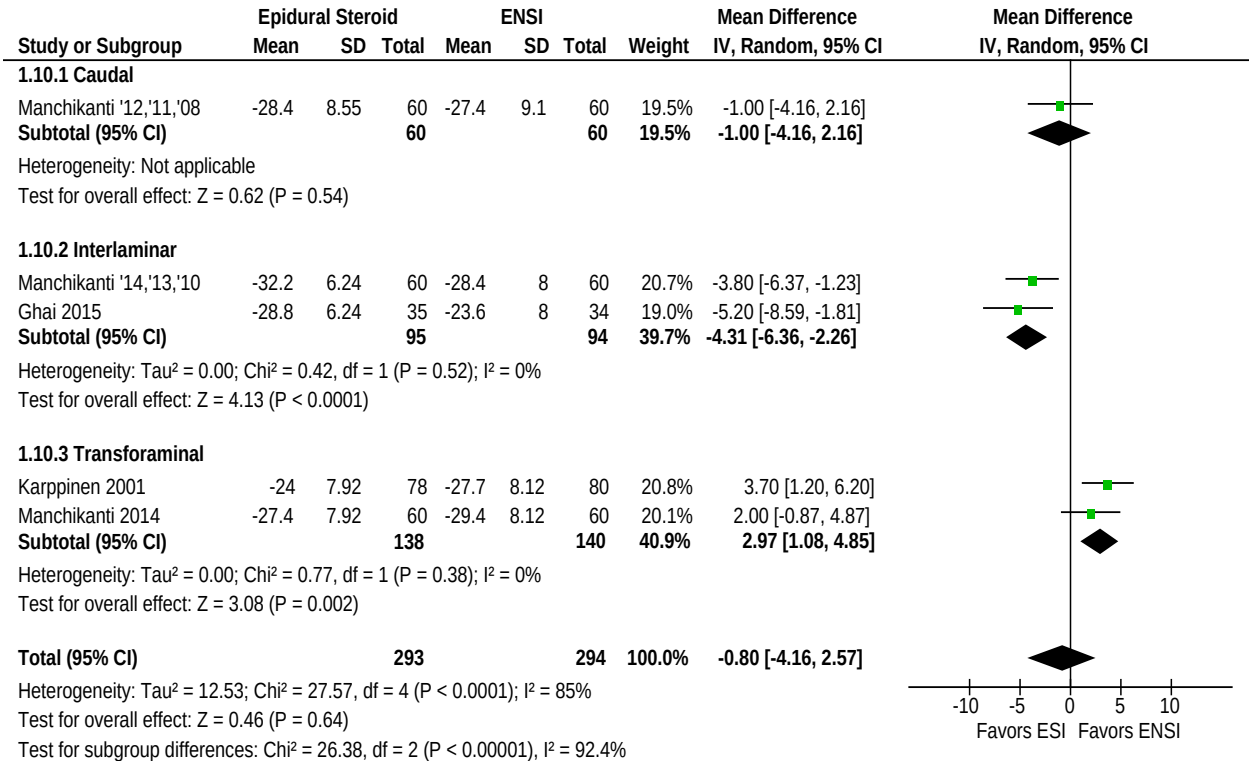
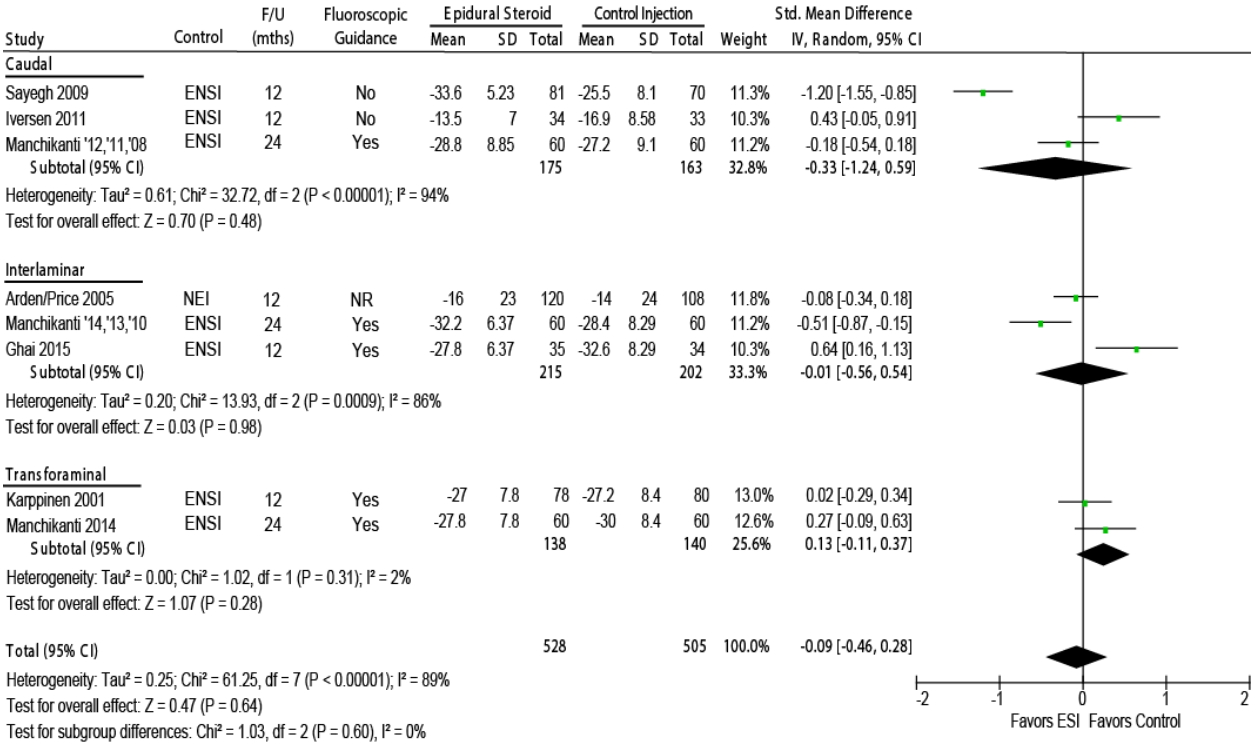


Figure 11. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED FUNCTION, LONG-TERM FOLLOW-UP



CI: confidence interval; ENSI: Epidural non-steroid injection; NEI: non-epidural steroid injection; F/U:follow-up; SD: standard deviation

Figure 11. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: IMPROVED FUNCTION, LONG-TERM FOLLOW-UP

DROPPED HIGH BIAS RISK

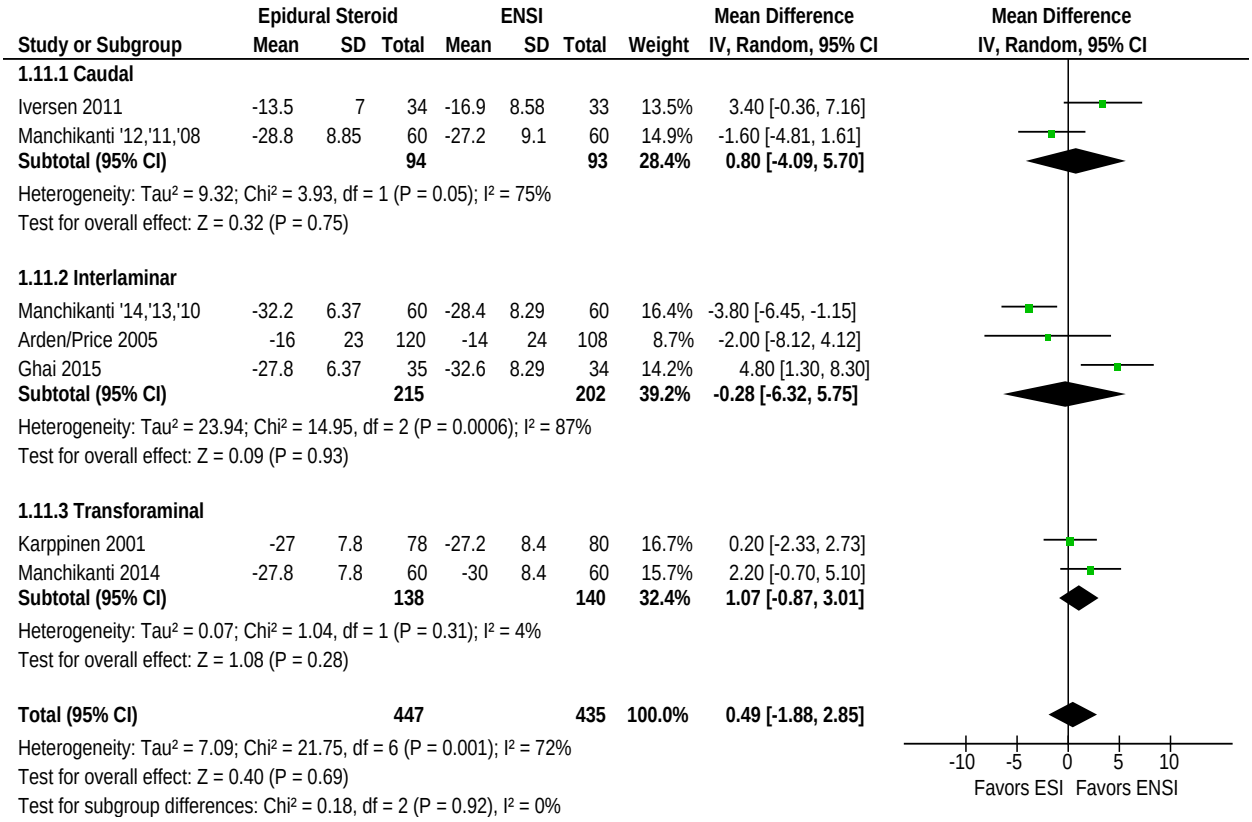


Figure 12. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH FUNCTION SUCCESS, SHORT-TERM FOLLOW-UP

