Washington State Health Care Authority

Health Technology Assessment

Spinal Injections – Re-review

UPDATED Final Evidence Report

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Health Technology Assessment Program (HTA)
Washington State Health Care Authority
PO Box 42712
Olympia, WA 98504-2712
(360) 725-5126
hca.wa.gov/hta
shtap@hca.wa.gov

Spinal Injections – Re-review

Provided by:

Spectrum Research, Inc.

Prepared by:

Joseph R. Dettori, PhD, MPH
Robin Hashimoto, PhD
Erika D. Brodt, BS
Krystle T. Pagarigan, BS
Eric C. Schnell, BS

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With assistance from:

Erin Anthony-Fick
Elena Dodge

The information in this assessment is intended to assist health care decision makers, clinicians, patients and policy makers in making sound evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.

Erratum

The following corrects errors in the strength of evidence table (Table 1 of the Executive Summary and Section 4.1):

- Lumbar radiculopathy due to disc and/or foraminal narrowing: ESI vs. Control Injections
    - Pain improvement, short-term: N=1696; WMD: -0.46 (-0.94 to 0.02)
    - Pain success, short-term: N=1201; RR: 1.27 (1.06 to 1.53)
    - Pain success, long-term: RR: 1.09 (0.95 to 1.26)
    - Risk of surgery: RR 0.83 (0.66 to 1.04)
- Lumbar spinal stenosis: ESI vs. Control Injections
    - Function improvement, short-term: SMD: -2.15 (-5.83 to 1.52); also deleted the phrase "insufficient evidence prevents firm conclusions" as this was included in error.

      This edit was also made to the corresponding text on page 118.

The following corrects an error in the strength of evidence table (Table 2 of the Executive Summary and the strength of evidence summary table in Section 5.2):

> "NDI" was changed to "NRS" in the conclusion statement, which should read, *"Cervical disc herniation with or without radiculopathy: ESI versus Control Injections, pain improvement on NRS, intermediate term*."

These edits do not change the report's conclusions.

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Abbreviations

CC: conservative care
CI: confidence interval
CoE: class of evidence
EANSI: extra-articular non-steroidal injection
EASI: extra-articular steroid injection
ENSI: epidural non-steroidal injection
ESI: epidural steroid injection
FDA: US Food and Drug Administration
f/u: follow-up
HTA: health technology assessment
HTE: heterogeneity of treatment effect
IANSI: intra-articular non-steroidal injection
IASI: intra-articular steroid injection
KQ: key question
MD: mean difference
mos.: months
N: number of patients
NEAI: non-extra-articular injection
NIAI: non-intra-articular injection
NR: not reported
NS: not statistically significant ($p \geq 0.05$)
RD: risk difference
RR: risk ratio
SD: standard deviation
SMD: standardized mean difference
SoE: strength of evidence
SR: systematic review
vs.: versus
WMD: weighted mean difference
yrs.: years

Executive Summary

Introduction

Back and neck pain are extremely common conditions; lifetime incidence is estimated to be 70% to 85% for low back pain,[1] and 14% to 71% for neck pain.[35] While back pain often resolves within a few months, surveys report that approximately 5% of the population has chronic back pain[5] (i.e., persists for more than three months). Similarly, while most cases of acute neck pain will resolve within 2 months,[24] 1 year chronic neck prevalence can range from 16.7% to 75.1%.[35]Back and neck pain have significant social and economic impacts. Back pain is the most common cause of activity limitation in people younger than 45 years, and about 2% of the United States workforce seek Worker's Compensation for back pain each year.[1] A registry study from Denmark also found that those suffering from neck pain had lower employment rates and incomes.[46] Additionally, back pain is the leading cause of years lost to disability, and neck pain is the fourth most common cause.[98] Lastly, back pain[9,21,44,111,116] and neck pain[9] have been reported to negatively impact quality of life, work status, functional activity, as well as satisfaction with pain treatment. The prevalence of back and neck pain is higher in certain populations, such as women and the elderly.[20]

Spinal imaging abnormalities are common in patients with back and neck pain, particularly in older adults. However, such findings poorly predict the presence or severity of pain.[121] Though often symptoms cannot be attributed to a specific disease or spinal pathology, spinal injections have been administered in patients with the following diagnosis or condition: disc degeneration, herniated nucleus pulposus, spinal stenosis, radiculopathy, failed back surgery syndrome, and facet joint syndrome (e.g., whiplash).

Treatment for back pain often involves a combination of interventions, and spinal injections are not usually performed until less invasive treatments have been tried and have not provided adequate relief. In general, spinal injections are indicated for intermittent or continuous pain causing functional disability or chronic pain that has failed to respond to more conservative therapies.[55,95] Spinal injections involve the injection of an anti-inflammatory agent such as a steroid and/or an anesthetic into the spine or space around the spinal nerves and joints. Types of spinal injections include epidural, facet joint, medial branch block, intradiscal, and sacroiliac joint injections. One of the theoretical advantages of spinal injections is direct delivery of treatment medication to the site involved in the source of pain.[43] Fluoroscopic or computed tomography (CT) visualization is often used to improve the accuracy of medication delivery.

While spinal injections can be used for diagnostic and therapeutic purposes, the focus of this report is only on those used therapeutically. The use of spinal injections has been growing; according to one study examining Medicare claims of lumbosacral injections, the number of epidural steroidal injections increased 271% and the number of facet injections increased 231% from 1994 to 2001.[31] Similar studies among the Medicare population indicate that from 2000 to 2011, average annual increases have been seen for epidural injections (7.5%),[80] facet joint injections (13.6%),[81] and sacroiliac injections (14.2%).[75] In the Washington State Medicare population alone, epidural injections, facet joint injections, sacroiliac injections, and percutaneous adhesiolysis (not discussed in this report) have increased on average 12% per year from 2000 to 2010.[76]

Treatment for chronic back pain typically begins with the identification of the underlying cause of pain. Depending upon the diagnosis, a variety of treatments can be administered. These treatments, collectively referred to as conventional medical management (CMM), include conservative/non-invasive interventions such as physical therapy and rehabilitation, pharmaceutical pain management, psychological therapy and coping skills, exercise, education, antidepressants, cognitive behavioral therapy and supported self-management, spinal manipulation, electrical stimulation, injections outside the spine, implanted devices, acupuncture/acupressure, and modified work.[22] Treatment strategies generally begin with the least invasive and low risk interventions, progressing to more invasive techniques if CMM treatments are not effective.

Policy Context

This topic was reviewed in March 2011 and selected for re-review by the Director of the Washington State Health Care Authority based on new literature identified. In addition, new safety concerns have emerged for epidural injections from the FDA.

Objectives

The objective of this Health Technology Assessment is to update the previous review on spinal injections. Specifically, the aim was to systematically review, critically appraise, analyze and synthesize research evidence evaluating the efficacy, comparative efficacy and safety of spinal injections in adults with subacute or chronic spinal pain.

Key Questions

When used in adult patients with subacute or chronic back or neck pain:

1. What is the evidence of efficacy and effectiveness of spinal injections? Including consideration of:
    a. Short-term and long-term measures, including measures related to repeated spinal injections, multilevel spinal injections, bilateral versus unilateral spinal injections
    b. Impact on clinically meaningful physical function and pain
    c. Impact on quality of life, patient satisfaction
    d. Opioid use, return to work, and any other reported surrogate measures

2. What is the evidence of the safety of spinal injections? Including:
    a. Adverse event type and frequency (mortality, major morbidity, other)
    b. Dural or arachnoid puncture
    c. Infection
    d. Epidural or intradural hematoma
    e. Allergic reaction
    f. Nerve or spinal cord injury
    g. Artery/vein damage/puncture
    h. Arachnoiditis

3. What is the evidence that spinal injections have differential efficacy or safety issues in sub populations? Including consideration of:
   a. Patient characteristics (gender, age, psychological or psychosocial co-morbidities, diagnosis, duration of pain)
   b. Injection characteristics (type of steroid [particulate, non-particulate], use of guidance, route of administration)e. Other patient characteristics or evidence based on patient selection criteria
   c. Provider type, setting, or other provider characteristics
   d. Payer/ beneficiary type: including worker's compensation, Medicaid, state employees

4. What is the evidence of cost implications and cost-effectiveness of spinal injections? Including:
   a. Direct costs over short term and over expected duration of effect
   b. Comparative costs

Inclusion/Exclusion Criteria

The inclusion and exclusion criteria are summarized below. Briefly, included studies met the following requirements with respect to participants, intervention, comparators, outcomes, and study design:

- *Population:* Adult patients with symptoms of subacute or chronic pain in the lumbar or cervical spine with or without radiculopathy or radiculitis. Subacute pain was defined as pain duration of 4 to 12 weeks prior to enrollment; chronic pain was defined as pain duration for longer than 12 weeks. We excluded studies of patients with back or neck pain due to acute major trauma, cancer, infection, cauda equina syndrome, spondyloarthropathy, osteoporosis or vertebral compression fracture.
- *Intervention:* For the intervention of epidural injections, results were stratified based on the condition: radicular lower or upper extremity pain, spinal stenosis, nonradicular axial pain, or pain from failed back or neck surgery. We accepted the authors' definition of radiculopathy, though the definition was not always explicit. Some authors simply used the term radiculopathy or sciatica, others described the presence of extremity pain, while some described motor or sensory deficit in a nerve root distribution. Facet joint injections for pain attributed to the facet joints were also included. These included injections into the joint (intraarticular), around the joint (extra- or peri- articular), or aimed at providing a therapeutic medial branch block. Studies of sacroiliac injections were included for low back pain presumed to originate from that joint. We excluded studies of extraspinal injections (botulinum toxin, paraspinal muscle injections, prolotherapy), chemonucleolysis, radiofrequency denervation, intradiscal electrothermal therapy, and coblation nucleoplasty. We also excluded studies that involved intervention injections of non-steroid medications such as hyaluronidase and clonidine.
- *Comparators:* Comparators of interest encompassed any treatment other than spinal steroid injections. To assess epidural steroid injections, we compared those injections with different control groups. Since some believe there is therapeutic benefit from an epidural injection of a non-steroid substance,[8] we initially separated control group injections into epidural non-steroid injections (ENSI) consisting of epidural anesthetic and or saline/water, and non-epidural

injections (NEI) that included dry needling, anesthetic and or saline/water into muscle or ligament (with studies of steroid NEI reported separately), procedures on the intervertebral disc (i.e., discectomy or disc ablation), and conservative care (i.e., physical therapy, exercise, no treatment).

- *Outcomes:* Outcomes of interest included pain, function, quality of life, opioid use, subsequent surgery, and complications. Primary outcomes were pain, function, subsequent surgery, and catastrophic adverse events.
- *Study design:* Randomized controlled trials were used for Key Questions (KQ) 1-3. For KQ 2 on safety, we also included observational studies of at least 100 patients where harm detection was a primary objective, and reviews and FDA reports of cases sustaining serious harms. Formal economic analyses that met the population, intervention, and comparators of interest were included to evaluate cost-effectiveness in KQ 4.

Methods

The scope of this report and final key questions were refined based on input from clinical experts from a variety of disciplines and public comments received on draft key questions. Clinical expert input was sought to confirm critical outcomes on which to focus.

A formal, structured systematic search of the peer-reviewed literature across a number of databases including PubMed to identify relevant peer reviewed literature as well as other sources (National Guideline Clearinghouse, Center for Reviews and Dissemination Database) to identify pertinent clinical guidelines and previously performed assessments.

Studies were selected for inclusion based on pre-specified criteria detailed in the full report. All records were screened by two independent reviewers. Selection criteria included a focus on studies with the least potential for bias that were written in English and published in the peer-reviewed literature.

Pertinent studies were critically appraised independently by two reviewers based on Spectrum's Class of Evidence (CoE) system which evaluates the methodological quality and potential for bias based on study design as well as factors which may bias studies. An overall Strength of Evidence (SoE) combines the appraisal of study limitations with consideration of the number of studies and the consistency across them, directness and precision of the findings to describe an overall confidence regarding the stability of estimates as further research is available. The SoE for all primary health outcomes was assessed by two researchers following the principles for adapting GRADE (Grades of Recommendation Assessment, Development and Evaluation).[4] The strength of evidence was based on the highest quality evidence available for a given outcome. Briefly, 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 (i.e., risk of bias, consistency of effect, directness of outcome, precision of effect estimate, and reporting bias). There are also situations where the studies could be upgraded if the study had large magnitude of effect (strength of association). The final strength of evidence was assigned an overall grade of high, moderate, low, or insufficient, which are defined as follows:

- High - Very confident that effect size estimates lie close to the true effect for this outcome; there are few or no deficiencies in the body of evidence; we believe the findings are stable.
- Moderate – Moderately confident that effect size estimates lie close to the true effect for this outcome; some deficiencies in the body of evidence; we believe the findings are likely to be stable but some doubt remains.
- Low – Limited confidence that effect size estimates lie close to the true effect for this outcome; major or numerous deficiencies in the body of evidence; we believe that additional evidence is needed before concluding that findings are stable or that the estimate is close to the true effect.
- Insufficient – We have no evidence, are unable to estimate an effect or have no confidence in the effect estimate for this outcome; OR no available evidence or the body of evidence has unacceptable efficiencies precluding judgment.

Included economic studies were also formally appraised based on criteria for quality of economic studies and pertinent epidemiological precepts.

Results: Summary of the evidence on critical outcomes

We included a total of 72 RCTs (in 95 publications) for efficacy: 63 randomized trials (80 publications) for the lumbar spine and nine randomized trials (15 publications) for the cervical spine. For safety, a total of 25 studies were included; 15 for lumbar (2 cohorts, 13 case-series), seven case-series for cervical, and three studies (1 cohort and 2 case-series) that reported on adverse events in both the lumbar and cervical spine. In addition, a summary report of the FDA adverse events reporting database was included to evaluate rare but serious adverse events. Three cost-effectiveness studies were included.

A summary of the critical outcomes for each key question are provided in the tables below and are sorted by comparator. Only primary outcomes and/or timepoints reported by one or more trials for a given treatment comparison are included in the summary tables below. Details of these and other outcomes are available in the report.

1. Serious risk of bias: the majority of studies violated one or more of the criteria for good quality RCT related to the outcome reported (see Appendix for details)
2. Inconsistency: differing estimates of effects across trials
3. Imprecise effect estimate for a continuous outcome: wide (or unknown) confidence interval and/or small sample size
4. Imprecise effect estimate for a dichotomous outcome: small sample size and/or confidence interval includes both negligible effect and appreciable benefit or harm with TT
5. Imprecise effect estimate for a dichotomous outcome: small sample size, rare outcome
6. Serious risk of bias in evaluation of HTE: the subgroup variables were specified at randomization, however the hypothesized direction was not stated; the subgroup hypothesis was not one of a smaller number tested

Efficacy Results for Lumbar Spinal Injections (Table 1)

Evidence base

Radiculopathy due to disc and/or foraminal narrowing

- ESI vs. Control injection: 23 RCTs (30 publications)[2,14,18,27-29,32,33,40-42,45,47,50,67,82-84,88,89,93,100,104,106-108,110,112,114,118]
- ESI vs. Control injection with other medication: 3 RCTs[13,25,27]
- ESI vs. Disc or decompression procedure: 4 RCTs[3,16,39,124]
- ESI vs. Conservative care: 2 RCTs[12,97]

Radiculopathy attributed to multiple causes

- ESI vs. Control Injection: 3 RCTs[7,10,123]

Stenosis

- ESI vs. Control Injection: 7 RCTs (10 publications)[28,33,36,38,56,57,59,63,64,99]
- ESI vs. Control injection with other medication: 1 RCT[101]
- ESI vs. Disc or decompression procedure: 1 RCT[11]
- ESI vs. Conservative care: 1 RCT[51]

Low back pain without radiculopathy

- ESI vs. Control Injection: 2 RCTs (6 publications)[58,60-62,65,66]
- Intradiscal steroid injection vs. Intradiscal control injection: 3 RCTs[17,49,113]
- Intradiscal non-steroid injection vs. Intradiscal control injection: 1 RCT[103]
- Intradiscal steroid injection plus Discography vs. Discography alone: 1 RCT[15]

Failed Back Syndrome

- ESI vs. Control Injection: 1 RCT (3 publications)[85-87]
- ESI vs. Control Injection with other medication: 3 RCTs[30,96,109]

Facet joint pain

- IASI vs Intra-articular control injection: 3 RCTs[19,37,53]
- IASI vs Intramuscular steroid injection: 1 RCT[105]
- IASI vs Medial branch radiofrequency denervation: 1 RCT[52]
- EASI vs Extra-articular control injection: 2 RCTs (3 publications)[79,91,92]
- EASI vs Medial branch radiofrequency denervation: 1 RCT[23]

Sacroiliac pain

- IASI vs Conservative care: 1 RCT[122]
- EASI vs Extra-articular control injection: 1 RCT[54]

Table 1. Strength of Evidence Summary: Efficacy Results for Lumbar Spinal Injections

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
Lumbar radiculopathy due to disc and/or foraminal narrowing: ESI vs. Control Injections								
Δ Pain	Short-term: n=1696	15 RCTs[2,14,18,27,29,40-42,45,47,50,67,82-84,88,89,93,104,118] N=1748	Yes (-1)	Yes (-1)	No	No	WMD: -0.46 ~~(-0.97 to 0.05~~ (-0.94 to 0.02) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	5 RCTs[41,47,67,82-84,88,89,93] N=587	Yes (-1)	Yes (-1)	No	No	WMD: -0.15 (-1.17 to 0.86) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	8 RCTs[2,14,41,45,47,67,82-84,88,89,93,104] N=905	Yes (-1)	Yes (-1)	No	No	WMD: -0.25 (-0.77 to 0.27) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain success	Short-term: n=1201	11 RCTs[2,27,29,32,40,41,67,82-84,88,89,93,104,110,118] N=1229	Yes (-1)	Yes (-1)	No	No	RR: ~~1.30~~ 1.27(1.06 to ~~1.58~~ 1.53) Conclusion: Greater proportion achieved pain success with ESI.	⊕⊕◯◯ LOW
	Intermediate-term	5 RCTs[27,41,67,82-	Yes (-1)	Yes (-1)	No	No	RR: 1.14 (0.93 to 1.39) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
		84,88,89,93 N=487						
	Long-term	7 RCTs[2,28,33,41,67,82-84,88,89,93,104] N=726	Yes (-1)	No	No	Yes (-1)	RR: ~~1.10 (0.92 to 1.30)~~ 1.09 (0.95 to 1.26) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Δ Function	Short-term	11 RCTs[2,18,27,41,45,47,67,82-84,88,89,93,104,112,118] N=1396	Yes (-1)	Yes (-1)	No	No	SMD: -0.21 (-0.56 to 0.14) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	6 RCTs[41,47,67,82-84,88,89,93,112] N=740	Yes (-1)	Yes (-1)	No	No	SMD: -0.27 (-0.76 to 0.21) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	8 RCTs[2,41,45,47,67,82-84,88,89,93,104,112] N=1033	Yes (-1)	Yes (-1)	No	No	SMD: -0.09 (-0.46 to 0.28) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function success	Short-term	7 RCTs[2,18,29,67,82-84,88,89,93,104,118]	Yes (-1)	Yes (-1)	No	No	RR: 1.04 (0.82 to 1.32) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
		N=988						
	Intermediate-term	3 RCTs[67,82-84,88,89,93] N=360	Yes (-1)	Yes (-1)	No	Yes (-1)	RR: 1.09 (0.86 to 1.38) Conclusion: No difference between groups. Insufficient evidence prevents firm conclusion.	⊕○○○ INSUFFICIENT
	Long-term	4 RCTs[2,67,82-84,88,89,93,104] N=588	Yes (-1)	No	No	No	RR: 1.07 (0.93 to 1.22) Conclusion: No difference between groups.	⊕⊕⊕○ MODERATE
Composite score success	Intermediate-term	3 RCTs[67,82-84,88,89,93] N=360	Yes (-1)	Yes (-1)	No	Yes (-1)	RR: 1.08 (0.86 to 1.35) Conclusion: No difference between groups. Insufficient evidence prevents firm conclusion.	⊕○○○ INSUFFICIENT
	Long-term	3 RCTs[67,82-84,88,89,93] N=360	Yes (-1)	No	No	Yes (-1)	RR: 1.04 (0.88 to 1.23) Conclusion: No difference between groups.	⊕⊕○○ LOW
Risk of Surgery	Not specified	16 RCTs[2,14,27-29,32,33,40,45,47,50,104,107,110,112,114,118] N=1705	Yes (-1)	No	No	Yes (-1)	RR: ~~0.82 (0.63 to 1.07)~~ **0.83 (0.66 to 1.04)** Conclusion: No difference between groups.	⊕⊕○○ LOW
Lumbar radiculopathy due to disc and/or foraminal narrowing: ESI vs. Control injections with other medications								
Δ Pain & function **Pain &**	Short-term	1 RCT[27] n=84	Yes (-1)	Unknown	No	Yes (-1)	ESI superior to etanercept on the ODI, MD: –16.2 (95% CI –26.0, –6.27). No differences in change in pain, proportions with successful outcomes, or	⊕⊕○○ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
function success **Risk of surgery**							risks of surgery.	
Δ Function	Short-term	1 RCT[13] n=26	Yes (-1)	Unknown	No	Yes (-1)	ESI superior to clonidine on the RMDQ, MD: -5.67 (95% CI: -10.12, -1.22).	⊕⊕◯◯ LOW
Δ Pain & function **Pain success**	Short-term	1 RCT[25] N=145	Yes (-1)	Unknown	No	Yes (-1)	No difference between ESI + oral placebo pills versus posterior ligament injection of saline + oral gabapentin in pain or function, or the likelihood of achieving pain success.	⊕⊕◯◯ LOW
Lumbar radiculopathy due to disc and/or foraminal narrowing: ESI vs. Disc or decompression procedures								
Δ Pain & function	Short-, intermediate- and long-term	2 RCTs[3,16] N=150	Yes (-1)	Yes (-1)	No	Yes (-1)	Insufficient evidence to determine the effects of ESI versus discectomy.	⊕◯◯◯ INSUFFICIENT
Δ Pain & function **Pain and function success** **Risk of surgery**	Short-, intermediate- and long-term	2 RCTs[39,124] N=169	Yes (-1)	No	No	Yes (-1)	ESI consistently performed poorer than radiofrequency nucleoplasty with respect to improvement in VAS pain and ODI function in the short-term (2 RCTs), intermediate-term (1 RCT), and long-term (1 RCT); and pain and function success in the intermediate- and long-term (1 RCT). There was no difference in risk of undergoing surgery in one trial.	⊕⊕◯◯ LOW
Lumbar radiculopathy due to disc and/or foraminal narrowing: ESI vs. Conservative Care								
Δ Pain & function	Short- and intermediate-term	2 RCTs[12,97] N=136	Yes (-1)	Yes (-1)	No	Yes (-1)	Insufficient evidence to determine effects of ESI versus conservative care.	⊕◯◯◯ INSUFFICIENT
Lumbar radiculopathy due to multiple causes: ESI vs. Control injections								
Pain success	Intermediate-term	1 RCT[10] N=35	Yes (-1)	Unknown	No	Yes (-1)	No difference between ESI versus epidural saline in pain relief. Diagnosis: arachnoiditis,	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
							prolapsed disc, no radiographic abnormalities or inconclusive findings	
Δ Pain & function	Short- and Intermediate-term	1 RCT[7] N=84	Yes (-1)	Unknown	No	Yes (-1)	No difference between ESI versus autologous conditioned serum administered via the interlaminar approach in pain or ODI scores. Diagnosis: Herniated nucleus pulposus or scarring after previous surgery.	⊕⊕◯◯ LOW
Δ Pain Risk of surgery	Short- and long-term	1 RCT[123] N=92	Yes (-1)	Unknown	No	Yes (-1)	ESI was associated with greater short-term pain relief (data NR; p<0.004) compared with intramuscular or interspinous ligament steroid injection. No difference in long-term pain relief or risk of surgery. Diagnosis: Disc prolapse or spinal stenosis	⊕⊕◯◯ LOW
Lumbar spinal stenosis: ESI vs. Control Injections								
Δ Pain	Short-term	4 RCTs[36,56,57,59,63,64,99] N=642	Yes (-1)	Yes (-1)	No	No	WMD: -0.17 (-0.62 to 0.29) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain success	Short-term	3 RCTs[36,56,57,59,63,64] N=606	No	No	No	No	RR: 1.03 (0.91 to 1.18) Conclusion: No difference between groups.	⊕⊕⊕⊕ HIGH
	Long-term	4 RCTs[28,33,56,57,59,63,64] N=287	Yes (-1)	No	No	Yes (-1)	RR: 1.04 (0.86 to 1.26) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Δ Function	Short-term	4 RCTs[36,56,57,59,63,64,99]	Yes (-1)	Yes (-1)	No	No	SMD: ~~-0.47 (-1.08 to 0.14)~~ **-2.15 (-5.83 to 1.52)** Conclusion: No difference between groups. ~~Insufficient evidence prevents firm~~	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
		N=642					~~conclusion.~~	
Function success	Short-term	3 RCTs[36,56,57,59,63,64] N=606	No	No	No	No	RR: 0.98 (0.84 to 1.15) Conclusion: No difference between groups.	⊕⊕⊕⊕ HIGH
Composite score success	Short-term	3 RCTs[56,57,59,63,64,99] N=256	Yes (-1)	Yes (-1)	No	Yes (-1)	RR: 1.07 (0.77 to 1.48) Conclusion: No difference between groups. Insufficient evidence prevents firm conclusion.	⊕◯◯◯ INSUFFICIENT
Risk of surgery	Not specified	3 RCTs[28,33,99] N=103	Yes (-1)	No	No	Yes (-1)	RR: 0.86 (0.48 to 1.52) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Lumbar spinal stenosis: ESI vs. Control injections with other medication								
Δ Pain and function	Short-term	1 RCT[101] N=80	Yes (-1)	Unknown	No	Yes (-1)	ESI was associated with less pain relief compared with etanercept injection (-2.3 ± 1.5 vs. -4.4 ± 1.4; p=0.03). No difference in ODI.	⊕⊕◯◯ LOW
Lumbar spinal stenosis: ESI vs. Decompression procedures								
Δ Pain and function **Pain success**	Short-term	1 RCT[11] N=38	Yes (-1)	Unknown	No	Yes (-1)	ESI was associated with a lower likelihood of pain success (≥2-point improvement on VAS) compared with the MILD procedure: 35% vs. 76%, RR 0.5 (0.2 to 0.9). No difference in VAS pain scores or ODI improvement.	⊕⊕◯◯ LOW
Lumbar spinal stenosis: ESI vs. Conservative care								
Δ Pain and function	Short- and intermediate-term	1 RCT[51] (N=29)	Yes (-1)	Unknown	No	Yes (-1)	No differences between groups in pain and function (RMDQ) improvement.	⊕⊕◯◯ LOW
Lumbar nonradicular axial pain: ESI vs. Control injections								

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
Δ Pain	Short term	2 RCTs[58,60-62,65,66] N=240	Yes (-1)	Yes (-1)	No	Yes (-1)	No consistent differences between groups. Insufficient evidence prevents firm conclusion.	⊕◯◯◯ INSUFFICIENT
	Intermediate and long term	2 RCTs[58,60-62,65,66] N=240	Yes (-1)	No	No	Yes (-1)	No differences between groups. MD at 6 months -0.3 (-0.68, 0.08) and 0 (-0.25 to 0.25); and at 24 months -0.3 (-0.73, 0.13) and 0 (-0.30 to 0.3.0)	⊕⊕◯◯ LOW
Pain and Function success	Short, intermediate and long term	2 RCTs[58,60-62,65,66] N=240	Yes (-1)	No	No	Yes (-1)	No differences between groups pain success or function success at any time-point.	⊕⊕◯◯ LOW
Δ Function	Short, intermediate and long term	2 RCTs[58,60-62,65,66] N=240	Yes (-1)	Yes (-1)	No	Yes (-1)	No consistent differences between groups. Insufficient evidence prevents firm conclusion.	⊕◯◯◯ INSUFFICIENT
Composite score success	Short, intermediate and long term	2 RCTs[58,60-62,65,66] N=240	Yes (-1)	No	No	Yes (-1)	No differences between groups.	⊕⊕◯◯ LOW
Lumbar nonradicular axial pain: Intradiscal steroid injections vs. Intradiscal control injections								
Δ Pain and Function	Short and intermediate term	1 RCT[17] N=80	Yes (-1)	Unknown	No	Yes (-1)	Greater improvement in both pain and function (ODI) with intradiscal injection of betamethasone versus saline at 3 months (MD -5.05, 95% CI -5.52 to -4.58; and MD -23.2, 95% CI -27.7 to -18.7, respectively) and 6 months (MD -4.55, 95% CI -5.0 to -4.1; and MD -23.3; 95% CI -27.8 to -18.9).	⊕⊕◯◯ LOW
	Long term	1 RCT[49] N=120	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups for pain or function improvement	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
Pain and function success	Short term	1 RCT[113] N=25	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups in pain or function success in the short term.	⊕⊕◯◯ LOW
Risk of surgery	Cumulative	1 RCT[49] N=120	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups in cumulative risk of surgery over 12 months.	⊕⊕◯◯ LOW
Lumbar nonradicular axial pain: Intradiscal non-steroid injections vs. Intradiscal control injections								
Δ Pain and Function	Intermediate and long term	1 RCT[103] N=72	Yes (-1)	Unknown	No	Yes (-1)	Greater improvement in pain and function (ODI) with intradiscal injection of methylene blue versus lidocaine at 6 months (MD -4.36, 95% CI -4.78 to -3.94; and MD -31.5, 95% CI -34.7 to -28.4, respectively) and 24 months (MD -4.56, 95% CI -4.98 to -4.14; and MD -33.9, 95% CI -37.5 to -30.4, respectively).	⊕⊕◯◯ LOW
Lumbar nonradicular axial pain: Discography plus intradiscal steroid injection vs. Discography alone								
Δ Pain and Function; and Risk of Surgery	Short, intermediate and long term	1 RCT[15] N=171	Yes (-1)	Unknown	No	Yes (-2)[1]	No differences between groups. No firm conclusions can be made regarding improvement in pain and function in the short, intermediate or long-term, and for cumulative risk of surgery due to insufficient evidence.	⊕◯◯◯ INSUFFICIENT
Failed back surgery syndrome: ESI vs. Control injections								
Δ Pain and Function; Function and composite score success	Short, intermediate and long term	1 RCT[85-87] N=140	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups for pain or function improvement, function success or composite outcome success.	⊕⊕◯◯ LOW
Failed back surgery syndrome: ESI vs. Control injections with other substances								
Δ Pain	Short and	2	Yes	No	No	Yes	No difference between groups for ESI	⊕⊕◯◯

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
	intermediate term	RCTs[96,109] N=69	(-1)			(-1)	compared with forceful saline or morphine.	LOW
Pain success	Short, intermediate and long term	3 RCTs[30,96,109] N=129	Yes (-1)	No	No	Yes (-1)	No difference between groups for ESI compared with forceful saline, morphine or hyaluronidase.	⊕⊕◯◯ LOW
Δ Function	Short and intermediate term	1 RCT[96] N=47	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups for improvement in function (Dallas ADL score) for ESI compared with forceful saline.	⊕⊕◯◯ LOW
Facet joint pain: Intra-articular steroid injection vs. Intra-articular control injection								
Δ Pain	Short and intermediate term	3 RCTs[19,37,53] N=227	Yes (-1)	No	No	Yes (-1)	No difference between groups.	⊕⊕◯◯ LOW
Δ Function	Short and intermediate term	1 RCT[37] N=60	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups.	⊕⊕◯◯ LOW
Facet joint pain: Intra-articular steroid injection vs. Intramuscular steroid injection								
Δ Pain	Short and intermediate term	1 RCT[105] N=60	No	Unknown	No	Yes (-1)	Significantly greater improvement following intra-articular versus intramuscular steroid injections in the short-term (MD -1.6; 95% CI -2.62 to -0.58); no difference between groups in the intermediate term.	⊕⊕⊕◯ MODERATE
Δ Function	Short and intermediate term	1 RCT[105] N=60	No	Unknown	No	Yes (-1)	Significantly greater improvement following intra-articular versus intramuscular steroid injections in the short-term (MD -2.7; 95% CI -4.71 to -0.69); no difference between groups in the intermediate term.	⊕⊕⊕◯ MODERATE
Facet joint pain: Intra-articular steroid injection vs. Radiofrequency denervation of the medial branch								
Δ Pain and	Intermediate	1 RCT[52]	No	Unknown	No	Yes	No differences between groups in pain or	⊕⊕⊕◯

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
Function	term	N=52				(-1)	function improvement.	MODERATE
Facet joint pain: Extra-articular steroid injection vs. Extra-articular control injection								
Δ Pain and function	Short and intermediate term	1 RCT[91,92] N=120	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups for pain or function improvement.	⊕⊕◯◯ LOW
	Long term	2 RCTs[79,91,92] N=204	Yes (-1)	Yes (-1)	No	Yes (-1)	No difference between groups for improvement in pain or function. Insufficient evidence prevents firm conclusion.	⊕◯◯◯ INSUFFICIENT
Pain success	Short, intermediate and long term	2 RCTs[79,91,92] N=204	Yes (-1)	No	No	Yes (-1)	No difference between groups.	⊕⊕◯◯ LOW
Function success	Short, intermediate and long term	1 RCT[91,92] N=120	Yes (-1)	Unknown	No	Yes (-1)	No differences between groups.	⊕⊕◯◯ LOW
Facet joint pain: Extra-articular steroid injection vs. Radiofrequency denervation of the medial branch								
Δ Pain and Pain success	Short, intermediate and long term	1 RCT[23] N=100	Yes (-1)	Unknown	No	Yes (-1)	Significantly less improvement in pain with methylprednisolone 40 mg plus lidocaine vs. radiofrequency denervation at intermediate (MD 1.6; 95% CI 1.27 to 1.93) and long-term (MD 2.0; 95% CI 1.79 to 2.21) follow-up; no difference between groups at short-term follow-up. Significantly fewer patients who received steroid injections reported pain success at all timepoints: short term, 80% vs. 100% (RR 0.80; 95% CI 0.70 to 0.92); intermediate term, 68% vs. 90% (RR 0.76; 95% CI 0.61 to 0.93); and long term, 62% vs. 88% (RR 0.70; 95% CI 0.55 to 0.90).	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
Sacroiliac joint pain: Intraarticular steroid injection vs. Conservative treatment								
Δ Pain and function; Pain success; Composite score success	Short term	1 RCT[122] (N=51)	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups in pain improvement, pain success, and composite score success. Significantly less improvement in function (RAND-36) with steroid injection versus physiotherapy and manual therapy, respectively: MD -31.2 (-44.1 to -18.2) and MD -37.9 (-46.2 to -29.7)	⊕⊕◯◯ LOW
Sacroiliac joint pain: Extraarticular steroid injection vs. Extraarticular control injection								
Δ Pain	Short term	1 RCT[54] (N=24)	Yes (-1)	Unknown	No	Yes (-1)	Greater improvement in pain with steroid vs. anesthetic injection: median -4.0 (range, -5.7 to -0.1) vs. -1.3 (range, -6.4 to 4.3); p=0.046	⊕⊕◯◯ LOW

CI: confidence interval; ESI: epidural steroid injection; MD: mean difference; ODI: Oswestry Disability Index; RCT: randomized controlled trial; RMDQ: Roland Morris Disability Questionnaire; RR: risk ratio; SMD: standardized mean difference; WMD: weighted mean difference.