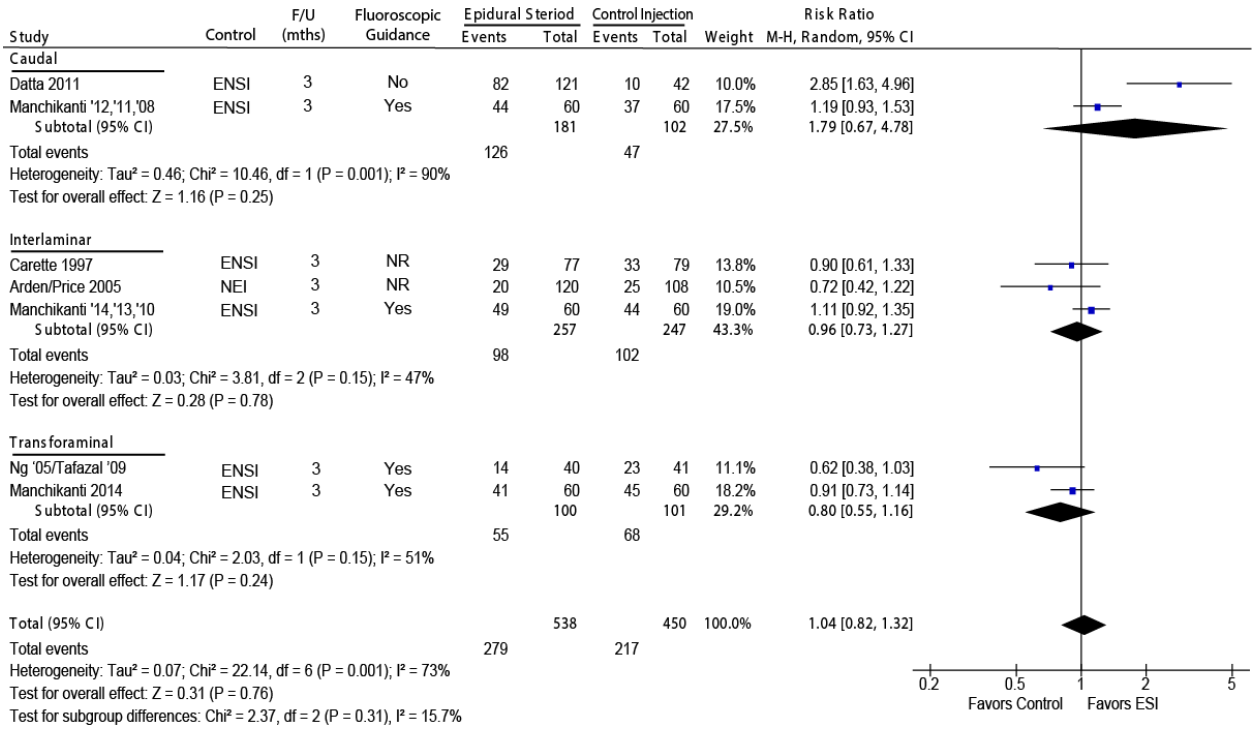


Figure 12. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH FUNCTION SUCCESS, SHORT-TERM FOLLOW-UP

DROPPED OUTLIER AND HIGH RISK OF BIAS

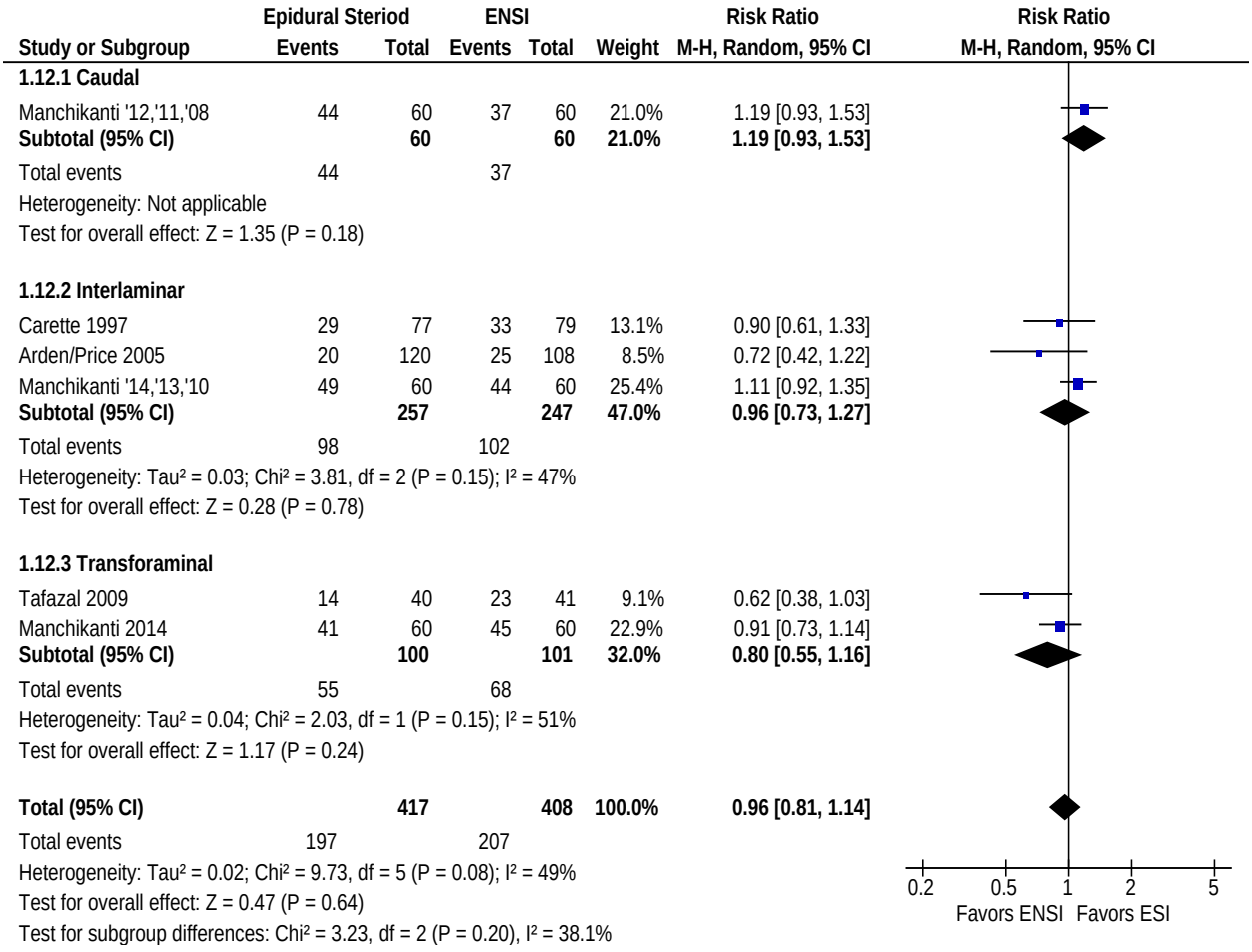


Figure 17. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: CUMULATIVE RISK OF SURGERY

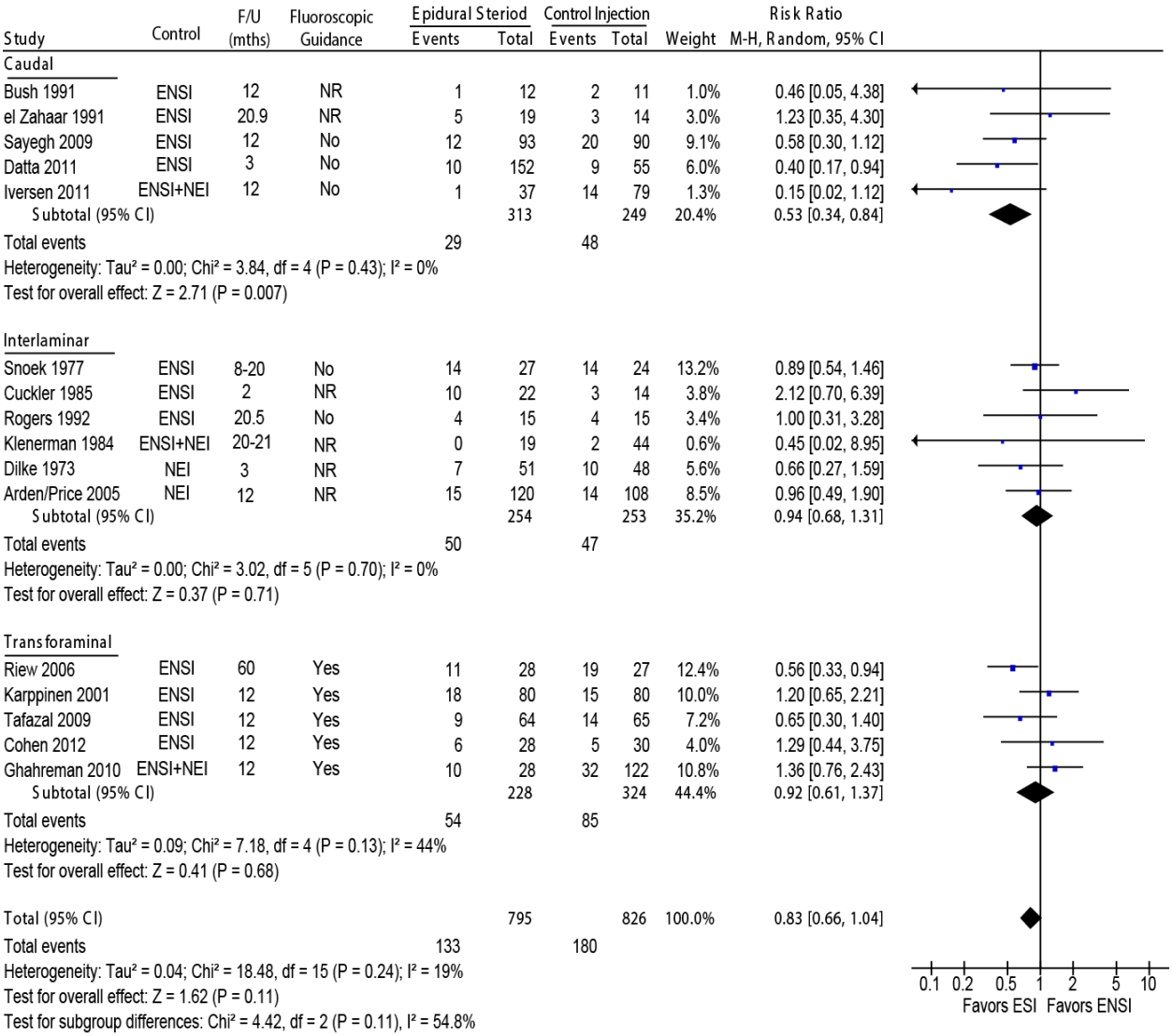


Figure 17. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: CUMULATIVE RISK OF SURGERY