1. Imprecise effect estimate: unknown confidence interval (all data estimated from graphs)

Efficacy Results for Cervical Spinal Injections (Table 2)

Evidence base

Radiculopathy attributed to disc pathology

- ESI vs. Conservative care: 1 RCT[26]

Cervicobrachialgia (neck pain with or without radiculopathy and/or stenosis)

- ESI vs. Control Injection: 1 RCT[115]

Disc herniation with or without radiculopathy

- ESI vs. Control Injection: 1 RCT (3 publications)[71-73]

Nonradicular neck pain

- ESI vs. Control Injection: 1 RCT (3 publications)[68-70]

Spinal stenosis

- ESI vs. Control Injection: 1 RCT[78]

Failed Surgery Syndrome

- ESI vs. Control Injection: 1 RCT[77]

Facet joint pain

- IASI vs. Intra-articular control Injection: 2 RCTs (4 publications)[6,74,90,94]
- IASI vs. Conservative care: 1 RCT[102]

Table 2. Strength of Evidence Summary: Efficacy Results for Cervical Spinal Injections

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
Cervical radiculopathy due to disc and/or foraminal narrowing: ESI vs. Conservative Care (CC)								
Arm pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[26] N=105	Yes (-1)	Unknown	No	Yes (-1)	ESI -3.2 ± 1.3, CC -2.8 ± 1.8 MD -0.4 (-1.0 to 0.2) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[26] N=104	Yes (-1)	Unknown	No	Yes (-1)	ESI -3.8 ± 1.3, CC -4.9 ± 1.8 MD 1.1 (0.5 to 1.7) Conclusion: Less improvement in arm pain with ESI versus CC.	⊕⊕◯◯ LOW
Function: NDI scores (0-100) (mean ± SD)	**Short-term**	1 RCT[26] N=105	Yes (-1)	Unknown	No	Yes (-1)	ESI 15.8 ± 2.9, CC 14.1 ± 2.7 MD 1.7 (0.6 to 2.8) Conclusion: Worse function with ESI versus CC.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[26] N=105	Yes (-1)	Unknown	No	Yes (-1)	ESI 11.0 ± 2.4, CC 5.4 ± 2.4 MD 5.6 (4.7 to 6.5) Conclusion: Worse function with ESI versus CC.	⊕⊕◯◯ LOW
Surgery	**Long-term**	1 RCT[26] N=114	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC 6%, CC 7% RR 0.80 (0.19 to 3.43) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Cervical radiculopathy due to disc and/or foraminal narrowing: ESI plus Conservative Care (CC) vs. Conservative Care (CC) alone								
Arm pain: ΔNRS scores (0-10) (mean ± SD (% improvement))	**Short-term**	1 RCT[26] N=107	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC -4.1 ± 1.5 (64%) CC -2.8 ± 1.8 (46%) MD -1.3 (-1.9 to -0.7) Conclusion: Greater improvement in arm pain with ESI+CC versus CC.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[26] N=105	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC -4.4 ± 1.6 (69%), CC -4.9 ± 1.8 (80%)	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
							MD 0.5 (-0.2 to 1.2) Conclusion: Less improvement in arm pain with ESI+CC versus CC.	
Function: NDI scores (0-100) (mean ± SD)	**Short-term**	1 RCT[26] N=107	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC 18.1 ± 3.0, CC 14.1 ± 2.7 MD 4.0 (2.9 to 5.1) Conclusion: Worse function with ESI+CC versus CC.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[26] N=105	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC 15.0 ± 2.5, CC 5.4 ± 2.4 MD 9.6 (8.7 to 10.5) Conclusion: Worse function with ESI+CC versus CC.	⊕⊕◯◯ LOW
Surgery	**Long-term**	1 RCT[26] N=114	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC 6%, CC 7% RR 0.80 (0.19 to 3.43) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Cervicobrachialgia (neck pain ± radiculopathy and/or stenosis): ESI versus Control Injections								
Pain: ≥50% improvement in NRS scores (% patients)	**Long-term**	1 RCT[115] N=42	Yes (-1)	Unknown	No	Yes (-1)	ESI 68%, NEI 12% RR 5.78 (1.53 to 21.84) Conclusion: More ESI patients achieved ≥50% improvement in pain than did NEI patients.	⊕⊕◯◯ LOW
Cervical disc herniation with or without radiculopathy: ESI versus Control Injections								
Pain: ≥50% improvement in NRS scores (% patients)	**Short-term**	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 75%, ENSI 85% RR 0.88 (0.74 to 1.06) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 73%, ENSI 83% RR 0.88 (0.73 to 1.06) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
	Long-term	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 68%, ENSI 72% RR 0.95 (0.75 to 1.21) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.1 ± 0.9, ENSI -4.2 ± 0.8 MD 0.1 (-0.2 to 0.4) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.0 ± 0.9, ENSI -4.4 ± 0.8 MD 0.4 (0.1 to 0.7) Conclusion: Slightly less improvement in ~~NDI~~ NRS scores with ESI vs. ENSI.	⊕⊕◯◯ LOW
	Long-term	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.1 ± 1.1, ENSI -4.1 ± 1.0 MD 0.0 (-0.4 to 0.4) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ≥50% improvement in NDI scores (% patients)	**Short-term**	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 85% RR 0.82 (0.68 to 1.00) Conclusion: Slightly fewer ESI patients achieved ≥50% improvement in pain than did ENSI patients.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 73%, ENSI 83% RR 0.88 (0.73 to 1.06) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 73% RR 0.95 (0.76 to 1.20) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ΔNDI scores	**Short-term**	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -13.6 ± 3.9, ENSI -14.9 ± 3.4 MD 1.3 (-0.02 to 2.6)	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
(0-100) (mean ± SD)							Conclusion: Slightly less improvement in NDI scores with ESI than ENSI.	
	Intermediate-term	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -13.9 ± 4.2, ENSI -15.8 ± 3.4 MD 1.9 (0.5 to 3.3) Conclusion: Slightly less improvement in NDI scores with ESI vs. ENSI.	⊕⊕◯◯ LOW
	Long-term	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.9 ± 4.2, ENSI -15.9 ± 3.5 MD 1.0 (-0.4 to 2.5) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
NRS & NDI scores (% patients)	**Intermediate-term**	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 73%, ENSI 82% RR 0.90 (0.74 to 1.09) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[72,73] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 68%, ENSI 72% RR 1.12 (0.91 to 1.37) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Nonradicular neck pain: ESI versus Control Injection								
Pain: ≥50% improvement in NRS scores (% patients)	**Short-term**	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 85%, ENSI 73% RR 1.16 (0.96 to 1.40) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 77%, ENSI 78% RR 0.98 (0.81 to 1.19) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 75%, ENSI 75% RR 1.00 (0.81 to 1.23) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.3 ± 0.6, ENSI -4.2 ± 0.9 MD -0.1 (-0.4 to 0.2) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.1 ± 0.8, ENSI -4.3 ± 0.9 MD 0.2 (-0.1 to 0.5) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.1 ± 0.9, ENSI -4.2 ± 1.0 MD 0.1 (-0.2 to 0.4) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ≥50% improvement in NDI scores (% patients)	**Short-term**	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 78%, ENSI 70% RR 1.12 (0.90 to 1.38) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 73%, ENSI 68% RR 1.07 (0.85 to 1.35) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 75% RR 0.93 (0.75 to 1.16) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ΔNDI scores (0-100) (mean ± SD)	**Short-term**	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.9 ± 4.3, ENSI -14.7 ± 3.6 MD -0.2 (-1.6 to 1.2) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.4 ± 4.3, ENSI -15.2 ± 3.4 MD 0.8 (-0.6 to 2.2) Conclusion: No difference between	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
							groups.	
	Long-term	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.8 ± 4.4, ENSI -16.1 ± 3.4 MD 1.3 (-0.1 to 2.7) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain + Function: ≥50% improvement in NRS & NDI scores (% patients)	**Short-term**	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 78%, ENSI 70% RR 1.12 (0.90 to 1.38) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 73%, ENSI 68% RR 1.07 (0.85 to 1.35) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[68,69] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 75% RR 0.93 (0.75 to 1.16) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Spinal stenosis: ESI versus Control Injection								
Pain: ≥50% improvement in NRS scores (% patients)	**Short-term**	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 87%, ENSI 87% RR 1.00 (0.82 to 1.22) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 80%, ENSI 90% RR 0.89 (0.72 to 1.10) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 73% RR 0.95 (0.69 to 1.31) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain:	**Short-term**	1 RCT[78]	Yes	Unknown	No	Yes	ESI -4.5 ± 0.6, ENSI -4.2 ± 0.7	⊕⊕◯◯

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
ΔNRS scores (0-10) (mean ± SD)		N=60	(-1)			(-1)	MD -0.3 (-0.6 to 0.04) Conclusion: No difference between groups.	LOW
	Intermediate-term	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.3 ± 0.6, ENSI -4.5 ± 0.6 MD 0.2 (-0.1 to 0.5) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.2 ± 0.7, ENSI -4.3 ± 0.7 MD 0.1 (-0.3 to 0.5) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ≥50% improvement in NDI scores (% patients)	**Short-term**	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 87%, ENSI 77% RR 1.13 (0.89 to 1.44) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 83%, ENSI 87% RR 0.96 (0.78 to 1.19) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 77% RR 0.91 (0.67 to 1.24) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ΔNDI scores (0-100) (mean ± SD)	**Short-term**	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -15.6 ± 3.6, ENSI -14.1 ± 3.5 MD -1.5 (-3.3 to 0.3) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -15.7 ± 3.5, ENSI -16.0 ± 3.2 MD 0.3 (-1.4 to 2.0) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
	Long-term	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -15.3 ± 3.5, ENSI -16.0 ± 3.4 MD 0.7 (-1.1 to 2.5) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain + Function: ≥50% improvement in NRS & NDI scores (% patients)	**Short-term**	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 87%, ENSI 77% RR 1.13 (0.89 to 1.44) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 80%, ENSI 87% RR 0.92 (0.74 to 1.16) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[78] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 73% RR 0.95 (0.69 to 1.31) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Failed surgery syndrome: ESI versus Control Injections								
Pain: ≥50% improvement in NRS scores (% patients)	**Short-term**	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 71%, ENSI 79% RR 0.91 (0.67 to 1.23) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 75%, ENSI 71% RR 1.05 (0.76 to 1.44) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 68%, ENSI 71% RR 0.95 (0.67 to 1.34) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -3.8 ± 0.7, ENSI -4.3 ± 0.8 MD 0.5 (0.1 to 0.9) Conclusion: Less improvement in pain with ESI versus ENSI.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.0 ± 0.7, ENSI -4.3 ± 0.7 MD 0.3 (-0.1 to 0.7) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -3.9 ± 0.9, ENSI -4.3 ± 0.7 MD 0.4 (-0.03 to 0.8) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ≥50% improvement in NDI scores (% patients)	**Short-term**	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 75%, ENSI 71% RR 1.05 (0.76 to 1.44) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 75%, ENSI 68% RR 1.11 (0.79 to 1.54) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 64%, ENSI 71% RR 0.90 (0.63 to 1.29) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ΔNDI scores (0-100) (mean ± SD)	**Short-term**	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.0 ± 3.5, ENSI -14.1 ± 3.3 MD 0.1 (-1.7 to 1.9) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.2 ± 3.5, ENSI -14.7 ± 3.2 MD 0.5 (-1.3 to 2.3) Conclusion: No difference between	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
							groups.	
	Long-term	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -13.8 ± 3.4, ENSI -15.0 ± 3.1 MD 1.2 (-0.5 to 2.9) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain + Function: ≥50% improvement in NRS & NDI scores (% patients)	**Short-term**	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 68%, ENSI 68% RR 1.00 (0.70 to 1.43) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 71%, ENSI 64% RR 1.11 (0.77 to 1.60) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[77] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 64%, ENSI 71% RR 0.90 (0.63 to 1.29) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Facet pain: IASI versus Intra-articular control injection								
Pain: ≥50% improvement in NRS scores (% patients)	**Short-term**	1 RCT[6] N=41	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~10%, IANSI ~11% RR ~0.9 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
	Intermediate-term	1 RCT[90,94] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI 95%, IANSI 87% RR 1.10 (0.98 to 1.23) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[90,94] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI 93%, IANSI 85% RR 1.10 (0.97 to 1.25)	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
							Conclusion: No difference between groups.	
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[90,94] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -4.5 ± 0.7, IANSI -4.4 ± 0.6 MD -0.1 (-0.3 to 0.1) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[90,94] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -4.8 ± 0.7, IANSI -4.6 ± 0.7 MD -0.2 (-0.5 to 0.1) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[90,94] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -5.0 ± 0.7, IANSI -4.7 ± 0.7 MD -0.3 (-0.6 to -0.05) Conclusion: More improvement in pain with IASI versus IANSI.	⊕⊕◯◯ LOW
Function: ≥50% improvement in NDI scores (% patients)	**Intermediate-term**	1 RCT[90,94] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI 65%, IANSI 60% RR 1.08 (0.82 to 1.43) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[90,94] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI 75%, IANSI 70% RR 1.07 (0.86 to 1.34) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ΔNDI scores (0-100) (mean ± SD)	**Short-term**	1 RCT[90,94] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -12.9 ± 3.1, IANSI -13.4 ± 3.5 MD 0.5 (-0.7 to 1.7) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[90,94] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -13.5 ± 3.0, IANSI -13.4 ± 3.6 MD -0.1 (-1.3 to 1.1) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
	Long-term	1 RCT[90,94] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -14.1 ± 3.1, IANSI -13.8 ± 3.4 MD -0.3 (-1.5 to 0.9) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Myofascial pain syndrome: IASI versus Conservative Care								
Tension headache (% patients)	**Short-term**	1 RCT[102] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~16%, CC ~24% RR ~0.7 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
	Intermediate-term	1 RCT[102] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~9%, CC ~21% RR ~0.4 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
	Long-term	1 RCT[102] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~3%, CC ~19% RR ~0.2 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[102] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~-3.7, IANSI ~-1.4 MD ~-2.3 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
	Intermediate-term	1 RCT[102] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~-3.9, IANSI ~-1.6 MD ~-2.3 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
	Long-term	1 RCT[102] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~-4.0, IANSI ~-1.6 MD ~-2.4 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT

CI: confidence interval; ESI: epidural steroid injection; ENSI: epidural non-steroid injection; CC: conservative care; IANSI: intraarticular non-steroid injection; IASI: intraarticular steroid injection; MD: mean difference; NC: not calculable; NEI: non-epidural injection; RCT: randomized controlled trial; RR: risk ratio.

~ indicates data estimated from graph; f/u: follow-up; MD: mean difference; NC: not calculable; RR: relative risk

1. Imprecise effect estimate: unknown confidence interval

Table 3. Strength of Evidence Summary: Harms

Catastrophic adverse events: non-transient paralysis (tetraplegia, paraplegia), blindness; as well as death, arachnoiditis, stroke, cardiac arrest, spinal cord infarction, spinal cord injury, and meningitis

Serious adverse events: epidural hematoma, deep infection, respiratory failure, spinal nerve injury, fever or infection attributed to the injection, hematoma, intravascular injection of steroid with neurologic sequelae, nerve root injury, retroperitoneal hematoma, subarachnoid injection, seroma, neurovascular complications, surgery or hospitalization necessary due to adverse events attributed to the procedure, and angina attributed to the procedure.

Non-serious adverse events: all other adverse events; note that the following were considered non-serious unless sufficient detail was reported to suggest that symptoms did not remit easily or were more severe: cerebrospinal fluid tap, dural pucture or tears, new neurological symptoms, sensory deficits, paresthesia and numbness in lower extremity, excessive pain, procedural bleeding, and procedural hypotension

Outcome	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
Catastrophic adverse events	60 RCTs* N=6290 1 report of FDA Adverse Events Reporting Database[34]	Yes (-1)	No	No	Yes (-1)[1]	Across all RCTs of epidural, facet joint and intradiscal injections in the lumbar or cervical spine that reported any adverse events, no catastrophic adverse events were reported to occur. Observational studies (3 cohort studies and 22 case series) were consistent with trials in reporting no instances of catastrophic events. One recent analysis of the FDA Adverse Events Reporting Database found a total of 131 major neurologic adverse events, which included five deaths (including suicide in two patients with arachnoiditis) and 41 cases of arachnoiditis; other events included (but aren't limited to) brainstem stroke, motor-incomplete tetraplegia, paraplegia, paralysis, spinal cord infarction, cardiac arrest, blindness, and meningitis, although total numbers of each event were unclear. In the majority of cases, the injection approach was unavailable, and the report did not attribute any major adverse events to any particular injection approach or imaging utilization; further, a causal relationship between particulate steroid	⊕⊕◯◯ LOW

Outcome	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
						injections and major adverse events has not been established.	
Serious adverse events	60 RCTs* N=6290 1 report of FDA Adverse Events Reporting Database[34]	Yes (-1)	No	No	No	Across all RCTs of epidural, facet joint and intradiscal injections in the lumbar or cervical spine that reported any adverse events, serious adverse events were rare, and no differences between treatment groups were detected. Aside from the following events, which were reported to occur in at least one patient, no serious adverse events were reported in the RCTs. Lumbar EI (with or without steroid): retroperitoneal hematoma (1%), subarachnoid entry or injection (0%-3%), hospitalization and/or surgery (2.0%-2.5%). Cervical EI (with or without steroid): subarachnoid puncture (0.3%-0.9%). Lumbar ESI vs. disc or decompression procedure: paresthesia and numbness in lower extremity for 3-4 days (4% (1/24) vs. 12% (3/26), p=0.34), seroma (0% vs. 1%) Observational studies were consistent with trials in finding low rates of serious adverse events.	⊕⊕⊕◯ MODERATE
Non-serious adverse events	60 RCTs* N=6290 1 report of FDA Adverse Events Reporting Database[34]	Yes (-1)	No	No	No	Across all RCTs of epidural, facet joint and intradiscal injections in the lumbar or cervical spine that reported any adverse events, reported that the majority of non-serious adverse events occurred infrequently. However, methods for assessing adverse events were not well reported. Observational studies were consistent with the randomized trials.	⊕⊕⊕◯ MODERATE

*All RCTs that reported on any harm was included in the study count based on the assumption that that study evaluated and reported any adverse event that occurred: the RCT count included 51 lumbar RCTs (N=5094) and 9 cervical RCTs (N=1196).

1. Imprecise effect estimate: rare outcomes

Differential Efficacy or Safety in Subpopulation

Lumbar spinal injections

Of 34 lumbar RCTs included in Key Question 1, nine trials[112 2,25,36,39,40,48,106,117-119] (one of which was reported across three publications) stratified results were reported for both treatment groups according to subgroups of interest (Table 4). Subgroups evaluated included baseline disc pathology; duration of pain; duration of symptoms; stenosis severity; injection approach; age; sex; race; ethnicity; body mass index; education; employment; smoking history; diabetes; neurological abnormalities; treatment expectations; previous episodes of sciatica; coexistent back pain; ODI scores; EQ-5D index scores; EQ-5D pain scores; Patient Health Questionnaire-8 scores; Generalized Anxiety Disorder-7 scores; Pain Catastrophizing Scale total scores; Pain Catastrophizing Scale helplessness, rumination, and magnification subscale scores; Fear-Avoidance Beliefs Questionnaire physical activities subscale scores; anxiety scores; and depression scores. No studies evaluated the differential efficacy or safety impact of Worker's Compensation, insurance status, or litigation.

Cervical or Sacroiliac spinal injections

None of the included RCTs of cervical or sacroiliac spinal injections evaluated the differential efficacy or effectiveness of any subpopulation or characteristic (i.e., none reported stratified results for both treatment groups according to subgroups of interest or reported the results of a formal test for interaction).

Table 4. Strength of Evidence Summary: Differential Efficacy or Safety in Subpopulations

Subgroup	Outcome	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Conclusion	Quality
Lumbar radiculopathy: ESI vs. Control injections								
Disc prolapse vs. foraminal narrowing	Short-term pain, function	1 RCT[118] N=124	Yes (-2)[1]	Yes (-1)	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias, inconsistency and imprecision to determine if the effect of ESI varies depending on reason for radiculopathy (disc prolapse or foraminal narrowing).	⊕◯◯◯ INSUFFICIENT
Disc herniation vs extrusion	≥75% improvement in leg pain, function, quality of life, and risk of surgery in the long-term	1 RCT[48] N=128	Yes (-2)[1]	Yes (-1)	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias, inconsistency and imprecision to determine if the effect of ESI varies depending on reason for radiculopathy (disc herniation or disc extrusion).	⊕◯◯◯ INSUFFICIENT
Disc herniation vs disc degeneration	Risk of surgery, short-term	1 RCT[112] N=183	Yes (-2)[1]	Unknown	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias and imprecision to determine if the effect of ESI varies depending on reason for radiculopathy (disc herniation or disc degeneration).	⊕◯◯◯ INSUFFICIENT
Symptom duration (<3 or 4 vs ≥3 or 4 months)	≥50% improvement in pain, short-term; or ≥75% improvement in function, short- and long-term	2 RCTs[2,40] N=378	Yes (-2)[1]	No	No	Yes (-1)	There was insufficient evidence from 2 trials based on serious risk of bias and imprecision to determine if the effect of ESI varies depending on symptom duration (<3 or 4 vs ≥3 or 4 months)	⊕◯◯◯ INSUFFICIENT
Baseline scores for anxiety or depression, SF-36, ODI,	"Response" (not defined), short- and long-term	1 RCT[2] N=228	Yes (-2)[1]	Unknown	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias and imprecision to determine if the effect of ESI varies depending on baseline	⊕◯◯◯ INSUFFICIENT

Subgroup	Outcome	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Conclusion	Quality
neurological abnormalities, prior episodes of sciatica, coexistent back pain, work status, or sex							characteristics.	
Lumbar radiculopathy: ESI vs. Disc decompression								
Symptom duration (<1 vs 1-3 vs >3 years)	Reduction in leg pain, intermediate-term (6 months)	1 RCT[39] N=90	Yes (-2)[1]	Unknown	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias and imprecision to determine if the effect of ESI varies depending on symptom duration (<1 vs 1-3 vs >3 years)	⊕◯◯◯ INSUFFICIENT
Lumbar stenosis: ESI vs. Control Injections Stenosis								
EQ-5D index score, employment status, treatment expectation, sex, race, ethnicity, education, smoking history, diabetes status, pain duration, stenosis severity, age, body mass index, EQ-5D pain scores,	Short-term pain, function, quality of life, patient satisfaction	1 RCT[119] N=400	Yes (-1)[2]	Yes (-1)	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias, inconsistency and imprecision to determine if the effect of ESI versus ENSI varies depending on any of several baseline characteristics or injection approach (tranforaminal vs. interlaminar)	⊕◯◯◯ INSUFFICIENT

Subgroup	Outcome	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Conclusion	Quality
Patient Health Questionnaire-8 scores, Generalized Anxiety Disorder-7 scores, Pain Catastrophizing Scale (total scores; helplessness, rumination, and magnification subscale scores), Fear-Avoidance Beliefs Questionnaire physical activities subscale scores, injection approach								

ESI: epidural steroid injection; RCT: randomized controlled trial.

1. Serious risk of bias in evaluation of HTE: unclear whether the subgroup variables were specified a priori; the hypothesized impact of subgroup on treatment effect was not stated
2. Serious risk of bias in evaluation of HTE: large number of subgroups tested (i.e., subgroup hypothesis not one of a smaller number tested); was unclear whether any of the subgroup variables were specified a priori; the hypothesized impact of subgroup on treatment effect was not stated

Strength of Evidence Summary: Cost Effectiveness

For lumbar radiculopathy due to disc pathology, two economic studies were included:

- One poorly conducted (QHES 49/100) cost-effectiveness study[48] conducted alongside an RCT[47] of fluoroscopically-guided ESI versus ENSI reported the cost per positive response (≥75% improvement in leg pain and absence of surgery); results were stratified based on MRI classification of disc herniation, extrusion, and bulge. For the disc herniation subgroup, ESI had a lower cost per positive response at 12 months compared with ENSI ($4432 vs. $17,098, p=0.0073); this difference was not observed at 3 months. In the extrusions subgroup, the opposite was true, with a significantly higher cost per positive response in the ESI versus ENSI group at 12 months ($7165 vs. $2484, p=0.0058); the difference was smaller and not significant at 3 months. In the bulge subgroup, there were no differences between groups in the cost per positive response at either 3 or 12 months. The analysis had major limitations, including a relatively short time horizon, lack of sensitivity analysis, long-term modeling, and statement of perspective. Further, results were only presented based on subgroups but not for the population as a whole. The authors stated that future work should be done to assess the impact of the cost-effectiveness of ESI versus ENSI when stratified based on MRI classification.
- One reasonably well-conducted (QHES 78/100) cost utility analysis[104] was performed using RCT[2] data that compared ESI (1-3 injections) to NEI (interligamentous saline injections); use of imaging was not reported in this trial. Utility values were derived from SF-36 scores through 12 weeks. The study found that based on 12-week data, the incremental cost per QALY of up to three ESIs (over NEI) was high, ranging from £44,701 to £354,172 for the provider and purchaser perspectives, respectively. Based on the same timeframe, the incremental cost per QALY of a single ESI (over NEI) was somewhat lower but remained high, ranging from £25,746 to £167,145 for the provider and purchaser perspectives, respectively. The authors concluded that the cost-effectiveness ratios are higher than the NICE thresholds and did not support NHS coverage. The main limitation of this study was its very short time horizon.

For lumbar spinal stenosis, one economic study was included:

- This cost utility analysis was relatively well-conducted (QHES 73/100) and compared serial ESI (i.e., 6 injections) to two different procedures (minimally invasive decompression and surgical decompression) in patients with moderate to severe symptomatic lumbar stenosis refractory to conservative care.[120] All data were derived from the literature, and all comparisons were indirect. No assumptions regarding use of imaging guidance for ESI were stated. Utility values were derived from EQ-5D, SF-6D, or ODI data. The study found that ESI was dominated by minimally invasive decompression, with cost per QALYs of $81,518 and $43,760, respectively. ESI dominated surgical decompression, which had a cost per QALY of $125,985. One-way sensitivity analysis showed that when three or less ESI were performed per year it dominated minimally invasive decompression; in no other scenario was it found to dominate minimally invasive decompression. The authors concluded that minimally invasive decompression was the most cost-effective treatment option in this patient population. However, the study made a number of assumptions that increase the risk of bias of their conclusions, including the assumption that patients had already failed ESI, which impacted the QALY values for this group. Other limitations included reliance on the published literature, and basing ESI QALY values on patients with mild stenosis rather than moderate to severe stenosis.

Comparison to Previous Report

The Body of Literature.

Our current report includes additional trials compared with our prior report. Of the 100 studies (across 123 citations) included in this updated report, a total of 39 studies (56 citations) were new. A total of 26 new trials were found that reported on the efficacy of ESI: 22 (35 citations) in the lumbar spine and four (9 citations) in the cervical spine. Of note, six lumbar trials and three cervical trials which were included in the previous report reported only preliminary results in a subset of patients. By the time of the re-review for this report, these trials had published longer-term follow-up studies in the entire study population (across 12 and 5 citations for the lumbar and cervical spine, respectively); these were not counted as new trials but as updates to previously included trials. For safety, 12 new studies were found, eight (2 cohorts, 6 case series) evaluating ESI in the lumbar spine, three case series of cervical ESI, and one case series of both lumbar and cervical ESI. In addition, a summary report of the FDA adverse events reporting database was included to evaluate rare but serious adverse events. For cost-effectiveness, one new study was found. Please see appendix CC, which identifies the studies in the previous and current report.

Methods.

Our earlier report relied on a previous systematic review by Chou et al (reference). It was a qualitative review which did not perform a meta-analysis. The current review conducted meta-analyses on several comparisons when two or more studies reported on the same outcome, had the same condition, and had similar controls (injections, conservative treatment, disc or decompression procedures). The update report added a long-term follow-up of ≥1 year which was not available in the earlier report.

The current review is consistent with the previous report in that there continues to be substantial heterogeneity (mixed results) in several of the pooled analyses. To address this, we used a random effects model to pool studies (Dersimonian-Laird (DL) random effects model). Given that the DL model in the presence of heterogeneity may result in overly small confidence intervals, we repeated the analyses using the profile likelihood method. The results in all cases were similar. We further explored heterogeneity using stratified analyses based on epidural approach, exclusion of outlier studies, the exclusion of poor-quality studies, and whether the control injection contained anesthetic or just saline. While statistical heterogeneity remained in a few analyses, the results for the rest were similar between the sensitivity and the primary analyses.

Results.

Lumbar radiculopathy due to disc and or foraminal narrowing, ESI versus control injections.

Our previous report (reference) found mixed evidence with respect to efficacy for lumbar epidural spinal injections vs. control injections for radiculopathy with some studies reporting no benefit or inferior results while others reported positive results in the short- and intermediate-term. The strength of evidence for those conclusions was LOW. That report did not perform meta-analysis, and based some conclusions on prior reviews. Our current report, as described above, performed meta-analysis when possible. Using meta-analysis for this report, we found, in the short-term, 30% more patients receiving ESI achieved a successful reduction in pain compared with a control injection, though there was no improvement in intermediate- or long-term pain success or short-, intermediate- or long-term change in function or function success. The strength of evidence for these results were mostly LOW. The risk of surgery following lumbar ESI is not reported in the last report. We found no difference in the risk of

surgery comparing ESI with control injections in this report. The strength of evidence for this finding was LOW.

Lumbar radiculopathy due to disc and or foraminal narrowing, ESI versus disc or decompression. procedures.
The prior report noted one trial that demonstrated ESI resulted in poorer outcomes compared with discectomy in patients with disc prolapse. The current review adds one new study comparing ESI to discectomy with opposite results. Strength of evidence, INSUFFICIENT. In addition, two new studies not available in the previous review both report ESI performed poorer than radiofrequency nucleoplasty with respect to short- and long-term pain and function.

Lumbar radiculopathy due to disc and or foraminal narrowing, ESI versus conservative care.
One additional trial was added for this report to the single trial in the earlier review comparing ESI to conservative care. Due to risk of bias, inconsistent results and imprecision, the quality of evidence remains insufficient.

Lumbar radiculopathy due to disc and or foraminal narrowing, ESI versus other medication.
The previous report did not distinguish trials that included other medication. This review reports on 3 trials that do so; one demonstrated better improvement in functional but not pain or overall success with ESI versus etanercept injection in the short-term. A second trial reported better improvement in function with ESI versus clonidine injection in the short-term. A third trial found no difference between ESI and posterior ligament injection of saline combined with oral gabapentin in the short-term. The quality of evidence from these studies were rated LOW.

Lumbar radiculopathy due to multiple causes, ESI versus control injections.
The previous report did not distinguish trials that included patients with radiculopathy due to multiple causes in the same trial. This review reports on 3 studies that included patients with radiculopathy due to 2 or more of the following conditions: arachnoiditis, prolapsed or herniated disc, spinal stenosis, or prior back surgery. There were no differences in pain in the intermediate-term (2 trials) or long-term (1 trial) pain or risk of surgery (1 trial) comparing ESI to control injections.

Lumbar stenosis, ESI versus control injections.
Our previous report found low to moderate evidence of no benefit (pain and function) comparing ESI to control injections in the short- or intermediate-term. We added two new studies to this report that reinforced the results from the previous review: no differences in pain or functional scores in the short-term (quality of evidence, LOW), no difference in pain or function success in the short-term (quality of evidence, HIGH), no difference in the risk of surgery (quality of evidence, LOW).

Lumbar nonradicular axial pain, ESI vs. control injections.
The prior report concluded no difference in short-term pain and function compared with control injections; quality of evidence, MODERATE. The current report adds long-term follow-up data to two studies included in the prior report and concludes no difference in short-, intermediate- or long-term follow-up; quality of evidence, LOW. In the previous report, we did not reduce the quality of evidence due to imprecision or risk of bias, which resulted in a higher quality of evidence rating. Re-evaluating the methodology and the precision of the results led us to downgrade the quality to LOW.

Failed back surgery syndrome, ESI vs. control injections with and without other medication

The current report distinguishes ESI vs. control injections with and without other medications while the prior report considered the controls together. There was no difference between ESI and control injections with respect to pain and function in the prior report or in the current report. However, the prior report rated the quality of evidence as MODERATE while the current report assessed the quality as LOW. In the previous report, we did not reduce the quality of evidence due to imprecision or risk of bias, which resulted in a higher quality of evidence rating. Re-evaluating the methodology and the precision of the results led us to downgrade the quality to LOW.

Lumbar facet joint pain, IASI vs. control injections.
No additional trials were identified; a total of three RCTs were included. While the new report assessed all three trials together as IASI versus control injections, the previous report divided these studies up into two comparisons: IASI vs. placebo (2 RCTs) and IASI vs. IAI with HA (1 RCT). Both reports concluded that there were no differences in pain or functional scores between groups in the short- and intermediate-term (quality of evidence, LOW).

Lumbar facet joint pain: EASI vs. control injections.
No additional trials were identified; a total of two trials (in three publications) were included. These studies were classified as lumbar medial branch (steroid) blocks versus medial branch sarapin injections. While the previous report concluded there was low strength of evidence of no difference between groups, the new reported evaluated the quality of evidence separately for different follow-up times and concluded that there was no difference between groups for pain or function scores in the short- or intermediate term based on low quality of evidence or in the long-term based on insufficient quality of evidence. Further, no differences were found between groups in pain or function success in the short-, intermediate-, or long-term based on low quality of evidence.
Cervicobrachialgia (neck pain ± radiculopathy and/or stenosis): ESI vs. Control injections.
One trial was included in both reports; no new trials were identified. The trial compared ESI to intramuscular steroid injections; the prior report referred to this comparison as ESI vs. non-placebo controls for neck pain with disc herniation and radiculitis. Both reports concluded that ESI was superior to control injections in terms of pain success in the long-term; the new report found the quality of evidence to be low while the old report considered it to be very low.

Cervical disc herniation with or without radiculopathy: ESI vs. Control injections.
The preliminary results from one trial were included in the prior report under the heading “neck pain with sciatica or radiculopathy”; this report included data on 70 patients. Since the prior HTA, two additional articles have been published and contain the results from the full trial of 120 patients. The new report concluded there were no differences between groups in: pain success (all timepoints), short- and long-term pain scores, intermediate- and long-term function scores, long-term function success, and intermediate- and long-term composite of pain and function success. However, there was significantly worse outcomes in the ESI group in the following: intermediate-term pain scores, short-term pain success, as well as short- and intermediate-term function. In all cases the new report found the quality of evidence to be low while the old report considered it to be very low.

Nonradicular neck pain: ESI vs. Control injections.
The preliminary results from one trial were included in the prior report under the heading “neck pain without sciatica or radiculopathy”; this report included data on 70 patients. Since the prior HTA, two additional articles have been published and contain the results from the full trial of 120 patients. The new report concluded there were no differences between groups in short-, intermediate- or long-term

pain success, pain scores, function success, function scores, or in a composite of pain and function success (quality of evidence for all, LOW).

Cervical spinal stenosis: ESI vs. Control injections.
Preliminary results from one new trial were included in the updated report; this RCT was published subsequent to the prior HTA. The updated HTA concluded there were no differences between groups in short-, intermediate- or long-term pain success, pain scores, function success, function scores, or in a composite of pain and function success (quality of evidence for all, LOW).

Cervical failed surgery syndrome: ESI vs. Control injections.
The preliminary results from one new trial were included in the updated report; this RCT was published following the prior HTA. The new report found no differences between groups in short-, intermediate- or long-term pain success, pain scores, function success, function scores, or in a composite of pain and function success (quality of evidence for all, LOW).

Cervical facet pain: IASI (medial branch block) vs. control injection.
Two trials (in three publications) were included in the new report. While both trials were included in the prior report, the second publication (Manchikanti 2010, 2 year results) of one trial had erroneously been omitted from the prior HTA. For IASI versus control injections, both reports concluded there were no differences between groups in short-term pain success based on insufficient (or very low in the prior report) quality of evidence. For medial branch blocks versus control injections, long-term pain scores were significantly better in the ESI group than the control group, but there were otherwise no differences between groups in any outcomes, including: pain or function success in the intermediate- and long-term, pain scores in the short- and intermediate-term, and function scores in the short-, intermediate-, and long-term. In all cases, the quality of evidence was considered to be low in the new report (and very low in the prior report).

The following new categories were included in the updated report that were not in the prior report; the new categories are based on the addition of new literature published after the following report:

Lumbar facet joint pain, IASI vs. intramuscular steroid injections.
One trial was identified in the new report that compared IASI to intramuscular steroid injections; the trial was published after our previous report. There were significantly greater improvements in pain and functional scores with IASI in the short-term but no differences between groups in the intermediate-term (quality of evidence, MODERATE).

Lumbar facet joint pain, IASI vs. Radiofrequency denervation of the medial branch.
One new trial was identified for the updated report that compared IASI to radiofrequency denervation of the medial branch; this trial was published after our previous report. No differences between groups were found in pain or functional scores in the intermediate-term (quality of evidence, MODERATE).

Lumbar facet joint pain, EASI vs. Radiofrequency denervation of the medial branch.
One new trial was identified that was published subsequent to the previous report and compared EASI to radiofrequency denervation of the medial branch. The new report concluded that while there were no differences between groups in pain scores in the short-term, there was less improvement in pain scores with EASI in the intermediate- and long-term. In addition, significantly fewer EASI patients

experienced pain success in the short-, intermediate-, or long-term. All conclusions were based on low quality of evidence.

Cervical radiculopathy due to disc and/or foraminal narrowing: ESI vs. Conservative Care (CC)
One new trial was identified and included in the updated report; this trial was published after the previous report. The new report concluded that there was low quality of evidence of the following: no difference between groups in short-term pain scores or surgery in the long-term; but worse intermediate-term pain scores as well as short- and intermediate-term function scores with ESI versus CC alone.

Cervical radiculopathy due to disc and/or foraminal narrowing: ESI + CC vs. Conservative Care (CC)
One trial was included in the new report; this trial was published after the previous report and was thus a new addition to the evidence base. The updated report found low quality of evidence for the following conclusions: greater improvement in short-term pain with ESI + CC but worse intermediate-term pain scores as well as short- and intermediate-term function scores with ESI + CC versus CC alone; no difference was found between groups in long-term surgery.

Myofascial pain syndrome: IASI vs. Conservative care (CC).
One new trial was published after our prior report and provided insufficient quality of evidence for all outcomes.

Safety
Both reports assessed all included RCTs for complications. A total of three cohort studies were included in the new report: from two recent cohort studies were added to the new report, and both reports included data from a cohort study on both cervical and lumbar injections. A total of 22 case series of lumbar and/or cervical injections were included in the new report, 10 of which were newly published since the prior report. While the prior HTA scanned published case reports for serious complications, the new HTA evaluated case reports of catastrophic adverse events using the report of the FDA Adverse Events Reporting Database. The new report concluded that catastrophic events were very rare but can occur following epidural steroid injections (quality of evidence, LOW). Both reports concluded that serious (or major) adverse events were rare and that non-serious (or minor) adverse events occurred relatively infrequently (moderate quality of evidence in new report and high strength of evidence in prior report).

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1. Appraisal

1.1. Rationale

Disease
Back and neck pain are common conditions, with sixty to eighty percent of U.S. adults afflicted at some time during their life. Back pain, and then neck pain, are the most common causes of disability and loss of productivity. In most patients reporting low back pain (>85%), symptoms cannot reliably be attributed to a specific spinal disease or pathology.[52] Some believe that a similar majority of neck pain is non-specific. Most patients' symptoms resolve satisfactorily within a relatively short time span (six weeks). In 5% to 10% of patients, pain does not satisfactorily resolve and the symptoms can be disabling and the social and economic impact of chronic pain is enormous. Discovering the cause for nonspecific low back and neck pain symptoms remains challenging. Some psychosocial risk factors for the progression to chronicity have been identified, but the origin and neurophysiologic pain sensations are poorly understood.

Treatments
Chronic pain treatment may include pharmacological treatment, physical therapy, psychological care and coping skills, exercise, education, antidepressants, cognitive behavioral therapy and supported self-management, spinal manipulations, electrical stimulation, injections, implanted devices, and other surgical treatment. Treatment strategies generally begin with the least invasive and low risk interventions and progress if the treatments are not effective. Treatment often involves a combination of interventions.

Technology
Spinal injections are not usually performed until non-surgical treatments have been given a fair trial and have not provided adequate relief. Intraspinal injections are intended to provide relief by injection of an anti-inflammatory agent (e.g. steroid); and/or anesthetic into the spine or space around the spinal nerves and joints. Intraspinal injections include epidural steroid injections, facet joint injections, medial branch block, sacroiliac joint injections and intradiscal steroid injections.

Prior Washington Health Care Authority Coverage Determination
Given that there were significant questions about the safety, efficacy and effectiveness (particularly long term), and the cost effectiveness of spinal injections, the Washington State HCA commissioned a Health Technology Assessment (HTA) on Spinal Injections and in 2011, the Health Technology Clinical Committee (HTCC) issued the following coverage determination:
Therapeutic Medial Branch Nerve Block injections, Intradiscal injections and Facet injections are not a covered benefit

Therapeutic Lumbar Epidural Injections; Cervical-thoracic Epidural Injections and Sacroiliac Joint Injections are a covered benefit for the treatment of chronic pain following certain specific conditions.

Current Situation
Since the last HTCC meeting, new literature has been identified addressing the topic. In addition, new safety concerns have emerged for epidural injections from the FDA. Therefore, the HCA selected this topic for re-review.

Objectives

The primary aim of this assessment is to update the previous review on spinal injections.

1.2. Key Questions

When used in adult patients with subacute or chronic back or neck pain:

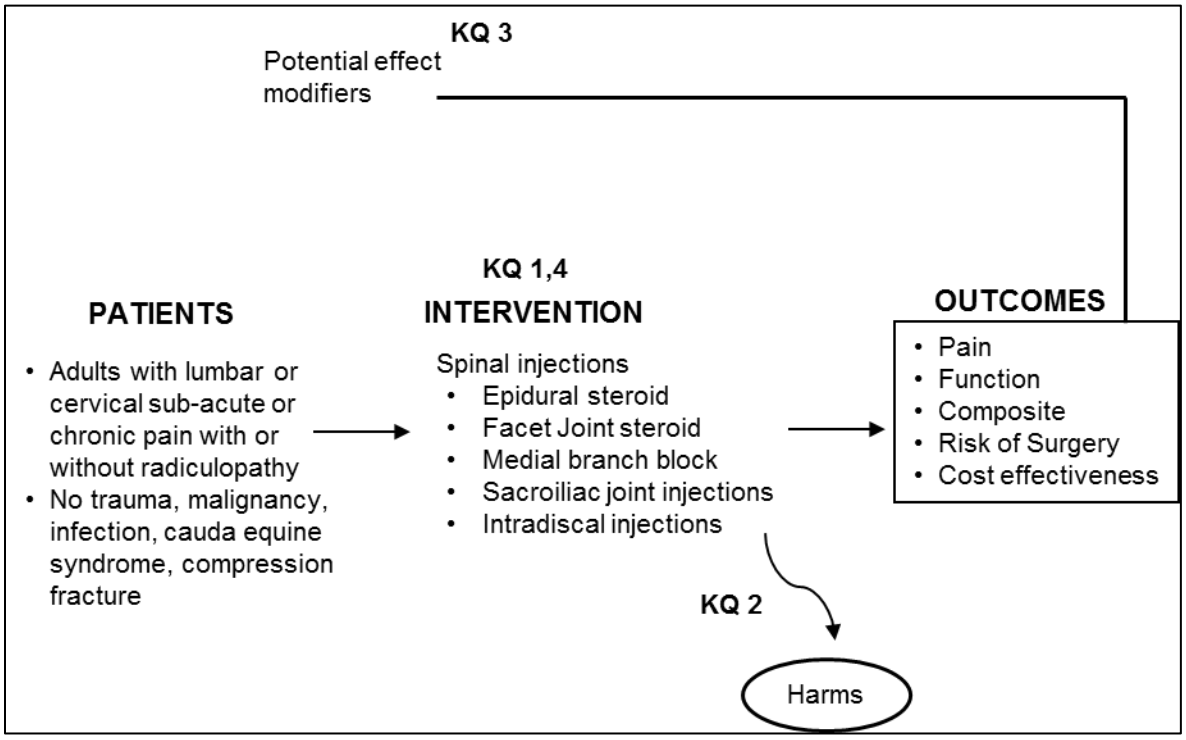
1. What is the evidence of efficacy and effectiveness of spinal injections? Including consideration of:
    a. Short-term and long-term measures, including measures related to:
        - repeated spinal injections
        - multilevel spinal injections
        - bilateral versus unilateral spinal injections
    b. Impact on clinically meaningful physical function and pain
    c. Impact on quality of life, patient satisfaction
    d. Opioid use, return to work, and any other reported surrogate measures

2. What is the evidence of the safety of spinal injections? Including:
    a. Adverse event type and frequency (mortality, major morbidity, other)
    b. Dural or arachnoid puncture
    c. Infection
    d. Epidural or intradural hematoma
    e. Allergic reaction
    f. Nerve or spinal cord injury
    g. Artery/vein damage/puncture
    h. Arachnoiditis

3. What is the evidence that spinal injections have differential efficacy or safety issues in sub populations? Including consideration of:
    a. Patient characteristics (gender, age, psychological or psychosocial co-morbidities, diagnosis, duration of pain)
    b. Injection characteristics (type of steroid [particulate, non-particulate], use of guidance, route of administration)e. Other patient characteristics or evidence based on patient selection criteria
    c. Provider type, setting, or other provider characteristics
    d. Payer/ beneficiary type: including worker‘s compensation, Medicaid, state employees

4. What is the evidence of cost implications and cost-effectiveness of spinal injections? Including:
    a. Direct costs over short term and over expected duration of effect
    b. Comparative costs

Figure 1. Analytic framework



1.3. Outcomes Assessed

Efficacy and effectiveness measures

The studies included in this assessment used a variety of measures to evaluate treatment outcomes, which are outlined in Table 1.

- Pain was assessed using the patient-reported visual analogue scale (VAS) and the Numerical Rating System (NRS). The 10-cm VAS was the most commonly used tool for assessing pain intensity and pain relief. Both the VAS and NRS are pain scales used as a tool for quantifying pain relief or improvement between pre- and post-treatment measurements; the changes in pain intensity are compared between treatment groups.
- Three patient-reported functional outcome measures were used: the Oswestry Disability Index (ODI), the Roland-Morris Disability Questionnaire (RDQ), and the Neck Disability Index (NDI).
    - The ODI evaluates patient back-related pain intensity, personal care, lifting, walking, sitting, standing, sleeping, sex life, social life, and travel on a scale of 0 to 100, with higher scores indicating greater back-related disability.
    - The RDQ evaluates patient back-related pain intensity, self-care, social life, walking, sitting, standing, sleeping bending, stairs, appetite, general activity and household chores on a scale of 0 to 24, where higher scores indicate greater back-related disability.
    - The NDI evaluates the subscales of patient neck-related pain intensity, personal care, lift, reading, headaches, concentration, work, driving, sleeping, and recreation each on a scale of 0 to 5 points. The subscale points are then doubled for a final score ranging from 0% to 100%, with higher scores indicating greater neck-related disability.

Table 1. Outcome measures

Outcome Measure	Instrument Type	Components		Score Range	Interpretation
ODI (Oswestry Disability Index) (version 2.0)[77]	Back	• Pain intensity • Personal care • Lifting • Walking • Sitting	• Standing • Sleeping • Sex life • Social life • Travelling	0–100*	Higher scores = greater disability
Roland-Morris Disability Questionnaire (RDQ)[214]	Back	• Pain intensity • Self-care • Social life • Walking • Sitting • Standing	• Sleeping • Bending • Stairs • Appetite • General activity • Household chores	0–24	Higher scores = greater disability
VAS pain (Visual Analogue Scale)	Generic	• Pain		0–10 cm or 0-100 mm	No pain: 0 Worst pain imaginable: 10
NRS (Numerical Rating System)[8]	Generic	• Pain		0 – 10	No pain: 0 Mild pain: 1 – 3 Moderate pain: 4 – 6 Severe pain: 7 – 10
NDI (Neck Disability Index)[48,234]	Neck	• Pain intensity • Personal care • Lifting • Reading • Headaches	• Concentration • Work • Driving • Sleeping • Recreation	0 – 50 or 0% – 100%*	Higher scores = greater disability

* ODI and NDI: Each of the ten subscales is scored on a scale of 0–5 points; the total score is then doubled for a final score ranging from 0% – 100%

1.4. Washington State Utilization and Cost Data

Spinal Injection – Re-Review

PARAMETERS: The spinal injection re-review analysis includes utilization data from PEBB/UMP (Public Employees Benefit Board Uniform Medical Plan), PEBB Medicare, the Department of Labor and Industries (L&I) Workers' Compensation Plan (forthcoming), and Medicaid Fee for Service and Managed Care. The original spinal injection study period covered 2006 to 2009; the Re-Review analysis periods addressed 2010 through 2014. Primary population inclusion criteria: age greater than 17 years old at time of service AND one of the following CPT/HCPCS codes:

27096	64476	64491
62310	64479	64492
62311	64480	94493
64470	64483	64494
64472	64484	64495
64475	64490	64520

In 2012, based upon a HTCC determination, the agencies implemented a strategy to ensure the efficacy of covered spinal injection procedures.

TABLE A
PEBB/UMP *(INCLUDES MEDICARE)*
POPULATION: ENROLLMENT
Number and Distribution by Gender and by Age Cohort

	2009	2010	2011	2012	2013	2014
PEBB/UMP ENROLLMENT	**184,538**	**191,368**	**214,106**	**212,682**	**219,801**	**226,052**
% PEBB/UMP >17 y.o.	**152,326** (82%)	**158,239** (79%)	**178,800** (83%)	**178,371** (84%)	**184,260** (84%)	**189,450** (84%)
GENDER Distribution PEBB/UMP > 17 years old						
All Males (%)	**N/A**	**N/A**	**44%**	**44%**	**44%**	**44%**
All Females (%)	**N/A**	**N/A**	**56%**	**56%**	**56%**	**56%**

TABLE B

MEDICAID FEE-FOR-SERVICE AND MANAGED CARE

Population: Enrollment

Number and Distribution by Gender and by Age Cohort

	2006	2007	2008	2009	2010	2011	2012	2013	2014
Medicaid	1,144,089	1,131,190	1,149,381	1,226,580	1,300,078	1,319,733	1,313,219	1,330,766	1,794,786
% Mbrs >17 y.o.	500,074 (44%)	480,356 (42%)	471,815 (41%)	494,906 (40%)	527,265 (41%)	526,252 (40%)	514,212 (39%)	521,159 (39%)	954,129 (53%)
GENDER Distribution > 17 years old									
Male (%)	26%	27%	28%	30%	31%	31%	31%	31%	41%
Female (%)	74%	73%	72%	70%	69%	69%	69%	69%	59%

TABLE C

PEBB/UMP (*Does not include Medicare*)

2006 -2014 UTILIZATION AND COSTS*: Spinal Injection

Year	Unique Patients (Pt.)	Procs	Avg Procs/Pt	Sub Amt	Allw Amt	Pd Amt	Avg Pd/ Proc
2006	1,008	3,654	3.6	*N/A*	*N/A*	$1,235,237	$338
2007	1,158	4,061	3.5	*N/A*	*N/A*	$1,414,372	$348
2008	1,481	5,591	3.8	*N/A*	*N/A*	$1,983,033	$355
2009	1,682	6,477	3.9	*N/A*	*N/A*	$2,302,815	$356
2010	1,912	6,078	3.2	$4,996,657	$2,668,749	$2,223,829	$366
2011	1,771	5,865	3.3	$4,882,599	$2,133,601	$1,806,534	$308
2012	1,606	4,463	2.8	$3,888,321	$1,762,015	$1,485,848	$333
2013	1,638	4,721	2.9	$4,371,236	$1,823,903	$1,541,538	$327
2014	1,604	4,531	2.8	$4,430,296	$1,945,924	$1,627,788	$359

**2006-2009 data was calibrated to ensure methodology matching between the original and re-review population analyses.*

TABLE D
PEBB/UMP (*DOES NOT INCLUDE MEDICARE*)
2006-2014 Spinal Injections by Type: Paid Dollars

Injection	2006	2007	2008	2009	2010	2011	2013	2014
Sacroilliac	$16,167	$22,515	$35,057	$42,255	$49,519	$29,528	$32,722	$32,700
Epidural	$532,910	$542,241	$702,524	$765,599	$795,580	$588,746	$591,946	$540,454
Facet Paravertebral	$320,849	$390,640	$527,416	$662,463	$563,131	$487,603	$283,995	$373,104
Foraminal	$363,566	$451,446	$711,383	$827,366	$795,194	$685,265	$626,488	$677,060
Nerve Block	$1,745	$7,529	$6,652	$5,132	$20,405	$15,392	$6,387	$4,470
Grand Total	**$1,235,237**	**$1,414,372**	**$1,983,033**	**$2,302,815**	**$2,223,829**	**$1,806,534**	**$1,541,538**	**$1,627,788**

CHART A
PEBB/UMP (DOES NOT INCLUDE MEDICARE)
2010 – 2014 UTILIZATION:
Select Spinal Injection Procedures by Type of Injection

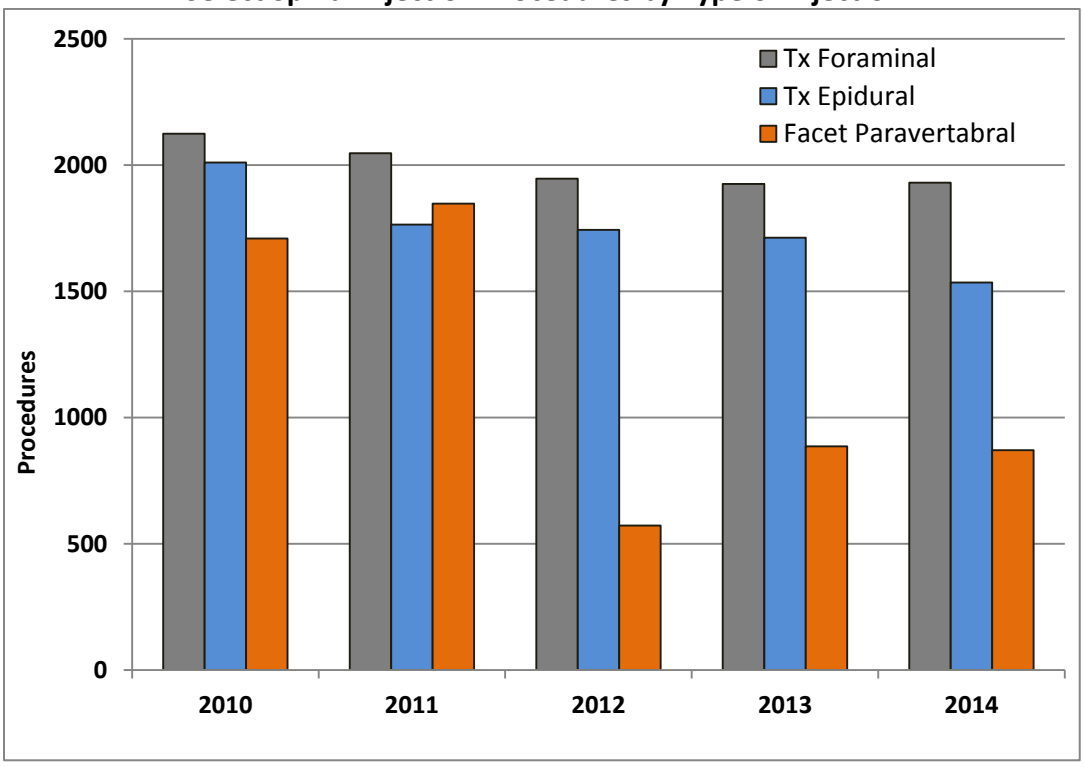


CHART B

PEBB/UMP (*DOES NOT INCLUDE MEDICARE*)

2006 - 2014 Paid Dollars: Select Spinal Injections by Type of Injection

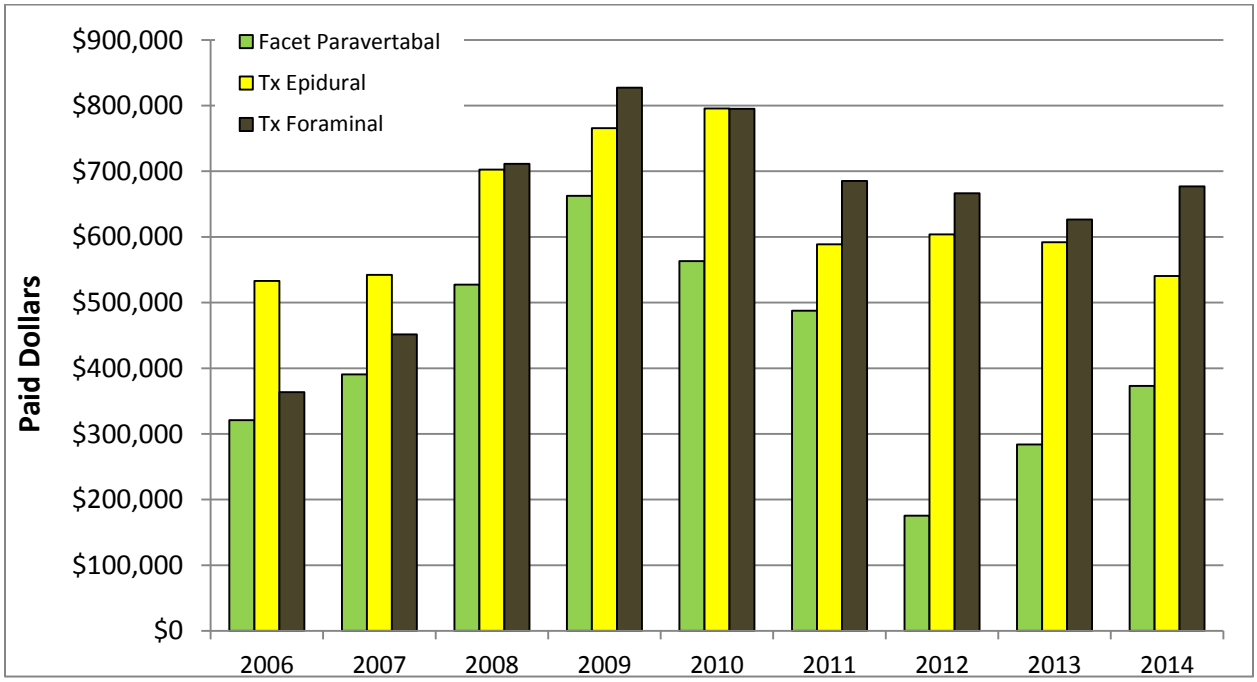


CHART C

UMP/PEBB (*DOES NOT INCLUDE MEDICARE*)

2006 – 2014 Utilization and Costs: Spinal Injection Procedures

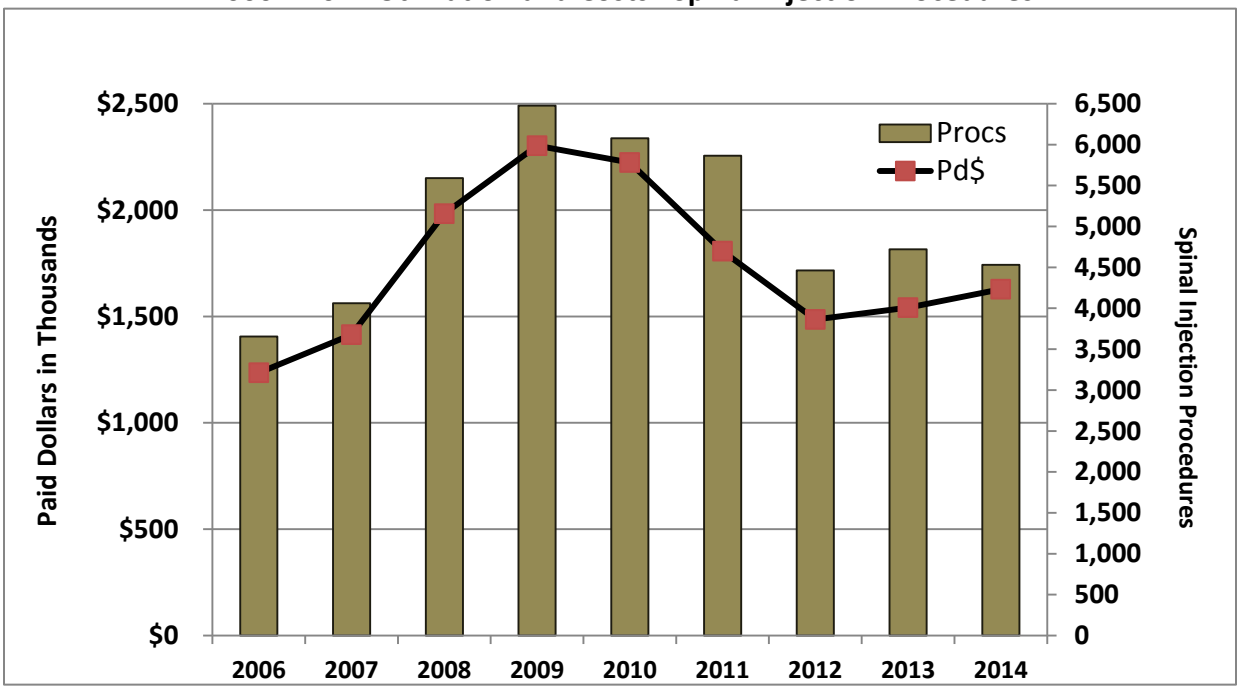


TABLE E

PEBB/UMP (DOES NOT INCLUDE *MEDICARE*)

2011 – 2012 Utilization: Change in Count of Top 15 Primary Diagnosis Codes Used for Facet Paravertebral Spinal Injections

Dx	Description	2011	2012
721.3	LUMBOSACRAL SPONDYLOSIS WITHOUT MYELOPATHY	693	225
721	CERVICAL SPONDYLOSIS WITHOUT MYELOPATHY	336	114
724.2	LUMBAGO	183	53
724.8	OTHER SYMPTOMS REFERABLE TO BACK	113	14
722.52	DEGENERATION OF LUMBAR OR LUMBOSACRAL INTERVERTEBRAL DISC	87	37
723.1	CERVICALGIA	79	18
721.2	THORACIC SPONDYLOSIS WITHOUT MYELOPATHY	57	33
724.4	THORACIC OR LUMBOSACRAL NEURITIS OR RADICULITIS, UNSPECIFIED	42	7
722.4	DEGENERATION OF CERVICAL INTERVERTEBRAL DISC	40	5
723.8	OTHER SYNDROMES AFFECTING CERVICAL REGION	30	3
338.29	CHRONIC PAIN NEC	27	11
722.93	OTHER AND UNSPECIFIED DISC DISORDER OF LUMBAR REGION	16	0
724.02	SPINAL STENOSIS, LUMBAR REGION, WITHOUT NEUROGENIC CLAUDICATION	15	0
723.4	BRACHIAL NEURITIS OR RADICULITIS NOS	14	1
722.1	DISPLACEMENT OF LUMBAR INTERVERTEBRAL DISC WITHOUT MYELOPATHY	13	1

TABLE F
PEBB/UMP MEDICARE
2006 – 2014 UTILIZATION: Spinal Injection Volume only*

YEAR	Unique Patients	Procs	Avg Procs/ Pt
2006	785	3,161	4.0
2007	859	3,525	4.1
2008	1019	4,167	4.1
2009	1,134	4,894	4.3
2010	1,627	2,880	1.8
2011	1,762	3,383	1.9
2012	1,846	2,938	1.6
2013	2,025	3,480	1.7
2014	1,900	3,372	1.8

**PEBB/UMP pays secondary to Medicare for these patents; therefore only a portion of PEBB paid dollars are captured in Medicare reporting. Including paid dollars in the analysis would give the appearance of significantly lower overall costs for this population.*

CHART D
PEBB/UMP (*INCLUDES MEDICARE*)
RATE: NUMBER OF SPINAL INJECTION PROCEDURES/1,000 MEMBERS >17 YEARS OLD

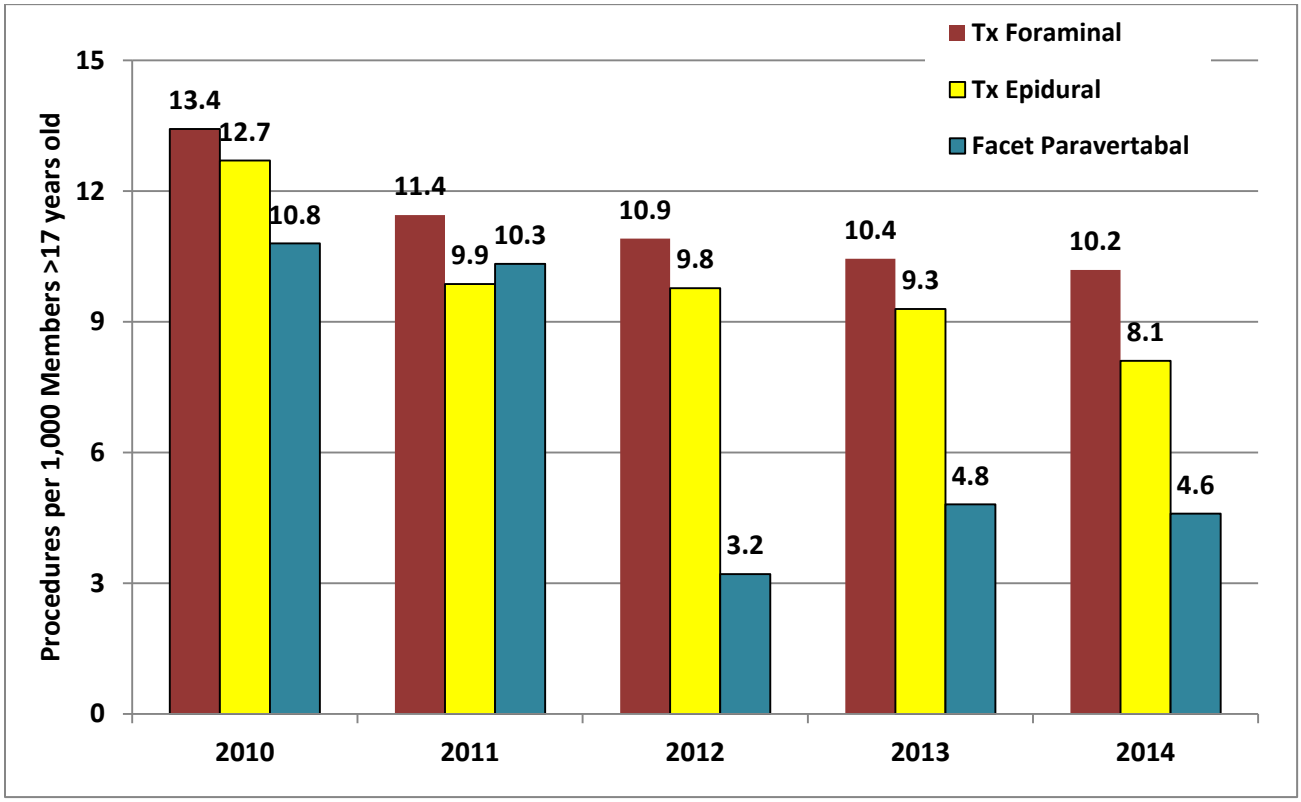


TABLE G

MEDICAID FEE-FOR-SERVICE

2011 – 2012 UTILIZATION: CHANGE IN COUNT OF TOP 15 PRIMARY DIAGNOSIS CODES USED FOR FACCET PARAVERTEBRAL SPINAL INJECTIONS

Dx	Description	2011	2012
7213	Lumbosacral spondylosis	834	669
7242	Lumbago	243	187
7210	Cervical spondylosis	153	168
33829	Chronic pain NEC	167	114
7248	Other back symptoms	104	132
7231	Cervicalgia	108	60
72252	Lumbar/lumbosacral disc degeneration	95	29
7244	Lumbosacral neuritis NOS	50	43
72283	Post-laminectomy syndrome-lumbar	13	36
7212	Thoracic spondylosis	23	23
7224	Cervical disc degeneration	38	8
7241	Pain in thoracic spine	24	17
3384	Chronic pain syndrome	8	24
7238	Cervical syndrome NEC	21	6
71698	Arthropathy NOS-other site	12	3

TABLE H

MEDICAID FEE-FOR-SERVICE & MEDICAID MANAGED CARE

2006- 2014 UTILIZATION: Spinal Injections

NOTE: THE ORIGINAL DATA (2006-2009) DID NOT DIFFERENTIATE BETWEEN FEE-FOR-SERVICE AND MANAGED CARE UTILIZATION.

Year	Patient (Pt.)	Procs	Avg Procs/ Pt	Sub Amt	Allw Amt	Pd Amt	Avg Pd/ Proc
2006	2,557	7,275	2.8	*n/a*	*n/a*	$1,321,088	$182
2007	2,650	6,694	2.5	*n/a*	*n/a*	$1,333,749	$199
2008	2,924	7,792	2.7	*n/a*	*n/a*	$1,520,215	$195
2009	3,385	8,625	2.5	*n/a*	*n/a*	$1,770,666	$205
2010	4,390	12,616	2.9	*n/a*	$3,513,688	$3,385,716	$268
2011	4,598	13,765	3.0	*n/a*	$4,725,242	$4,614,234	$335
2012	4,166	12,222	2.9	*n/a*	$3,951,106	$3,854,283	$315
2013	3,587	9,433	2.6	*n/a*	$2,771,360	$2,638,845	$280
2014	4,594	10,375	2.3	*n/a*	$2,961,301	$2,851,284	$275

TABLE I

MEDICAID FEE-FOR-SERVICE

2010 – 2014 UTILIZATION: Spinal Injections

NOTE: MEDICAID FEE-FOR-SERVICE POPULATION UNDERGOING MIGRATION TO MANAGED CARE

Year	Patient (Pt.)	Procs	Avg Procs/ Pt	Sub Amt	Allw Amt	Pd Amt	Avg Pd/ Proc
2010	2,721	8,867	3.3	*n/a*	$2,844,180	$2,737,921	$309
2011	2,735	9,233	3.4	*n/a*	$3,628,134	$3,577,816	$388
2012	2,171	7,194	3.3	*n/a*	$2,704,985	$2,643,105	$367
2013	747	1,944	2.6	*n/a*	$754,476	$727,464	$374
2014	294	529	1.8	*n/a*	$182,578	$163,655	$309

TABLE J

MEDICAID MANAGED CARE

2010 – 2014 UTILIZATION: Spinal Injections

NOTE: MEDICAID MANAGED CARE POPULATION GREW BY 35% IN 2014

Year	Patient (Pt.)	Procs	Avg Procs/ Pt	Sub Amt	Allw Amt	Pd Amt	Avg Pd/ Proc
2010	1,669	3,749	2.2	*n/a*	$669,509	$647,795	$217
2011	1,863	4,532	2.4	*n/a*	$1,097,108	$1,036,418	$291
2012	1,995	5,028	2.5	*n/a*	$1,246,121	$1,211,179	$299
2013	2,840	7,489	2.6	*n/a*	$2,016,883	$1,911,381	$331
2014	4,300	9,846	2.3	*n/a*	$2,778,723	$2,687,630	$351

CHART E

MEDICAID FEE-FOR-SERVICE & MEDICAID MANAGED CARE

2010 – 2014 UTILIZATION: Select Spinal Injections by Count of Procedures

NOTE: 2014 RECORDED A 35% INCREASE IN THE MEDICAID POPULATION

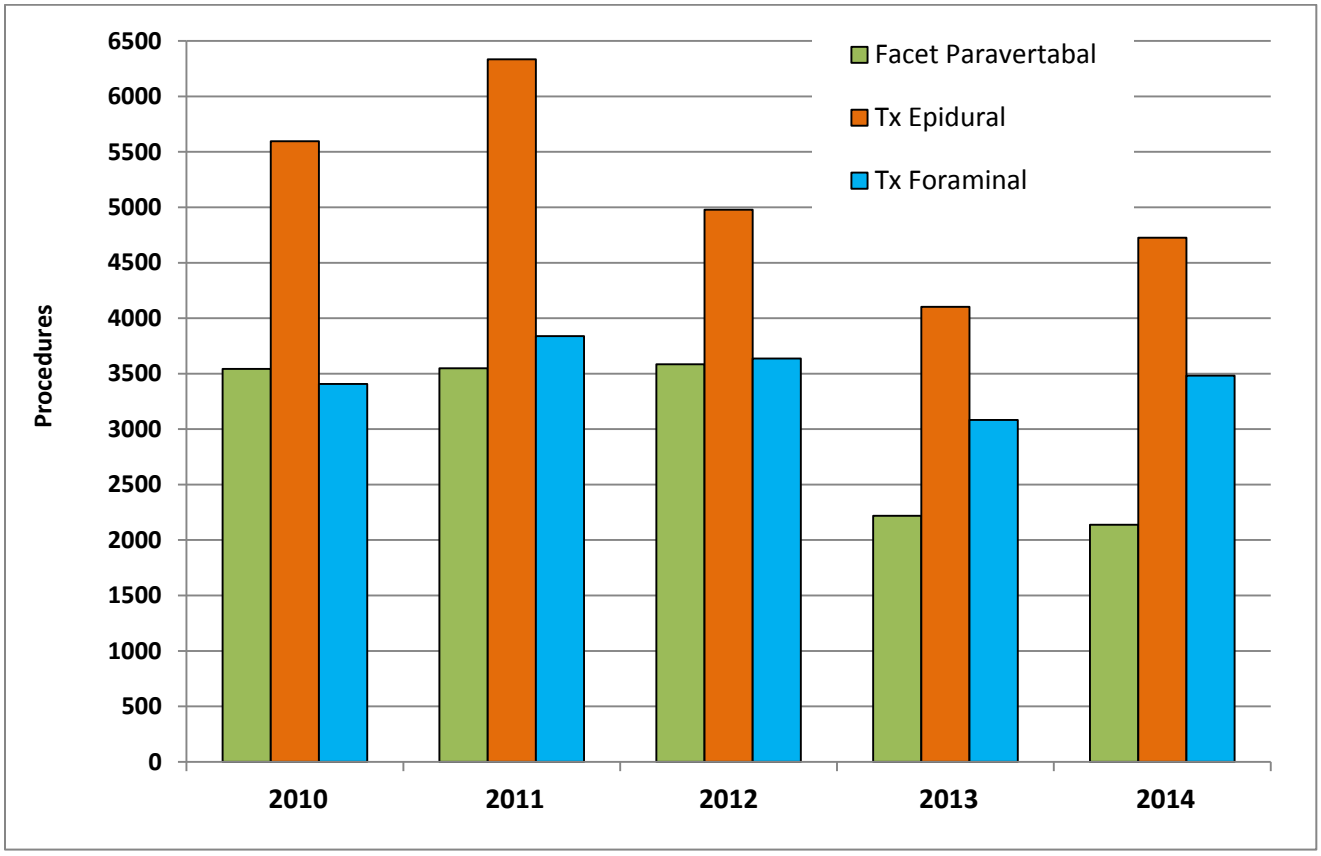


CHART F

MEDICAID FEE-FOR-SERVICE & MEDICAID MANAGED CARE

2014 RATE: NUMBER OF SPINAL INJECTION PROCEDURES/1,000 MEMBERS >17 YEARS OLD

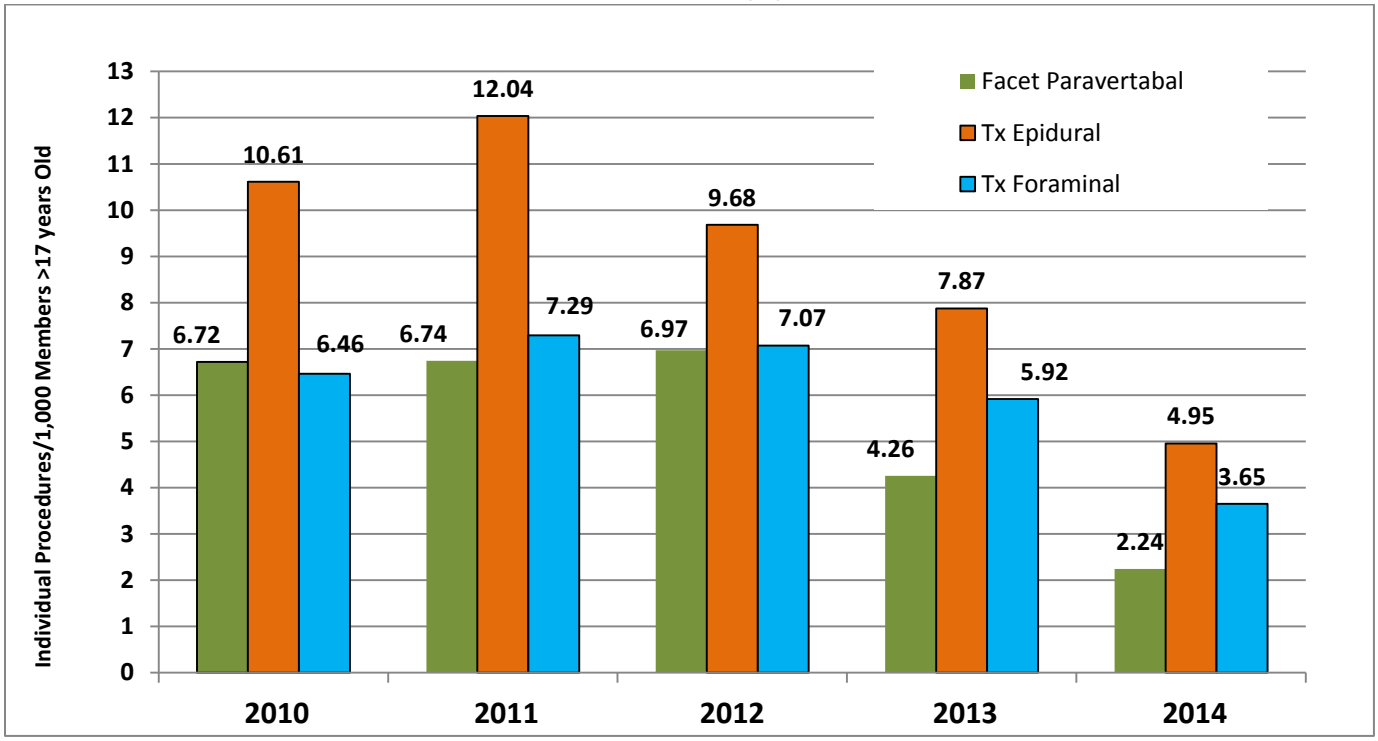


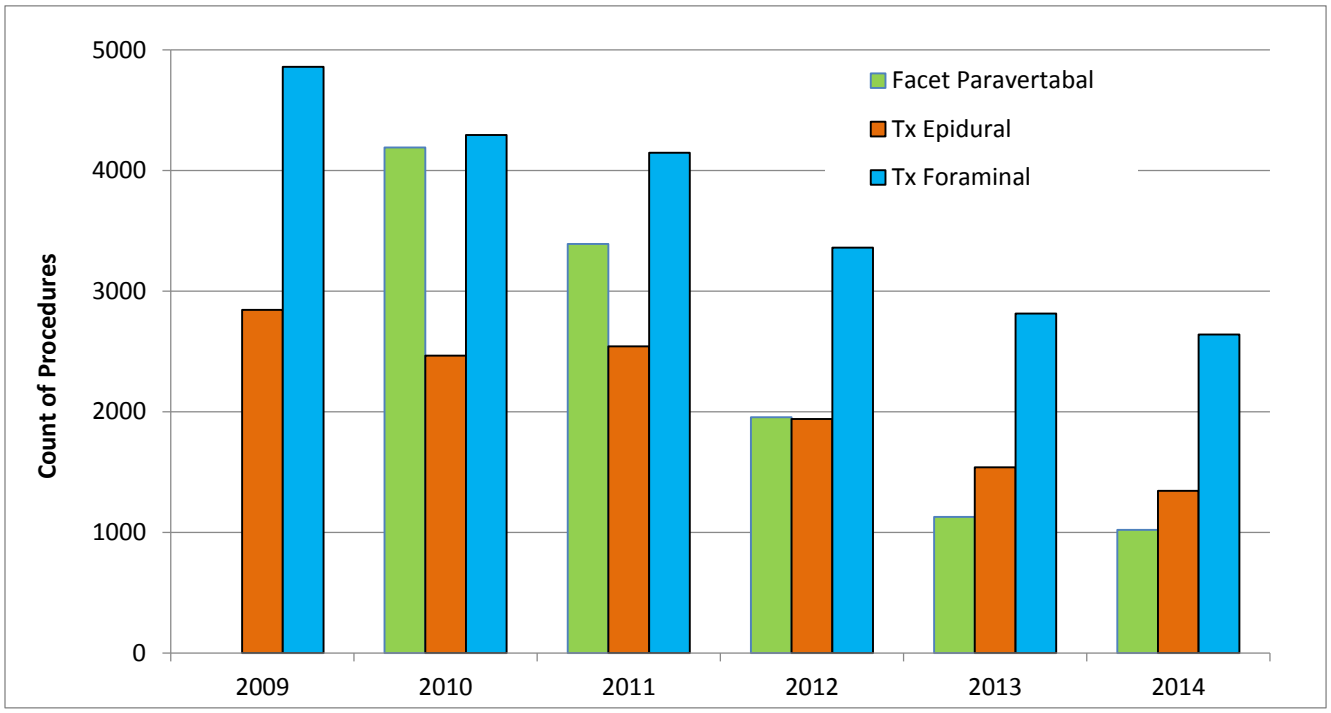
TABLE K

LABOR & INDUSTRIES

2006 - 2014 UTILIZATION AND COSTS: Spinal Injections

Year	Unique Patients (Pt.)	Procs	Avg Procs/ Pt	Allw Amt	Pd Amt	Avg Pd/ Proc
2006	4,667	12,055	2.58	$9,903,630	$4,572,458	$379
2007	4,414	11,476	2.60	$9,845,963	$4,450,219	$388
2008	4,408	11,524	2.61	$10,033,815	$4,302,110	$373
2009	4,887	8,387	1.72	$5,075,410	$4,031,757	$481
2010	4,434	11,544	2.60	$7,263,546	$4,720,276	$409
2011	4,226	10,611	2.51	$6,381,964	$4,103,952	$387
2012	3,658	7,783	2.13	$4,483,229	$3,132,197	$402
2013	3,185	6,002	1.88	$3,277,139	$2,397,713	$399
2014	2,992	5,498	1.84	$2,683,732	$2,240,763	$408