DROPPED HIGH BIAS RISK

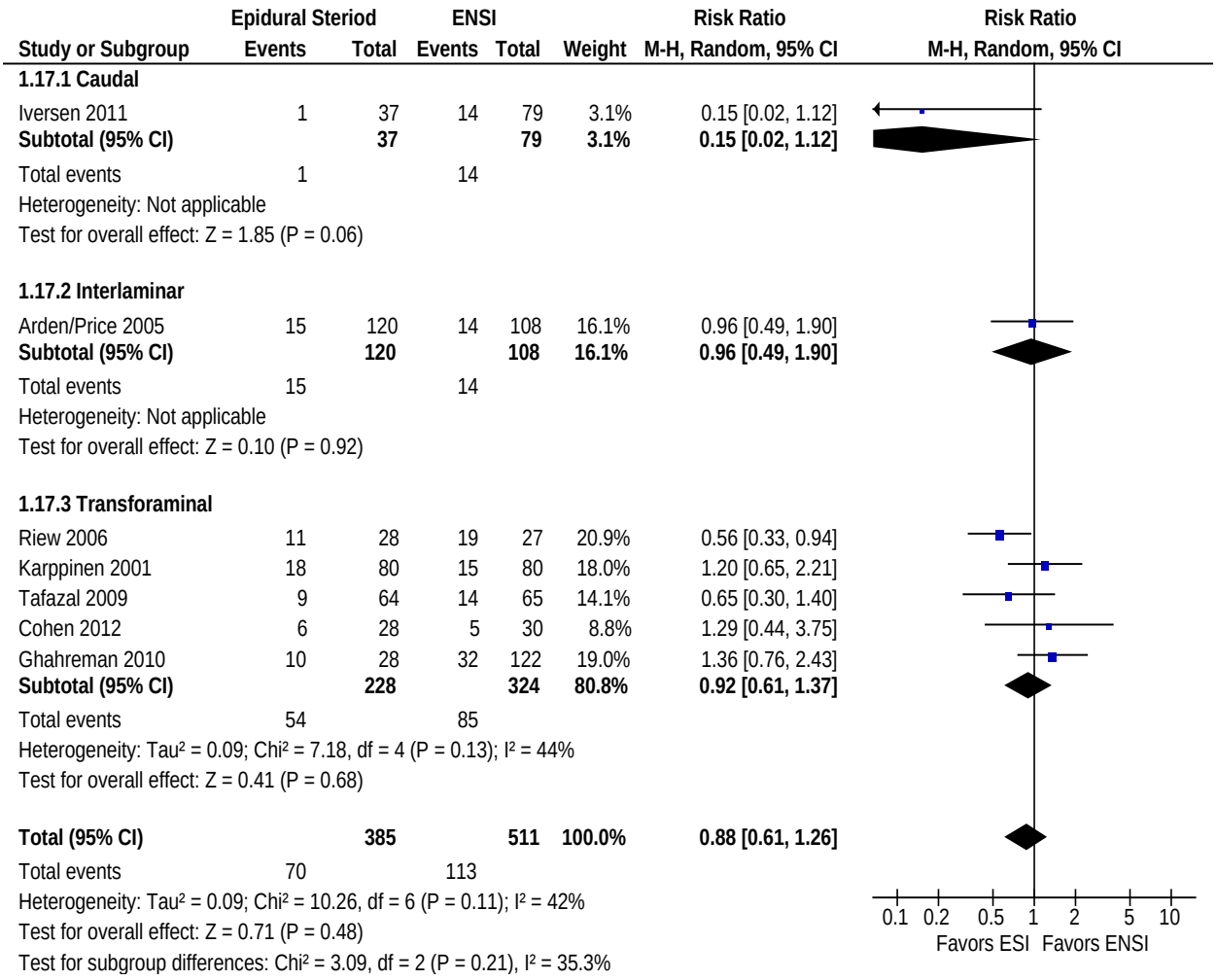


Figure 20. Epidural steroid injections (ESI) vs. control injections for spinal stenosis: PROPORTION WITH PAIN SUCCESS, LONG-TERM FOLLOW-UP

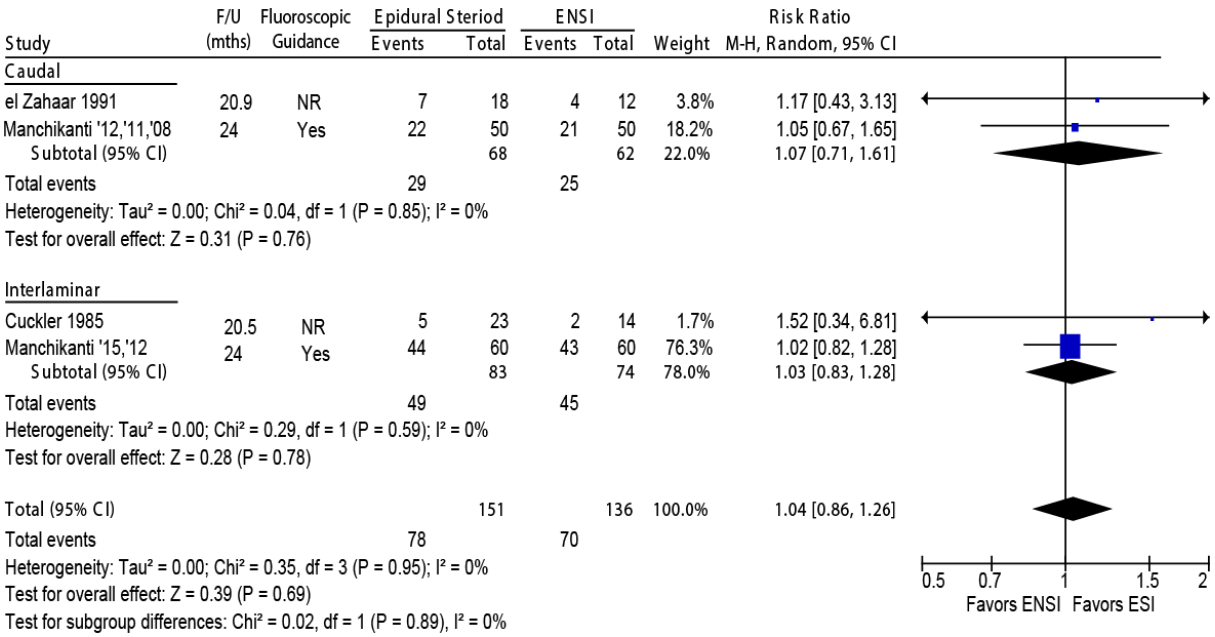


Figure 20. Epidural steroid injections (ESI) vs. control injections for spinal stenosis: PROPORTION WITH PAIN SUCCESS, LONG-TERM FOLLOW-UP

DROPPED HIGH BIAS RISK

	Epidural Steriod		ENSI			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**M-H, Random, 95% CI**
1.20.1 Caudal							
Manchikanti '12,'11,'08	22	50	21	50	19.2%	1.05 [0.67, 1.65]	
Subtotal (95% CI)		**50**		**50**	**19.2%**	**1.05 [0.67, 1.65]**	
Total events	22		21				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.20 (P = 0.84)							
1.20.2 Interlaminar							
Manchikanti '15,'12	44	60	43	60	80.8%	1.02 [0.82, 1.28]	
Subtotal (95% CI)		**60**		**60**	**80.8%**	**1.02 [0.82, 1.28]**	
Total events	44		43				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.20 (P = 0.84)							
Total (95% CI)		**110**		**110**	**100.0%**	**1.03 [0.84, 1.25]**	
Total events	66		64				
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.92); I² = 0%							
Test for overall effect: Z = 0.27 (P = 0.79)							
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.93), I² = 0%							

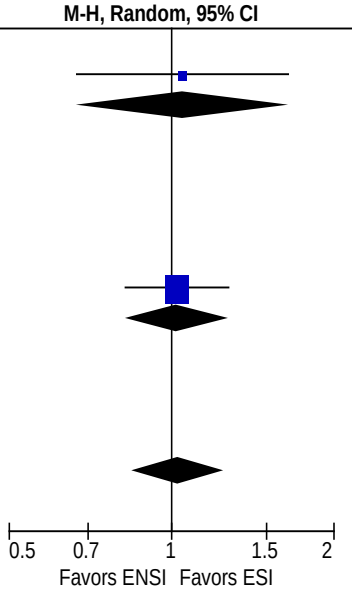


Figure 21. Epidural steroid injections (ESI) vs. control injections for spinal stenosis: IMPROVED FUNCTION, SHORT-TERM FOLLOW-UP

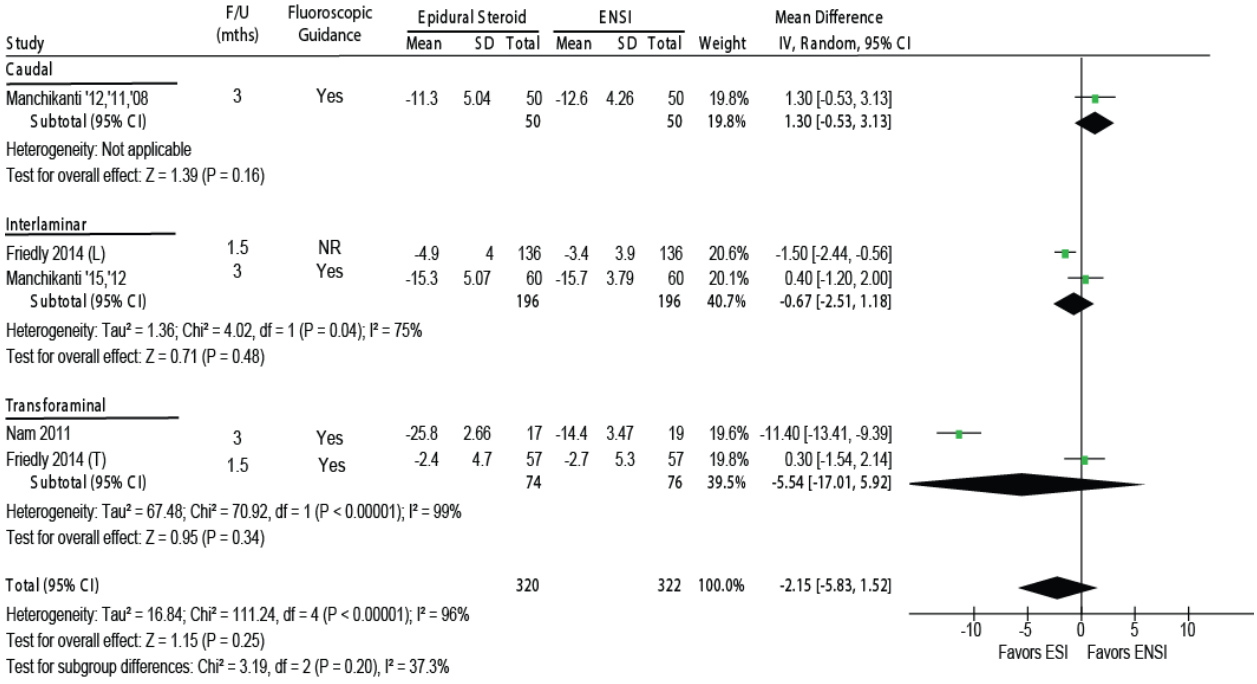
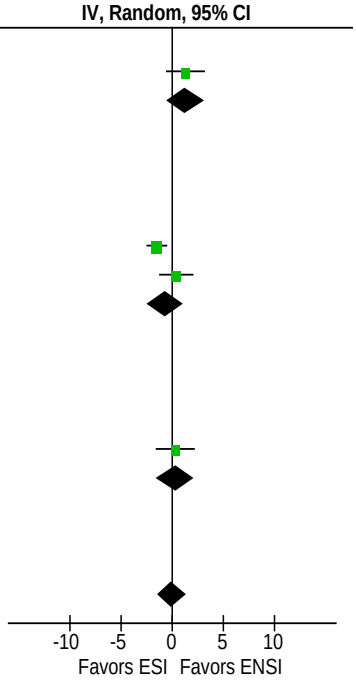


Figure 21. Epidural steroid injections (ESI) vs. control injections for spinal stenosis: IMPROVED FUNCTION, SHORT-TERM FOLLOW-UP

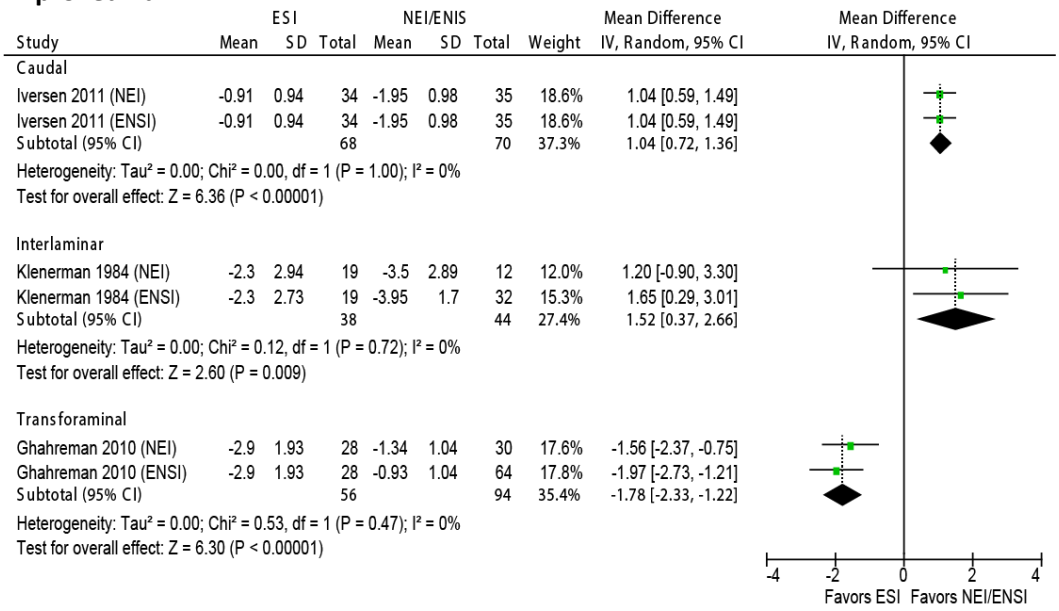
DROPPED OUTLIER

	Epidural Steroid			ENSI				Mean Difference	Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**IV, Random, 95% CI**
1.21.1 Caudal									
Manchikanti '12,'11,'08	-11.3	5.04	50	-12.6	4.26	50	22.2%	1.30 [-0.53, 3.13]	
Subtotal (95% CI)			**50**			**50**	**22.2%**	**1.30 [-0.53, 3.13]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.39 (P = 0.16)									
1.21.2 Interlaminar									
Friedly 2014 (L)	-4.9	4	136	-3.4	3.9	136	31.2%	-1.50 [-2.44, -0.56]	
Manchikanti '15,'12	-15.3	5.07	60	-15.7	3.79	60	24.4%	0.40 [-1.20, 2.00]	
Subtotal (95% CI)			**196**			**196**	**55.7%**	**-0.67 [-2.51, 1.18]**	
Heterogeneity: Tau² = 1.36; Chi² = 4.02, df = 1 (P = 0.04); I² = 75%									
Test for overall effect: Z = 0.71 (P = 0.48)									
1.21.3 Transforaminal									
Friedly 2014 (T)	-2.4	4.7	57	-2.7	5.3	57	22.1%	0.30 [-1.54, 2.14]	
Subtotal (95% CI)			**57**			**57**	**22.1%**	**0.30 [-1.54, 2.14]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.32 (P = 0.75)									
Total (95% CI)			**303**			**303**	**100.0%**	**-0.02 [-1.39, 1.36]**	
Heterogeneity: Tau² = 1.35; Chi² = 10.02, df = 3 (P = 0.02); I² = 70%									
Test for overall effect: Z = 0.02 (P = 0.98)									
Test for subgroup differences: Chi² = 2.20, df = 2 (P = 0.33), I² = 8.9%									

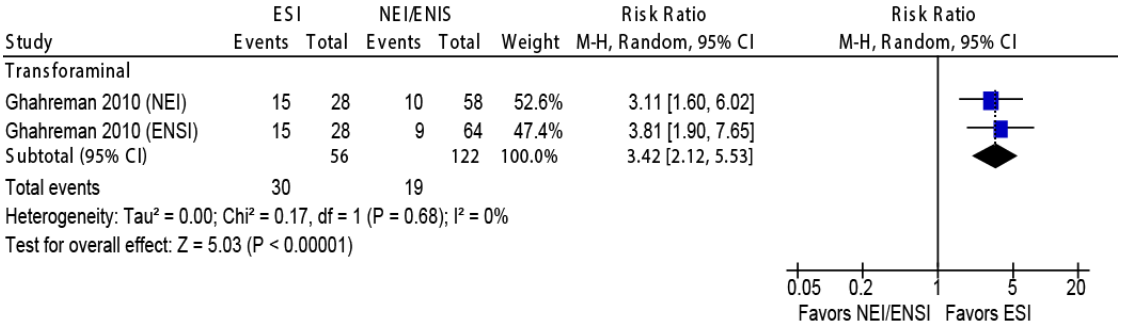


Direct comparisons between epidural steroid injection (ESI) versus epidural non-steroid injection (ENSI) or non-epidural injection (NEI) for improved pain, pain success, and risk of surgery.

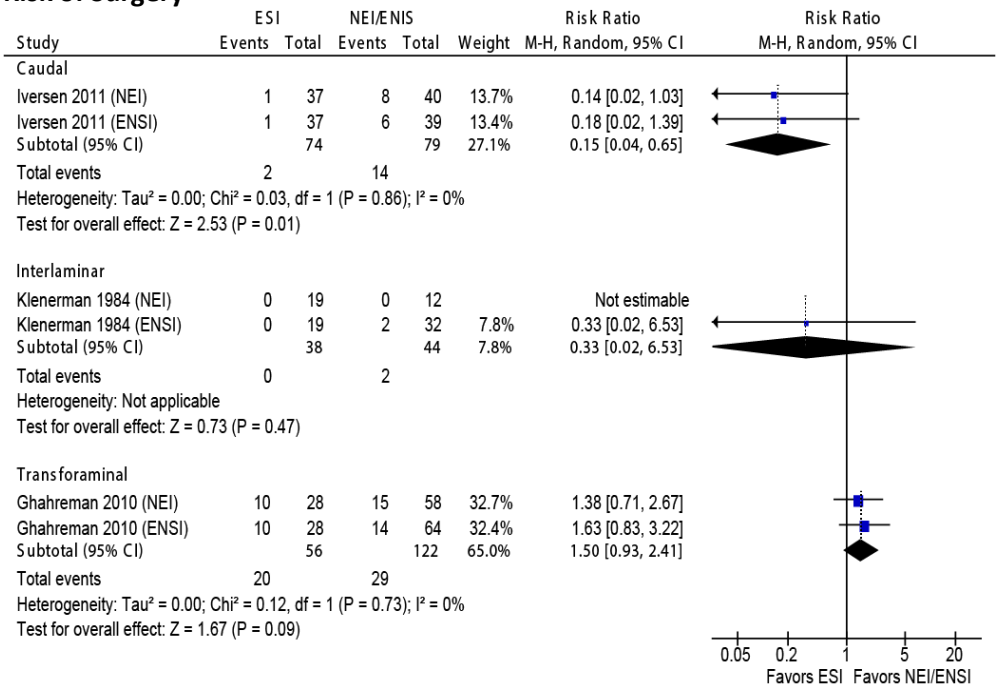
Improved Pain



Pain Success



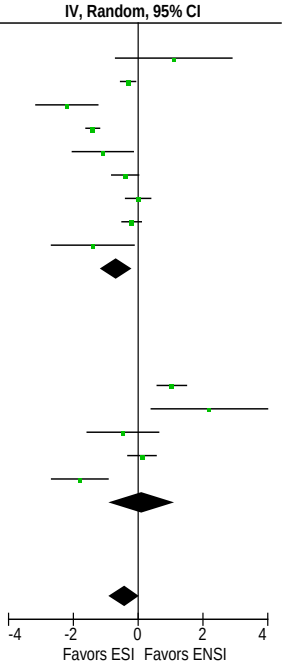
Risk of Surgery



Sensitivity analysis comparing ESI vs. control injections with and without anesthetic.