CHART G
LABOR & INDUSTRIES
2009 - 2014 UTILIZATION: Select Spinal Injections Procedures by Type of Injection



2. Background

2.1. Epidemiology and Burden of disease

Back and neck pain are extremely common conditions; lifetime incidence is estimated to be 70% to 85% for low back pain,[12] and 14% to 71% for neck pain.[79] While back pain often resolves within a few months, surveys report that approximately 5% of the population has chronic back pain[17] (i.e., persists for more than three months). Similarly, while most cases of acute neck pain will resolve within two months,[55] one-year chronic neck prevalence can range from 16.7% to 75.1%.[79] Back and neck pain have significant social and economic impacts. Back pain is the most common cause of activity limitation in people younger than 45 years, and about 2% of the United States workforce seek Worker's Compensation for back pain each year. [12] A registry study from Denmark also found that those suffering from neck pain had lower employment rates and incomes.[113] Additionally, back pain is the leading cause of years lost to disability, and neck pain is the fourth most common cause.[189] Lastly, back pain[33,50,101,216,224] and neck pain[33] have been reported to negatively impact quality of life, work status, functional activity, as well as satisfaction with pain treatment.

Back and neck pain is more prevalent in certain populations. Women report greater incidence of both back and neck pain; the National Health Interview Survey 2013 survey of over 30,000 United States adults indicated that low back pain was self-reported in 30.2% of women versus 26.5% of men, while 16.5% of women versus 12.2% of men self-reported neck pain.[47] Additionally, those aged 45 to 64 have a higher risk for neck pain, with an estimated 19.4% Americans self-reporting the condition; with regards to low back pain, those who are older than 75 years of age are at a higher risk with 34.2% of Americans self-reporting the condition.[47] Further, back pain is more common in countries with high-income economies compared to countries with medium- and low-income economies.[104]

Spinal imaging abnormalities are common in patients with back and neck pain, particularly in older adults. However, such findings poorly predict the presence or severity of pain.[233] Though often symptoms cannot be attributed to a specific disease or spinal pathology, spinal injections have been administered in patients with the following diagnosis or condition:

- **Disc degeneration** refers to the naturally-occurring wear-and-tear of spinal discs associated with aging. As people age, discs desiccate and lose elasticity, becoming susceptible to disc compression and tears that can cause spinal pain. Disc degeneration occurs most often in the cervical or lumbar spinal regions and in those who are obese, smokers, or perform heavy physical work.[2] A case control study of 158 adults age 65 years or older found that 40% of participants with chronic low back pain also had severe disc degeneration.[99] Additionally, a systematic review found that prevalence of disc degeneration increased with age; 37% of individuals in their twenties were estimated to have some level of disc degeneration while 80% of individuals in their fifties and 96% of individuals in their eighties were estimated to have some level of degeneration.[35]
- **Herniated nucleus pulposus (HNP)** occurs when the central portion of the disc (nucleus pulposus) bulges into the spinal canal, causing compression of surrounding nerves. This can result in weakness, numbness, or pain in an arm or leg. In particular, lumbar disc herniation is

the main cause for radicular pain.[242] Herniated discs are more common in the lumbar region and in middle-aged and older men, especially accompanying strenuous physical activity.

- **Spinal stenosis** describes the narrowing of the spinal canal, and leg and back pain can result from the compression of neuronal structures and intra-spinal vasculature.[127] Stenosis is most common in people older than 65 years, and is characterized by pain, paresthesia, and cramping in one or both legs.[127] Lumbar spinal stenosis (LSS) is estimated to occur in 8% to 11% of the US population, and it is estimated that 2.4 million Americans will be affected by LSS by 2021.[11] Those over the age of 50, female, or with a history of spinal injury or surgery are at increased risk.

- **Radiculopathy** describes nerve root impingement or inflammation that has progressed to cause neurologic symptoms in areas that are innervated by the affected nerve roots.[132] This can occur in the lumbar and cervical spine regions, but is more common in the lumbar region.[132] Causes of radiculopathy include disc herniation, foraminal narrowing, and osteoarthritis. Related conditions are:

    - Radiculitis— an inflammation of a spinal nerve root, causing radicular pain;[215]
    - Sciatica— pain or numbness in a leg, radiating along the sciatic nerve, that is caused by a herniated disc with nerve-root compression in approximately 90% of cases;[231]
    - Cervicobrachialgia— pain in the neck radiating down the arm that can be the result of cervical radiculopathy.[1]

- **Failed back surgery syndrome (FBSS)** describes a condition of persistent pain after back surgery. As number of lumbar and cervical spine surgeries increase, so do the number of failed surgeries and thus, the incidence of FBSS.[106] A study by Javid[112] indicated that lumbar laminectomy was unsuccessful for 30.4%, 22.8%, and 34.8% of patients with central stenosis, stenosis with HNP, and lateral stenosis, respectively. Treating FBSS patients is challenging, as additional surgery and conservative therapies may not relieve pain.[232]

- **Facet joint syndrome** describes pain occurring in the facet joints (also referred to as zygapophysial or Z joints), which allow the spine to bend and twist. It can be characterized by trauma, inflammation and disc degeneration that subsequently pinches the facet joint nerves. [3] Facet joint pain increases with age and is most often found in the elderly due to the degeneration of the cartilage covering the face joints over time.[85]

- **Whiplash** describes an extension/flexion injury occurring as the result of a vehicle accident, most often a rear-end collision.[4,225,227] Common symptoms are neck pain and stiffness as well as reduced and painful neck movements.[5] There are a variety of resulting conditions, such as joint dysfunction, disc herniation, chronic pain, faulty muscle movement, and cognitive or mental function problems. Women are more frequently and more seriously affected by whiplash.[4] Additionally, advanced age and pre-existing health conditions such as arthritis can also increase the severity of the condition. Whiplash frequently improves without further complications, but chronic whiplash in which pain lasts >6 months can develop. Although reports on whiplash have increased, there are no epidemiologic studies regarding the prevalence of chronic whiplash.[5]

2.2. Technology: Spinal Injections

Treatment for back pain often involves a combination of interventions, and spinal injections are not usually performed until less invasive treatments have been tried and have not provided adequate relief. Spinal injections involve the injection of an anti-inflammatory agent such as a steroid and/or an anesthetic into the spine or space around the spinal nerves and joints. One of the theoretical advantages of spinal injections is direct delivery of treatment medication to the site involved in the source of pain.[98] Fluoroscopic or computed tomography (CT) visualization is often used to improve the accuracy of medication delivery.

Types of spinal injections include epidural, facet joint, medial branch block, intradiscal, and sacroiliac joint injections. While spinal injections can be used for diagnostic and therapeutic purposes, the focus of this report is only on those used therapeutically. The use of spinal injections has been growing; according to one study examining Medicare claims of lumbosacral injections, the number of epidural steroidal injections increased 271% and the number of facet injections increased 231% from 1994 to 2001.[70] Similar studies among the Medicare population indicate that from 2000 to 2011, average annual increases have been seen for epidural injections (7.5%), [167] facet joint injections (13.6%), [168] and sacroiliac injections (14.2%). [160] In the Washington State Medicare population alone, epidural injections, facet joint injections, sacroiliac injections, and percutaneous adhesiolysis (not discussed in this report) have increased on average 12% per year from 2000 to 2010.[161]

2.2.1. ***Procedures***

Epidural Injections deliver medication into the epidural space of the spine to decrease inflammation of the nerve root.[7] Three approaches are possible; which is used depends on the location and source of pain as well as on the physician's preference and experience.[185] Caudal and interlaminar/translaminar injections have been traditionally used, but transforaminal injections are gaining in popularity, particularly in treating unilateral radiculopathy.[185]

- *Interlaminar/translaminar:* This is the most commonly used approach, and is thought to deliver the medication directly to the treatment site.[63,135] Sometimes referred to as a paramedian translaminar epidural, this approach involves placement of the needle between the lamina of the vertebrae, delivering medication to both the right and left sides of the inflamed area.[7] The interlaminar/translaminar approach requires significant dexterity for accurate treatment,[129] yet requires less medication than the caudal approach and has a lower risk of damaging the nerve root.[185]
- *Transforaminal:* This approach requires the smallest volume to the primary site of pathology.[63,135] The transforaminal approach involves placement of the needle in the neural foramen, treating one side at a time. The transforaminal approach offers a closer delivery of the medication to the nerve root compared with the interlaminar approach, allowing the use of lower doses of medication. This approach is particularly useful in treating large disk or lateral disk herniations and foraminal stenosis, but has a higher risk of damaging the nerve root.
- *Caudal:* The caudal lumbar approach is performed via the sacral hiatus.[130] The caudal approach is considered to be less demanding and has a lower risk of intradural injection, but requires larger volumes of injectate.

Facet/Zygapophysial Joint Injections deliver medication into the facet joints. Prior to steroid injections, controlled diagnostic blocks of the joint or the nerves that supply the joint are often performed using local anesthetic.[28] Pain reduction indicates that the affected nerve has been identified as the source of pain.[26,68,125] There is some controversy as to the amount of pain relief that constitutes a positive response, varying from 50% to 100%.[27] Repeated blocks with anesthetics of different duration of action can verify the exact location of facet joint pain, but must be done in a controlled manner to be valid.

For therapeutic (and diagnostic) purposes, the choice between a medial branch block and intraarticular injection is somewhat dependent on the physician's preference and training. There are several approaches, including:

- *Intraarticular injections:* Injection into the facet (zygapophysial) joints. Intraarticular injections carry the risk of leakage of fluid into the epidural space and nerve roots, are more difficult to perform, especially if age-related changes or trauma cause difficulty entering the facet joint, and are more time consuming.[28]
- *Extra-articular/pericapsular injections:* Inject into the space around the joints, as opposed to into the joints as in intraarticular injections.
- *Medial branch blocks:* Medial branch blocks involve injection of the medication into the area of the medial branch of the posterior primary ramus.[6,27,125] The procedure for medial branch blocks can be performed with a lower dose of corticosteroids.

Sacroiliac Joint Injections: Diagnostic and therapeutic sacroiliac joint injections deliver local anesthetic and/or corticosteroids into or around the sacroiliac joint.[51] The use of this type of injection in patients without spondylarthropathy remains controversial.[51] A positive response from a diagnostic injection is poorly defined and dependent upon individual physician preferences.[94] A positive diagnostic block can identify either sacroiliac joint structures or joint malfunction as a potential source of pain.[28,94] Diagnostic sacroiliac joint blocks can be among the most challenging of spinal injection procedures, with false-positive and false-negative blocks possible.[94]

Intradiscal Injections deliver steroids directly into the intervertebral disc[51] and can be used for both diagnostic and therapeutic purposes. Intradiscal injections of steroids are thought to promote stabilization by causing a contraction of the disc tissue and suppressing inflammation within the disc.[190] Risks of the procedure seem to be minimal, but this remains a controversial topic.[190]

2.2.2. ***Guidance***

Fluoroscopy for spinal injections is routinely used to ensure correct needle placement, accurate delivery of the injectate, and avoidance of complications, as it provides a quick and cost-effective method for injection guidance.[183] Incorrect needle placement during spinal injections without the use of fluoroscopy has been reported by various studies in 12.5% to 38.3% of patients,[31] although recent analysis of the FDA Adverse Event Report System database to investigate incidence of serious neurological events indicated that imaging use does not eradicate the risk of serious neurologic outcomes.[78] A C-arm fluoroscope allows the X-ray tube to be moved around the prone patient and an image intensifier enhances the image, making it easier to interpret.[32] Although studies have shown that radiation exposure to physicians using fluoroscopy for spinal injections is within safety limits,[29,32,147-149] other methods, including ultrasound and CT, are being investigated as non-radioactive or lower radioactive methods of needle guidance.

2.2.3. *Mechanism of Action*

Referred to as corticosteroids, glucocorticosteroids, glucorticoids or steroids,[20] usage of steroid spinal injections were first used to treat back and leg pain within the last century.[185] Corticosteroids administered for therapeutic spinal pain relief work by inhibiting the synthesis or action of neural peptides; inhibiting the synthesis or release of inflammatory substances, including phospholipase A_2, arachidonic acid and its metabolites, tumor necrosis factor alpha, interleukin 1, and prostaglandin E_2; suppress the sensitization of dorsal horn neurons; and suppress ongoing neuronal discharge.[98,185] In the case of radiculopathy, glucocorticoids relieve both the early and late effects of inflammation.[185] For patients with referred back pain from disc degeneration, the corticosteroids likely work by reducing impulses from the posterior longitudinal ligament and the outer annulus of the intervertebral disc.[185] For patients with stenosis, steroids appear to inhibit nerve root edema, reducing microcirculation and reducing ischemia, prostaglandin synthesis, and inflammation.[95] Common glucocorticosteroids are cortisone, hydrocortisone, prednisone, methylprednisolone, dexamethasone, betamethasone, and triamcinolone.

The local anesthetic administered for both diagnostic and therapeutic steroid injection use works by dampening C-fiber activity and interrupting the nociceptive input and reflex mechanisms of the afferent limb of local pain fibers, interrupting the pain-spasm cycle.[98] It is theorized that the anesthetic acts on the free glutamate released by herniated disc material and clears adhesions or inflammatory exudates from the affected neural structure.[98] Common anesthetics utilized in conjunction with corticosteroid injections are lidocaine, procaine, and bupivacaine.

2.2.4. *Indications for Steroid Spinal Injections*

In general, epidural, facet joint, and sacroiliac joint injections are indicated for intermittent or continuous pain causing functional disability, or chronic pain that has failed to respond to more conservative therapies.[135,185]

- **Lumbar transforaminal injections** are indicated in patients with chronic low back and/or lower extremity pain resulting from disc herniation, FBSS without extensive scar tissue and hardware, spinal stenosis with radiculitis, or discogenic pain with radiculitis.[82,134,135,185]
- **Lumbar interlaminar and caudal epidural injections** are indicated in patients with disc herniation/lumbar radiculitis; lumbar spinal stenosis; post lumbar surgery syndrome; epidural fibrosis; disc degeneration/discogenic low back pain; and negative for facet joint pain. [82,134,135,185]
- **Cervical interlaminar epidural injections** are indicated in patients with a herniated, protruded, or extruded disc with or without radiculitis; cervical spinal stenosis; post cervical surgery syndrome; disc degeneration; and negative for facet joint pain.[135] It is recommended that they be performed at the C7-T1 level, but no higher than C6-C7 level.[206]
- **Cervical transforaminal epidural injections** are indicated for patients with cervical radicular pain.[75,109]
- **Lumbar or cervical facet joint blocks** are indicated in patients with chronic somatic or non-radicular low back/cervical pain or headache and lower/upper extremity pain; no evidence of either discogenic or sacroiliac joint pain; no evidence of disc herniation or radiculitis; inability to undergo physical or chiropractic therapy; inability to tolerate non-steroidal anti-inflammatory

medications; or patients with pain originating from lumbar facet joints.[135,203] Therapeutic facet joint nerve blocks are indicated in patients with a positive response (80% relief) to a controlled anesthetic block.[135]

- **Intradiscal injections** are indicated in patients with internal disc disruption with Modic changes on an MRI and signs of end-plate inflammatory changes,[190] chronic discogenic low back pain,[51] and lumbar disc prolapse with sciatica or radiculopathy.[51]
- **Sacroiliac joint injections** are indicated in patients with chronic somatic or nonradicular low back and lower extremity pain that is greatest below the level of L5, and lack of evidence for disc-related or facet joint pain.[135] A therapeutic sacroiliac joint injection is indicated with a positive sacroiliac diagnostic block of at least 80% pain relief.[135] It also may be considered for symptomatic pain relief of sacroiliac joint pain.[10]

2.2.5. *Particulate and Non-Particulate Steroids*

Although the FDA does not formally distinguish between particulate and non-particulate steroids,[78] existing literature frequently makes this distinction in studies of steroid spine injections. It is the belief among some clinicians that particulate steroids have greater positive effects than non-particulate steroids, though the data are inconclusive.[56] Particulate steroids include methylprednisolone acetate, triamcinolone acetonide or hexacetonide, betamethasone acetate, and prednisolone acetate.[71] These steroid types are highly insoluble in water and form microcrystalline aggregates that are larger than a red blood cell.[219] Non-particulate steroids include dexamethasone sodium phosphate. There is concern regarding the safety of particulate steroids, as there is general consensus that particulate steroids result in more embolic events in the case of accidental intravascular injection. An FDA report evaluating case reports found that most cases of adverse events reported administration of particulate steroid injections.[78] Futhermore, there is growing consensus that the risk associated with the use of particulate steroids is greater with utilizing the transforaminal approach.[206] However, the FDA acknowledged that any implication for differential risk is limited due to lack of reliable information about utilization of different formulations.

2.2.6. *Contraindications*

Spinal injections are not indicated in patients with a history of allergy to any of the medications used.[27,135] Lumbar epidural injections are not indicated for uncompensated coagulopathy including bleeding disorders; ongoing use of anticoagulant medications; thrombocytopenia; infection; diabetes mellitus, prominent motor deficit or paresis suggestive of severe root or cauda equina compression; failure of previous injections to provide benefit; severe spinal stenosis as demonstrated by imaging studies; local malignancy; and acute spinal cord compression. [66,82,185] In addition, some factors that can negatively affect the outcome include smoking, chronic pain syndrome, previous back surgery, axial-only pain or diffuse pain, opioid dependence, and disability claims.[183,185]

2.2.7. *Potential Complications and Harms*

Complications of the various types of spinal injections can arise from the procedure itself or from any of the injectates used, and may include:[9,19,23,28,46,54,78,82,91,94,98,114,133,135,154,164,165,185,192,207]

- **Major and minor procedural complications** include infection; hematoma; intravascular uptake resulting in systemic instead of localized exposure to medication; nerve damage; dural puncture

(possibly resulting in a post-dural puncture headache); unintentional subarachnoid, intrathecal, or subdural injection; disc entry; permanent spinal cord injury; air embolism; pneumocephalus; brain/spinal cord infarction; brain/spinal cord edema; intracranial hypotension; retinal hemorrhage or cortical blindness; transient neurologic deficits; vasovagal syncope; arachnoiditis; myelopathy/cauda equina syndrome; local discomfort or swelling; increased general or radicular pain; local bleeding; profuse bleeding urinary complications; epidural granuloma; abscess; radiation exposure; direct needle trauma; intravascular puncture. Serious but rare neurological complications from epidural injection of corticosteroids include loss of vision, stroke, paralysis, and death, as described in a 2014 FDA Drug Safety Announcement.[78]

- **Complications from the corticosteroids** include suppression of the hypothalamic-pituitary axis; elevation of blood sugar in diabetics; elevated blood pressure; fluid retention in patients with congestive heart failure; dizziness; nausea/vomiting; weakness; headache; tachycardia; facial erythema; transient hypotension/hypertension; gastritis; mood swings; pruritus; insomnia; menstrual irregularities; Cushingoid syndrome; meningitis; and electrolyte imbalance. Epidural injection of particulate steroids (methylpredinoslone acetate, triamcinolone acetonide or hexacetonide, betamethasone acetate, betamethasone acetate/betamethasone sodium phosphate) were associated more frequently with rare, serious adverse events in the FDA's Adverse Events Reporting System database compared to nonparticulate steroid (dexamethasone sodium phosphate, betamethasone sodium phosphate, methylprednisolone sodium succinate, hydrocortisone sodium succinate). This increase may be due to the embolization of particulate steroids that can possibly lead to infarction.
- **Complications related to any of the injectates or additives** include allergic reactions; facial flushing; high spinal anesthesia; and hypersensitivity or anaphylactoid reactions.
- **Other possible complications** include seizure; transient global amnesia; organic brain syndrome; and muscle spasm.

2.3. Comparator Treatments

Treatment for chronic back pain typically begins with the identification of the underlying cause of pain. Depending upon the diagnosis, a variety of treatments can be administered. These treatments, collectively referred to as conventional medical management (CMM), include conservative/non-invasive interventions such as physical therapy and rehabilitation, pharmaceutical pain management, psychological therapy and coping skills, exercise, education, antidepressants, cognitive behavioral therapy and supported self-management, spinal manipulation, electrical stimulation, injections outside the spine, implanted devices, acupuncture/acupressure, and modified work.[51] Treatment strategies generally begin with the least invasive and low risk interventions, progressing to more invasive techniques if CMM treatments are not effective.

2.4. Clinical Guidelines

The National Guideline Clearinghouse (NGC) and Google were searched for guidelines related to spinal corticosteroid injections in adults presenting with subacute or chronic lumbar or cervical pain. Key word searches were performed: ("spinal injections") AND ("chronic" OR "subacute").

Guidelines from the following sources are summarized below in Table 2:

- American society of Anesthesiologists Task Force on Chronic Pain Management & the American Society of Regional Anesthesia and Pain Medicine
- Colorado Division of Workers' Compensation
- Institute for Clinical Systems Improvement
- American Society of Interventional Pain Physicians
- Toward Optimized Practice
- United States Food and Drug Administration Safe Use Initiative, an expert multidisciplinary working group, and 13 specialty stakeholder societies

Table 2. Clinical Guidelines

Organization(s) Title (year)	Search Dates	Population Investigated	Intervention	Evidence Base Available	Recommendations	Level of Evidence
Manchikanti/ American Society of Interventional Pain Physicians[134] *An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part II: guidance and recommendations. (2013)*	1966 – 2012	Individuals with chronic spinal pain	• Epidural injections • Cervical interlaminar epidural injections • Cervical facet joint nerve blocks • Lumbar facet joint nerve blocks • Sacroiliac joint injections Sacroiliac joint blocks	NR	• Caudal, interlaminar, and transforaminal steroid injections may be used for lumbar radiculitis • Caudal, interlaminar, and transforaminal steroid injections may be used for lumbar spine stenosis	Good* Caudal & interlaminar injections : Fair* Transforaminal injections: limited*
American Society of Anesthesiologists Task Force/ American Society of Regional Anesthesia and Pain Management[10] *Practice Guidelines for Chronic Pain Management. An updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia*	1944 – 2009	Patients with chronic non-cancer neuropathic, somatic, or visceral pain syndromes	• Intraarticular facet joint injections • Sacroiliac joint injections • Epidural steroid injections (both transforaminal and interlaminar)	RCTs & Observational studies (study number NR) NR RCTs & Observational studies (study number NR)	• Intraarticular facet joint injections may be used for symptomatic relief of facet-mediated pain • Sacroiliac joint injections may be considered for symptomatic pain relief of sacroiliac joint pain • Epidural steroid injections may be used as part of a multimodal treatment regimen in select patients with radicular pain or radiculopathy	C2/ B2† D† Ranges: A3 – D†

Organization(s) Title (year)	Search Dates	Population Investigated	Intervention	Evidence Base Available	Recommendations	Level of Evidence
and Pain Medicine. (2010)						
Colorado Division of Workers' Compensation[60] *Chronic pain disorder medical treatment guidelines (2012)*	2001 – 2010	Individuals qualifying under Colorado's Workers' Compensation Act as injured workers with chronic pain	• Epidural steroid injections • Facet injections • Sacroiliac joint injections Intradiscal steroid injections	NR	• Intradiscal steroid injections are not recommended for discogenic back pain • Epidural injections should be limited to acute exacerbations of radicular pain • Facet joint injections are not recommended in subacute low back pain, and are only permitted in chronic low back pain • Sacroiliac joint injections are not recommended in subacute low back pain, and are only permitted in chronic low back pain.	NR
Colorado Division of Workers' Compensation[62] *Low back pain medical treatment guidelines. (2014)*	2006 – 2012	Individuals who qualify as injured workers with low back pain under Colorado Workers' Compensation Act	• Epidural injections • Intradiscal injections • Sacroiliac joint injections • Transforaminal injections with Etanercept Facet injections	NR	• There is no proven benefit from adding steroids to local anesthetic spinal injections, with the possible exception of patients who are strong candidates for surgery based on a herniated disc and clear nerve impingement. • Intradiscal steroid injections are not recommended for patients with non-radicular pain. • Sacroiliac joint injections may be used for low back pain. • Transforaminal injections with Etanercept are not recommended.	NR

Organization(s) Title (year)	Search Dates	Population Investigated	Intervention	Evidence Base Available	Recommendations	Level of Evidence
					• Facet injections are strongly not recommended for relief of non-radicular low back pain.	
Colorado Division of Workers' Compensation[61] *Cervical spine injury medical treatments. (2014)*	2006 – 2012	Those who qualify as injured workers with cervical spine injuries under the Colorado Workers' Compensation act.	• Epidural steroid injections (including transforaminal and interlaminar) • Intradiscal steroid injections • Transforaminal injections with Etanercept Facet injections	NR	• Epidural injections are not recommended for non-radicular cervical pain • Intradiscal injections in patients with non-radicular back pain are not recommended • Transforaminal injections with Etanercept is not recommended • Facet injections may be recommended	NR
Goertz/ Institute for Clinical Systems Improvement[89] *Adult acute and subacute low back pain. (2012)*	May 2011 – June 2012	≥18 years old in primary care who have symptoms of acute or subacute low back pain or radiculopathy	Epidural steroid injections	5 sources (study type NR)	• Epidural steroid injections may be used for LBP, with a radicular component to assist with short-term pain relief	Weak‡

Organization(s) Title (year)	Search Dates	Population Investigated	Intervention	Evidence Base Available	Recommendations	Level of Evidence
Hooten/Institute for Clinical Systems Improvement[103] *Assessment and management of chronic pain. (2013)*****	August 2011 – August 2013	≥18 years old with chronic pain	• Facet joint injections • Epidural corticosteroid injections • Transforaminal epidural injections Sacroiliac joint injections	1 SR 3 studies (type NR) 3 case reports, 2 studies (type NR) NR	• Facet joint injections have not been found to provide sustained therapeutic benefits • There is limited evidence to support the efficacy of epidural corticosteroid injections • Transforaminal epidural injections may be used for cervical procedures, when used as part of a longitudinal care plan • More studies are needed before a recommendation can be made for sacroiliac joint injections	Low§ High§ Low§ NR
Toward Optimized Practice[203] *Guideline for the evidence-informed primary care management of low back pain. (2011)*	January 2002 – December 2010	≥18 years old in primary care setting with nonspecific low back pain. Excluding: pregnant women; diagnosis or treatment of specific causes of low back pain such as: inpatient treatments; referred pain (from abdomen, kidney, ovary, pelvis, bladder); inflammatory conditions; infections; degenerative and structural changes; fracture; neoplasm; metabolic bone disease	• Epidural steroid injections • Medial branch blocks Intraarticular facet joint blocks	SRs (study number NR) & 8 Guidelines SR & IHE database	• Epidural steroid injections are recommended for those with chronic low back pain • Do not use epidural steroid injections in patients with acute or subacute low back pain without radiculopathy • Epidural steroid injections may be helpful in patients with acute or subacute low back pain in the presence of radiculopathy • Medial branch blocks and intraarticular facet joint blocks may be beneficial for patients with pain originating from lumbar facet joints	NR

Organization(s) Title (year)	Search Dates	Population Investigated	Intervention	Evidence Base Available	Recommendations	Level of Evidence
U.S. Food and Drug Administration Safe Use Initiative, an expert multidisciplinary working group, and 13 specialty stakeholder societies††[206] *Safeguards to Prevent Neurologic Complications after Epidural Steroid Injections (2015)*	NR	NR	Epidural steroid injections	Best available scientific evidence or expert opinion‡‡	• All cervical interlaminar ESIs should be performed using image guidance, with appropriate anteroposterior, lateral, or contralateral oblique views and a test dose of contrast medium. • Cervical transforaminal ESIs should be performed by injecting contrast medium under real-time fluoroscopy and/or digital subtraction imaging, usingan anteroposterior view, before injecting any substance that may be hazardous to the patient. • Cervical interlaminar ESIs are recommended to be performed at C7-T1, but preferably not higher than the C6-C7 level. • Particulate steroids should not be used in therapeutic cervical transforaminal injections. • All lumbar interlaminar ESIs should be performed using image guidance, with appropariate anteroposterior, lateral, or contralateral oblique views and a test dose of contrast medium. • Lumbar transforaminal ESIs should be performed by injecting contrast medium	NR

Organization(s) Title (year)	Search Dates	Population Investigated	Intervention	Evidence Base Available	Recommendations	Level of Evidence
					under real-time fluoroscopy and/or digital subtraction imaging, using an anteroposterior view, before injecting any substance that may be hazardous to the patient. • A nonparticulate steroid (e.g., dexamethasone) should be used for the initial injection in lumbar transforaminal epidural injections. • There are situations where particulate steroids could be used in the performance of lumbar transforaminal ESIs.	

ESI: Epidural Steroid Injection

* United States Preventative Task Force criteria:

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (at least 2 consistent, higher-quality RCTs or studies of diagnostic test accuracy).

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (at least one higher-quality trial or study of diagnostic test accuracy of sufficient sample size; 2 or more higher quality trials or studies of diagnostic test accuracy with some inconsistency; at least 2 consistent, lower-quality trials or studies of diagnostic test accuracy, or multiple consistent observational studies with no significant methodological flaws).

Poor or Limited: Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality trials, important flaws in trial design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

† Guideline definitions for Scientific Evidence:

Category A: supportive literature; RCTs that report statistically significant ($p<0.01$) differences between clinical interventions for a specified clinical outcome.

- Level 1: the literature contains multiple RCTs, and the aggregated findings are supported by meta-analyses
- Level 2: the literature contains multiple RCTs but there in an insufficient number of studies to conduct a viable meta-analysis
- Level 3: the literature contains a single RCT

Category B: suggestive literature; information from observational studies permits inference of beneficial or harmful relationships among clinical interventions and clinical outcomes.

- Level 1: the literature contains observational comparisons of clinical interventions or conditions and indicates statistically significant differences between clinical interventions for a specified clinical outcome
- Level 2: the literature contains non-comparative observational studies with associative or descriptive statistics
- Level 3: the literature contains case reports

Category C: equivocal literature; literature cannot determine whether there are beneficial or harmful relationships among clinical interventions and clinical outcomes.
Level 1: meta-analysis did not find significant differences among groups or conditions
Level 2: there is an insufficient number of studies to conduct meta-analysis and (1) RCTs have not found significant differences among groups or conditions or (2) RCTs report inconsistent findings
Level 3: observational studies report inconsistent findings or do not permit interference of beneficial or harmful relationships
Category D: insufficient evidence from literature; the lack of scientific evidence in the literature. (1) No identified studies address the specified relationships among interventions and outcomes. (2) The available literature cannot be used to assess relationships among clinical interventions and clinical outcomes. The literature either does not meet the criteria for content as defined in the "focus" of the guidelines or does not permit a clear interpretation of findings due to methodological concerns.

‡ Institute for Clinical Systems Improvement evidence grading:
High: further research is very unlikely to change our confidence in the estimate of effect.
Weak: The work group recognizes that the evidence, though of high quality, shows a balance between estimates of harms and benefits. The best action will depend on local circumstances, patient values or preferences.
Strong: The work group is confident that the desirable effects of adhering to this recommendation outweigh the undesirable effects. This is a strong recommendation for or against. This applies to most patients.
Moderate: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Weak: The work group recognizes that there is a balance between harms and benefit, based on moderate quality evidence, or that there is uncertainty about the estimates of the harms and benefits of the proposed intervention that may be affected by new evidence. Alternative approaches will likely be better for some patients under some circumstances.
Strong: The work group is confident that the benefits outweigh the risks, but recognizes that the evidence has limitations. Further evidence may impact this recommendation. This is a recommendation that likely applies to most patients.
Low: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change. The estimate or any estimate of effect is very uncertain.
Weak: The work group recognizes that there is significant uncertainty about the best estimates of benefits and harms.
Strong: The work group feels that the evidence consistently indicates the benefit of this action outweighs the harms. This recommendation might change when higher quality evidence becomes available.

§ Crosswalk between Institute for Clinical Systems Improvement evidence grading system and GRADE:
High: further research is very unlikely to change our confidence in the estimate of effect
Moderate: further research is likely to have an impact on our confidence in the estimate of effect and may change the estimate
Low: further research is very likely to have an impact on our confidence in the estimate of effect and is likely to change the estimate or any estimate of effect is very uncertain

** Guideline is an updated version of one included in previous report.

†† The U.S. FDA Safe Use Initiative group convened and facilitated teleconferences conducted by the working group (details not provided), which drafted, discussed, and formulated a set of clinical considerations. Once clinical considerations were drafted, representatives from a number of national pain organizations were invited to review and vote on them. New studies published after the initial vote were summarized by the working group and presented to the national organizations, who them revoted on clinical considerations given the new data.

‡‡ When evidence was lacking, expert opinion was sought both within the working group and from leading scientific societies or associations with interest or expertise in the subject of epidural injections.

2.5. Previous Systematic Reviews/Technology Assessments

We searched for systematic reviews and Health Technology Assessments addressing spinal injections and published since 2010. Systematic reviews were found by searching for systematic reviews in PubMed using the search strategy in Appendix B. We identified eight systematic reviews; all eight reported on epidural steroid injections, and one of the eight also evaluated facet joint injections. We summarize the systematic reviews in Table 3.