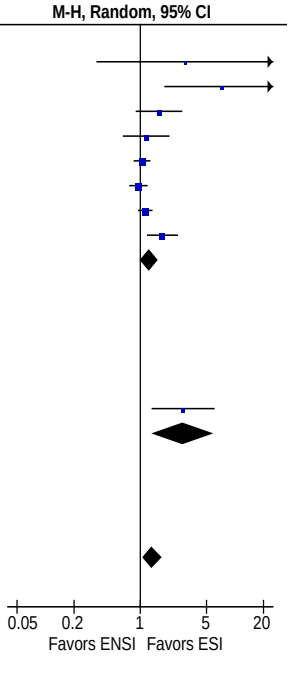
Short-term improved pain:

Study or Subgroup	Epidural Steroid Mean	SD	Total	ENSI Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
8.1.1 Anesthetic								
Klenerman 1984 1	-2.3	2.73	19	-3.4	2.68	16	3.9%	1.10 [-0.70, 2.90]
Tafazal 2009	-2.74	0.47	42	-2.43	0.55	34	8.9%	-0.31 [-0.54, -0.08]
Ghahreman 2010 1	-2.9	1.93	28	-0.7	1.69	27	6.6%	-2.20 [-3.16, -1.24]
Datta 2011	-2.4	0.84	121	-1	0.5	42	9.0%	-1.40 [-1.61, -1.19]
Cohen 2012	-3.57	1.24	28	-2.48	2.3	30	6.6%	-1.09 [-2.03, -0.15]
Manchikanti '12,'11,'08	-4.4	1.12	60	-4	1.21	60	8.5%	-0.40 [-0.82, 0.02]
Manchikanti 2014	-4.2	0.95	60	-4.2	1.21	60	8.6%	0.00 [-0.39, 0.39]
Manchikanti '14,'13,'10	-4.5	0.63	60	-4.3	1.01	60	8.8%	-0.20 [-0.50, 0.10]
Ghai 2015	-4.9	2.73	35	-3.5	2.68	34	5.4%	-1.40 [-2.68, -0.12]
Subtotal (95% CI)			**453**			**363**	**66.3%**	**-0.68 [-1.17, -0.19]**
Heterogeneity: Tau² = 0.42; Chi² = 92.26, df = 8 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 2.74 (P = 0.006)								
8.1.3 Saline / Water								
Iversen 2011	-0.91	0.94	34	-1.95	0.98	35	8.4%	1.04 [0.59, 1.49]
Klenerman 1984 2	-2.3	2.73	19	-4.5	2.68	16	3.9%	2.20 [0.40, 4.00]
Carette 1997	-2.67	3.6	77	-2.2	3.44	79	6.0%	-0.47 [-1.58, 0.64]
Karppinen 2001	-3.97	1.3	79	-4.09	1.5	79	8.5%	0.12 [-0.32, 0.56]
Ghahreman 2010 2	-2.9	1.93	28	-1.1	1.56	37	6.9%	-1.80 [-2.67, -0.93]
Subtotal (95% CI)			**237**			**246**	**33.7%**	**0.11 [-0.91, 1.13]**
Heterogeneity: Tau² = 1.11; Chi² = 39.23, df = 4 (P < 0.00001); I² = 90%								
Test for overall effect: Z = 0.22 (P = 0.83)								
Total (95% CI)			**690**			**609**	**100.0%**	**-0.43 [-0.89, 0.04]**
Heterogeneity: Tau² = 0.62; Chi² = 169.31, df = 13 (P < 0.00001); I² = 92%								
Test for overall effect: Z = 1.79 (P = 0.07)								
Test for subgroup differences: Chi² = 1.90, df = 1 (P = 0.17), I² = 47.5%								



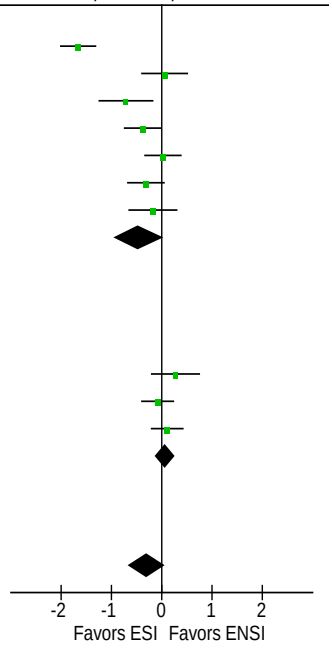
Short-term pain success:

Study or Subgroup	Epidural Steriod Events	Total	ENSI Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
8.2.1 Anesthetic						
Rogers 1992	3	15	1	15	1.1%	3.00 [0.35, 25.68]
Ghahreman 2010 1	15	28	2	27	2.6%	7.23 [1.82, 28.67]
Datta 2011	50	121	11	42	9.8%	1.58 [0.91, 2.74]
Cohen 2012	14	28	13	30	9.8%	1.15 [0.66, 2.00]
Manchikanti '12,'11,'08	48	60	46	60	18.6%	1.04 [0.86, 1.26]
Manchikanti 2014	44	60	46	60	18.1%	0.96 [0.78, 1.18]
Manchikanti '14,'13,'10	53	60	47	60	19.2%	1.13 [0.96, 1.33]
Ghai 2015	30	35	17	34	14.1%	1.71 [1.19, 2.46]
Subtotal (95% CI)		**407**		**328**	**93.3%**	**1.24 [1.00, 1.54]**
Total events	257		183			
Heterogeneity: Tau² = 0.05; Chi² = 21.15, df = 7 (P = 0.004); I² = 67%						
Test for overall effect: Z = 1.97 (P = 0.05)						
8.2.3 Saline / Water						
Ghahreman 2010 2	15	28	7	37	6.7%	2.83 [1.34, 6.00]
Subtotal (95% CI)		**28**		**37**	**6.7%**	**2.83 [1.34, 6.00]**
Total events	15		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.72 (P = 0.007)						
Total (95% CI)		**435**		**365**	**100.0%**	**1.34 [1.06, 1.69]**
Total events	272		190			
Heterogeneity: Tau² = 0.07; Chi² = 29.06, df = 8 (P = 0.0003); I² = 72%						
Test for overall effect: Z = 2.42 (P = 0.02)						
Test for subgroup differences: Chi² = 4.29, df = 1 (P = 0.04), I² = 76.7%						



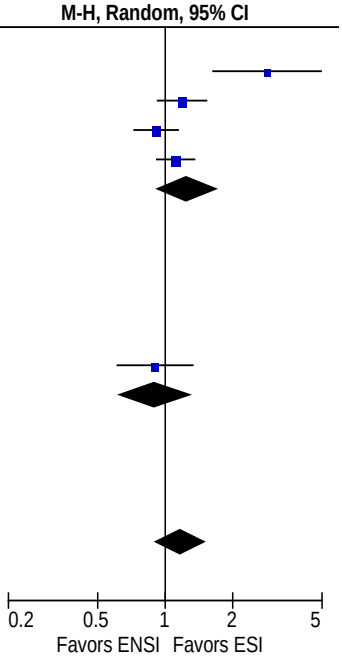
Short-term improved function:

Study or Subgroup	Epidural Steroid Mean	SD	Total	ENSI Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
8.3.1 Anesthetic								
Sayegh 2009	-29.8	9.92	89	-15	7.61	85	10.3%	-1.66 [-2.01, -1.32]
Tafazal 2009	-13.6	3.1	42	-13.8	3.7	34	9.7%	0.06 [-0.39, 0.51]
Cohen 2012	-20.47	10.28	28	-12.1	12.74	30	9.2%	-0.71 [-1.24, -0.18]
Manchikanti '12,'11,'08	-28.6	7.84	60	-25.4	8.95	60	10.2%	-0.38 [-0.74, -0.02]
Manchikanti 2014	-26.6	7.69	60	-26.8	8.85	60	10.3%	0.02 [-0.33, 0.38]
Manchikanti '14,'13,'10	-31.2	6.24	60	-29	7.59	60	10.2%	-0.31 [-0.67, 0.05]
Ghai 2015	-25.8	16	35	-22.6	19.88	34	9.6%	-0.18 [-0.65, 0.30]
Subtotal (95% CI)			**374**			**363**	**69.5%**	**-0.45 [-0.94, 0.03]**
Heterogeneity: Tau² = 0.38; Chi² = 61.33, df = 6 (P < 0.00001); I² = 90%								
Test for overall effect: Z = 1.84 (P = 0.07)								
8.3.3 Saline / Water								
Iversen 2011	-7.5	9.14	34	-9.9	8.19	35	9.5%	0.27 [-0.20, 0.75]
Carette 1997	-17.3	20.6	77	-15.4	25.5	79	10.5%	-0.08 [-0.40, 0.23]
Karppinen 2001	-20	7.31	79	-20.9	9.03	79	10.5%	0.11 [-0.20, 0.42]
Subtotal (95% CI)			**190**			**193**	**30.5%**	**0.06 [-0.14, 0.26]**
Heterogeneity: Tau² = 0.00; Chi² = 1.65, df = 2 (P = 0.44); I² = 0%								
Test for overall effect: Z = 0.59 (P = 0.55)								
Total (95% CI)			**564**			**556**	**100.0%**	**-0.29 [-0.65, 0.08]**
Heterogeneity: Tau² = 0.31; Chi² = 81.97, df = 9 (P < 0.00001); I² = 89%								
Test for overall effect: Z = 1.53 (P = 0.12)								
Test for subgroup differences: Chi² = 3.71, df = 1 (P = 0.05), I² = 73.0%								



Short-term function success:

Study or Subgroup	Epidural Steriod Events	Total	ENSI Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
8.4.1 Anesthetic						
Datta 2011	82	121	10	42	12.5%	2.85 [1.63, 4.96]
Manchikanti '12,'11,'08	44	60	37	60	22.4%	1.19 [0.93, 1.53]
Manchikanti 2014	41	60	45	60	23.3%	0.91 [0.73, 1.14]
Manchikanti '14,'13,'10	49	60	44	60	24.3%	1.11 [0.92, 1.35]
Subtotal (95% CI)		**301**		**222**	**82.5%**	**1.25 [0.91, 1.73]**
Total events	216		136			
Heterogeneity: Tau² = 0.09; Chi² = 17.56, df = 3 (P = 0.0005); I² = 83%						
Test for overall effect: Z = 1.36 (P = 0.17)						
8.4.3 Saline / Water						
Carette 1997	29	77	33	79	17.5%	0.90 [0.61, 1.33]
Subtotal (95% CI)		**77**		**79**	**17.5%**	**0.90 [0.61, 1.33]**
Total events	29		33			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.52 (P = 0.60)						
Total (95% CI)		**378**		**301**	**100.0%**	**1.17 [0.90, 1.52]**
Total events	245		169			
Heterogeneity: Tau² = 0.07; Chi² = 17.11, df = 4 (P = 0.002); I² = 77%						
Test for overall effect: Z = 1.16 (P = 0.25)						
Test for subgroup differences: Chi² = 1.62, df = 1 (P = 0.20), I² = 38.3%						



APPENDIX CC. Studies included in the updated versus the original report

	Citation	Update	Original
	EFFICACY – LUMBAR		
1.	Arden NK, Price C, Reading I, et al. A multicentre randomized controlled trial of epidural corticosteroid injections for sciatica: the WEST study. Rheumatology (Oxford) 2005;44:1399-406.	X	X*
2.	Aronsohn J, Chapman K, Soliman M, et al. Percutaneous microdiscectomy versus epidural injection for management of chronic spinal pain. Proc West Pharmacol Soc 2010;53:16-9.	X	
3.	Becker C, Heidersdorf S, Drewlo S, de Rodriguez SZ, Kramer J, Willburger RE. Efficacy of epidural perineural injections with autologous conditioned serum for lumbar radicular compression: an investigator-initiated, prospective, double-blind, reference-controlled study. Spine (Phila Pa 1976) 2007;32:1803-8.	X	
4.	Breivik H, Hesla, P., Molnar, I., et al. . Treatment of chronic low back pain and sciatica. Comparison of caudal epidural injections of bupivacaine and methylprednisolone with bupivacaine followed by saline. Adv Pain Res Ther 1976;1:927-32.	X	X*
5.	Brown LL. A double-blind, randomized, prospective study of epidural steroid injection vs. the mild(R) procedure in patients with symptomatic lumbar spinal stenosis. Pain Pract 2012;12:333-41.	X	
6.	Buchner M, Zeifang F, Brocai DR, Schiltenwolf M. Epidural corticosteroid injection in the conservative management of sciatica. Clin Orthop Relat Res 2000:149-56.	X	X*
7.	Burgher AH, Hoelzer BC, Schroeder DR, Wilson GA, Huntoon MA. Transforaminal epidural clonidine versus corticosteroid for acute lumbosacral radiculopathy due to intervertebral disc herniation. Spine (Phila Pa 1976) 2011;36:E293-300.	X	
8.	Bush K, Hillier S. A controlled study of caudal epidural injections of triamcinolone plus procaine for the management of intractable sciatica. Spine (Phila Pa 1976) 1991;16:572-5.	X	X*
9.	Buttermann GR. Treatment of lumbar disc herniation: epidural steroid injection compared with discectomy. A prospective, randomized study. J Bone Joint Surg Am 2004;86-A:670-9.	X	X*
10.	Buttermann GR. The effect of spinal steroid injections for degenerative disc disease. Spine J 2004;4:495-505.	X	X*
11.	Cao P, Jiang L, Zhuang C, et al. Intradiscal injection therapy for degenerative chronic discogenic low back pain with end plate Modic changes. Spine J 2011;11:100-6.	X	
12.	Carette S, Leclaire R, Marcoux S, et al. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. N Engl J Med 1997;336:1634-40.	X	X*
13.	Carette S, Marcoux S, Truchon R, et al. A controlled trial of corticosteroid injections into facet joints for chronic low back pain. N Engl J Med 1991;325:1002-7.	X	X*
14.	Civelek E, Cansever T, Kabatas S, et al. Comparison of effectiveness of facet joint injection and radiofrequency denervation in chronic low back pain. Turk Neurosurg 2012;22:200-6.	X	
15.	Cohen SP, Hanling S, Bicket MC, et al. Epidural steroid injections compared with gabapentin for lumbosacral radicular pain: multicenter randomized double blind comparative efficacy study. BMJ 2015;350:h1748.	X	
16.	Cohen SP, White RL, Kurihara C, et al. Epidural steroids, etanercept, or saline in	X	

	Citation	Update	Original
	subacute sciatica: a multicenter, randomized trial. Ann Intern Med 2012;156:551-9.		
17.	Cuckler JM, Bernini PA, Wiesel SW, Booth RE, Jr., Rothman RH, Pickens GT. The use of epidural steroids in the treatment of lumbar radicular pain. A prospective, randomized, double-blind study. J Bone Joint Surg Am 1985;67:63-6.	X	X*
18.	Datta R, Upadhyay, K. . A randomized clinical trial of three different steroid agents for treatment of low backache through the caudal route. Med J Armed Forces India 2011;67:25-33.	X	
19.	Devulder J, Deene P, De Laat M, Van Bastelaere M, Brusselmans G, Rolly G. Nerve root sleeve injections in patients with failed back surgery syndrome: a comparison of three solutions. Clin J Pain 1999;15:132-5.	X	X*
20.	Dilke TF, Burry HC, Grahame R. Extradural corticosteroid injection in management of lumbar nerve root compression. Br Med J 1973;2:635-7.	X	X*
21.	el Zahaar MS. The value of caudal epidural steroids in the treatment of lumbar neural compression syndromes. . J Neurol Orthop Med Surg 1991;12:181-4.	X	X*
22.	Friedly JL, Comstock BA, Turner JA, et al. A randomized trial of epidural glucocorticoid injections for spinal stenosis. N Engl J Med 2014;371:11-21.	X	
23.	Fuchs S, Erbe T, Fischer HL, Tibesku CO. Intraarticular hyaluronic acid versus glucocorticoid injections for nonradicular pain in the lumbar spine. J Vasc Interv Radiol 2005;16:1493-8.	X	X*
24.	Fukusaki M, Kobayashi I, Hara T, Sumikawa K. Symptoms of spinal stenosis do not improve after epidural steroid injection. Clin J Pain 1998;14:148-51.	X	X*
25.	Gerszten PC, Smuck M, Rathmell JP, et al. Plasma disc decompression compared with fluoroscopy-guided transforaminal epidural steroid injections for symptomatic contained lumbar disc herniation: a prospective, randomized, controlled trial. J Neurosurg Spine 2010;12:357-71.	X	
26.	Ghahreman A, Ferch R, Bogduk N. The efficacy of transforaminal injection of steroids for the treatment of lumbar radicular pain. Pain Med 2010;11:1149-68.	X	X
27.	Ghai B, Kumar K, Bansal D, Dhatt SS, Kanukula R, Batra YK. Effectiveness of Parasagittal Interlaminar Epidural Local Anesthetic with or without Steroid in Chronic Lumbosacral Pain: A Randomized, Double-Blind Clinical Trial. Pain Physician 2015;18:237-48.	X	
28.	Helliwell M, Robertson J, Ellis R. Outpatient treatment of low-back pain and sciatica by a single extradural corticosteroid injection. British Journal of Clinical Practice 1985;39:228-31.	X	X*
29.	Iversen T, Solberg TK, Romner B, et al. Effect of caudal epidural steroid or saline injection in chronic lumbar radiculopathy: multicentre, blinded, randomised controlled trial. BMJ 2011;343:d5278.	X	
30.	Karppinen J, Malmivaara A, Kurunlahti M, et al. Periradicular infiltration for sciatica: a randomized controlled trial. Spine (Phila Pa 1976) 2001;26:1059-67.	X	X*
31.	Khot A, Bowditch M, Powell J, Sharp D. The use of intradiscal steroid therapy for lumbar spinal discogenic pain: a randomized controlled trial. Spine (Phila Pa 1976) 2004;29:833-6; discussion 7.	X	X*
32.	Klenerman L, Greenwood R, Davenport HT, White DC, Peskett S. Lumbar epidural injections in the treatment of sciatica. Br J Rheumatol 1984;23:35-8.	X	X*
33.	Koc Z, Ozcakir S, Sivrioglu K, Gurbet A, Kucukoglu S. Effectiveness of physical therapy	X	X

	Citation	Update	Original
	and epidural steroid injections in lumbar spinal stenosis. Spine (Phila Pa 1976) 2009;34:985-9.		
34.	Lakemeier S, Lind M, Schultz W, et al. A comparison of intraarticular lumbar facet joint steroid injections and lumbar facet joint radiofrequency denervation in the treatment of low back pain: a randomized, controlled, double-blind trial. Anesth Analg 2013;117:228-35.	X	
35.	Lilius G, Laasonen EM, Myllynen P, Harilainen A, Gronlund G. Lumbar facet joint syndrome. A randomised clinical trial. J Bone Joint Surg Br 1989;71:681-4.	X	X*
36.	Luukkainen RK, Wennerstrand PV, Kautiainen HH, Sanila MT, Asikainen EL. Efficacy of periarticular corticosteroid treatment of the sacroiliac joint in non-spondylarthropathic patients with chronic low back pain in the region of the sacroiliac joint. Clin Exp Rheumatol 2002;20:52-4.	X	X*
37.	Manchikanti L, Cash KA, McManus CD, Pampati V, Smith HS. Preliminary results of a randomized, equivalence trial of fluoroscopic caudal epidural injections in managing chronic low back pain: Part 1--Discogenic pain without disc herniation or radiculitis. Pain Physician 2008;11:785-800.	X	X
38.	Manchikanti L, Cash KA, McManus CD, Pampati V, Smith HS. One-year results of a randomized, double-blind, active controlled trial of fluoroscopic caudal epidural injections with or without steroids in managing chronic discogenic low back pain without disc herniation or radiculitis. Pain Physician 2011;14:25-36.	X†	
39.	Manchikanti L, Cash KA, Pampati V, Falco FJ. Transforaminal epidural injections in chronic lumbar disc herniation: a randomized, double-blind, active-control trial. Pain Physician 2014;17:E489-501.	X	
40.	Manchikanti L, Singh V, Cash KA, et al. Preliminary results of a randomized, equivalence trial of fluoroscopic caudal epidural injections in managing chronic low back pain: Part 2--Disc herniation and radiculitis. Pain Physician. 2008 Nov-Dec;11(6):801-15. PMID: 19057627.	X	X
41.	Manchikanti L, Singh V, Cash KA, Pampati V, Damron KS, Boswell MV. A randomized, controlled, double-blind trial of fluoroscopic caudal epidural injections in the treatment of lumbar disc herniation and radiculitis. Spine (Phila Pa 1976) 2011;36:1897-905.	X†	
42.	Manchikanti L, Singh V, Cash KA, Pampati V, Damron KS, Boswell MV. Effect of fluoroscopically guided caudal epidural steroid or local anesthetic injections in the treatment of lumbar disc herniation and radiculitis: a randomized, controlled, double blind trial with a two-year follow-up. Pain Physician 2012;15:273-86.	X†	
43.	Manchikanti L, Singh V, Cash KA, Pampati V, Falco FJ. The role of fluoroscopic interlaminar epidural injections in managing chronic pain of lumbar disc herniation or radiculitis: a randomized, double-blind trial. Pain Pract 2013;13:547-58.	X†	
44.	Manchikanti L, Singh V, Cash KA, Pampati V, Falco FJ. A randomized, double-blind, active-control trial of the effectiveness of lumbar interlaminar epidural injections in disc herniation. Pain Physician 2014;17:E61-74.	X†	
45.	Manchikanti L, Singh V, Falco FJ, Cash KA, Pampati V. Evaluation of the effectiveness of lumbar interlaminar epidural injections in managing chronic pain of lumbar disc herniation or radiculitis: a randomized, double-blind, controlled trial. Pain Physician 2010;13:343-55.	X	X
46.	Manchikanti L, Cash KA, McManus CD, Damron KS, Pampati V, Falco FJ. Lumbar interlaminar epidural injections in central spinal stenosis: preliminary results of a	X	