HTAs were found by searching for ("spinal injection"), ("epidural" AND "spine"), and ("spinal injection health technology assessment") in PubMed, the University of York Centre for Reviews and Dissemination database, and Google Scholar. We found a total of four Health Technology Assessments (HTAs). All report on epidural steroid injections (ESIs), two report on facet joint injections, two report on sacroiliac injections, and one reports on intradiscal injections (Table 4).

Table 3. Previous Systematic Reviews

Assessment (year) Search dates	Purpose	Condition	Treatments Vs Controls	Primary Outcomes	Evidence Base Used	Risk Of Bias Assessed	Quantitative Synthesis?	Primary Conclusions
Bicket (2013)[24] Database inception to 10/2012	To examine whether epidural injections of noncorticosteroid mixtures constitute a treatment or true placebo in patients with spinal pain	Back or neck pain w/or w/o radiculopathy	ESI vs. ENSI vs. non-epidural injection	Pain, positive response*	43 RCTs (3,641 patients)	Yes	Yes	Epidural nonsteroid injections may provide improved benefit compared with nonepidural injections on some measures, though few, low-quality studies directly compared controlled treatments, and only short-term outcomes (≤12 weeks) were examined.
Bicket (2015)[25] Database inception to 1/2013	To determine whether ESI reduce the need for surgery, compared with control treatments	Back pain w/ or w/o radiculopathy	ESI vs. any non-epidural steroid injection	Surgery†	26 RCTs (3,271 patients)	Yes	Yes	In the short-term (<1 year), 5 studies indicated that ESI showed a nonsignificant reduction in need for surgery; in the long term (≥1 year), 16 studies indicated that ESI did not significantly affect the need for surgery. Combining both long and short-term outcomes, 22 studies indicated that ESI showed a nonsignificant reduction in need for surgery.
Choi (2013)[49] 1950 to 10/2011	To assess the long term benefits of ESI	Lower back pain w/ radiculopathy	ESI vs. non-steroidal injection vs. other treatment (conservative, epiduroscopy, or interspinous lig injection)	Pain, disability, surgery‡	29 RCTs (2,040 patients)	Yes	Yes	After adjusting for baseline pain score, no significant differences in pain outcomes (17 studies) were found at 6 months or over longer terms. ESI did not improve disability (11 studies) or reduce the number of patients who underwent surgery (17 studies).
Henschke (2010)[97] NR to 11/2009	To evaluate the effectiveness and safety of injection therapies and denervation procedures for the	Chronic lower back pain	Facet joint corticosteroid injections vs. placebo vs. other treatments	Pain intensity, functional status§	9 RCTs (594 patients)	Yes	Yes	There is low to very low quality of evidence to support injection therapy over placebo or other treatments for patients with chronic low-back pain. Intra-articular facet joint corticosteroid

Assessment (year) Search dates	Purpose	Condition	Treatments Vs Controls	Primary Outcomes	Evidence Base Used	Risk Of Bias Assessed	Quantitative Synthesis?	Primary Conclusions
	management of chronic low-back pain		(local anesthetic, mixture of anesthetics and corticosteroids with home stretching, sodium hyaluronate, Sarapin) Epidural space corticosteroid injections vs. other treatment (anesthetic, benzodiazepine or spinal endoscopy)					injections are slightly more effective for short-term pain relief than placebo (1 study) or facet nerve blocks (1 study). However, no significant differences in pain intensity and functional status were indicated between intra-articular facet joint corticosteroid injections and a mixture of local anesthetics, corticosteroids and home stretching (1 study), sodium hyaluronate injections (1 study), or medial branch blocks with or without corticosteroids (1 study). There was no significant difference for pain relief over the short to intermediate follow-up term for epidural corticosteroids vs. benzodiazepine injection or targeted epidural anesthetics.
Liu (2015)[127] NR to 9/2014	To investigate the effectiveness and safety of ESI in patients with lumbar spinal stenosis (LSS)	Lumbar spinal stenosis	ESI vs. placebo injection (local anesthetic) or control (no further details provided)	Pain, walking ability, adverse effects of ESI**	10 RCTs (1,010 patients)	Yes	Yes	Minimal or no significant differences were found between ESI and local anesthetic injection in terms of short-term benefit. However, significant differences were found between the ESI and local anesthetic injection groups regarding change in bodily pain (BP) at both 3 and 4 years, as well as the physical function (PF) subscale scores at 4 years.

Assessment (year) Search dates	Purpose	Condition	Treatments Vs Controls	Primary Outcomes	Evidence Base Used	Risk Of Bias Assessed	Quantitative Synthesis?	Primary Conclusions
Zhai (2015)[242] NR to 10/2014	To assess the effects of ESI in managing various chronic low and lower extremity pain	Chronic pain of disc herniation or radiculitis	ESI vs. placebo injection (local anesthetic)	Pain, functional assessment, opioid intake††	10 RCTs (1,111 patients)	Yes	Yes	No significant differences were found between ESI and placebo injection in terms of pain relief, functional assessment, or opioid intake.
Pinto (2012)[201] Database inception to 4/27/2012	To determine efficacy of ESI for sciatica, compared with placebo	Sciatica	ESI vs. placebo (inert or innocuous substance injection)	Pain, disability‡‡	23 RCTs (2,334 patients)	Yes	Yes	In the short-term (>2 weeks, ≤3 months), ESI provided small improvements in pain and disability compared with placebo in patients with sciatica however; the effects were less than the proposed threshold for clinically important change. Long-term effects (≤12 months) were not statistically significant and ESI showed no effect on low back pain.
Quraishi (2012)[205] 1966 to 2009	To assess the effectiveness of transforaminal ESI for treating low back and lumbar radicular pain	Low back or lumbar pain w/ radiculopathy	ESI vs. non-steroidal injections	Pain, disability§§	5 RCTs (499 patients)	NR	Yes	Transforaminal ESI improved pain but not disability outcomes. However, the 3 studies that followed patients to 3 months and the 1 study that followed patients to 12 months did not find any significant differences.

ESI: epidural steroid injection; ENSI: epidural non-steroid injection; RCT: Randomized Controlled Trial
* Positive response reported in studies as "positive response," "success," "relief of pain," and "50% or more reduction in pain"
† Surgery reported in studies as ''surgery,'' ''need for surgery,'' ''proceeding to surgery,'' ''transfer to surgery,'' ''referral to surgery'' or a specific surgical procedure
‡ Pain was reported in studies with the Visual Analogue Score (VAS) and disability with the Oswestry Disability Index (ODI)
§ Pain intensity was reported in studies with the VAS, numerical rating scale (NRS), or McGill pain questionnaire. Functional status was reported in studies with the Roland-Morris Disability Questionnaire (RMDQ), ODI, perceived recovery, or return to work
** Studies reported outcomes in terms of: RMDQ, VAS, Brief Pain Inventory (BPI), Swiss Spinal Stenosis Questionnaire (SSSQ), SF-36, EQ-5D, PHQ-8, GAD-7, Low Back Pain Bothersomness Scale (LBPBS), ODI, NRS, Low back outcome score (LBOS), Sciatica Bothersomeness Index (SBI), Leg Pain Bothersomeness Scale (LPBS), or Roland Morris Disability (RMDI)
†† The "overwhelming majority" of studies used the NRS to assess pain and the ODI to measure functional ability. No further details provided
‡‡ Scores for pain intensity and disability were converted to scales from 0 to 100
§§ Pain was reported in studies with the VAS and disability with the ODI

Table 4. Previous Health Technology Assessments

Assessment (year)	Search dates	Diagnosis	Treatments Evaluated	Evidence base available	Primary Conclusions	Critical Appraisal*
Chou (2015)[110] Agency for Health Care Research and Quality (AHRQ) *Pain Management Injection Therapies for Low Back Pain*	2008 to 10/2014	Low back pain	Epidural corticosteroid injections Facet joint corticosteroid injections Medial branch blocks Sacroiliac corticosteroid injections	<u>Epidural Injection</u> 78 RCTs; 29 compared steroid injection to placebo <u>Facet Joint Injection</u> 13 RCTs <u>Medial branch blocks</u> 0 studies <u>Sacroiliac Injection</u> 1 RCT	**Efficacy:** <u>Epidural injection:</u> - Significant effect on mean improvement in pain at immediate-term F/U for ESI compared to placebo. MCID was not reached regarding pain and function at long-term F/U. No heterogeneity of treatment effect found regarding injection technique, patient characteristics, or comparators. - ESI vs. nonplacebo interventions did not clearly demonstrate effectiveness. <u>Facet joint injections:</u> - There are no clear differences between various facet joint corticosteroid injections (intraarticular, extra-articular, or medial branch) and placebo interventions. <u>Sacroiliac Injections:</u> - Insufficient evidence to determine efficacy of sacroiliac joint corticosteroid injections. **Safety**: <u>Epidural injection:</u> - Trials comparing ESI to placebo reported no serious AEs & few harms. Observational studies consistent with the finding of low risk of serious AEs. - Trials comparing ESI vs. other therapies reported no serious AEs and few harms. <u>Facet Injections:</u> - Trials reported no serious harms and few adverse events. <u>Sacroiliac Injections:</u> - NR **Economic: NR**	**Yes, SOE in AHRQ Methods Guide**
Ollendorf (2011)[197] Institute for	1/2000 to 2/2011	• All diagnoses had subacute or chronic low	Epidural steroid injections	Epidural steroid injections: NR	**Efficacy**: <u>Epidural injection, lumbar disc herniation</u>: - Mixed evidence regarding treatment success in studies comparing ESI to various control groups.	**Yes, U.S. Preventive Services Task Force**

Assessment (year)	Search dates	Diagnosis	Treatments Evaluated	Evidence base available	Primary Conclusions	Critical Appraisal*
Clinical and Economic Review (ICER) *Management Options for Patients With Low Back Disorders* Ollendorf (2011) (continued)		back and/or leg pain who have continued symptoms following a minimum of 4-6 weeks of simple conservative management Lumbar spinal stenosis Lumbar disc herniation Degenerative /isthmic spondylolisthesis Non-specific low back/leg pain			- Mixed evidence regarding pain and function improvement over short-term F/U in patients with lumbar disc herniation in studies of ESI. - Evidence is inconclusive regarding ESI impact on Quality of Life and employment status <u>Epidural injection, lumbar spinal stenosis:</u> - Limited evidence that there is no significant difference in patients achieving pain relief >50% at short-, intermediate-, and long-term follow-up when comparing ESI to saline/local anesthetic. - ESI confers no incremental benefit in pain or function in short- or long-term follow-up. - One RCT reported no significant between-group difference between ESI and PT or control injections for Quality of Life outcomes. - Employment status did not differ significantly between ESI and control patients. <u>Degenerative spondylolisthesis:</u> - No studies were found for this patient population comparing ESI to other treatments. <u>Non-specific low back pain:</u> - There is no difference in “treatment success” in the long- or short-term follow-up between treatment with ESI or local anesthetic. - There is no difference in “treatment success” in the long- or short-term follow-up between treatment with medial branch blocks or local anesthetic injections. - There is no difference in benefit on pain or function for ESI, intradiscal steroid injections, or therapeutic medical branch blocks. - There is limited evidence indicating significant improvement in pain from sacroiliac steroid injections vs. local anesthetic injections. - ESI confers no additional benefit regarding return to work. - 1 SR indicates that lumbar spinal injections of any	**(AHRQ 2008)**

Assessment (year)	Search dates	Diagnosis	Treatments Evaluated	Evidence base available	Primary Conclusions	Critical Appraisal*
					type range from 2 to 4 annually - There is sparse data indicating that the need for surgical intervention arises in 14-36% of patients with nonspecific low back pain, lumbar disc herniation, or foraminal stenosis by 12 months following initial injection. **Safety**: - There is limited evidence to support low rates of major and minor complications resulting from spinal injections. **Economic: NR**	
Armon (2007)[14] American Academy of Neurology (AAN) *Assessment: Use of epidural steroid injections to treat radicular lumbosacral pain*	NR to 2/2005	Radicular lumbosacral pain	Epidural steroid injections	Epidural steroid injections : 6 RCTs	**Efficacy:** - ESIs may result in some improvement in radicular lumbosacral pain between 2 to 6-weeks follow-up when compared to control. - ESIs confer no additional benefit compared to control on function, need for surgery, or long-term pain relief beyond 3 months. Routine use for these indications is not recommended. **Safety: NR** **Economic: NR**	**Yes, details not provided**
Nielens (2006)[194] KCE Belgian Health Care Knowledge Centre *Chronic low back pain, KCE reports vol. 48 C*	NR	Chronic >3 months low back pain, with or without sciatica	Epidural corticosteroid injections Facet injections Sacroiliac joint injections Intradiscal injections	Epidural corticosteroid injections: 2 guidelines Facet injections: 3 guidelines Sacro-iliac joint injections: 1 guideline Intradiscal injections:	**Efficacy:** <u>Epidural corticosteroid injections:</u> - No evidence for the effectiveness of ESI in non-specific, non-radicular common low back pain. - Evidence is conflicting for the effectiveness of ESIs in CLBP patients with radicular pain. - There is low-quality evidence in a mixed chronic and sub-acute population of CLBP with sciatica for the effectiveness of transforaminal ESIs for sciatica (but not in extruded disc herniations). <u>Facet injections:</u> - There is insufficient evidence to establish effectiveness of facet injections in CLBP.	**Yes, details not provided**

Assessment (year)	Search dates	Diagnosis	Treatments Evaluated	Evidence base available	Primary Conclusions	Critical Appraisal*
Nielens (2006) (CONTINUTED)				1 guideline	Sacro-iliac joint injections: - Very limited evidence to support the effectiveness of sacroiliac injections in short-term follow-up. Intradiscal injections: - Efficacy of therapeutic intradiscal injections is unestablished. **Safety:** Epidural corticosteroid injections: - Safety of ESIs is unknown. - Minor side effects appear frequent but transient; major side effects or complications are uncommon but can be dramatic. Facet injections: - Safety of facet injections is unknown. Sacroiliac joint injections: - Safety of sacroiliac injections is unknown. Intradiscal injections: - There is concern about important adverse effects such as septic discitis, spondylodiscitis, progressive degeneration of disc related to corticosteroids, and anaphylaxis due to radio-opaque solutions. AEs remain understudied. **Economic: NR**	

NR: Not Reported; RCT: Randomized Controlled Trial; SR: Systematic Review
* Critical appraisal refers to formal evaluation of individual study quality using criteria such as the GRADE methods of scoring and the determination of overall strength of evidence.

2.6. Medicare and Representative Private Insurer Coverage Policies

Payer websites previously cited in the 2010 report were searched for updated coverage decisions on the use of epidural steroid injections for the treatment of spinal pain. Policy decisions were identified from four national bell weather payers and two local payer policies. Coverage policies are consistent for the coverage of epidural steroid injection in select patients, although criteria for patient selection vary across plans. Documented success with diagnostic injections is frequently required to proceed to therapeutic injection. Coverage is not consistent for facet joint injections, sacroiliac joint injections, and intradiscal injections. When covered, injections are subject to spacing requirements between procedures, yearly and/or lifetime maximums.

Table 5, below, provides an updated overview of policy decisions as reported in Table 3 in the 2010 report.

National policy decisions:

- **Medicare**
  - No national coverage decisions were found for any spinal injections.

- **Aetna (2015)**
  Aetna will cover the following procedures as specified, but only one procedure will be covered at a time:
  - Epidural injections: Aetna will cover epidural injections of corticosteroid preparations with or without anesthetic agents in the outpatient setting to relieve back or neck pain when **all** of the following conditions are met:
    - Intraspinal tumor or other space-occupying lesion, or non-spinal origin for pain, has been ruled out as the cause of pain;
    - Two or more weeks of treatment with conservative measures (e.g. rest, systemic analgesics and/or physical therapy) have not improved pain;
    - Epidural injections beyond the first set of three injections are provided as part of a comprehensive pain management program, which includes physical therapy, patient education, psychosocial support, and oral medications, where appropriate.

    Repeat epidural injections beyond the first set of 3 injections are considered medically necessary when provided as part of a comprehensive pain management program, which includes physical therapy, patient education, psychosocial support, and oral medications, where appropriate. Repeat epidural injections more frequently than every 7 days are not considered medically necessary. Up to 3 epidural injections are considered medically necessary to diagnose a member's pain and achieve a therapeutic effect; if the member experiences no pain relief after three epidural injections, additional epidural injections are not considered medically necessary. Once a therapeutic effect is achieved, it is rarely medically necessary to repeat epidural injections more frequently than once every 2 months. In selected cases where more definitive therapies (e.g., surgery) cannot be tolerated or provided, additional epidural injections may be considered medically necessary. Repeat injections extending beyond 12 months may be reviewed for continued medical necessity.

Epidural injections are considered experimental and investigational for all other indications.

- Selective nerve root blocks/selective transforaminal epidural injection: Aetna will cover selective nerve root blocks for patients with radiculopathy when other non-invasive measures (e.g. physical therapy, non-narcotic analgesics) have failed or become intolerant and **any one** of the following conditions is met:
    - Radicular pain that is due to post-surgical or post-traumatic scarring;
    - Radicular pain when surgically correctable lesion cannot be identified;
    - Radicular pain in persons with surgically correctable lesions but who are not surgical candidates.

  Selective nerve root blocks should be administered as part of a comprehensive pain management program. Administration of more than three injections over six months is subject to review.

  Aetna will cover diagnostic selective nerve root blocks for patients with chronic radiculopathy, where diagnosis remains uncertain after standard evaluation (e.g., neurological examination, radiological and neurodiagnostic studies)

  Selective nerve root blocks are considered experimental and investigational for all other indications.

- Facet joint injections: Aetna only considers diagnostic facet joint injections to be medically necessary. Therapeutic injections are classified as experimental and investigational as treatment for back and neck pain and for all other indications. Therapeutic facet joint injections are found to have no proven value.
- Sacroiliac joint injections: Aetna will cover sacroiliac joint injections when they are used to relieve pain associated with lower lumbosacral disturbances in patients, provided the patient meets **both** of the following conditions:
    - The patient has back pain for more than three months;
    - The injections are provided as part of a comprehensive pain management program, including physical therapy, patient education, psychosocial support, and oral medication where appropriate.

  Aetna will cover up to two sacroiliac injections for diagnosis and treatment; additional injections are not covered if the patient experiences no symptom relief or functional improvement from two injections. It is not considered medically necessary to repeat these injections more frequently than once every 7 days. Once the diagnosis is established, it is rarely medically necessary to repeat sacroiliac injections more frequently than once every two months. Repeat injections extending beyond 12 months may be reviewed for continued medical necessity.

Sacroiliac joint injections are considered experimental and investigational for all other indications.

- **Cigna (2015)**
  Cigna will cover the following procedures as specified below. Ultrasound guidance for injections is considered experimental, investigational, or unproven and is not covered.
  - Epidural steroid injection/selective nerve root block: CIGNA covers epidural steroid injection for acute or recurrent radicular pain when a trend toward improvement is not seen after at least six weeks of conservative treatment (e.g. pharmacological therapy, physical therapy, exercise).
    CIGNA will cover subsequent epidural steroid injections/selective nerve root blocks as medically necessary when prior injections resulted in beneficial clinical response, cervical, thoracic or lumbar radicular pain has persisted or worsened and there is a minimum interval of two months between injection sessions.

    Long-term, repeated, or maintenance injection is not covered. Epidural steroid injection for acute, subacute, or chronic back pain is considered experimental, investigational, or unproven.
    - Sacroiliac joint injection: CIGNA will cover sacroiliac joint injection for the treatment of back pain associated with localized sacroiliac joint confirmed on imaging studies.
    - Intradiscal steroid injection: CIGNA does not cover intradiscal steroid injection because it is considered experimental, investigational, or unproven.

- **Humana (2015)**
  Humana will cover the following procedures as specified below. Ultrasound guidance for injections is considered experimental, investigational, or unproven and is not covered.
  - Epidural steroid injections: Humana may cover epidural steroid injections when **all** of the following conditions are met by the patient:
    - Failure to improve after three months of conservative therapy including, but not limited to, rest, systematic medications and/or physical therapy
    - Pain is radicular
    - No more than three nerve root levels are injected per session
    - Diagnostic epidural steroid injection (two injections) is successful
    - Injections must be at least two months apart, provided the patient has at least 50% relief in pain and/or symptoms for six weeks;
    - A total of four therapeutic injections per region (i.e., cervical, thoracic, lumbar) may be given per rolling calendar year upon return of pain and/or deterioration in function and only when responsiveness to prior injections has occurred.

    Patients may also be eligible if pain has been unresponsive to conservative measures and is related to diagnoses of cancer, reflex sympathetic dystrophy, lumbar spinal stenosis, or herpes zoster/post-herpetic neuralgia.

- Facet joint injections/medial branch blocks: Humana may cover facet joint injections or medial branch nerve blocks for back or neck pain when facet joint syndrome is suspected and **all** of the following criteria are met:
  - Absence of radiculopathy
  - Diagnosis of back or neck pain was at least three months ago and has been unresponsive to conservative treatment (e.g. rest, systematic medications and/or physical therapy)
  - No more than three levels of facet joint injections per side, per region may be injected per session
  - Pain is aggravated by extension, rotation or lateral bending of the spine and is not typically associated with neurological deficits.
  - Diagnostic injection (two series of injections) is successful
  - A total of four therapeutic facet injections per region per rolling calendar year may be covered upon return of pain and/or deterioration in function and only when responsiveness to prior injections has occurred.

- Sacroiliac joint injections: Humana may cover sacroiliac joint injections when **all** of the following criteria are met:
  - Chronic low back pain with symptoms present for at least three months
  - Failure of conservative treatment (e.g., medications, and/or rest and/or physical therapy)
  - Diagnostic injection (two series of injections) is successful with 50% reduction in pain and/or symptoms
  - Injections are at least two months apart provided that the patient has at least a 50% relief in pain and/or symptoms for six weeks.
  - A total of four therapeutic injections per rolling calendar year may be performed only upon return of pain and/or deterioration in function and only when responsiveness to prior injections has occurred.

- **United Health Care**
  United Health Care will cover the following procedures as specified below.

  - Epidural steroid injection: United Health Care will cover epidural steroid injection for patients with acute and sub-acute sciatica or radicular pain caused by spinal stenosis, disc herniation, or degenerative changes in the vertebrae. They are approved for short-term use provided the following conditions are met by the patient:

    - The pain is associated with symptoms of nerve root irritation and/or low back pain due to disc extrusions and/or contained herniations;

    - The pain has been unresponsive to conservative treatment (e.g. medications, physical therapy, exercise).

  - Facet joint injection: United Health Care will only cover diagnostic facet joint injection. Therapeutic facet joint injection is considered unproven due to conflicting clinical

evidence for facet joint syndrome and a lack of evidence for the effectiveness of facet joint injections over placebo at reducing chronic spinal pain.

Local policy decisions:

- **BCBS Regence Group (Idaho, Oregon, Utah, and most of Washington) (2009)**
  - Facet joint injection: Therapeutic facet joint injection may be covered when performed under fluoroscopy for the management of chronic neck or back pain (pain lasting at least three months despite conservative treatment such as physical therapy and non-steroidal anti-inflammatory medication). Facet joint injections for the treatment of acute back or neck pain are not considered medically necessary. Patients must meet the following criteria for injections to be considered medically necessary:
    - One injection per level per side every two months or longer provided the patient has achieved at least 50% pain relief in six weeks. The medical record must clearly document responsiveness to prior injections indicating improvement in physical and functional status;
    - Injections are limited to a maximum of six per year;
    - A maximum of 16 injections in a lifetime is rarely considered medically necessary. Exceptions to the lifetime limit include:
      - Pathology involving both cervical and lumbar spine;
      - Bilateral facet joint injections;
      - Recurrence of symptoms at least two years after previous successful facet joint injection treatments.

- **Nordian Healthcare Solutions (Washington)**
  Nordian Healthcare Solutions will cover the following procedures as indicated below (see Table 5 for procedural requirements):
  - Lumbar epidural steroid injection: Covered after failure of four weeks of non-surgical, non-injection care (with specific exceptions) for patients with pain associated with suspected radicular pain, neurogenic claudication and/or moderate to severe low back pain (NPRS ≥ 3/10) associated with significant impairment of activities of daily living and one of the following:
    - Substantial imaging abnormalities such as a central disc herniation
    - Severe degenerative disc disease or central spinal stenosis

  - Facet joint injection or medial branch blocks: covered when the following indications are met: at least three months of moderate to severe pain with functional impairment and an inadequate response to conservative care; pain is predominately axial and, with the exception of facet joint cysts, not associated with radiculopathy or neurogenic claudication; and clinical assessment implicates the facet joint as the putative source of pain and there is no non-facet pathology that could explain the source of pain. Repeat intraarticular injections or medial branch blocks may be covered if the first injection results in > 50% pain relief for at least three months. A maximum of five facet joint injection sessions may be performed per rolling twelve month year in the cervical/thoracic spine and five in the lumbar spine.

Table 5. Overview of payer technology assessments and policies for spinal injections

Payer (Year)	Evidence Base Available	Policy	Rationale / Comments
National policies			
Aetna Clinical Policy Bulletin: Back Pain – Invasive Procedures (0016) (2015) Last review: 06/02/15 Next review: 01/07/2016 Clinical Policy Bulletin: Selective Nerve Root Blocks (0722) (2014) Last Review: 11/05/15 Next Review: 08/27/15	<u>Epidural injection:</u> 2 Practice Guidelines (AAN & APS) <u>Facet joint injection:</u> 2 RCTs 1 SR 1 technology assessment 3 practice guidelines (APS, AANS, ACOEM) <u>Sacroiliac joint injection:</u> NR <u>Selective nerve root blocks:</u> 1 RCT 1 meta-analysis 5 observational studies 2 SR 1 technology assessment (ICSI)	Aetna will cover the following procedures as specified, but only one procedure will be covered at a time: <u>Epidural injection:</u> Aetna will cover epidural injections of corticosteroid preparations with or without anesthetic agents in the outpatient setting to relieve back or neck pain when all of the following conditions are met: • Intraspinal tumor or other space-occupying lesion, or non-spinal origin for pain, has been ruled out as the cause of pain; • Two or more weeks of treatment with conservative measures (e.g. rest, systemic analgesics and/or physical therapy) have not improved pain; • Epidural injections beyond the first set of three injections are provided as part of a comprehensive pain management program, which includes physical therapy, patient education, psychosocial support, and oral medications, where appropriate. Repeat epidural injections beyond the first set of 3 are covered when provided as part of a comprehensive pain management program <u>Facet joint injections:</u> Aetna will cover diagnostic facet joint injections only. <u>Sacroiliac joint injections</u> Aetna will cover sacroiliac joint injections when they are used to relieve pain associated with lower lumbosacral disturbances in patients, provided the patient meets both of the following conditions: The patient has back pain for more than three months; The injections are provided as part of a comprehensive pain management program, including physical therapy, patient education, psychosocial support, and oral medication where appropriate. <u>Selective nerve root blocks:</u> Aetna will cover selective nerve root blocks with imaging guidance for patients with radiculopathy when other non-invasive measures (e.g. physical therapy, non-narcotic analgesics) have failed or become intolerant and any one of the following conditions is met: • Radicular pain that is due to post-surgical or post-traumatic scarring; • Radicular pain when surgically correctable lesion	

Payer (Year)	Evidence Base Available	Policy	Rationale / Comments
		cannot be identified; • Radicular pain in persons with surgically correctable lesions but who are not surgical candidates. Selective nerve root blocks should be administered as part of a comprehensive pain management program. Administration of more than 3 SNRBs per 6 months is subject to review for medical necessity.	
CIGNA Medical Coverage Policy: Minimally Invasive Treatment of Back Pain (0139) (2015) Last Review: 07/15/2015 Next Review: 07/15/2016	Epidural injection: 2 SR 5 practice guidelines (ASIPP, ACOEM, AANS, ASA, NASS) 1 technology assessment (AAN) Facet joint injection: 1 SR 1 technology assessment CADTH 4 practice guidelines (ASIPP, ACOEM, AANS, ASA/ASRA) Sacroiliac joint injection: 4 practice guidelines (ASIPP, ACOEM, ASA/ASRA, APS) Intradiscal injection: 1 practice guideline (ACOEM)	Epidural steroid injection/selective nerve root block: CIGNA covers epidural steroid injection for acute or recurrent radicular pain when a trend toward improvement is not seen after at least three weeks of conservative treatment (e.g. pharmacological therapy, physical therapy, exercise). CIGNA will cover subsequent epidural steroid injections/selective nerve root blocks as medically necessary when prior diagnostic/stabilization injections resulted in beneficial clinical response (e.g., improvement in pain, functioning, activity tolerance) and BOTH of the following criteria are met: • Cervical, thoracic or lumbar radicular pain (e.g., sciatica) has persisted or worsened • Minimum interval of two months between injection sessions A maximum of four therapeutic injection treatment sessions may be covered for the same diagnosis/condition within a 12-month period, if preceding therapeutic injection resulted in more than 50% relief for at least two months. Long-term repeated or maintenance injections, injections without radiculopathy, and injections with ultrasound guidance are not covered. Facet joint injection: CIGNA will cover a diagnostic facet joint injections only Sacroiliac joint injection: CIGNA will cover sacroiliac joint injection for the treatment of back pain associated with localized sacroiliac joint pathology confirmed on imaging studies. Intradiscal steroid injection: Not covered.	CPT codes if conditions met: 27096, 62310, 62311, 64479, 64480, 64481, 64482, 64483, 64484, 66490, 66491, 66492, 66493, 66494, 66495 HCPCS code if conditions met: G0269
Humana Medical Coverage Policy: Injections for Pain Conditions (CLPD-	NR	Epidural steroid injections: Humana may cover epidural steroid injections when all of the following conditions are met by the patient: • Failure to improve after three months of conservative therapy including, but not limited to, rest, systematic medications and/or physical therapy	CPT codes if conditions met: 27096, 62310, 62311, 64479, 64480, 64483, 64484, 64490,

Payer (Year)	Evidence Base Available	Policy	Rationale / Comments
0486-013) (2015)		• Pain is radicular • No more than three nerve root levels may be injected per session • Diagnostic epidural steroid injection (two injections) is successful • Injections must be at least two months apart, provided the patient has at least 50% relief in pain and/or symptoms for six weeks; • A total of four therapeutic injections per region (i.e., cervical, thoracic, lumbar) may be given per rolling calendar year upon return of pain and/or deterioration in function and only when responsiveness to prior injections has occurred. Patients may also be eligible if pain has been unresponsive to conservative measures and is related to diagnoses of cancer, reflex sympathetic dystrophy, lumbar spinal stenosis, or herpes zoster/post-herpetic neuralgia. <u>Facet joint injections/medial branch blocks</u>: Humana may cover facet joint injections or medial branch nerve blocks for back or neck pain when facet joint syndrome is suspected and all of the following criteria are met: • Absence of radiculopathy • Diagnosis of back or neck pain was at least three months ago and has been unresponsive to conservative treatment (e.g. rest, systematic medications and/or physical therapy) • No more than three levels of facet joint injections per side, per region may be injected per session • Pain is aggravated by extension, rotation or lateral bending of the spine and is not typically associated with neurological deficits. • Diagnostic injection (two series of injections) is successful • A total of four therapeutic facet injections per region per rolling calendar year may be covered upon return of pain and/or deterioration in function and only when responsiveness to prior injections has occurred. <u>Sacroiliac joint injections:</u> Humana may cover sacroiliac joint injections when all of the following criteria are met: • Chronic low back pain with symptoms present for at least three months • Failure of conservative treatment (e.g., medications,	64491, 64492, 64493, 64494, 64495, 77003 HCPCS codes if conditions met: G0260

Payer (Year)	Evidence Base Available	Policy	Rationale / Comments
		and/or rest and/or physical therapy) • Diagnostic injection (two series of injections) is successful • Injections are at least two months apart provided that the patient has at least a 50% relief in pain and/or symptoms for six weeks. • A total of four therapeutic injections per rolling calendar year may be performed only upon return of pain and/or deterioration in function and only when responsiveness to prior injections has occurred.	
UnitedHealthcare Medical Policy: Epidural Steroid and Facet Injections for Spinal Pain (2015T0004U) (2015) Last Update: 06/01/15	Epidural steroid injection: 10 RCTs 1 prospective cohort 1 SR 1 literature review 5 practice guideline (ASA, AAN, ASIPP, AANS, NASS) Facet joint injection: 7 RCTs 3 observational studies 2 SR 2 practice guideline (ACR & ASIPP)	Epidural steroid injection: UnitedHealthcare will cover epidural steroid injection for patients with acute and sub-acute sciatica or radicular pain caused by spinal stenosis, disc herniation, or degenerative changes in the vertebrae. They are approved for short-term use provided the following conditions are met by the patient: • The pain is associated with symptoms of nerve root irritation and/or low back pain due to disc extrusions and/or contained herniations; and • The pain has been unresponsive to conservative treatment (e.g. medications, physical therapy, exercise). Facet joint injection: UnitedHealthcare will cover diagnostic facet joint injection and/or facet nerve block only.	CPT codes if conditions met: 62311, 64483, 64484, 64490, 64491, 64492, 64493, 64494, 64495
Local policies			
BCBS Regence Group (ID, OR, UT, much of WA) Medical Policy: Facet Joint Injections (135) (2014)	Facet joint injection: 1 practice guideline (ASIPP)	Facet joint injection: Diagnostic or therapeutic facet joint injection may be covered when performed under fluoroscopy for the management of chronic neck or back pain (pain lasting at least three months despite conservative treatment such as physical therapy and non-steroidal anti-inflammatory medication). Facet joint injections for the treatment of acute back or neck pain are not considered medically necessary. Patients must meet the following criteria for injections to be considered medically necessary: • One injection per level per side every two months or longer provided the patient has achieved at least 50% pain relief in six weeks. The medical record must clearly document responsiveness to prior injections	CPT codes if conditions are met: 64490, 64491, 64492, 64493, 64494, 64495, 77003, 0213T, 0214T, 0215T, 0216T, 0217T, 0218T

Payer (Year)	Evidence Base Available	Policy	Rationale / Comments
		indicating improvement in physical and functional status; • Injections are limited to a maximum of six per year; • A maximum of 16 injections in a lifetime is rarely considered medically necessary. Exceptions to the lifetime limit include: • Pathology involving both cervical and lumbar spine; • Bilateral facet joint injections; • Recurrence of symptoms at least two years after previous successful facet joint injection treatments.	
Nordian Healthcare Solutions, LLC LCD: Lumbar Epidural Injections (L34980)	Lumbar epidural injection: 2 RCT 1 sub-study from an RCT 4 SR	Lumbar epidural injections: Nordian Healthcare will cover lumbar epidural steroid injection after failure of four weeks of non-surgical, non-injection care (with specific exceptions) for patients with pain associated with suspected radicular pain, neurogenic claudication and/or moderate to severe low back pain (NPRS ≥ 3/10) associated with significant impairment of activities of daily living and one of the following: • Substantial imaging abnormalities such as a central disc herniation • Severe degenerative disc disease or central spinal stenosis Procedural requirements include: • Real-time imaging guidance for all steroid and transforaminal injections • For each session, no more than 80 mg of triamcinolone, 80 mg of methylprednisolone, 12 mg of betamethasone, 15 mg of dexamethasone or equivalent corticosteroid dosing may be used • No more than two transforaminal, one caudal interlaminar or one lumbar interlaminar may be performed per session • No more than three epidurals may be performed in a six month period or no more than six epidural injection sessions may be performed in a twelve month period	CPT/HCPCS Codes: 62311, 62319, 64483, 64484
Nordian Healthcare Solutions, LLC LCD: Facet Joint Injections, Medial Branch Blocks, and Facet Joint Radiofrequency Neurotomy (L34995)	Facet joint injection and medial branch blocks: 1 RCT Facet joint radiofrequency neurotomy: 4 RCT 1 literature review 2 prospective	Nordian Healthcare will cover the following procedures as specified when the following indications are met: • At least three months of moderate to severe pain with functional impairment and an inadequate response to conservative care • Pain is predominately axial and, with the exception of facet joint cysts, not associated with radiculopathy or neurogenic claudication • Clinical assessment implicates the facet joint as the putative source of pain and there is no non-facet pathology that could explain the source of	CPT/HCPCS Codes: 64490, 64491, 64492, 64493, 64494, 64495, 64633, 64634, 64635, 64636, 0213T, 0214T, 0215T, 0216T, 0217T, 0218T

Payer (Year)	Evidence Base Available	Policy	Rationale / Comments
	cohort 2 retrospective chart review	pain Procedural requirements include: • Facet joint interventions must be performed under fluoroscopic or CT guidance. Facet joint interventions performed under ultrasound guidance will not be reimbursed. • Total IA injection volume must not exceed 1.0 mL per cervical joint or 2 mL per lumbar joint • Total MBB anesthetic volume must not exceed 0.5 mL per MB nerve for diagnostic purposes and 2 mL for therapeutic. • No more than 100 mg of triamcinolone or methylprednisolone or 15 mg of betamethasone or dexamethasone or equivalents shall be injected during any single session <u>Facet joint injection or medial branch blocks:</u> Nordian Healthcare may cover repeat intraarticular injections or medial branch blocks if the first injection results in > 50% pain relief for at least three months. A maximum of five facet joint injection sessions may be performed per rolling twelve month year in the cervical/thoracic spine and five in the lumbar spine <u>Thermal medial branch radiofrequency neurotomy:</u> Nordian Healthcare may cover facet joint denervation with RF medial branch neurotomy when dual medial branch blocks provide ≥ 80% pain relief and duration of pain is consistent with the agent employed. Repeat denervation procedures involving the same joint will only be considered necessary if the patient experienced ≥ 50% improvement of pain and improvement in patient specific ADLs for at least six months. For each covered spinal region, no more than two thermal RF sessions may be reimbursed in any rolling twelve-month year, involving no more than four joints per session. <u>Non-thermal radiofrequency:</u> Not covered. <u>Intraarticular and/or extraarticular facet joint prolotherapy:</u> Not covered.	