	Citation	Update	Original
	randomized, double-blind, active control trial. Pain Physician 2012;15:51-63.		
47.	Manchikanti L, Cash KA, McManus CD, Damron KS, Pampati V, Falco FJ. A randomized, double-blind controlled trial of lumbar interlaminar epidural injections in central spinal stenosis: 2-year follow-up. Pain Physician 2015;18:79-92.	X	
48.	Manchikanti L, Cash KA, McManus CD, Pampati V, Abdi S. Preliminary results of a randomized, equivalence trial of fluoroscopic caudal epidural injections in managing chronic low back pain: Part 4--Spinal stenosis. Pain Physician 2008;11:833-48.	X	X
49.	Manchikanti L, Cash KA, McManus CD, Pampati V, Fellows B. Fluoroscopic caudal epidural injections with or without steroids in managing pain of lumbar spinal stenosis: one-year results of randomized, double-blind, active-controlled trial. J Spinal Disord Tech 2012;25:226-34.	X†	
50.	Manchikanti L, Cash KA, McManus CD, Pampati V, Fellows B. Results of 2-year follow-up of a randomized, double-blind, controlled trial of fluoroscopic caudal epidural injections in central spinal stenosis. Pain Physician 2012;15:371-84.	X†	
51.	Manchikanti L, Cash KA, McManus CD, Pampati V. Fluoroscopic caudal epidural injections in managing chronic axial low back pain without disc herniation, radiculitis, or facet joint pain. J Pain Res 2012;5:381-90.	X†	
52.	Manchikanti L, Cash KA, McManus CD, Pampati V, Benyamin R. Fluoroscopic lumbar interlaminar epidural injections in managing chronic lumbar axial or discogenic pain. J Pain Res 2012;5:301-11.	X†	
53.	Manchikanti L, Cash KA, McManus CD, Pampati V, Benyamin RM. Preliminary results of a randomized, double-blind, controlled trial of fluoroscopic lumbar interlaminar epidural injections in managing chronic lumbar discogenic pain without disc herniation or radiculitis. Pain Physician 2010;13:E279-92.	X	X
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55.	Manchikanti L, Singh V, Cash KA, Pampati V, Datta S. Preliminary results of a randomized, equivalence trial of fluoroscopic caudal epidural injections in managing chronic low back pain: Part 3--Post surgery syndrome. Pain Physician 2008;11:817-31.	X	X
56.	Manchikanti L, Singh V, Cash KA, Pampati V, Datta S. Management of pain of post lumbar surgery syndrome: one-year results of a randomized, double-blind, active controlled trial of fluoroscopic caudal epidural injections. Pain Physician 2010;13:509-21.	X†	
57.	Manchikanti L, Singh V, Cash KA, Pampati V, Datta S. Fluoroscopic caudal epidural injections in managing post lumbar surgery syndrome: two-year results of a randomized, double-blind, active-control trial. Int J Med Sci 2012;9:582-91.	X†	
58.	Manchikanti L, Pampati V, Bakhit CE, et al. Effectiveness of lumbar facet joint nerve blocks in chronic low back pain: a randomized clinical trial. Pain Physician 2001;4:101-17.	X	X*
59.	Manchikanti L, Singh V, Falco FJ, Cash KA, Pampati V. Lumbar facet joint nerve blocks in managing chronic facet joint pain: one-year follow-up of a randomized, double-blind controlled trial: Clinical Trial NCT00355914. Pain Physician 2008;11:121-32.	X	X

	Citation	Update	Original
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61.	Meadeb J, Rozenberg S, Duquesnoy B, et al. Forceful sacrococcygeal injections in the treatment of postdiscectomy sciatica. A controlled study versus glucocorticoid injections. Joint Bone Spine 2001;68:43-9.	X	X*
62.	Murakibhavi VG, Khemka AG. Caudal epidural steroid injection: a randomized controlled trial. Evid Based Spine Care J 2011;2:19-26.	X	
63.	Nam HS, Park YB. Effects of transforaminal injection for degenerative lumbar scoliosis combined with spinal stenosis. Ann Rehabil Med 2011;35:514-23.	X	
64.	Ng L, Chaudhary N, Sell P. The efficacy of corticosteroids in periradicular infiltration for chronic radicular pain: a randomized, double-blind, controlled trial. Spine (Phila Pa 1976) 2005;30:857-62.	X	X*
65.	Ohtori S, Miyagi M, Eguchi Y, et al. Epidural administration of spinal nerves with the tumor necrosis factor-alpha inhibitor, etanercept, compared with dexamethasone for treatment of sciatica in patients with lumbar spinal stenosis: a prospective randomized study. Spine (Phila Pa 1976) 2012;37:439-44.	X	
66.	Peng B, Pang X, Wu Y, Zhao C, Song X. A randomized placebo-controlled trial of intradiscal methylene blue injection for the treatment of chronic discogenic low back pain. Pain 2010;149:124-9.	X	X
67.	Price C, Arden N, Coglan L, Rogers P. Cost-effectiveness and safety of epidural steroids in the management of sciatica. Health Technol Assess 2005;9:1-58, iii.	X	X
68.	Ribeiro LH, Furtado RN, Konai MS, Andreo AB, Rosenfeld A, Natour J. Effect of facet joint injection versus systemic steroids in low back pain: a randomized controlled trial. Spine (Phila Pa 1976) 2013;38:1995-2002.	X	
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70.	Riew KD, Park JB, Cho YS, et al. Nerve root blocks in the treatment of lumbar radicular pain. A minimum five-year follow-up. J Bone Joint Surg Am 2006;88:1722-5.	X	X*
71.	Riew KD, Yin Y, Gilula L, et al. The effect of nerve-root injections on the need for operative treatment of lumbar radicular pain. A prospective, randomized, controlled, double-blind study. J Bone Joint Surg Am 2000;82-A:1589-93.	X	X*
72.	Rocco AG, Frank E, Kaul AF, Lipson SJ, Gallo JP. Epidural steroids, epidural morphine and epidural steroids combined with morphine in the treatment of post-laminectomy syndrome. Pain 1989;36:297-303.	X	X*
73.	Rogers P, Nash, T., Schiller, D., et. al,. Epidural steroids for sciatica. Pain Clinic 1992;5:67-72.	X	X*
74.	Sayegh FE, Kenanidis EI, Papavasiliou KA, Potoupnis ME, Kirkos JM, Kapetanos GA. Efficacy of steroid and nonsteroid caudal epidural injections for low back pain and sciatica: a prospective, randomized, double-blind clinical trial. Spine (Phila Pa 1976) 2009;34:1441-7.	X	X
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76.	Snoek W, Weber H, Jorgensen B. Double blind evaluation of extradural methyl	X	X*

	Citation	Update	Original
	prednisolone for herniated lumbar discs. Acta Orthop Scand 1977;48:635-41.		
77.	Tafazal S, Ng L, Chaudhary N, Sell P. Corticosteroids in peri-radicular infiltration for radicular pain: a randomised double blind controlled trial. One year results and subgroup analysis. Eur Spine J 2009;18:1220-5.	X	X
78.	Visser LH, Woudenberg NP, de Bont J, et al. Treatment of the sacroiliac joint in patients with leg pain: a randomized-controlled trial. Eur Spine J. 2013 Oct;22(10):2310-7. PMID: 23720124.	X	
79.	Wilson-MacDonald J, Burt G, Griffin D, Glynn C. Epidural steroid injection for nerve root compression. A randomised, controlled trial. J Bone Joint Surg Br 2005;87:352-5.	X	X*
80.	Wu S, Li X, Lin C, et al. CT-guided nucleoplasty with radiofrequency energy for the treatment of lumbar disk herniation. J Spinal Disord Tech. 2015 Feb;28(1):E9-16. PMID: 25023711.	X	
	EFFICACY – CERVICAL		
1.	Barnsley L, Lord SM, Wallis BJ, Bogduk N. Lack of effect of intraarticular corticosteroids for chronic pain in the cervical zygapophyseal joints. N Engl J Med 1994;330:1047-50.	X	X
2.	Cohen SP, Hayek S, Semenov Y, et al. Epidural steroid injections, conservative treatment, or combination treatment for cervical radicular pain: a multicenter, randomized, comparative-effectiveness study. Anesthesiology 2014;121:1045-55.	X	
3.	Manchikanti L, Cash KA, Pampati V, Wargo BW, Malla Y. Management of chronic pain of cervical disc herniation and radiculitis with fluoroscopic cervical interlaminar epidural injections. Int J Med Sci 2012;9:424-34.	X†	
4.	Manchikanti L, Cash KA, Pampati V, Wargo BW, Malla Y. A randomized, double-blind, active control trial of fluoroscopic cervical interlaminar epidural injections in chronic pain of cervical disc herniation: results of a 2-year follow-up. Pain Physician 2013;16:465-78.	X†	
5.	Manchikanti L, Cash KA, Pampati V, et al. The effectiveness of fluoro-scopic cervical interlaminar epidural injections in managing chronic cervical disc herniation and radiculitis: preliminary results of a randomized, double-blind, controlled trial. Pain Physician. 2010; 13:223-36.	X	X
6.	Manchikanti L, Cash KA, Pampati V, Malla Y. Two-year follow-up results of fluoroscopic cervical epidural injections in chronic axial or discogenic neck pain: a randomized, double-blind, controlled trial. Int J Med Sci 2014;11:309-20.	X†	
7.	Manchikanti L, Cash KA, Pampati V, Malla Y. Fluoroscopic cervical epidural injections in chronic axial or disc-related neck pain without disc herniation, facet joint pain, or radiculitis. J Pain Res 2012;5:227-36.	X†	
8.	Manchikanti L, Cash KA, Pampati V, Wargo BW, Malla Y. Cervical epidural injections in chronic discogenic neck pain without disc herniation or radiculitis: preliminary results of a randomized, double-blind, controlled trial. Pain Physician. 2010;13(4):E265–E278.	X	X
9.	Manchikanti L, Malla Y, Cash KA, McManus CD, Pampati V. Fluoroscopic cervical interlaminar epidural injections in managing chronic pain of cervical postsurgery syndrome: preliminary results of a randomized, double-blind, active control trial. Pain Physician 2012;15:13-25.	X	
10.	Manchikanti L, Malla Y, Cash KA, McManus CD, Pampati V. Fluoroscopic epidural	X	