AAN: American Academy of Neurology; AANS: American Association of Neurological Surgeons; ACOEM: American College of Occupational and Environmental Medicine; ACR: American College of Radiology; APS: American Pain Society; ASA: American Society of Anesthesiologists ; ASIPP: American Society of Interventional Pain Physicians; ASRA: American Society of Regional Anesthesia and Pain Medicine; CADTH: Canadian Agency for Drugs and Technologies in Health; CPT: Current Procedural Terminology; HCPCS: The Healthcare Common Procedure Coding System; ICSI: Institute for Clinical Systems Improvement; NASS: North American Spine Society; NR: not reported.

3. The Evidence

3.1. Methods of the Systematic Literature Review

3.1.1. Objectives and key questions

This topic was reviewed in March 2011 and selected for re-review by the Director of the Washington State Health Care Director based on new literature identified. In addition, new safety concerns have emerged for epidural injections from the FDA. The objective of this Health Technology Assessment is to update the previous review on spinal injections. Specifically, the aim was to systematically review, critically appraise, analyze and synthesize research evidence evaluating the efficacy, comparative efficacy and safety of spinal injections in adults with subacute or chronic spinal pain.

Key Questions:

When used in adult patients with subacute or chronic back or neck pain:

1. What is the evidence of efficacy and effectiveness of spinal injections? Including consideration of:
    e. Short-term and long-term measures, including measures related to repeated spinal injections, multilevel spinal injections, bilateral versus unilateral spinal injections
    f. Impact on clinically meaningful physical function and pain
    g. Impact on quality of life, patient satisfaction
    h. Opioid use, return to work, and any other reported surrogate measures

2. What is the evidence of the safety of spinal injections? Including:
    i. Adverse event type and frequency (mortality, major morbidity, other)
    j. Dural or arachnoid puncture
    k. Infection
    l. Epidural or intradural hematoma
    m. Allergic reaction
    n. Nerve or spinal cord injury
    o. Artery/vein damage/puncture
    p. Arachnoiditis

3. What is the evidence that spinal injections have differential efficacy or safety issues in sub populations? Including consideration of:
    e. Patient characteristics (gender, age, psychological or psychosocial co-morbidities, diagnosis, duration of pain)
    f. Injection characteristics (type of steroid [particulate, non-particulate], use of guidance, route of administration. Other patient characteristics or evidence based on patient selection criteria
    g. Provider type, setting, or other provider characteristics
    h. Payer/ beneficiary type: including worker‘s compensation, Medicaid, state employees

4. What is the evidence of cost implications and cost-effectiveness of spinal injections? Including:
    c. Direct costs over short term and over expected duration of effect
    d. Comparative costs

3.1.2. Inclusion/exclusion

The inclusion and exclusion criteria are summarized in Table 6. Briefly, included studies met the following requirements with respect to participants, intervention, comparators, outcomes, and study design.

- *Population:* Adult patients with symptoms of subacute or chronic pain in the lumbar or cervical spine with or without radiculopathy or radiculitis. Subacute pain was defined as pain duration of 4 to 12 weeks prior to enrollment; chronic pain was defined as pain duration for longer than 12 weeks. We excluded studies of patients with back or neck pain due to acute major trauma, cancer, infection, cauda equina syndrome, spondyloarthropathy, osteoporosis or vertebral compression fracture.

- *Intervention:* For the intervention of epidural injections, results were stratified based on the condition: radicular lower or upper extremity pain, spinal stenosis, nonradicular axial pain, or pain from failed back or neck surgery. We accepted the authors' definition of radiculopathy, though the definition was not always explicit. Some authors simply used the term radiculopathy or sciatica, others described the presence of extremity pain, while some described motor or sensory deficit in a nerve root distribution. Facet joint injections for pain attributed to the facet joints were also included. These included injections into the joint (intraarticular), around the joint (extra- or peri- articular), or aimed at providing a therapeutic medial branch block. Studies of sacroiliac injections were included for low back pain presumed to originate from that joint. We excluded studies where the intervention was extraspinal injections (botulinum toxin, paraspinal muscle injections, prolotherapy), chemonucleolysis, radiofrequency denervation, intradiscal electrothermal therapy, and coblation nucleoplasty.

- *Comparators:* Comparators of interest encompassed control injections (injections with anesthetic and or saline/water, dry needling, or steroid injected into soft tissue). To assess epidural steroid injections, we compared those injections with different control groups. Since some believe there is therapeutic benefit from an epidural injection of a non-steroid substance,[24] we initially separated control group injections into epidural non-steroid injections (ENSI) consisting of epidural anesthetic and or saline/water, and non-epidural injections (NEI) that included dry needling, anesthetic and or saline/water into muscle or ligament (with studies of steroid NEI reported separately), procedures on the intervertebral disc (i.e., discectomy or disc ablation), and conservative care (i.e., physical therapy, exercise, no treatment).

- *Outcomes:* Outcomes of interest included pain, function, quality of life, opioid use, subsequent surgery, and complications. Primary outcomes were pain, function, subsequent surgery, and serious or catastrophic adverse events.

- *Study design:* Randomized controlled trials were used for Key Questions (KQ) 1-3. For KQ 2 on safety, we also included observational studies of at least 100 patients where harm detection was a primary objective, and reviews and FDA reports of cases sustaining serious harms. Formal economic analyses that met the population, intervention, and comparators of interest were included to evaluate cost-effectiveness in KQ 4.

Table 6. Summary of inclusion and exclusion criteria

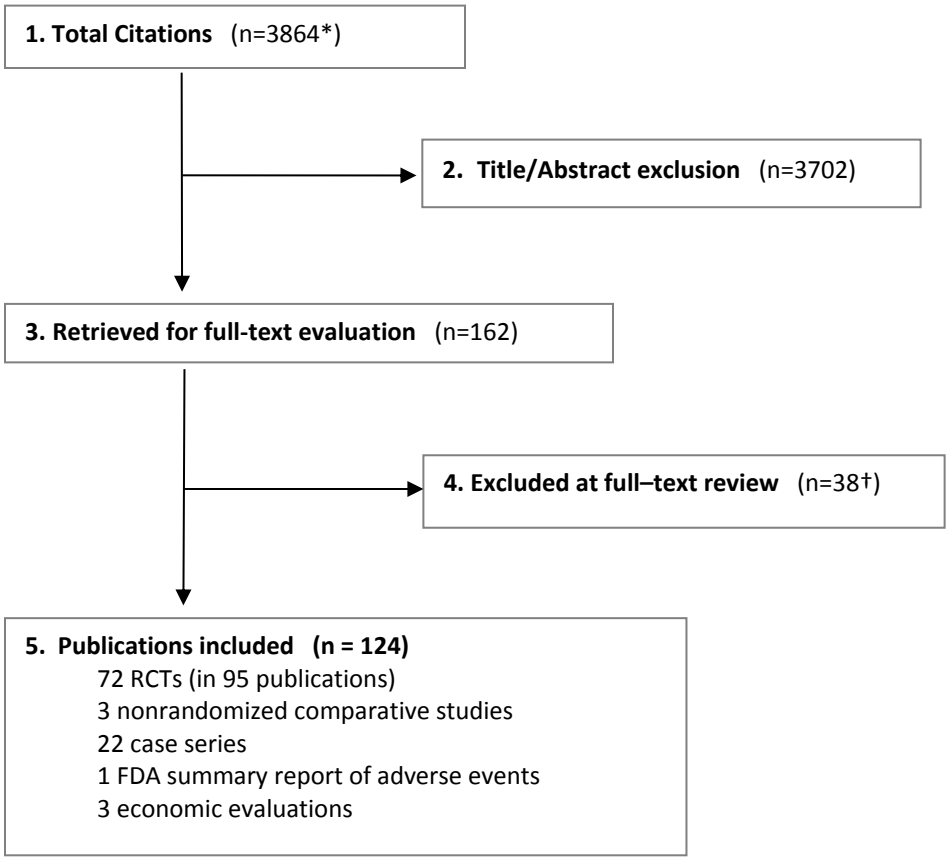
Study Component	Inclusion	Exclusion
Participants	Adults with: ◆ Cervical or lumbar sub-acute or chronic pain with or without radiculopathy or radiculitis	◆ Children ◆ Acute major trauma ◆ Cancer ◆ Infection ◆ Cauda equina syndrome ◆ Fibromyalgia ◆ Spondyloarthropathy ◆ Osteoporosis ◆ Vertebral compression fracture
Intervention	Lumbar, sacral or cervical therapeutic spinal injections to include: ◆ Epidural injections ◆ Facet joint injections ◆ Medial branch block ◆ Sacroiliac joint injections ◆ Intradiscal injections	◆ Extraspinal injections (Botulinum toxin injections, local injections, paraspinal muscle injections, prolotherapy) ◆ Chemonucleolysis ◆ Radiofrequency denervation, intradiscal electrothermal therapy, coblation nucleoplasty and related procedures ◆ Drugs added to corticosteroids such as hyaluronidase and clonidine
Comparators	◆ Control injections or non-injection controls	◆ Spinal steroid injections
Outcomes	◆ Pain ◆ Physical function ◆ Health-related quality of life ◆ Patient satisfaction ◆ Opioid use ◆ Prevention of surgery ◆ Complications and adverse effects (e.g. procedural complications and technical failures).	◆ Non-clinical outcomes
Study Design	◆ KQs 1 & 3: RCTs ◆ KQ 2: RCTs, observational studies with harm detection as primary purpose, and reviews of case reports of serious harms ◆ KQ 4: Formal economic studies	◆ Case series other than those with N ≥ 100 for key question 2 ◆ Case reports other than for context ◆ Non-clinical studies (e.g., technical reports) ◆ Studies in which < 75% (or an unreported percentage) of patients have any of the excluded diagnoses (see above)
Publication	◆ Studies published in English in peer reviewed journals, published HTAs or publicly available FDA reports ◆ Full formal economic analyses (e.g. cost-utility studies) published in English in an HTA, or in a peer-reviewed journal published after those represented in previous HTAs.	◆ Abstracts, editorials, letters ◆ Duplicate publications of the same study which do not report on different outcomes ◆ Single reports from multicenter trials ◆ Studies reporting on the technical aspects spinal injections ◆ White papers ◆ Narrative reviews ◆ Articles identified as preliminary reports when results are published in later versions ◆ Incomplete economic evaluations such as costing studies

3.1.3. Literature search and study selection

We searched electronic databases from January 1, 2010 to July 24, 2015 to identify new publications since our original report. Electronic databases searched include PubMed, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, and the National Guideline Clearinghouse (see Appendix B for full search strategy). We also hand searched the reference lists of all included studies and the bibliographies of several systematic reviews published since our last report (see Table 3 in the previous section).

The clinical studies included in this report were identified using the algorithm shown in Appendix A. The search took place in four stages. The first stage of the study selection process consisted of the comprehensive electronic search and bibliography check. We then screened all possible relevant articles using titles and abstracts in stage two. This was done by two individuals independently. Those articles that met a set of a priori retrieval criteria were included. Articles were selected for full-text review if they included epidural injections, facet joint injections, therapeutic medial branch injections, intradiscal injections or sacroiliac injections for lumbar or cervical radicular pain, spinal stenosis, or nonradicular axial pain. We excluded conference abstracts, non-English-language articles, and studies of nonhuman subjects. Any disagreement between screeners that were unresolved resulted in the article being included for the next stage. Stage three involved retrieval of the full text articles remaining. The final stage of the study selection algorithm consisted of the selection of those studies using a set of a priori inclusion criteria, again, by two independent investigators. Discrepancies were resolved through discussion and if necessary adjudicated by a third investigator. A list of excluded articles along with the reason for exclusion is available in Appendix C. The remaining articles form the evidence base for this report.

Figure 2. Flow chart of literature search results



*Number derived from literature search from 2011 HTA plus 2010-2015 updated search: 2760 + 1104 references
†Studies listed with reason for exclusion in Appendix C.

3.1.4. Data extraction

Reviewers extracted the following data from the clinical studies: study design, study period, setting, country, sample size, inclusion and exclusion criteria, study population characteristics, preoperative diagnoses, study interventions, follow-up time, use of imaging guidance, characteristics of the control intervention, and study outcomes (pain, function, health-related quality of life, opioid usage, and "success"), and adverse events. After discussion with our clinical expert (PS), we separated adverse events into catastrophic, serious and non-serious adverse events. We defined catastrophic adverse events as non-transient paralysis (tetraplegia, paraplegia), blindness, death, arachnoiditis, stroke, cardiac arrest, spinal cord infarction, spinal cord injury, and meningitis. Serious adverse events included epidural hematoma, deep infection, respiratory failure, spinal nerve injury, fever or infection attributed to the injection, hematoma, intravascular injection of steroid with neurologic sequelae, nerve root injury, retroperitoneal hematoma, subarachnoid injection, seroma, neurovascular complications, surgery or hospitalization necessary due to adverse events attributed to the procedure, and angina attributed to the procedure. The following were considered non-serious unless sufficient detail was reported to suggest that symptoms did not remit easily or were more severe: cerebrospinal fluid tap, dural pucture or tears, new neurological symptoms, sensory deficits, paresthesia and numbness in lower

extremity, excessive pain, procedural bleeding, and procedural hypotension. All other adverse events were considered to be non-serious in nature.

For economic studies, data related to sources used, economic parameters and perspectives, results, and sensitivity analyses were abstracted. An attempt was made to reconcile conflicting information among multiple reports presenting the same data.

3.1.5. Study quality and risk of bias (RoB) assessment

The method used by Spectrum Research, Inc. (SRI) for assessing the quality of evidence of individual studies as well as the overall strength of evidence (SoE) for each primary outcome incorporates aspects of the rating scheme developed by the Oxford Centre for Evidence-based Medicine,[187] precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group,[16] and recommendations made by the Agency for Healthcare Research and Quality (AHRQ).[238] Economic studies were evaluated according to The Quality of Health Economic Studies (QHES) instrument developed by Ofman et al.[195] Based on these quality criteria, each study chosen for inclusion for a Key Question was given a RoB (or QHES) rating; details of each rating are available in Appendix E. Standardized abstraction guidelines were used to determine the RoB (or QHES) rating for each study included in this assessment.

The SoE for all primary health outcomes was assessed by two researchers following the principles for adapting GRADE.[18,92,93] The strength of evidence was based on the highest quality evidence available for a given outcome. In determining the strength of body of evidence regarding a given outcome, the following domains were considered:

- Risk of bias: the extent to which the included studies have protection against bias
- Consistency: the degree to which the included studies report results that are similar in terms of range and variability.
- Directness: describes whether the evidence is directly related to patient health outcomes.
- Precision: describes the level of certainty surrounding the effect estimates.
- Publication bias: is considered when there is concern of selective publishing.

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 studies could be upgraded if the study had large magnitude of effect (strength of association). The final strength of evidence was assigned an overall grade of high, moderate, low, or insufficient, which are defined as follows:

- High - Very confident that effect size estimates lie close to the true effect for this outcome; there are few or no deficiencies in the body of evidence; we believe the findings are stable.
- Moderate – Moderately confident that effect size estimates lie close to the true effect for this outcome; some deficiencies in the body of evidence; we believe the findings are likely to be stable but some doubt remains.
- Low – Limited confidence that effect size estimates lie close to the true effect for this outcome; major or numerous deficiencies in the body of evidence; we believe that additional evidence is needed before concluding that findings are stable or that the estimate is close to the true effect.

- Insufficient – We have no evidence, are unable to estimate an effect or have no confidence in the effect estimate for this outcome; OR no available evidence or the body of evidence has unacceptable efficiencies precluding judgment.

Similar methods for determining the overall quality (strength) of evidence related to economic studies have not been reported, thus the overall strength of evidence for outcomes reported in Key Question 4 was not assessed.

3.1.6. Evidence synthesis and analysis

We summarized evidence for lumbar and cervical injections separately and by the indications for which treatment was given. The indications identified in included studies for the lumbar spine were radiculopathy attributed to disc pathology and or foraminal narrowing, radiculopathy due to multiple causes (e.g., disc pathology or spinal stenosis), low back pain without radiculopathy, spinal stenosis, failed back syndrome, facet joint pain, and sacroiliac pain. Indications included in studies for the cervical spine were cervical radicular pain attributed to disc pathology, cervicobrachialgia, disc herniation with and without radiculopathy, nonradicular neck pain, spinal stenosis, failed surgery syndrome, and pain attributed to the facet joint(s).

We conducted meta-analyses when there were at least three studies with similar indications, interventions, control groups and outcomes. We grouped control treatments for radiculopathy, stenosis, axial pain or failed back syndrome according to whether the control was an epidural non-steroid injection (ENSI); a non-epidural injection (i.e., intramuscular injection, ligament injection or dry needling in the ligament); a disc or decompression procedure (e.g., discectomy, nucleoplasty), or conservative care (i.e., physical therapy, rehabilitation). Comparisons for which evidence was deemed suitable for pooling were lumbar epidural steroid injection versus ENSI (epidural local anesthetic injection, epidural saline injection, or both) for radiculopathy and stenosis; epidural steroid injection versus NEI (soft tissue local anesthetic injection, soft tissue saline injection, needling with no injection) for radiculopathy. We assessed the meta-analyses results of the epidural steroid injection versus ENSI and compared it with the epidural steroid injection versus NEI and found no difference in the results. In addition, we identified three studies that directly compared epidural steroid injection versus ENSI and versus NEI within the same study and found no difference. Therefore, we chose to combine the two control groups into one "control injection" group and report this comparison in the report. The results tables included at the end of this report contain the analyses separated by ENSI and NEI control groups.

Outcomes were stratified by duration of follow-up as short term (1 week to ≤3 months), intermediate term (>3 months to <1 year), and long term (≥1 year). When more than one follow-up time was reported within a category, we used data from the longest duration available within that category. We analyzed two continuous outcomes: pain and function. Most studies reported axial and extremity pain. For our analysis, we used leg or arm pain when available. Pain was measured on a visual analog scale (VAS) or a numerical rating scale (NRS) of 0 to 10 or 0 to 100 (higher scores indicate greater pain). We converted all pain scales to 0 (no pain) to 10 (worst possible pain). Function was assessed using the Oswestry Disability Index (ODI) (range 0 to 100, higher scores indicate greater disability), the Roland Disability Questionnaire (RDQ) (range 0 to 24, higher scores indicate greater disability), and the Neck Disability Index (NDI) (range 0 to 100, higher scores indicate greater disability). Other continuous outcome measures not used in the meta-analyses are detailed in the evidence tables. In the primary analyses in the meta-analyses, we pooled weighted mean difference (WMD) for pain and standardized mean difference (SMD) for function. The mean difference was calculated using the change between the

follow-up and baseline scores. We imputed missing standard deviations using the mean standard deviation from other studies in the analysis. We calculated a risk ratio (RR) for dichotomous outcomes of pain or function "success" (e.g., >50% improvement in pain scores or function scores, or as otherwise defined in the trials), composite measures of success (e.g., >50% improvement in pain and >50% function as measured by the ODI or RDQ), and risks of subsequent surgery. Each study was weighted and pooled using the Mantel-Haenszel method. For interpreting the clinical importance of mean changes in outcome scores, we defined a minimum clinically important difference as an improvement in 1.5 points on a 0 to 10 pain scale, 10 points on the Oswestry Low Back Pain Disability Questionnaire (ODI), and 5 points on the Roland Morris Disability Questionnaire (RDQ)[198] and 8.5 points on the NDI.[241]

We used a random effects model to account for inter-study variability. Effect sizes were reported and displayed along with their respective 95% confidence intervals. For the primary analyses of epidural injections versus control injections, we pooled across approaches (caudal, interlaminar, or transforaminal), but also stratified the results by approach. We assessed the presence of statistical heterogeneity among the studies by using the standard Cochran's chi-square test, and the magnitude of heterogeneity by using the I^2 statistic.[100] When statistical heterogeneity was present, we performed sensitivity analyses first by omitting obvious outliers. In cases where there were no obvious outliers, we repeated the analysis excluding poor quality studies. When an analysis only contained high quality studies, we did sensitivity analysis using the profile likelihood method[64] and compared results. In all the sensitivity analyses, the results were similar to the primary analyses and not reported further. All results and figures were produced using Review Manager v5.2.6.

4. Results

4.1. Key Question 1: Efficacy and effectiveness

4.1.1. Number of studies retained

We included 63 randomized trials (80 publications) for the lumbar spine and nine randomized trials (15 publications) for the cervical spine. The selection of the studies are summarized in Figure 2. The comparisons evaluated and their respective studies are listed in Table 7.

Table 7. The number of studies for each comparison of efficacy for conditions of the lumbar and cervical spine.

Comparisons	N Studies
LUMBAR	
Radiculopathy due to disc pathology and/or foraminal narrowing	
ESI vs. Control injection*	23 RCTs (30 publications)[13,39,44,59,65,67,72,74,87,88,96,108,115,120,151,169-171,175,176,180,193,204,209-211,213,217,221,228]
ESI vs. Control injection with other medication	3 RCTs[38,57,59]
ESI vs. Disc or decompression procedure	4 RCTs[15,41,86,240]
ESI vs. Conservative care	2 RCTs[37,188]
Radiculopathy attributed to multiple causes	
ESI vs. Control Injection*	3 RCTs[22,34,239]
Stenosis	
ESI vs. Control Injection*	7 RCTs (10 publications)[65,74,81,84,136,137,139,143,144,191]
ESI vs. Control injection with other medication	1 RCT[196]
ESI vs. Decompression procedure	1 RCT[36]
ESI vs. Conservative care	1 RCT[122]
Low back pain without radiculopathy	
ESI vs. Control Injection*	2 RCTs (6 publications)[138,140-142,145,146]
Intradiscal steroid injection vs. Intradiscal control injection*	3 RCTs[43,118,220]
Intradiscal non-steroid injection vs. Intradiscal control injection*	1 RCT[200]
Intradiscal steroid injection plus Discography vs. Discography alone	1 RCT[40]
Failed Back Syndrome	
ESI vs. Control Injection*	1 RCT (3 publications)[172-174]
ESI vs. Control Injection with other medication	3 RCTs[69,186,212]
Facet joint pain	
IASI vs Intra-articular control injection*	3 RCTs[45,83,126]
IASI vs Intramuscular steroid injection	1 RCTs[208]
IASI vs Medial branch radiofrequency denervation	1 RCT[123]
EASI vs Extra-articular control injection*	2 RCTs (3 publications)[166,178,179]
EASI vs Medial branch radiofrequency denervation	1 RCT[53]

Sacroiliac pain	
IASI vs Conservative care	1 RCT[235]
EASI vs Extra-articular control injection*	1 RCT[128]
CERVICAL	
Radiculopathy attributed to disc pathology	
ESI vs. Conservative care	1 RCT[58]
Cervicobrachialgia (neck pain with or without radiculopathy and/or stenosis)	
ESI vs. Control Injection*	1 RCT[223]
Disc herniation with or without radiculopathy	
ESI vs. Control Injection*	1 RCT (3 publications)[156-158]
Nonradicular neck pain	
ESI vs. Control Injection*	1 RCT (3 publications)[152,153,155]
Spinal stenosis	
ESI vs. Control Injection*	1 RCT[163]
Failed Surgery Syndrome	
ESI vs. Control Injection*	1 RCT[162]
Facet joint pain	
IASI vs. Intra-articular control Injection*	2 RCTs (4 publications)[21,159,177,181]
IASI vs. Conservative care	1 RCT[199]

ESI: epidural steroid injection; EASI: extraarticular steroid injection; IASI: intraarticular steroid injection
*Injection with anesthetic and or water/saline.

Lumbar Spinal injections

4.1.2. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing

Thirty four randomized trials (in 41 publications) evaluated lumbar epidural steroid injections (ESI) for radiculopathy attributed to disc pathology and/or foraminal narrowing (Appendix F). Overall, four trials were considered low risk of bias,[44,57,87,115] 14 moderately low risk of bias[13,59,86,88,108,151Becker, 2007 #13,169-171,175,176,180,193,209-211,228,239,240] and 16 moderately high risk of bias.[15,34,37-39,41,65,67,72,74,96,120,188,213,217,221] Of the 23 trials that compared ESI with control injections, 22 contributed data to the metaanalyses (two reported outcomes for patients with herniated disc and spinal stenosis separately and are included in both sections).[65,74] Three trials were low risk of bias,[44,87,115] nine were moderately low risk of bias,[13,59,88,108,151,169-171,175,176,180,193,204,210,211,228] and 10 were considered to be moderately high risk of bias.[39,65,67,72,74,96,120,213,217,221] Sample sizes ranged from 23 to 228 and duration of follow-up from 2 weeks to 3 years. Four trials enrolled patients with subacute symptoms (4 to 12 weeks);[44,59,115,221] the remainder included patients with chronic back pain, back pain of mixed duration, or did not report the duration of symptoms. In ten trials, [44,59,65,67,74,87,88,115,193,210,211,217,228] the inclusion criteria required MRI or CT imaging findings that correlated with symptoms, specifically disc herniation in six[44,59,65,67,74,87] Other imaging findings included foraminal stenosis and disc degeneration. Five studies did perform imaging (X-ray, MRI) on all patients; however, inclusion in the trial was not necessarily dependent on these results.[13,39,72,96,108,204] Most trials required that patients had failed conservative treatment prior to enrollment. Ten trials employed an interlaminar approach,[13,44,65,72,88,96,120,175,176,180,204,221] six a caudal approach,[37,67,74,108,169-171,217] and six a transforminal approach.[59,87,115,151,193,210,211,228] The most commonly

used steroid was methylprednisolone (12 trials);[44,59,65,67,72,88,96,115,120,175,193,213,221,228] other steroids used included triamcinolone (5 trials),[13,39,87,108,200] betamethasone (5 trials), [151,169-171,175,176,180,210,211,217] dexamethasone (1 trial),[67] and hydrocortisone (1 trial).[74] Comparator injections included various anesthetics (bupivacaine, lidocaine, carbocaine, procaine) with or without saline/water or saline alone. The majority of trials included control patients also receiving epidural injections; five of the trials included non-epidural injection controls consisting of interspinous ligament injections, intramuscular injections, and subcutaneous injections superficial to the sacral hiatus and outside the spinal canal.[13,87,96,108,120,204] Flouroscopic guidance was used in all trials evaluating a transforaminal approach, one trial evaluating a caudal approach,[169-171] and two evaluating an interlaminar approach.[88,175,176,180] One trial of caudal injections used ultrasound guidance.[108] For the remainder, guidance was not used or was not reported. The major methodological shortcomings of these trials included unclear random sequence generation and concealed allocation, and unclear reporting of differential loss-to-follow-up between groups. For trials that were not amenable to meta-analysis, a brief description of the trial and patient characteristics is included with the individual results below.

ESI vs. Control Injections

Control: Injection with anesthetic and or saline/water, dry needling

Pain Improvement from Baseline (0-10 scale)

There was no difference between epidural steroid injections and control injections with respect to improvement in pain scores at short-term (Figure 3), 15 trials, mean difference -0.46 (95% CI: -0.94, 0.02),[13,39,44,67,88,96,108,120,169-171,175,176,180,204] intermediate-term (Figure 4), five trials, mean difference -0.15 (95% CI: -1.17, 0.86),[115,146,169-171,175,176,180] or long-term follow-up (Figure 5), eight trials, mean difference -0.25 (95% CI: -0.77, 0.27),[13,39,88,108,115,151,169-171,175,176,180,204] (Table 8).

Proportion of Patients Achieving Pain Success

A greater proportion of patients receiving epidural steroid injections compared with control injections achieved short-term successful pain relief defined as ≥20%,[193,228] ≥50%,[13,59,87,88,169-171,175,176,180,204] or 100%[67,72,213] pain reduction (Figure 6, Table 9), 11 trials, RR 1.27 (95% CI: 1.06, 1.53). However, there were no differences between epidural steroid injections and epidural non-steroid interventions in the likelihood of a successful pain outcome in the intermediate (Figure 7), five trials, RR 1.14 (95% CI: 0.93, 1.39), [59,88,169-171,175,176,180] or long-term follow-up (Figure 8), seven trials, RR 1.09 (95% CI: 0.95, 1.26),[13,65,74,88,151,169-171,175,176,180,204] (Table 9).

Function Improvement from Baseline

There were no differences between epidural steroid injections and control injections in improvement in function at short-term (Figure 9), 11 trials, SMD –0.21 (95% CI –0.56, 0.14),[13,44,59,88,108,115,151,169-171,175,176,180,204,217,228] intermediate-term (Figure 10), six trials, SMD –0.27 (95% CI: –0.76, 0.21), [88,115,151,169-171,175,176,180,217] or long-term follow-up (Figure 11), eight trials, SMD –0.09 (95% CI: –0.46, 0.28),[13,88,108,115,151,169-171,175,176,180,204,217] (Table 10).

Proportion of Patients Achieving Function Success

There were no differences between epidural steroid injections and control injections in the proportion of patients achieving a short-term successful outcome defined as improvement of ≥10%,[193,228] ≥50%,[151,169-171,175,176,180] or ≥75%[13,200] from baseline in ODI, ODI score ≤20 on a 0-50 scale,[44] or

improvement of >5 points from baseline in RMDQ,[67] at short-term (Figure 12, seven trials, RR 1.04 (95% CI: 0.82, 1.32),[13,44,67,151,169-171,175,176,180,204,228] intermediate-term (Figure 13, three trials, RR 1.09 (95% CI: 0.86, 1.38),[151,169-171,175,176,180] or long-term follow-up (Figure 14), four trials, RR 1.07 (95% CI: 0.93, 1.22),[13,151,169-171,175,176,180,204] (Table 11).

Composite Score

There were no differences between epidural steroid injections and control injections in the proportion of patients achieving an intermediate or long-term successful composite outcome defined as improvement of ≥50% from baseline in pain AND function (ODI or RDQ) (Figures 15 and 16; Table 12), three trials, RR 1.08 (95% CI: 0.86, 1.35) and RR 1.04, (95% CI: 0.88, 1.23), respectively.[151,169-171,175,176,180]

Risk of Surgery

There were no differences between epidural steroid injections and control injections in the cumulative risk of surgery at final follow-up (Figure 17, Table 13), 16 trials, RR 0.83 (95% CI 0.66, 1.04).[13,39,65,67,72,74,108,120,204,213,217,221]

Opioid Use

Two moderately low risk of bias trials assessed the proportion of patients achieving ≥20% decrease in opioid use (Table 14). Patients in both studies were required to have leg pain as or more severe than back pain and MRI or CT evidence of a pathologic disc condition correlating with symptoms. Mean symptom durations differed between the studies: 2.7 months versus 11.5 months. One reported no difference between fluoroscopically guided transforaminal epidural injection with methylprednisolone 60 mg + bupivacaine + water (n=28) versus epidural non-steroid injections with bupivacaine + water (n=30) in achieving a ≥20% decrease in opioid use in the short- and intermediate-term.[59] The other reported no difference between ultrasound guided caudal epidural injection with triamcinolone 40 mg + saline (n=37) versus saline injection (n=35) in achieving a ≥20% decrease in opioid use in the short-term.[108]

Three trials from the same author group assessed opioid use based on morphine equivalents and compared epidural steroid injection in 120 patients (each study) with disc herniation and function-limiting low back and lower extremity pain of greater than 6 months duration, each with a different approach. The first used a caudal approach and compared fluoroscopically guided methylprednisolone 40 mg + lidocaine versus epidural lidocaine alone.[169-171] The second trial used an interlaminar approach and compared fluoroscopically guided betamethasone 6 mg + lidocaine 0.5% versus lidocaine 0.5%.[175,176,180] The third trial used a transforaminal approach and compared fluoroscopically guided betamethasone 3 mg + lidocaine 1% versus lidocaine 1% + saline.[151] All three trials report no difference between groups in intake of opioids at short-, intermediate- or long-term (Table 15).

Other outcomes

One moderately low risk of bias trial evaluated the quality of life in patients with unilateral lumbar radiculopathy (confirmed on CT or MRI) >12 weeks with leg pain below the knee and leg pain worse than back pain.[108] They reported no difference in the EQ-5D comparing ultrasound guided caudal epidural injection with 40 mg triamcinolone (n=37) versus caudal epidural injection with 0.9% saline (n=39) versus subcutaneous injection superficial to the sacral hiatus and outside spinal canal with 0.9% saline (n=40) at short- or long-term follow-up (Table 16).

One moderately low risk of bias trial found no difference between single-level interlaminar epidural injection with 80 mg methylprednisolone (2 ml) plus isotonic saline (8 ml) (n=78) and interlaminar epidural injection with isotonic saline (1 ml) (n=80) in quality of life as measured by the Sickness Impact Profile at short-term follow-up, MD -1.2 (95% CI: -5.2, 2.8).[44] Further, there were no differences on physical or psychosocial dimensions subscales (Table 16). This trial included patients with sciatica (>4 weeks but <1 year duration) with constant or intermittent pain in one or both legs radiating below knee and CT evidence of herniated disk corresponding to clinical findings.

One moderately low risk of bias used the Lifestyle/Function Questionnaire (scale, 6 worse to 18 best) to assess any effects on lifestyle in patients with unilateral sciatica associated with paresthesia (>1 month duration) and positive straight leg raise. They found no difference between caudal epidural injection with 80 mg triamcinolone acetonide in normal saline with 0.5% procaine hydrochloride (total 25 ml) (n=12) versus caudal epidural injection with saline (25 ml) (n=11) in the short- or long-term (Table 16).[39]

Control: Non-Steroid Injection with Other Medications

Various Outcomes

Two trials evaluated epidural steroid injections versus epidural non-steroid injections with clonidine,[38] or etanercept,[59] and one trial versus posterior ligament injection of saline plus oral gabapentin[57] (Tables 17 and 18).

Burgher et al.[38] compared fluoroscopically guided transforaminal epidural injections of triamcinolone 40 or 80 mg (n=15) versus clonidine 200 or 400 mcg (n=11); both groups also received epidural injections of lidocaine 2% (1 ml). Included patients had CT- or MRI-confirmed disc herniation with unilateral low back and leg pain ≤3 months and a positive nerve root tension sign at a single level of the lumbosacral spine. In the short-term, steroid injections were superior to clonidine on the RDQ; difference in change from baseline at 4 weeks, -5.67 (95% CI: -10.12, -1.22); p=0.02. This study had moderate risk of bias.

One moderately low risk of bias study (n=58) found transforaminal epidural steroid injection (methylprednisolone acetate 60 mg + bupivacaine 0.5% + water) superior to transforaminal epidural etanercept 4 mg (+ bupivacaine 0.5% + water) on the ODI at 1 month, difference –16.2 (95% CI: –26.0, –6.27).[59] There were no differences in other outcomes, including change in pain from baseline, proportions with successful outcomes, reduction in opioid use or risks of surgery. All injections were performed under fluoroscopic guidance. For inclusion, patients were required to have leg pain as or more severe than back pain and MRI or CT evidence of a pathologic disc condition correlating with symptoms (mean duration 49.9 weeks).

One recent study with moderately low risk of bias evaluated fluoroscopically-guided interlaminar or transforaminal injection of methylprednisolone 60 mg, bupivacaine 0.25% and saline plus oral placebo medication (n=73) compared with posterior ligament injection of saline (3 ml) plus oral gabapentin 300 mg (n=72).[57] Patients were included if they had symptomatic lumbosacral radicular pain (>6 weeks but ≤4 years duration) and findings of single-level disc herniation on MRI imaging concordant with their presentation. The study found no difference between groups in the likelihood of achieving pain success, RR 1.27 (95% CI: 0.79, 2.03); a reduction of pain from baseline, mean difference -0.3 (95% CI: -1.2, 0.5); or a change in function from baseline, mean difference 3.9 (95% CI: -1.1, 9.0) at 3 month follow-up.

ESI vs. Disc or Decompression Procedures

Discectomy

Various Outcomes

Two trials compared epidural steroid injections versus discectomy for lumbar radiculopathy (Tables 19 and 20).

One study with a moderately high risk of bias enrolled 100 patients with radiculopathy from a lumbar herniated disc verified by imaging.[41] Patients failed 6 weeks of conservative care prior to enrollment. Fifty patients received epidural steroid injection of betamethasone (10-15 mg), 76% under fluoroscopic guidance, and 50 received a discectomy (procedure not described). The epidural steroid injection group had an increased likelihood of motor deficit compared with discectomy at the 1 to 3 month follow-up (72% vs. 38%), RR 1.89 (95% CI: 1.28, 2.80), There was a significant reduction in leg pain in the discectomy group at the short- and intermediate-term, but no differences in back pain or ODI scores. Results are difficult to interpret due to high rates of crossover from the epidural injection group to discectomy (54% of patients allocated to epidural injection underwent discectomy).

A second study with a moderately high risk of bias randomly assigned 50 patients with chronic, single-level lumbar disc herniation confirmed by CT or MRI to either epidural steroid injection of 40 mg methylprednisolone plus 0.25% bupivacaine (3 ml) under fluoroscopic guidance or percutaneous microdiscectomy.[15] The authors reported lower back but not leg pain in the microdiscectomy group after 6 weeks. There was no difference in opioid use.

Nucleoplasty

Various Outcomes

Two studies, both moderately low risk of bias, compared transforaminal epidural steroid injection versus radiofrequency nucleoplasty (Tables 19 and 20).

One trial compared transforaminal epidural injection of betamethasone plus lidocaine under fluoroscopic guidance (n=40) versus nucleoplasty immediately followed by nerve root injection of betamethasone plus lidocaine (n=39) versus nucleoplasty alone (n=39).[240] Patients with a minimum of 6 months' radicular pain caused by single-level lumbar disc herniation confirmed by MRI, who had failed conservative treatment and had no history of prior surgical intervention were included. Compared with nucleoplasty, epidural steroid injections performed poorer with respect to short- and long-term pain and function (ODI), mean difference for pain 0.9 (95% CI: 0.57, 1.23) and 1.0 (95% CI: 0.7, 1.3), and for function 4.8 (95% CI: 1.27, 8.33) and 4.7 (95% CI: 1.06, 8.34), respectively. Results were similar when epidural steroids were compared with nucleoplasty plus steroids.