	Citation	Update	Original
	injections in cervical spinal stenosis: preliminary results of a randomized, double-blind, active control trial. Pain Physician 2012;15:E59-70.		
11.	Manchikanti L, Singh V, Falco FJ, Cash KA, Fellows B. Comparative outcomes of a 2-year follow-up of cervical medial branch blocks in management of chronic neck pain: a randomized, double-blind controlled trial. Pain Physician 2010;13:437-50.	X†	
12.	Manchikanti L, Singh V, Falco FJ, Cash KM, Fellows B. Cervical medial branch blocks for chronic cervical facet joint pain: a randomized, double-blind, controlled trial with one-year follow-up. Spine (Phila Pa 1976) 2008;33:1813-20.	X†	X
13.	Manchikanti, L., Damron, K., Cash, K., Manchukonda, R., & Pampati, V. (2006). Therapeutic cervical medical branch blocks in managing chronic neck pain: a preliminary report of randomized, double-blind, controlled trial: clinical trial NCT0033272. Pain Physician, 9(346), 1533-3159.	X	X
14.	Park SC, Kim KH. Effect of adding cervical facet joint injections in a multimodal treatment program for long-standing cervical myofascial pain syndrome with referral pain patterns of cervical facet joint syndrome. J Anesth 2012;26:738-45.	X	
15.	Stav A, Ovadia L, Sternberg A, Kaadan M, Weksler N. Cervical epidural steroid injection for cervicobrachialgia. Acta Anaesthesiol Scand 1993;37:562-6.	X	X
	SAFETY – LUMBAR: COHORTS		
1.	Fotiadou A, Wojcik A, Shaju A. Management of low back pain with facet joint injections and nerve root blocks under computed tomography guidance. A prospective study. Skeletal Radiol 2012;41:1081-5.	X	
2.	Mandel S, Schilling J, Peterson E, Rao DS, Sanders W. A retrospective analysis of vertebral body fractures following epidural steroid injections. J Bone Joint Surg Am 2013;95:961-4.	X	
	SAFETY – LUMBAR: CASE SERIES		
1.	Botwin KP, Gruber RD, Bouchlas CG, Torres-Ramos FM, Freeman TL, Slaten WK. Complications of fluoroscopically guided transforaminal lumbar epidural injections. Archives of physical medicine and rehabilitation 2000;81:1045-50.	X	X
2.	Botwin KP, Gruber RD, Bouchlas CG, et al. Complications of fluoroscopically guided caudal epidural injections. American journal of physical medicine & rehabilitation / Association of Academic Physiatrists 2001;80:416-24.	X	X
3.	Candido KD, Katz JA, Chinthagada M, McCarthy RA, Knezevic NN. Incidence of intradiscal injection during lumbar fluoroscopically guided transforaminal and interlaminar epidural steroid injections. Anesthesia & Analgesia 2010;110:1464-7.	X	X
4.	Everett CR, Baskin MN, Novoseletsky D, Speech D, Patel R. Flushing as a side effect following lumbar transforaminal epidural steroid injection. Pain Physician 2004;7:427-30.	X	X
5.	Goodman BS, Lincoln CE, Deshpande KK, Poczatek RB, Lander PH, DeVivo MJ. Incidence of intravascular uptake during fluoroscopically guided lumbar disc injections: a prospective observational study. Pain Physician 2005;8:263-6.	X	X
6.	Hong JH, Kim SY, Huh B, Shin HH. Analysis of inadvertent intradiscal and intravascular injection during lumbar transforaminal epidural steroid injections: a prospective study. Reg Anesth Pain Med 2013;38:520-5.	X	
7.	Huang AJ, Palmer WE. Incidence of inadvertent intra-articular lumbar facet joint injection during fluoroscopically guided interlaminar epidural steroid injection. Skeletal Radiol 2012;41:157-62.	X	

	Citation	Update	Original
8.	Jaimes R, 3rd, Rocco AG. Multiple epidural steroid injections and body mass index linked with occurrence of epidural lipomatosis: a case series. BMC Anesthesiol 2014;14:70.	X	
9.	Kim SJ, Lee MH, Lee SW, Chung HW, Lee SH, Shin MJ. Radiation exposure for fluoroscopy-guided lumbosacral epidural steroid injections: comparison of the transforaminal and caudal approaches. J Spinal Disord Tech 2014;27:E37-40.	X	
10.	Lee HI, Park YS, Cho TG, Park SW, Kwon JT, Kim YB. Transient adverse neurologic effects of spinal pain blocks. J Korean Neurosurg Soc 2012;52:228-33. *(also provides data for cervical)*	X	
11.	McGrath JM, Schaefer MP, Malkamaki DM. Incidence and characteristics of complications from epidural steroid injections. Pain Med 2011;12:726-31. *(also provides data for mixed population)*	X	
12.	Manchikanti L, Cash KA, Pampati V, Damron K, McManus C. Evaluation of lumbar transforaminal epidural injections with needle placement and contrast flow patterns: a prospective, descriptive report. Pain Physician 2004;7:217-24.	X	X
13.	Stalcup ST, Crall TS, Gilula L, Riew KD. Influence of needle-tip position on the incidence of immediate complications in 2,217 selective lumbar nerve root blocks. The Spine Journal 2006;6:170-6.	X	X
	SAFETY – CERVICAL: CASE SERIES		
1.	Kennedy DJ, Schneider B, Casey E, et al. Vasovagal rates in flouroscopically guided interventional procedures: a study of over 8,000 injections. Pain Med 2013;14:1854-9.	X	
2.	Kloth DS, Calodney AK, Derby R, et al. Improving the safety of transforaminal epidural steroid injections in the treatment of cervical radiculopathy. Pain Physician 2011;14:285-93.	X	
3.	Ma DJ, Gilula LA, Riew KD. Complications of fluoroscopically guided extraforaminal cervical nerve blocks. The Journal of Bone & Joint Surgery 2005;87:1025-30.	X	X
4.	Pobiel R, Schellhas K, Eklund J, et al. Selective cervical nerve root blockade: prospective study of immediate and longer term complications. American Journal of Neuroradiology 2009;30:507-11.	X	X
5.	Schellhas K, Pollei S, Johnson B, Golden M, Eklund J, Pobiel R. Selective cervical nerve root blockade: experience with a safe and reliable technique using an anterolateral approach for needle placement. American Journal of Neuroradiology 2007;28:1909-14.	X	X
6.	Wald JT, Maus TP, Geske JR, et al. Safety and efficacy of CT-guided transforaminal cervical epidural steroid injections using a posterior approach. AJNR Am J Neuroradiol 2012;33:415-9.	X	
7.	Waldman SD. Complications of cervical epidural nerve blocks with steroids: a prospective study of 790 consecutive blocks. Regional Anesthesia and Pain Medicine 1989;14:149-51.	X	X
	SAFETY – LUMBAR OR CERVICAL (MIXED): COHORTS		
1.	Huston CW, Slipman CW, Garvin C. Complications and side effects of cervical and lumbosacral selective nerve root injections. Archives of physical medicine and rehabilitation 2005;86:277-83.	X	X
	SAFETY – LUMBAR OR CERVICAL (MIXED): CASE SERIES		

	Citation	Update	Original
1.	El Abd O, Amadera J, Pimentel DC, Gomba L. Immediate and acute adverse effects following transforaminal epidural steroid injections with dexamethasone. Pain Physician 2015;18:277-86.	X	
2.	Johnson BA, Schellhas KP, Pollei SR. Epidurography and therapeutic epidural injections: technical considerations and experience with 5334 cases. AJNR Am J Neuroradiol 1999;20:697-705.	X	X
	COST-EFFECTIVENESS		
1.	Karppinen J, Ohinmaa A, Malmivaara A, et al. Cost effectiveness of periradicular infiltration for sciatica: subgroup analysis of a randomized controlled trial. Spine (Phila Pa 1976) 2001;26:2587-95.	X	X
2.	Price C, Arden N, Coglan L, Rogers P. Cost-effectiveness and safety of epidural steroids in the management of sciatica. Health Technol Assess 2005;9:1-58, iii.	X	X
3.	Udeh BL, Costandi S, Dalton JE, Ghosh R, Yousef H, Mekhail N. The 2-year cost-effectiveness of 3 options to treat lumbar spinal stenosis patients. Pain Pract 2015;15:107-16.	X	

*This trial was included the Chou 2009 systematic review.
†These studies provided longer-term follow-up for preliminary studies included in the original report; these preliminary studies only reported on a subset of patients and are included for completeness, while the follow-up studies included the entire population.

APPENDIX DD. Clinical Experts

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- Associate Professor, Deparment of Rehabilitation Medicine
- Investigator, Cost Effectiveness Cost and Outcomes Research Center VA Puget Sound Healthcare System; Seattle, Washington
- Attending Physician, Rehabilitation Care Services
- Investigator, Seattle Epidemiologic Research and Information Center

Daryl R. Fourney, M.D., F.R.C.S.C. (Neurosurgery), F.A.C.S.
Royal University Hospital; Saskatoon, Saskatchewan, Canada

- Professor, Division of Neurosurgery

James Babington, M.D.
Virginia Mason Medical Center; Seattle, Washington

- Medical Co-Director, Comprehensive Spine Program
- Medical Director, Spine Clinics
- Member, Section of Physical Medicine and Rehabilitation