The second trial (n=90) evaluated patients with chronic radicular symptoms and a focal lumbar disc protrusion.[86] Compared with nucleoplasty, epidural steroid injections (various) performed poorer with respect to short- and intermediate term pain and function (ODI), mean difference for pain 2.3 (95% CI: 2.1, 2.5) and 2.6 (95% CI: 2.4, 2.8), and for function 9.0 (95% CI: 7.9, 10.1) and 10.0 (95% CI: 8.3, 11.7), respectively. Similarly, the trial found transforaminal epidural steroid injection associated with lower likelihood than nucleoplasty of achieving ≥2.5 point improvement in leg pain in the intermediate- (21% versus 29%), RR 0.42 (95%CI: 0.21, 0.84) and long-term (21% versus 42%), RR 0.49 [95% CI 0.24, 1.0]);

≥13 point improvement in ODI in the intermediate- (15% versus 32%), RR 0.47 (95%CI: 0.2, 1.1) and long-term (10% versus 30%), RR 0.34 (95%: CI 0.34, 0.95). There was no difference in risk of undergoing surgery (5% vs. 11%) RR 0.45, 95% CI 0.09, 2.19). The trial was funded by a manufacturer of a plasma disc decompression device.

ESI vs. Conservative Care

Various Outcomes

Two trials compared epidural injection versus conservative care (Tables 21 and 22).

One trial with a moderately high risk of bias compared caudal epidural injection with 80 mg triamcinolone acetate (2 ml), 2% lidocaine (2 ml), and normal saline (20 ml), with fluoroscopic guidance (n=50) versus conservative treatment consisting of tizanidine 6-12 mg/d, diclofenac 50-100 mg/d, amitriptyline 10-50 mg qhs, bilateral skin traction and physical therapy (TENS, short-wave diathermy, back extension exercises) (n=50).[188] Included patients had low back pain with unilateral or bilateral sciatica for ≥3 months not responding to rest and analgesics, and MRI evidence of disc degeneration. The steroid group had greater improvement in pain compared with baseline (5.4 vs. 2.0 on 0-10 VAS), better ODI scores (mean difference from baseline, 23.7 vs. 4.0 on 0 to 100 scale), and higher likelihood of complete pain relief (86% versus 24%) than conservative care at 6 month follow-up. Methodological shortcomings included inadequate description of allocation concealment and no blind assessment.

Another moderately high risk of bias trial (N=36) of patients with a herniated disk ≥5 mm confirmed by MRI with clinical symptoms of nerve root compression, positive straight leg raise test at <60 degrees and age <50 years found neither pain nor mobility following single-level interlaminar epidural injection with 100 mg methylprednisolone in 0.25% bupivacaine plus conservative care (n=17) significantly different than conservative care consisting of bed rest, analgesics, NSAIDS or tramadol, graded rehabilitation, hydrotherapy, electroanalgesia, and spinal mobilization physiotherapy (n=19).[37] Methodological shortcoming included unclear random sequence generation, inadequate description of allocation concealment, lack of blind assessment and differences between groups in baseline prognostic factors.

4.1.3. Lumbar radiculopathy attributed to multiple causes

ESI vs. Control Injections

Various Outcomes

Three trials included patients with radiculopathy attributed to multiple causes (Appendix G).

One moderately low risk of bias trial included patients with MRI or CT confirmed herniated nucleus pulposus or scarring after previous surgery and lumbar radicular symptoms of at least 6 weeks duration and compared fluoroscopically guided, single-level interlaminar epidural injection of either 10 mg triamcinolone plus anesthetic (n = 25) or 5 mg triamcinolone plus anesthetic (n = 27) versus interlaminar autologous conditioned serum (n = 32).[22] At short- and intermediate term, epidural autologous conditioned serum resulted in a larger reduction in pain from baseline compared with epidural steroid (Table 23). There was no difference in function as measured by the ODI.

One small (N=35) older trial with a moderately high risk of bias included patients with the following findings on radiculography: arachnoiditis, prolapsed disc, no radiographic abnormalities or inconclusive

findings.[34] All patients presented with incapacitating chronic low back pain and sciatica unresponsive to conservative therapies. The trial compared caudal epidural injection with 80 mg methylprednisolone and 20 ml bupivacaine with caudal epidural injection of 20 ml bupivacaine followed by 100 cc of saline. There was no statistical difference between groups in "considerable" pain relief (defined as diminution of pain and/or paresis to enable return to work or rehabilitation for other work) at final follow-up of a mean 9.4 months (range, 3 to 20 months), 65% (9/16) vs. 26% (5/19) RR 2.14 (95% CI: 0.90, 5.09) (Table 24). Methodological shortcoming included, inadequate description of allocation concealment, unclear accounting of the number of patients lost to follow-up, and differences between groups in baseline prognostic factors.

One moderately low risk of bias trial of patients with lumbosacral nerve root pain >6 weeks of sufficient intensity to warrant surgery and an MRI showing disc prolapse and/or spinal stenosis reported greater short-term pain relief (data not reported; p<0.004) with interlaminar epidural steroid injection with 80 mg methylprednisolone (2 ml) plus 40 mg 0.5% bupivacaine (8 ml) (n=44) compared with intramuscular or interspinous ligament injection with 80 mg methylprednisolone (2 ml) plus 40 mg 0.5% bupivacaine (8 ml) (n=48); however, there was no difference between groups in the long-term.[239] There was no difference in risk of surgery at a minimum 12 months follow-up, RR 1.31 (95% CI: 0.76, 2.27) (Table 24).

4.1.4. Lumbar spinal stenosis

Ten trials in 13 publications evaluated epidural steroid injections for the treatment of lumbar spinal stenosis.(Appendix H). One trial was rated as low risk of bias,[81] two as moderately low risk of bias[136,137,139,143,144] and seven as moderately high risk of bias[36,65,74,84,122,191,196] (Appendix E). Control groups included control injections (i.e., non-steroid injections with anesthetic and or saline/water) (7 RCTs),[65,74,81,84,136,137,139,143,144,191] control injections with other medication (i.e., etanercept) (1 RCT),[196] decompression procedures (1 RCT),[36] and conservative care (1 RCT).[122] Patients were included if they had chronic function-limiting back and/or leg pain or signs of neurogenic claudication; MRI and/or CT confirmation of spinal stenosis was required in eight studies.[36,65,74,81,84,122,191,196] Six of the seven trials that compared ESI with control injections contributed data to the meta-analyses for this comparison (1 low risk of bias,[81] 2 moderately low risk of bias,[136,137,139,143,144] and 3 moderately high risk of bias[65,74,191]), two of which reported outcomes for patients with herniated disc and spinal stenosis separately and are included in both sections.[65,74] Sample sizes across these six studies ranged from 37 to 400. One study specifically included patients with degenerative scoliosis (>10 degrees) combined with spinal stenosis.[191] The mean duration of pain varied (range, 7.2 months to 115 months across trials) and the majority of studies required patients to have failed conservative treatment prior to enrollment. A variety of steroids were used, including betamethasone (3 trials),[81,136,137,139,143,144] methylprednisolone (2 trials)[65,81] triamcinolone (1 trial),[191] dexamethasone (1 trial),[81] and hydrocortisone (1 trial).[74] Control injections included various anesthetics (procaine, carbocaine, lidocaine) with or without saline. The most common approach was interlaminar in three trials,[65,81,136,137] by transforaminal in two[81,191] and caudal in two;[74,139,143,144] one trial reported primary outcomes stratified by approach.[81] Injections were performed under fluoroscopic guidance in four trials;[81,136,137,139,143,144,191] the use of imaging guidance was unclear in the remaining two. Single-level injections were performed in three trials[65,74,191] and one allowed multilevel and bilateral injections;[81] the remaining studies did not specify the number of levels treated but they are assumed to be single-level.[136,137,139,143,144] Co-interventions appeared to be applied equally between treatment groups. The major methodological shortcoming of these trials was unclear allocation

concealment. For the remaining trials that were not amenable to meta-analysis, a brief description of the trial and patient characteristics is included with the individual results below.

ESI vs. Control injections

Non-steroid injection with anesthetic and or saline/water

Pain Improvement from Baseline (0-10 scale)

There was no difference between epidural steroid injections and epidural non-steroid with anesthetic and or saline/water injections in patients with spinal stenosis with respect to improvement in pain scores at short-term follow-up (Figure 18, Table 25), four trials, mean difference -0.17 (95% CI: -0.62, 0.29).[81,136,137,139,143,144,191] Due to the large amount of heterogeneity (I^2=55%), we excluded one outlier trial (mean difference -0.81 compared with all others ranging from -0.20, 0.30). Excluding the outlier trial decreased statistical heterogeneity, I^2=0%), reduced the overall point estimate, mean difference 0.08 (95% CI: -0.12, 0.28) but did not change the overall results.

Proportion of Patients Achieving Pain Success

There were no differences between epidural steroid injections and epidural non-steroid injections (ENSI) with anesthetic and or saline/water in patients with spinal stenosis in the proportion achieving pain success in the short-term (Figure 19), three trials, RR 1.03 (95% CI: 0.91, 1.18), [81,136,137,139,143,144] or long-term follow-up (Figure 20), four trials, RR 1.04 (95% CI: 0.86, 1.26),[65,74,136,137,139,143,144] (Table 26).

Function Improvement from Baseline

There was no difference between epidural steroid injections and epidural non-steroid with anesthetic and or saline/water injections in patients with spinal stenosis with respect to improvement in function improvement at short-term (Figure 21, Table 27), four trials, ~~SMD -0.47 (95% CI: -1.08, 0.14)~~ **-2,15 (95% CI: -5.83, 1.52)**.[81,136,137,139,143,144,191] Due to the large amount of heterogeneity (I^2=93%), we evaluated pain improvement using the profile likelihood method. The estimates were similar.

Proportion of Patients Achieving Function Success

There were no differences between epidural steroid injections and epidural non-steroid injections (ENSI) with anesthetic and or saline/water in patients with spinal stenosis in the proportion achieving function success at short-term follow-up (Figure 22, Table 28), three trials, RR 0.98 (95% CI: 0.84, 1.15).[81,136,137,139,143,144]

Composite Score

There were no differences between epidural steroid injections and epidural non-steroid injections (ENSI) with anesthetic and or saline/water in patients with spinal stenosis in the proportion achieving a short-term successful composite outcome defined as improvement of ≥50% from baseline in pain AND function (ODI or RDQ) (Figure 23, Table 29), three trials, RR 1.07 (95% CI: 0.77, 1.48).[136,137,139,143,144,191]

Risk of Surgery

There was no differences between epidural steroid injections and epidural non-steroid injections (ENSI) with anesthetic and or saline/water in patients with spinal stenosis in the risk of surgery (Figure 24, Table 30), RR 0.86 (5% CI: 0.48, 1.52).[65,74,191]

Opioid use

Two trials from the same author group assessed opioid use based on morphine equivalents and compared epidural steroid injection in patients with spinal stenosis, each with a different approach. The first used a caudal approach and compared fluoroscopically guided betamethasone 6 mg + lidocaine 0.5% versus lidocaine 0.5% alone.[139,143,144] The second trial used an interlaminar approach and compared fluoroscopically guided betamethasone 1 mg + lidocaine 0.5% versus lidocaine 0.5%.[136,137] Both trials report no difference between groups in intake of opioids at short-, intermediate- or long-term (Table 31)

Other outcomes

One low risk of bias trial (n=386)[81] enrolled patients with symptoms (duration ranged from <3 months to >5 years) of neurogenic claudication and imaging findings of central lumbar spinal stenosis on advanced imaging, average pain of >4 on a 0 to 10 scale, score of 7 or higher on the RDQ, and pain the lower back, buttock, leg, or a combination of these sites on standing, walking, or spinal extension in the past week, with pain worse in the buttock, leg, or both than in the back. Patients were randomized to fluoroscopically-guided interlaminar or transforaminal epidural injection with various steroids versus epidural injection with local anesthetic. There were no significant differences in the short-term (6 weeks) between the treatment groups with respect to the EQ-5D quality of life questionnaire (Table 31) or the Swiss Spinal Stenosis Questionnaire (SSSQ) symptoms and physical function subscales (Table 27). However, on the satisfaction subscale of the SSSQ, 67% versus 54% of patients who received steroids plus lidocaine reported being very or somewhat satisfied with their treatment, as compared with 54% of those who received lidocaine alone, RR 1.24 (95% CI: 1.05, 1.46) (Table 32).

One moderately high risk of bias trial evaluated walking distance in patients diagnosed with chronic spinal stenosis suffering from pseudoclaudication with leg pain following treatment with a caudal epidural injection with 40 mg methylprednisolone (n=19) versus an epidural injection with local anesthetic or saline (n=34).[84] The groups were comparable in terms of age (72 vs. 70 years), sex (68% vs. 72% male), and clinical characteristics. The authors found no differences between groups in mean walking distance or likelihood of being able to walk >20 meters at 1 month follow-up (Table 28).

ESI vs. Control injections with Other Medication

One trial (n=80) at moderately high risk of bias compared fluoroscopically guided transforaminal epidural injection with 3.3 mg dexamethasone versus epidural etanercept (Table 33). Patients were included if they had low back and leg pain for >1 month and central, lateral recess, or foraminal narrowing. Treatment groups were comparable in terms of age (67 vs. 65 years), duration of symptoms (2.3 vs. 2.5 months), and used of non-steroid anti-inflammatory drugs at baseline (85% vs. 87%); however, there were fewer males in the steroid group (45% vs. 55%). The trial found that steroid injections were associated with worse leg pain than the control injection at 1 month (5.2 vs. 3.5, p=0.03), but no difference in ODI.[196]

ESI vs. Decompression Procedures

One moderately low risk of bias trial (n=38) compared fluoroscopically guided interlaminar epidural steroid injection with 80 mg triamcinolone acetate (40 mg in diabetic patients) versus minimally invasive lumbar decompression (the MILD® procedure) in patients with MRI evidence of spinal stenosis and hypertrophic ligamentum flavum (Tables 33 and 34).[36] Though no statistically significant differences were noted, the steroid and MILD groups did vary somewhat on several baseline variables, respectively, including age (79 vs. 74 years), proportion of males (47% vs. 62%), two or more levels treated (59% vs.

67%) and conservative care for over 6 months prior to the procedures (76% vs. 62%). The steroid injection group had a lower likelihood of experiencing ≥2-point improvement in pain than the MILD procedure at the 2 week follow-up (35% vs. 76%). By the 6 week follow-up, there was no difference between groups. There was no difference in functional outcomes (ODI) or patient satisfaction at 2 or 6 weeks.

ESI vs. Conservative Care

One small, moderately high risk of bias trial (n=29) evaluated interlaminar epidural injection with 60 mg triamcinolone acetonide under fluoroscopic guidance compared with either passive physical therapy (ultrasound, hot packs and TENS) 5 days/week for 2 weeks, or no physical therapy for long-standing chronic spinal stenosis (mean >5 years).[122] The treatment groups varied somewhat, respectively, with regard to age (61 vs. 63 vs. 53 years), proportion of males (80% vs. 50% vs. 89%), and symptom duration (5.0 vs. 5.7 vs. 5.7 years). There were no differences between groups in mean pain intensity, the RDQ or the Nottingham Health Profile at 3 or 6 months (Table 33).

4.1.5. Lumbar nonradicular axial pain

Seven randomized trials (in 13 publications) evaluated spinal injections for low back pain without radiculopathy; two evaluated epidural injections and five evaluated intradiscal injections (Appendix I).

ESI vs. Control Injections

Two trials from the same author group, both with a moderately low risk of bias, compared epidural steroid injections versus epidural non-steroid injections with anesthetic at short-term (3 months), intermediate-term (6 months), and long-term (24 months) follow-up. Both trials included 120 patients, 60 in each group, with non-radicular low back pain who had failed to improve with conservative care. One trial randomized patients to receive a caudal epidural injection of betamethasone 6 mg or methylprednisolone 40 mg plus lidocaine versus lidocaine only.[138,145,146] In the second trial patients received an epidural injection of betamethasone 6 mg plus lidocaine versus lidocaine only via an interlaminar approach.[140-142] All injections were performed under fluoroscopic guidance. The mean duration of back pain was 96 months and 117 months, respectively; the number of levels treated were not reported in either study. There were no significant differences reported by either study between epidural steroid versus local anesthetic injection at short-, intermediate-, or long-term follow-up on all outcomes, including mean pain scores (0-10 NRS), likelihood of ≥50% pain relief, mean ODI score, likelihood of ≥50% improvement in ODI, likelihood of success (≥50% improvement in both pain and ODI) and use of opioids (Tables 35 and 36).

Intradiscal Steroid Injection vs. Intradiscal Control Injections

Three trials, all at moderately high risk of bias, compared intradiscal steroid injections versus intradiscal non-steroid injections with anesthetic and/or saline/water.

One trial randomized 40 patients to receive an intradiscal steroid injection of betamethasone (dose not reported) and 40 to receive an intradiscal injection of saline.[43] The use of guidance was not reported. Only patients with single-level disc degeneration confirmed by imaging and positive discography were enrolled. Patients who received steroid injections showed significantly greater improvement in both the short and intermediate term compared with those who received saline: mean difference between groups for pain scores on VAS was -5.05 (95% CI: -5.52, -4.58) at 3 months and -4.55 (95% CI: -5.0, -4.1)

at 6 months and for function scores on ODI was -23.2 (95% CI: -27.7, -18.7) and -23.3 (95% CI: -27.75, -18.85), respectively (Table 37).

A second trial included 25 patients with single-level disc degeneration confirmed by imaging and positive discography and who had failed at least 6 weeks of conservative treatment and randomized them to either an intradiscal injection of methylprednisolone 80 mg (n=14) or bupivacaine (n=11).[220] Fluoroscopic guidance was used in all cases. There were no significant differences noted between the two groups on any outcome in the short-term (10-14 days), including the likelihood of pain relief on VAS (not defined further), likelihood of function improvement on ODI (not defined further), or likelihood of subjective overall improvement (considered treatment success, not defined further) (Table 38).

The third trial enrolled 120 patients with disc degeneration confirmed by imaging and who had failed at least 6 weeks of conservative treatment and randomized 60 patients each to receive an intradiscal injection of methyloprednisolone 40 mg or saline.[118] All injections were performed under fluoroscopic guidance. There were no differences at long-term follow-up between the steroid and the saline groups for pain or function improvement on VAS and ODI, respectively. A similar proportion of patients in both groups had undergone surgery by 12 months (Tables 37 and 38).

Intradiscal Non-Steroid Injection vs. Intradiscal Control Injections

One trial at moderately low risk of bias enrolled 72 patients with evidence of disc degeneration confirmed by imaging and who had failed at least 6 weeks of conservative treatment and randomized 36 to receive an intradiscal injection of methylene blue 10 mg and lidocaine and 36 to receive lidocaine and saline only.[200] All injections were performed under fluoroscopic guidance. For all outcomes measured, those who received methylene blue reported significantly better outcomes at both intermediate- and long-term follow-up (Tables 37 and 38). The mean difference between groups in pain improvement on VAS was -4.36 (95% CI: -4.78, -3.94) at 6 months and -4.56 (95% CI: -4.98, -4.14) at 24 months and for function improvement on ODI, -31.5 (95% CI: -34.65, -28.35) and -33.9 (95% CI: -37.45, -30.35), respectively. Almost twice as many patients in the methylene blue group reported a reduction in medication use (defined as no use or only occasional use of NSAIDs or opioids) at 24 months, 91.7% versus 57.1% (RR 1.6; 95% CI 1.18, 2.17), with the vast majority of those reporting no medication use compared with the control group (83.3% vs. 5.7%; RR 14.58; 95% CI 3.77, 56.46). Patient satisfaction (defined as completely satisfied or satisfied) was reported by 91.7% of patients in the methylene group compared with 14.3% in the anesthetic group; RR 6.42 (95% CI: 2.83, 14.53).

Intradiscal Steroid Injection plus Discography vs. Discography alone

One trial at moderately high risk of bias randomized 86 patients to discography plus intradiscal injection of betamethasone (mean 9.7 mg) and 85 to discography alone.[40] Patients were enrolled if they had symptoms related to disc degeneration as diagnosed by a combination of clinical examination, medical history and imaging and had failed conservative treatment. Fluoroscopic guidance was used in all cases. The discography plus steroid groups reported better results for all outcomes measured (Tables 37 and 38). The mean difference between groups in VAS pain score was -1.2 at 3 months, -0.9 at 6 months, and -0.4 at 24 months, and for ODI function scores was -7.3, -4.9, and -12.8, respectively. The likelihood of a success treatment (as reported by the patient) was 40.7% versus 0% at 1-3 months, 22.1% versus 0% at 7-12 months, and 17.4% vs. 1.2% at 12-24 months (RR 14.8; 95% CI 2.0, 109.8). The likelihood of a

reduction in narcotic or NSAID use was greater in the discography plus steroid group, 19.7% vs. 3.5% (RR 5.6; 95% CI 1.7, 18.4). The risk of surgery was 65% versus 83%, favoring the discography plus steroid group (RR 0.77, 95% CI 0.65, 0.93).

4.1.6. Failed back surgery syndrome

Four randomized trials (in 6 publications) evaluated epidural steroid injections (ESI) for low back pain due failed back surgery syndrome (Appendix J).

ESI vs. Control injections

Control: Epidural non-steroid injection with anesthetic and or saline/water

One trial at a moderately low risk of bias randomized 140 to receive epidural steroid injections of betamethasone 6 mg plus lidocaine and saline (n=70) or lidocaine and saline alone (n=70).[172-174] All injections were performed via the caudal approach under fluoroscopic guidance. Patients were required to have failed conservative management prior to enrollment. The authors reported no significant differences between the treatment groups on any outcome measured at short-term (3 months), intermediate-term (6 months), or long-term follow-up (24 months), including pain improvement on VAS, likelihood of ≥50% pain relief on VAS, function improvement on ODI, likelihood ≥50% improvement in ODI, likelihood of treatment success (defined as improvement of ≥50% in both pain and function), or use of opioids (Tables 39 and 40).

ESI vs. Control injections with Other Medications

Control: Epidural steroid injection or epidural non-steroid injection with other medication

One trial at moderately high risk of bias randomized patients to three groups: epidural injection with triamcinolone 75 mg plus lidocaine and saline (n=7), with triamcinolone 75 mg plus morphine 8 mg and lidocaine (n=8), and with morphine 8 mg plus lidocaine only (n=7), Tables 39 and 40.[212] The approach and use of guidance was not reported. A significant difference favoring epidural steroid injections was seen for pain improvement at 6 months when the triamcinolone plus lidocaine group was compared with the morphine plus lidocaine group, -3.9 (95% CI: -5.28, -2.52), but not when the triamcinolone plus morphine and lidocaine group was compared with the morphine plus lidocaine group. There were no difference in the likelihood of a patient self-reporting their pain as better at 6 months for any of the treatment comparisons.

A second trial at moderately high risk of bias randomized 60 patients with persistent pain following spinal surgery for disc herniation and electromyography showing chronic nerve pathology without acute irritation to receive either an epidural injection into the nerve root sleeve with methylprednisolone 40 mg plus bupivacaine alone (n=20) or with the addition of hyaluronidase (n=20) and hyaluronidase plus bupivacaine only (n=20).[69] All injections were performed via the transforaminal approach under fluoroscopic guidance. There were no difference in the likelihood of a successful pain outcome, defined as ≥50% improvement on the verbal pain rating scale, between groups at either short- (3 months) or intermediate-term (6 months) follow-up (Table 40).

Another trial at moderately high risk of bias included 47 patients with postoperative sciatica with or without low back pain and CT or MRI findings and randomized them to one of three treatment groups: epidural injection with prednisolone 125 mg (n=16), forceful injection with prednisolone acetate (n=15), or forceful injection of saline (n=16).[186] All injections were performed via the caudal approach under fluoroscopic guidance. There were no significant differences between groups on any outcome measured over both short- (2 months) and intermediate-term (4 months) follow-up, including pain improvement on VAS, likelihood of ≥15% pain relief on VAS, and function improvement as measured by the Dallas Activities of Daily Living domain (Tables 39 and 40).

4.1.7. Facet joint pain

Eight randomized trials evaluated facet joint steroid injections for facet joint pain (Appendix K). Six evaluated intraarticular steroid injections (IASI) and three evaluated extra-articular steroid injections (EASI).

IASI vs. Intraarticular Control injections

One trial at moderately high risk of bias compared intra-articular facet joint injection with methylprednisolone acetate 80 mg plus local anesthetic (n=28) versus saline (n=42) under fluoroscopic guidance.[126] Mean duration of back pain was not reported (>3 months per inclusion) and neither diagnostic facet joint block nor imaging was required for inclusion. Patients received one unilateral injection at two levels. There were no differences between intra-articular versus extra-articular steroid injections in mean VAS score at 3 months (mean difference between groups 0.8, 95% CI -0.09, 1.69) (Table 41). There was also no difference in symptom improvement or disability score (data not reported).

A second trial at moderately low risk of bias compared intra-articular facet joint injection with methylprednisolone acetate 20 mg (without local anesthetic) (n= 51) versus saline (n=50),[45] (Tables 41 and 42). Fluoroscopic guidance was used in all cases. Patients had chronic back pain (median 18-24 months) and a positive (≥50% pain relief) response to a single diagnostic intra-articular facet joint block. Imaging was not required for enrollment. Patients received an average of 3.6 injections at two levels; most (80%) received bilateral injections. At 1 month, there was no difference between the steroid versus saline injections in likelihood of patient-reported global improvement (i.e., “very marked” or “marked” improvement), pain improvement (on VAS and McGill pain questionnaire pain rating index), or Sickness Impact Profile scores. At 6 months the steroid injection was associated with greater improvement in pain on VAS (mean difference in change scores -1.1; 95% CI -1.8, -0.4), greater likelihood of global improvement (46% vs. 15%; RR 3.08, 95% CI 1.64, 6.51), and better Sickness Impact Profile physical dimension scores (4.3 vs. 7.9, p<0.05), with no differences on other outcomes. However, 6-month results may have been confounded by differential receipt of cointerventions such as physical therapy, antidepressant medication, or other injections (22% vs. 12%). In a sensitivity analysis based on outcomes at the last evaluation prior to cointerventions carried forward, there was no difference in likelihood of improvement at 6 months (31% vs. 17%, p=0.17). There was also no difference in the likelihood of sustained improvement (improvement at 6 months in patients with improvement at 1 month) (55% vs. 31%).

A third RCT at moderately high risk of bias compared intra-articular facet injection with triamcinolone acetonide 10 mg (n=30) versus hyaluronic acid (n=30).[83] The rationale for the hyaluronic acid was to provide viscosupplementation to the joint. Patients were required to have nonradicular low back pain for at least 3 months and CT scan evidence of facet joint arthropathy with osteophytes. Diagnostic blocks were not used for patient selection. Patients received bilateral injections at three levels over 3 weeks, with one joint treated per week. There were no differences between groups on any outcome at 1 month or 6 months, including mean pain score, RDMQ, ODI, or the SF-36 (Table 41).

IASI vs. Intramuscular steroid injection

One trial at low risk of bias randomized patients to receive intra-articular facet joint (n=31) versus an intramuscular injection (n= 29) of 20 mg triamcinolone hexacetonide under fluoroscopic guidance (Tables 41 and 42).[208] Patients did not receive a diagnostic facet joint block. Mean duration of pain was 52 months. Patients who received the intra-articular steroid injection showed greater improvement in pain on VAS (mean difference in change scores -1.6; 95% CI -2.62, -0.58) and function on RMDQ (mean difference in change scores -2.7, 95% CI -4.71, -0.69) in the short term (3 months). No clear differences were seen between groups in the intermediate term (up to 6 months). Regarding quality of life as measured by the Short Form (SF)-36, greater improvement was seen over time in patients who received an intra-articular steroid injection compared with an intramuscular injection for the "role physical" domain (p=0.02); no differences were found between groups for the other SF-36 domains.

IASI vs. Medial Branch Radiofrequency Denervation

One trial at low risk of bias randomized patients to an intra-articular steroid injection with betamethasone 3 mg plus local anesthetic with sham neurotomy (n=29) versus medial branch radiofrequency neurotomy plus local anesthetic injection (n=27).[123] Both interventions were performed under fluoroscopic guidance and additional electrostimulation confirmation in the neurotomy group. Patients had chronic (≥24 months) symptoms, MRI-confirmed facet joint osteoarthritis and hypertrophy, and a positive response (≥50% pain relief) to a single diagnostic intra-articular facet joint block. The number of treatments was not reported. At 6 months, there were no differences between the steroid injection and neurotomy in pain improvement on VAS, function improvement on ODI and RMDQ (Table 41), or analgesic usage (data not reported).

EASI vs. Extraarticular Control injections

One RCT at moderately low risk of bias compared medial branch injection with betamethasone 0.075 mg to 0.225 mg plus local anesthetic (n=60) versus local anesthetic (bupivacaine 0.25%) alone (n=60).[178,179] Patients were also randomized to Sarapin (extract from pitcher plant, thought to have analgesic properties) versus no Sarapin, however results were similar and the Sarapin and non-Sarapin groups were combined for the final analysis. All injections were performed using fluoroscopic guidance. The median duration of back pain was 108 months and all patients had a positive response (defined as ≥80% pain relief) to two diagnostic facet joint blocks. Imaging was not required for patient selection. Patients received a mean of six to seven injections over a period of approximately 24 months; the number of levels treated was not reported. There were no differences between medial branch steroid versus local anesthetic injection at all time points through 24 months on all outcomes, including mean pain scores

(0-10 NRS), likelihood of ≥50% pain relief, mean ODI score, likelihood of ≥40 percent improvement in ODI, and use of opioids (Tables 41 and 42).

The second trial, considered to be at moderately high risk of bias, randomized patients to receive methylprednisolone 0.5mg to 1.5 mg plus local anesthetic (n=42) versus local anesthetic (bupivacaine 0.25%) plus Sarapin (n=42).[166] The mean duration of back pain was 21 months and all patients had a positive response (not defined) to two diagnostic facet joint blocks. Imaging was not required for patient selection. Patients received a mean of six to seven injections over a period of approximately 2.5 years in four levels per patient. There were no differences between medial branch steroid versus local anesthetic injection at all time points through 12 months on all outcomes, including mean pain scores (0-10 NRS), likelihood of ≥50% pain relief, mean ODI score, likelihood of ≥40 percent improvement in ODI, use of opioids, or depression or generalized anxiety disorder as measure by the Millon Clinical Multiaxial Inventory and Beck Depression Inventory (Tables 41 and 42).

EASI vs. Medial Branch Radiofrequency Denervation

One trial at moderately low risk of bias randomized 100 patients with chronic low back (mean duration 19 months) to receive medial branch injection with 40 mg methylprednisolone plus local anesthetic (n=50) versus radiofrequency neurotomy (n=50),[53] (Tables 41 and 42). Both interventions were performed under fluoroscopic guidance and additional electrostimulation confirmation in the neurotomy group. Patients were required to have failed at least 6 weeks of conservative therapy prior to enrollment. Although patients in the injection group were not required to undergo diagnostic block, patients in the neurotomy group were required to have a positive response (criteria not reported) to a diagnostic block for inclusion. There were no imaging requirements for patient selection. Patients underwent a single treatment at one to four levels; the number of levels treated was similar in both treatment groups. The steroid injection was associated with worse outcomes than neurotomy at intermediate- and long-term follow-up based on VAS pain scores (mean difference 1.6 [95% CI: 1.27 to 1.93] at 6 months and 2.0 [95% CI: 1.79 to 2.21] at 12 months; no significant difference was seen in the short-term) and at all follow-up times regarding the likelihood of a successful pain outcome, defined as >50% improvement on VAS: 80% vs. 100% at 1 month (RR 0.8; 95% CI 0.7, 0.92), 68% vs. 90% at 6 months (RR 0.76; 95% CI 0.61, 0.93], and 62% vs. 88% at 12 months (RR 0.7; 95% CI 0.55, 0.9). There were no differences between groups in quality of life as measured by the EuroQOL Five Dimensions Questionnaire (EQ-5D) scores. Patient satisfaction was higher with neurotomy at 12 months (mean 2.0 vs. 1.5 on the North American Spine Society Patient Satisfaction Scale) though differences were not statistically significant at earlier time points. Results are difficult to interpret, as they may have been differential use of diagnostic blocks for selection of patients in the steroid injection and neurotomy groups.

4.1.8. Sacroiliac join pain

Two randomized trials evaluated sacroiliac joint injections for sacroiliac joint pain (Appendix L). Both trials were considered moderately high risk of bias.

IASI vs. Conservative treatment

One trial randomized patients with sacroiliac joint-related pain of at least 1 month but less than 12 months duration to receive one of three treatments: intraarticular injections with kenacort 20 mg plus lidocaine using fluoroscopic guidance (n=18), physiotherapy (n=15), or manual therapy (n=18),[235] (Tables 43 and 44). Physiotherapy consisted of a fixed exercise schedule over 6 weeks aimed at improving flexibility and strengthening back and pelvic floor muscles with exercises to be performed five to six time per day during week 1, then 3 times a day in subsequent weeks; guided exercises with a physiotherapist occurred 1 time per week. Manual therapy consisted of high-velocity thrust manipulation techniques to mobilize the sacroiliac joint over two sessions with an interval of 2 weeks. The mean age of all participants was 46 (range 20-73) years (not reported by group); the proportion of males in each group varied (11% for steroid, 27% for physiotherapy, and 44% for manual therapy). Patients with previous back surgery were excluded. There were no significant differences between groups in pain improvement on VAS in the short-term (up to 3 months). The likelihood of pain success (defined as an improvement of ≥2 points on VAS) and overall treatment success (complete relief of complaints at 6 weeks or 3 months, or 3 month mean VAS pain score less than baseline VAS score) was not significantly different at 3 months between patients who received steroid injections versus physiotherapy and versus manual therapy. Regarding function improvement, the steroid injection group showed a deterioration of function at 3 months as measured by the RAND-36 physical functioning domain while both the physiotherapy and manual therapy groups improved significantly, mean difference between groups, respectively: -31.15 (95% CI: -44.11, -18.19) and -37.9 (95% CI: -46.15, -29.65).

EASI vs. Extra-articular Control Injections

One trial randomized patients with chronic pain of the sacroiliac joint (SIJ) region to receive to single-level periarticular injections of methylprednisolone 60 mg plus lidocaine (n=13) or periarticular injections of lidocaine only (n=11).[128] Patients were included if they had pain and tenderness for at least 3 months, no signs of spondylarthropathy, and showed positive results on one or more of the following tests: Gaenslen's test, Patrick's test, or thigh flexion test. The two groups were similar, respectively, in mean age (50 vs. 49 years) but differed somewhat regarding sex (77% vs. 64% female) and duration of symptoms (5.4 vs. 4.4 years). The use of imaging guidance was not reported. One month post-injection, patients who received a steroid injection reported greater improvement in pain compared with patients who received only anesthetic: median change in VAS score from baseline -4.0 (range, -5.7 to -0.1) versus -1.3 (range, -6.4 to 4.3), p=0.046 (Table 43).

Cervical Spinal Injections

4.1.9. Cervical radicular pain due to disc pathology

ESI vs. Conservative Care

One moderately low risk of bias trial[58] assessed the impact of fluoroscopically guided interlaminar ESI of 60 mg depo-methylprednisolone plus saline (3 ml total volume) alone (n=55) versus conservative care (CC) consisting of medical (gabapentin and/or nortriptyline) and physical therapy (n=59) versus ESI plus CC (n=55) in patients with cervical radiculopathy attributed to disc pathology; the trial also compared ESI plus conservative care (ESI + CC) to CC alone (Appendix M).

Injections were done at C6-C7 or C7-C1; repeat injections were permitted at the one- and three- month follow-up. Both ESI groups received a mean of 1.3 injections per patient. The trial had an exit protocol such that patients with treatment failure (patient perceived worsening of pain, dissatisfaction with treatment, and >2-point decrease in NRS arm pain scores) at any point starting at the one-month follow-up appointment were able to leave the study in order to obtain other treatment(s). A relatively high percentage of patients in the ESI, CC, and ESI + CC groups exited the study per protocol: 45% vs. 47% vs. 33% after the one month follow-up appointment and 11% vs. 7% vs. 24% after the 3-month appointment; cumulatively, 56% of all patients (56% vs. 53% vs. 56% in each group, respectively) exited the trial. Once a patient left the trial, the last available data were carried forward. Baseline differences were present among the groups: median duration of pain was slightly longer in the CC alone group (12 months) compared with the ESI (10 months) or ESI + CC (8 months) groups, slightly more patients in the CC group were obese (36%) than those in the ESI (26%) or ESI + CC (22%) groups, while fewer patients in the CC group were using opioids (31%) than those in the ESI + CC group (44%).

Pain

There was no difference between the ESI alone group versus the CC group in improvement in arm pain at 3 months, MD -0.4, (5% CI: -1.0 to 0.2). At 6 months the ESI group had significantly less improvement than the CC group, MD 1.1 (95% CI: 0.5, 1.7). There was a greater improvement in neck pain versus the CC group at the 3 month follow-up, but by 6 months the ESI group had significantly less improvement in neck pain than the CC group. Arm pain improvement was significantly better with ESI plus CC versus CC alone at 3 months, MD -1.3, 95% CI -1.9 to -0.7), but not at 6 months, MD 0.5 (95% CI: -0.2 to 1.2,) (Tables 45). This pattern was similar with respect to neck pain at 3 months, but by 6 months the ESI plus CC group had significantly less improvement in neck pain than the CC group (Table 46).

Function

The ESI (± CC) groups had significantly worse NDI scores than the CC group both in short- and intermediate-term follow-ups (Table 47).

Other outcomes

There was no difference between groups at 3 months in the percent of patients with positive global perceived effect (GPE); a composite outcome of a positive GPE plus a reduction in arm pain by at least 50%; medication reduction (≤20% decrease in use of opioids or discontinuation of non-opioids); or the proportion of patients receiving surgery (Table 48). Using another composite outcome of a positive GPE, a ≥2-point decrease in NRS arm pain score, and no additional procedural intervention, there was no difference between the ESI alone versus CC groups at either 3 or 6 months. However, significantly more patients in the ESI + CC group had a positive outcome than the CC group at both 3 months (RR 2.12, 95% CI: 1.29, 3.48) and 6 months (RR 1.86, 95% CI: 1.05 to 3.29) (Table 48). This result suggests that the addition of conservative care to ESI may confer additional benefit to the patient in this composite outcome.

4.1.10. Cervicobrachialgia (neck pain with or without radiculopathy and/or stenosis)

ESI vs. Control Injections

One moderately high risk of bias trial evaluated 80 mg methylprednisolone and 5 ml 1% lidocaine administered in the epidural space (approach not specified) (n=25) versus in the posterior neck muscle (n=25) in patients with cervicobrachialgia attributed to disc degeneration and/or osteoarthritis, with or without radiculopathy, and with or without stenosis (Appendix N).[223]

Eight patients (all randomized to the intramuscular injection group) were excluded from all analyses after the patients became involved in insurance claim litigations during the follow-up period leading to differential loss to follow-up between the ESI and control group (100% vs. 68% follow-up).

This study was considered to be at moderately high risk of bias due to methodological limitations surrounding random sequence generation, allocation concealment, non-adherence to the intention to treat principle, blind assessment of the primary outcome (pain), and differential loss to follow-up between groups.

Pain

More ESI patients had pain success (≥50% improvement) versus patients with intramuscular steroid injection (68% vs. 12%, RR 5.78, 95% CI: 1.53, 21.84). The authors provided additional results for different categories of pain relief, stratified as very good (≥75%), good (50-74%), satisfactory (31-49%), poor (0-30%), or worse (≤0%); results are presented in Table 49.

Opioid use

Significantly more patients in the ESI group than the intramuscular steroid injection group had a decrease in the daily analgesic dose at 12 months (64% vs. 9%, $p<0.05$). It was not clear if the reduction was required to be from baseline or from another prior date; it was also not clear how many patients in each group were used for these calculations.

4.1.11. Cervical disc herniation with or without radiculopathy

ESI vs. Control Injections

One moderately low risk of bias trial randomized 120 patients to fluoroscopically guided interlaminar epidural injections with "non-particulate" betamethasone (6 mg in 1 ml) plus 4 ml 0.5% lidocaine injections (n=60) (ESI) or interlaminar epidural injections of 5 ml 0.5% lidocaine (n=60) (ENSI) for chronic disc herniation with or without radiculopathy (Appendix O).[156-158] Patients continued medical therapy, were involved in an exercise therapy program, and were instructed to continue work (if they had been working previously). Patients could receive repeat injections if they developed increasing pain levels as well as a decrease in functional ability and pain levels to below 50%. Baseline characteristics were similar between ESI and ENSI groups with the exception of weight, which was significantly lower in the ESI group (168.1 ± 35.2 vs. 208.3 ± 53.3, units not reported).

Data for all 120 patients were included in the analyses by carrying forward the last available data for missing patients. The study was considered to be at moderately low risk of bias due to methodological limitations surrounding unclear details on how allocation concealment was ensured as well as not controlling for the potentially confounding difference in weight between treatment groups.

Pain

There was no significant differences between ESI and ENSI in terms of the percentage of patients who achieved ≥50% pain relief in the short-, intermediate- and long-term (Table 50). The difference in change from baseline in mean NRS scores was similar between groups at 3 and 24 months but not a 6 months where the ESI group had less improved pain versus the ENSI group, MD 0.4 (95% CI: 0.1, 0.7) (Table 51). The mean duration of ≥50% pain relief per procedure was similar between the ESI and ENSI groups for the first two injections, for the injections subsequent to the first two, and for each procedure.

Function

Fewer patients in the ENSI group achieved ≥50% improvement in NDI scores at 3 months (70% vs. 85%, RR 0.82, 95% CI 0.68, 1.00), but not at 6 or 24 months (Table 52). The ESI group had less improvement in disability scores versus the ENSI group at 3 months, MD 1.3 (95% CI: -0.02, 2.6) and 6 months, MD 1.9 (95% CI: 0.5 to 3.3) but not at 24 months (Table 53).

Other outcomes

There was no difference at 6 or 24 month follow-up between the ESI and ENSI groups in the proportion of patients achieving a composite outcome which included ≥50% improvement from baseline in both NRS pain and NDI scores (Table 54). There was no difference in in opioid intake (as measured in morphine equivalence) between groups at any time period.

4.1.12. Nonradicular neck pain

ESI vs. Control Injections

One moderately low risk of bias trial evaluated fluoroscopically guided interlaminar epidural injections with "non-particulate" betamethasone (6 mg in 1 ml) plus 4 ml 0.5% lidocaine injections (n=60) (ESI) versus interlaminar epidural injections of 5 ml 0.5% lidocaine (n=60) (ENSI) in patients with chronic axial or discogenic neck pain of at least six months' duration without disc herniation, radiculopathy, stenosis, or spondylosis, or facet pain (Appendix P).[152,153,155] All patients were instructed to participate in a structured exercise program as well as to continue both medical therapy and work. Repeat injections were permitted in patients who experienced increased pain and a decrease in functional ability to below 50%. In general, baseline characteristics were similar between groups with the exception of weight, which was significantly lower in the ESI group (164.7 ± 39.3 vs. 183.6 ± 57.5 (units not reported).

Pain

There were no significant differences between groups in the proportion of pain reduction of ≥50% from baseline in the short-, intermediate- and long-term (Table 55). The difference in change from baseline in mean NRS scores was similar between groups at all follow-ups (Table 56). The mean duration of ≥50% pain relief per procedure was statistically similar between the ESI and ENSI groups for the first two injections (8.2 vs. 8.6 weeks), for the injections subsequent to the first two (11.5 vs. 13.1 weeks), or for each procedure (11.7 vs. 12.2 weeks).

Function

There were no differences between groups in the proportion of patients achieving ≥50% improvement in NDI scores in the short-, intermediate-, and long-term follow-up periods (Table 57). Further, the change from baseline in NDI scores were statistically similar between groups at all follow-up time points (Table 58).

Other outcomes

There was no difference at 3, 6 or 24 month follow-up between the ESI and ENSI groups in the proportion of patients achieving a composite outcome which included ≥50% improvement from baseline in both NRS pain and NDI scores (Table 59). There was no difference in opioid intake (as measured in morphine equivalence) between groups at any time period.

4.1.13. Cervical spinal stenosis

ESI vs. Control Injections

Studies included

One moderately low risk of bias trial evaluated fluoroscopically guided interlaminar epidural injections with "non-particulate" betamethasone (6 mg in 1 ml) plus 4 ml 0.5% lidocaine injections (n=30) (ESI) versus interlaminar epidural injections of 5 ml 0.5% lidocaine (n=30) (ENSI) in patients with spinal stenosis and at least six months' pain in the neck and upper extremity that was rated a 6 on a 10-point VAS scale and limited function (Appendix Q).[163] Patients continued exercise programs as well as both medical therapy and work; no specific co-intervention was prescribed. Repeat injections were permitted in patients who experienced increased pain and a decrease in functional ability to below 50%. In general, baseline characteristics were similar between groups with the exception of weight, which was significantly lower in the ESI group (170.7 ± 32.7 vs. 196 ± 54.2 (units not reported).

The trial was considered to be at moderately high risk of bias due to methodological limitations regarding unclear details regarding how allocation was concealed, failure to adhere to the intention to treat principle, unclear whether outcomes were evaluated in a blinded manner, follow-up of less than 80% randomized patients, lack of information regarding complete follow-up of patients randomized to each group (and thus an inability to determine whether there was <10% difference in follow-up between groups), as well as not controlling for the potentially confounding difference in weight between treatment groups.

Pain

There were no significant differences between groups in the proportion of pain reduction of ≥50% from baseline in the short-, intermediate- and long-term (Table 60). The difference in change from baseline in mean NRS scores was similar between groups at all follow-ups (Table 61). The mean duration of ≥50% pain relief per procedure was statistically similar between the ESI and ENSI groups for the first two injections (8.2 vs. 8.6 weeks), for the injections subsequent to the first two (11.5 vs. 13.1 weeks), or for each procedure (11.7 vs. 12.2 weeks).

Function

There were no differences between groups in the proportion of patients achieving ≥50% improvement in NDI scores in the short-, intermediate-, and long-term follow-up periods (Table 62). The ESI group experienced significantly less time with ≥50% pain relief per procedure (8.6 ± 3.6 weeks vs. 11.3 ± 5.8 weeks) Further, the change from baseline in NDI scores were statistically similar between groups at all follow-up time points (Table 63).

Other outcomes

There was no difference at 3, 6 or 24 month follow-up between the ESI and ENSI groups in the proportion of patients achieving a composite outcome which included ≥50% improvement from baseline in both NRS pain and NDI scores (Table 64). There was no difference in opioid intake (as measured in morphine equivalence) between groups at any time period.

4.1.14. Failed neck surgery syndrome

ESI vs. Control Injections

One moderately high risk of bias trial evaluated fluoroscopically guided interlaminar epidural injections with "non-particulate" betamethasone (6 mg in 1 ml) plus 4 ml 0.5% lidocaine injections (n=28) (ESI) versus interlaminar epidural injections of 5 ml 0.5% lidocaine (n=28) (ENSI) in patients with cervical surgery performed at least 12 months ago and who had chronic (≥6 months) pain in the neck and upper extremity that limited function, and that was unresponsive to medical, exercise, and physical therapy (Appendix R).[162] All patients were instructed to participate in a structured exercise program as well as to continue both medical therapy and work. Repeat injections were permitted in patients who experienced increased pain and a decrease in functional ability to below 50%. In general, baseline characteristics were similar between groups with the exception sex (males comprising 68% of the ESI group but only 36% of the ENSI group) and height (patients in the ESI group were slightly taller than those in the ENSI group).

The trial was considered to be at moderately high risk of bias due to methodological limitations regarding unclear details regarding how allocation was concealed, failure to adhere to the intention to treat principle, unclear whether outcomes were evaluated in a blinded manner, follow-up of less than 80% randomized patients, lack of information regarding complete follow-up of patients randomized to each group (and thus an inability to determine whether there was <10% difference in follow-up between groups), as well as not controlling for the potentially confounding difference in sex and height between treatment groups.

Pain

There were no significant differences between groups in the proportion of pain reduction of ≥50% from baseline in the short-, intermediate- and long-term (Table 65). However, at three months, the ESI group had significantly less pain reduction from baseline than the ENSI group, as measured by the mean NRS score change from baseline, MD 0.5 (95% CI: 0.1, 0.9). This difference was not sustained later time points (Table 66).

Function

There were no differences between groups in the proportion of patients achieving ≥50% improvement in NDI scores in the short-, intermediate-, and long-term follow-up periods (Table 67). Further, the change from baseline in NDI scores were statistically similar between groups at all follow-up time points (Table 68).

Other outcomes

There was no difference at 3, 6 or 24 month follow-up between the ESI and ENSI groups in the proportion of patients achieving a composite outcome which included ≥50% improvement from baseline in both NRS pain and NDI scores (Table 69). There was no difference in daily opioid use (as measured in morphine equivalence) between groups at any time period.

4.1.15. Facet joint pain

IASI vs. Intra-articular control injections

Two moderately low risk of bias trials[21,177,181] compared the impact of a fluoroscopically guided intra-articular (medial branch) steroid injection (IASI) versus a non-steroid intra-articular injection (IANSI)

control in patients with chronic facet joint neck pain (≥3-6 months) and who had a positive response on two diagnostic blocks given on separate occasions and with two different local anesthetics (Appendix S).

One trial[159,177,181] injected "non-particulate" betamethasone (0.15 mg/ml; volume NR) plus 0.25% bupivacaine (volume NR) with or without equal volumes of Sarapin (dose NR) in the IASI group (n=60) and 0.25% bupivacaine (volume NR) with or without equal volumes of Sarapin (dose NR) in the IANSI group (n=60). Although this study originally randomized patients to four groups (two groups without Sarapin and two groups with Sarapin), the authors found no impact of Sarapin on the results and thus pooled results based on the presence versus absence of steroid. The study offered repeat injections to patients who achieved at least 50% pain relief after the first therapeutic injection and whose pain levels decreased to below 50% compared with pre-injection pain levels. The second study[21] injected 0.57 mg betamethasone (1 ml) in the IASI group (n=21) and 0.5% bupivacaine (1 ml) in the IANSI group (n=20) and only allowed one injection per patient.

Baseline characteristics were similar between IASI and IANSI groups in both studies. In general, trials were considered to be at moderately low risk of bias due to methodological limitations regarding unclear details regarding how allocation was concealed; the trial by Manchikanti et al.[177,181] also did not report whether outcomes were evaluated in a blinded manner. The Manchikanti trial was considered to be at moderately high risk of bias for long-term outcomes as the follow-up rate for 24 month outcomes was not reported.

Pain

Both studies reported no difference between treatment and control groups in the proportion of patients reporting ≥50% pain relief, though one study reported only 10% versus 11% achieving ≥50% at 2.7 month follow-up[21] while the other study reported 95% vs 87% at 6 month and 93% versus 85% at 24 month follow-up (Table 70).[177,181] There was no difference between groups in mean pain improvement at 3 or 6 months in one study.[177,181] At 24 months, the IASI group had a statistical but not clinically important improvement in pain versus the IANSI group, MD -0.3, (95% CI: -0.6, -0.05) (Table 71).

Function

One study found no difference between groups in the proportion of patients achieving ≥50% improvement in NDI scores in the intermediate- or long-term (Table 72).[177,181] Similarly, there was no statistical difference between groups in change from baseline in mean NDI scores at any time point measured (Table 73).

Opioid use

No difference in daily opioid usage (as measured in morphine equivalence) between ESI and ENSI groups at 24 months.[177,181]

IASI vs. Conservative care

One moderately high risk of bias trial[199] compared bilateral fluoroscopically guided inter-articular steroid injections (IASI) with 5 mg triamcinolone, 187.5 IU hyaluronidase, and 0.5 ml 1% lidocaine at both C5-C6 and C6-C7 (n=200) versus no injection (n=200) in patients with chronic myofascial pain syndrome attributed to the facet joints (see Appendix X for study's definition of this condition). All patients received conservative care, which consisted of an exercise program and opioid and non-opioid analgesics plus a muscle relaxant. Patients in the IASI group could receive additional trigger point

injections with 1 ml 1% lidocaine on the first two follow-up visits, and at the third visit were offered Botox injections in any remaining trigger points in the trapezius muscles. This study had high loss to follow-up (23.5%), no information on random sequence generation, allocation concealment, or blinded outcomes assessment; co-interventions were not applied equally (the injections group only could receive additional and Botox intra-muscular injections during the follow-up period); and less than 80% complete follow-up. In addition, the study did not provide data on baseline characteristics for patients randomized, thus there was a concern regarding controlling for potentially confounding baseline characteristics.

Pain

There were fewer patients in the IASI group reporting tension-type headaches than patients in the no injection group at 3, 6, and 12 months follow-up (Table 74). Further, the IASI group had significantly greater pain improvement from baseline compared with the no injection group on a 0-10 NRS scale at 3, 6, and 12 months (Table 75). All data in the Table are approximate, as they were estimated from graphs. The IASI group had approximately 3 more months being symptom-free between the injection and 12 months compared with the no injection group (7.2 vs. 4.2 months).

4.1.16. Repeat, multilevel, and bilateral spinal injections

Many studies included repeat, multilevel, and bilateral injections. However, like the previous review, we did not find any studies that compared repeat with single injections, multilevel with one-level injections, or bilateral with unilateral spinal injections.

4.2. Key Question 2: Harms

4.2.1. Number of studies retained

For this key question, all adverse events reported in the RCTs included in key question 1 were included. A total of four nonrandomized comparative studies (cohort studies) were reviewed at full-text for inclusion, three of which were included after full-text review.[80,107,182] In addition, the full-text articles of 37 case series of harms were reviewed for inclusion, 22 of which met the inclusion criteria.[30,31,42,73,76,90,102,105,111,114,117,119,121,124,131,150,184,202,218,222,236,237] Details on studies excluded after full text review are available in the Appendix C.

4.2.2. Adverse event categorization

Adverse events were categorized as catastrophic, serious, or non-serious. Catastrophic adverse events included non-transient paralysis (tetraplegia, paraplegia), blindness; as well as death, arachnoiditis, stroke, cardiac arrest, spinal cord infarction, spinal cord injury, and meningitis. Serious events included epidural hematoma, deep infection, respiratory failure, spinal nerve injury, fever or infection attributed to the injection, hematoma, intravascular injection of steroid with neurologic sequelae, nerve root injury, retroperitoneal hematoma, subarachnoid injection, seroma, neurovascular complications, surgery or hospitalization necessary due to adverse events attributed to the procedure, and angina attributed to the procedure. The following were considered non-serious unless sufficient detail was reported to suggest that symptoms did not remit easily or were more severe: cerebrospinal fluid tap, dural puncture or tears, new neurological symptoms, sensory deficits, paresthesia and numbness in

lower extremity, excessive pain, procedural bleeding, and procedural hypotension. All other adverse events were considered to be non-serious in nature.

Lumbar Spinal Injections

4.2.3. Randomized controlled trials

For the comparison of lumbar ESI to ENSI (any approach), all adverse events are listed in Appendix T. The only catastrophic event formally evaluated was meningitis by one trial, with no cases (0% vs. 0%). Serious adverse events that occurred included retroperitoneal hematoma in one trial (1% (1/80) vs. 0%, p=0.3), subarachnoid entries in 2.2% of all ESI and ENSI procedures (no other details reported) in one tria[136,137]l and subarachnoid punctures without headache in 3.0% of all ESI and ENSI procedures in another trial.[140-142] In addition, one trial reported that "serious adverse events" (hospitalization and/or surgery) occurred similarly between ESI and ENSI groups (2.5% vs. 2.0%, RR 1.25, 95% CI 0.34 to 4.58, p=0.74); no further details on these incidents were reported. The following serious events were reported to occur in no patients in either group: epidural hematoma[67] (1 RCT), hematoma[196] (1 RCT), deep infection[196] (1 RCT), nerve root injury (1 RCT),[67] spinal nerve injury (1 RCT),[196] subarachnoid injection[68,84] (2 RCTs), and "major adverse events" (1 RCT).[139,143,144] While one RCT reported the need to administer naloxone for reversal of respiratory depression in 3 ESI patients, these events were specifically attributed to the combination of triamcinolone and morphine injected. Non-serious adverse events included (but are not limited to) sensory deficits (13%-28% vs 48%),[68] worsening pain/symptoms (4%-13% vs. 19%-36%),[38,59] nausea (13%-20% vs. 9%-17%),[38,59] local pain (5.2%-21% vs. 5.2%-7.1%),[67,108] headache (0%-38% vs. 0%-31%),[44,55,67,175,176,180] and discomfort at injection site (27% vs. 18%).[38]

For the comparison of lumbar ESI versus NEI, adverse events are detailed in Appendix T. Catastrophic events and serious adverse events were not reported. Non-serious adverse events included (but are not limited to) accidental CSF tap (6%-10.5% vs. 0%-6%),[72,209] post-dural puncture headache (0.8% vs. 0%), headache (1.2%-3% vs. 0%-4%),[13,204,209] local pain (5.2% vs. NR),[108] and nausea (1.6% vs. 1.8%).[13,204]

For the comparison of lumbar ESI versus disc or decompression procedures (discectomy, decompression, nucleoplasty) adverse events are listed in Appendix T. Catastrophic events were not reported. Serious adverse events that occurred included paraesthesia and numbness in the lower extremity that resolved spontaneously within 3 to 4 days (4% vs. 13%, RR 0.36, 95% CI 0.04 to 3.24, p=0.34) (1 RCT)[15] and seroma (0% vs. 1.3%, p=0.42) (1 RCT).[41] The following serious events were reported to occur in no patients in either treatment group: hematoma (1 RCT),[36] infection (1 RCT),[36] nerve root damage (1 RCT),[240] neurovascular complications (1 RCT), [36] blood transfusion (1 RCT),[36] and re-hospitalization due to injection-related adverse events (1 RCT).[36] Non-serious adverse events included (but are not limited to) dural puncture/tear/durotomy (0%-4% vs. 0%-2.6%), injection site pain (5% vs. 4.4%)[86] and increased back/radicular pain (2.5% vs. 8.9-11%).[86]

For the comparison of lumbar ESI versus conservative care, adverse events can be found in Appendix T Catastrophic events were not reported. Only one study reported serious adverse events, with "major side-effects" occurring in no patients (0% vs. 0%). Non-serious adverse events in the ESI group included angina pectoris (3%),[122] bleeding during procedure (4%),[188] dural puncture (0%),[188] and hypotension leading to vasovagal response (24% (12/50))[188] which was managed immediately, transient bilateral lower extremity numbness (40% (20/40)),[188] and headache (18%).[188]

For the comparison of lumbar IASI versus IANSI, adverse events are summarized in Appendix T. No catastrophic adverse events were reported. Serious adverse events were reported by one study as "significant adverse events", and none occurred (0% vs. 0%).[83] Other adverse events were reported as "adverse events" (0% vs. 0%)[45] and "side effects" (6.6%).[126]

For the comparison of lumbar IASI versus NIAI, adverse events can be found in Appendix T. Neither catastrophic nor serious events were reported. Non-serious side effects included (but aren't limited to) death from heart failure (not attributed to procedure, 3% vs. 0%) dizziness (5%), increased blood glucose (8.3%), nausea (5%), and post-procedural pain (15%).[208]

For the comparison of lumbar IASI versus radiofrequency denervation, adverse events are listed in Appendix T. No catastrophic events were reported. Serious adverse events were reported as "major adverse events" and none occurred (0% vs. 0%). No other adverse events were reported.

For the comparison of lumbar EASI versus EANSI, adverse events can be found in Appendix T. Neither catastrophic nor serious adverse events were reported. Non-serious adverse events were assessed, but did not occur, and included post-puncture headache,[166] infection,[166] rash,[166] weight gain,[166] and "adverse events".[166]

For the comparison of lumbar EASI versus NEAI, adverse events can be found in Appendix T. There were no catastrophic or serious adverse events reported. Minor adverse events only included "side-effects" which occurred in 6.6% of patients.[126]

For the comparison of lumbar EASI versus disc or decompression procedures, adverse events are detailed in Appendix T. There were no catastrophic adverse events reported. The only serious adverse event reported was infection, which did not occur in any patients in either group in one trial.[53] Other adverse events assessed included new motor deficit, and new sensory deficit, but none occurred (0% vs. 0%).[53] However, some patients experienced increased severity of low back pain (0% vs. 4%).[53]

4.2.4. Cohort studies

Adverse events for lumbar ESI versus conservative care can be found in Appendix U. Catastrophic or serious adverse events were not reported. Non-serious adverse events reported included (but are not limited to) lumbar disc displacement (37% vs 35%), lumbar disc degeneration (38.8% vs 34.8%), lumbar spinal stenosis (54.7% vs 51.9%), lumbago (90.0% vs 91.9%), spinal stenosis (54.7% vs 51.9%), and radiculopathy (59.3% vs 62.0%).[182]

For the comparison of lumbar EASI versus EANSI, adverse events can be found in Appendix U. No catastrophic or serious adverse events were reported. Other adverse events were reported as "any complication", and did not occur (0% vs 0%).[80]

No cohort studies met the inclusion criteria for the following comparators: lumbar epidural spinal injections versus non-steroid epidural injections, lumbar epidural steroid injections versus non-epidural injections, lumbar epidural steroid injections versus disc or decompression procedures, lumbar epidural steroid injections versus conservative care.

4.2.5. Case series

Adverse events for lumbar epidural spinal injections (any approach) can be found in Appendix V. No catastrophic events were reported; those evaluated included quadriparesis, paraplegia, respiratory depression, and respiratory failure.[124] One case of transient paraplegia[124] occurred following an interlaminar ESI with 40 mg triamcinolone acetonide plus local anesthetic performed under fluoroscopic guidance; the patient recovered within 90 minutes of the procedure; epidural lipomatosis was reported in one trial to occur in 6.1%[111] of ESI injections with methylprednisolone. Other serious adverse events reported to occur in no patients included fever[150], infection,[42] and respiratory depression or failure.[124] Non-serious adverse included (but are not limited to) chest pain or discomfort (0%),[124] dural puncture (0%-1.1%),[31,102,184] intravascular injection[102]/uptake[90] of steroid (0%-14.3%),paresthesia during procedure (2.0%),[102] flushing (1.2%-11.3%),[30,76] headache (1%-4.8%),[30,150] and pain/soreness at the injection site (0.23%-6%).[30,31,102,150,184]

Adverse events for lumbar intra-articular injections are summarized in Appendix V. No catastrophic events were reported. The only serious adverse event reported was medication entrance into the subarachnoid space in 0.06% patients, however no adverse sequelae occurred.[222] Non-serious adverse events included (but are not limited to) puncture of the dural sac (0.06%),[222] and increased or new pain (2.3%).[222]

Adverse events for lumbar extra-articular injections (medial branch block) can be found in Appendix V. No catastrophic events occurred, including paraplegia or quadriparesis.[124] There were five events (in three patients) of transient paraplegia[124] occurred following an medial branch block with 40 mg triamcinolone acetonide plus local anesthetic performed under fluoroscopic guidance; all patients recovered within 1.3 to 8 hours of the procedure. There were no cases of respiratory depression or failure.[124] Other adverse events evaluated included leg weakness, nausea, and chest pain or discomfort, of which there were no reported cases.[124]

Cervical Spinal Injections

4.2.6. Randomized controlled trials

For the comparison of cervical ESI versus ENSI, adverse events are detailed in Appendix W. No catastrophic events were reported. Serious adverse events reported were subarachnoid puncture in 0.3% to 0.9%[152,153,157,158,163,174] of all injections across four trials.[152,153,157,158,163,174] Non-serious adverse events included (but are not limited to) intravascular penetration/entry (0.5%-1.5%)[152,153,157,158,163,174] and nerve root irritation (0.4%-0.8%).[152,153,157,158]

For the comparison of cervical ESI versus NEI, adverse events can be found in Appendix W. The only reported events included “complications of ESI”, which did not occur in any patients (0%).[223]

For the comparison of cervical ESI versus conservative care, adverse events are reported in Appendix W. No catastrophic or serious events were reported. Other adverse events occurring in the ESI group included (but weren’t limited to) wet tap associated with neurological sequelae in the ESI group, (no other details were reported) (0.7%),[58] headache (1.4%),[58] tachycardia (0.7%), and vasovagal episodes (0.7%).[58]

Adverse events for cervical IASI versus IANSI can be found in Appendix W. No catastrophic events were reported. The only serious adverse events reported were nerve root or spinal trauma[177,181] and

infection[177,181] there were no cases of either of which there were no cases. One non-serious adverse event was reported- facial flushing (4.9%).

4.2.7. Cohort studies

No cohort studies of cervical spinal injections were identified that met the inclusion criteria.

4.2.8. Case series

Adverse events for cervical epidural steroid injections (any approach) can be found in Appendix X. Catastrophic events (paraplegia, quadriparesis, respiratory depression/failure) were evaluated by one study,[124] with no cases occurring. One study reported a case of superficial infection and abscess at the injection site that required incision, drainage, and antibiotics (0.5%),[237] another reported that no "serious/significant complications" occurred.[236] Non-serious adverse events included (but weren't limited to) chest pain/discomfort (0%),[124] dural puncture and associated headache (1.0%),[237] intra-arterial injection (1.7%),[121] vascular trespass (19.7%), inadequate epiradiucular flow (4.1%),[121] and operative nerve pain or paresthesia (15.6%).

None of the included case series reported on cervical intra-articular injections.

Adverse events for cervical extra-articular (medial branch) injections are detailed in Appendix X. There were no catastrophic events, including brain stem injury/infarct,[218] cerebellar/cerebral injury/infarct,[218] death,[131] stroke,[131] spinal cord injury/infarct,[131,218] paraplegia,[124] or paralysis. [131] Other serious events included one case each of respiratory depression and respiratory failure;[124] both patients recovered within 10 to 60 minutes. One patient had transient quadriparesis[124] (with no respiratory depression) and recovered within 60 minutes; the event was attributed to accidental intravascular injection of steroid and local anesthetic. Another patient was diagnosed with conversion disorder after reporting quadriparesis[124] following MBB injection and subsequent hospitalization; the quadriparesis[124] event was attributed to this disorder. Additional serious adverse events reported included grand mal seizure (0.02%),[218] life-threatening anaphylactic reaction (0.02%),[218] increased clinical pain for ten or more days (10%),[218] nerve root injury/infarct (0%),[218] vertebral artery injury (0%),[131] suspected hematoma (0.2%),[202] infection (0%),[131,218] and "any major complication" (0%).[202] Non-serious adverse events included (but weren't limited to) chest discomfort (1.0%),[124] chest pain (0.5%),[124] and an increase in pain (2.0%-10%).[202,218]

Lumbar or Cervical Spinal Injections

4.2.9. Cohort studies

Adverse events for mixed cervical and lumbar steroid injections versus no injection can be found in Appendix Y. Neither catastrophic nor serious adverse events were reported. Other adverse events included "agitation" (17% vs. 53%), fatigue/malaise (19% vs. 43%), increased pain at injection site (30% vs. 8%), increased radicular pain (37% vs. 36%), increased spine pain (37% vs. 33%), insomnia (9-11% vs. 38-40%), and lower extremity numbness (11% vs. 32%).[107]

4.2.10. Case series

Adverse events for mixed cervical and lumbar epidural steroid injections (any approach) are available in Appendix Z. Catastrophic events were not reported. Serious adverse events included presentation to ED and admitted for leg weakness (0.05%), presentation to ED on day of injection for chest pain with overnight hospitalization (0.05%), epidural hematoma (0.019%),[114] fever and pain at the injection site

(0.05%),[184] infection (0%),[114] and "major complications" (0%).[184] Non-serious events included (but are not limited to) transient hypotensive episode (0.019%),[114] chest and back pain (0.05%-0.16%),[184] increased radicular pain (12%),[73] increased spine pain (6%),[73] headache (0%-13.3%),[73,184] heart burn (6%),[73] hyperactivity/euphoria/anxiety (0%-5.3%),[73] increased pain (0.05%-14.6%),[73,184] insomnia (13.3%),[73] nausea (0% to 5.3%),[73] numbness (0%-10%),[73,184] puritus (4.7%),[73] and tingling (2.7%-4.7%).[73]

4.2.11. Case reports of catastrophic adverse events

It has been widely acknowledged that rarely, catastrophic neurologic events may occur in patients who undergo ESI. In 2014, the FDA assembled a report[78] that reviewed major neurologic adverse events (AEs) reported in the FDA Adverse Event Reporting System (FAERS) as well as those published in the peer-reviewed literature.

The FAERS database was searched for all adverse events reported between 11/1/97 and 4/23/14; a separate search of this database for arachnoiditis was also conducted through 4/23/14. A total of 131 major neurologic adverse events associated with ESI were reported between November 1997 and April 2014. The most common adverse event reported was arachnoiditis, with a total of 41 cases. The majority of these cases did not have information regarding injection route (1 interlaminar), site (4 lumbar, 1 lumbosacral, 1 sacral, and 1 cervical), or use of imaging (contrast media used in 1, none specified in 2 patients). The primary reported outcome of arachnoiditis in these 41 cases included disability (41%), hospitalization (27%), death (5%), need for intervention (2%), and "other serious" outcomes (24%). All but two of these cases occurred in patients who had been injected with particulate steroids (methylprednisolone in 85% and triamcinolone in 10%); the remaining 5% of patients had received a non-particulate steroid (betamethasone). The event outcome was listed as persisting in all of the 17 reports with this information. Of the remaining 90 major neurologic adverse events reported in the FAERS database, the primary outcome was listed as hospitalization (39%), disability (19%), death (3%), life threatening (1%), and "other serious" outcome (38%). Adverse events listed included (but aren't limited to) a brainstem stroke, motor-incomplete tetraplegia, paraplegia, paralysis, spinal cord infarction, cardiac arrest, spinal epidural lipomatosis, severe spasm pain leading to laminectomy and epidural hematoma evacuation, seizures, blindness, hemorrhages of the eyes, meningitis, and personality and behavioral changes. As for arachnoiditis, all but two patients had received a particulate steroid. Injection site varied, as did route of injection. Of the 43 cases reporting, the event outcome was documented as persisting in 79% and as resolving or resolved in 21%. In total, there were five deaths reported in the FAERS database, including suicide in two patients with arachnoiditis; all five of these patients had received particulate steroid injections.

Two separate searches of the published literature were conducted using Pubmed: one in which all major adverse events were sought (8/1/12-8/1/14), and one in which only arachnoiditis events were sought (through 10/20/14). A complete list of adverse events retrieved from this search was not provided, however the report includes discussion of intravascular steroid injection (lumbar transforaminal and caudal ESI), paraplegia (lumbar transforaminal and interlaminar ESI), cauda equine syndrome (caudal ESI), cervical spinal cord injury (interlaminar ESI), and infective arachnoiditis (lumbar caudal ESI).

The FDA report concluded that catastrophic or major neurologic adverse events following ESI can occur but are rare. These events have not been clearly attributed to any particular injection approach or imaging utilization, and while the vast majority of events occurred in patients who received particulate steroid injections, a causal relationship between particulate steroid injections and catastrophic events has not been established.

4.3. Key Question 3: Differential Efficacy and Harms in Subpopulations

Lumbar Spinal Injections

4.3.1. Number of studies retained

Of 34 lumbar RCTs included in Key Question 1, nine trials [217 13,57,81,86,87,116,209,226,228,229] (one of which was reported across three publications) stratified results for both treatment groups according to subgroups of interest. Subgroups evaluated included baseline disc pathology; duration of pain; duration of symptoms; stenosis severity; injection approach; age; sex; race; ethnicity; body mass index; education; employment; smoking history; diabetes; neurological abnormalities; treatment expectations; previous episodes of sciatica; coexistent back pain; ODI scores; EQ-5D index scores; EQ-5D pain scores; Patient Health Questionnaire-8 scores; Generalized Anxiety Disorder-7 scores; Pain Catastrophizing Scale total scores; Pain Catastrophizing Scale helplessness, rumination, and magnification subscale scores; Fear-Avoidance Beliefs Questionnaire physical activities subscale scores; anxiety scores; and depression scores. No studies evaluated the differential efficacy or safety impact of Worker's Compensation, insurance status, litigation, or steroid particulate size.

4.3.2. Differential efficacy and safety: lumbar spinal injections

ESI versus injection control in patients with radiculopathy due to HNP:

One small trial[228] of patients with radiculopathy due to disc pathology compared transforaminal ESI of 40 mg methylprednisolone and bupivacaine to transforaminal ESI of bupivacaine alone; all injections were performed using fluoroscopic guidance. This study formally evaluated the impact of disc pathology and found:

- Disc pathology (disc prolapse versus foraminal narrowing, may modify treatment effect with respect to short-term (3 months) change in ODI scores: patients with disc prolapse (n=76) had similar improvement in ODI scores between ESI and ENSI groups (13.6 ± 3.1 (n=42) vs. 13.8 ± 3.7 (n=34), MD -0.2, 95% CI -1.8 to 1.4, p=0.80), while those with stenosis (n=48) did significantly better when treated with ESI versus ENSI (1.5 ± 2.6 (n=23) vs. 6.5 ± 3.4 (n=25), MD -5.0, 95% CI -6.8 to -3.2, p<0.01); the test for interaction suggested that disc prolapse versus foraminal narrowing modified the treatment effect (p=0.042).
- Disc pathology (disc prolapse versus foraminal narrowing, did not modify treatment effect with respect to short-term (3 months) change in leg pain VAS scores, with reported interaction p-values of at least 0.05.

Another small trial[116], with a total enrollment of 128 patients, compared transforaminal ESI injections (methylprednisolone plus bupivacaine) to transforaminal ENSI injections (saline); all injections were fluoroscopically-guided. This study found:

- Disc pathology on MRI (disc herniation(s) versus extrusion(s)) may modify treatment effect with respect to 12-month leg pain (≥75% improvement) and surgery based on a formal test for interaction. For leg pain improvement of ≥75%, in the disc herniation subgroup, 23% (95% CI -2% to 49%) more ESI patients improved compared with ENSI patients, while in the disc extrusion subgroup, 24% fewer (2% to 45%) ESI patients improved than ENSI patients. For surgery, in the disc herniation subgroup, 21% (95% CI -4% to 46%) fewer patients in the ESI group underwent surgery compared with ENSI patients, while in the extrusions subgroup, 18% (-0.4% to 36%) more ESI than ENSI patients were treated surgically. These results suggest that patients with disc herniation have better long-term results in terms of leg pain relief and need for surgery

when treated with ESI, while patients with disc extrusion may do worse with respect to these two outcomes when treated with ESI (versus ENSI). This was a very small trial, with a total enrollment of 128 patients.

- Disc pathology did not appear to modify any of the following outcomes as reported in short- (3 months), intermediate- (6 months), and long-term (12 months): ≥75% improvement in leg pain (short-and intermediate-term only), leg pain VAS scores, ODI scores, or Nottingham Health Profile pain and emotional subscale scores (quality of life outcome measure). A formal test for interaction was not performed for these outcomes; data are available in Appendix AA.

In three other trials[217] [13,87] comparing ESI to injection control, none of the following characteristics modified (or appeared to modify in cases where the p-value for interaction was not reported) treatment effect:

- Disc pathology (disc herniation versus disc degeneration) for the outcome of surgery in the short-term (1 month).[217]
- Symptom duration (<3 versus ≥3 months) for ≥50% pain improvement in the short-term (1 month) (regardless of whether ESI was compared to ENSI with local anesthetic alone or with saline alone, and regardless of whether ESI was compared to intramuscular injection with steroid or with local anesthetic).[87]
- Symptom duration (<4 versus ≥4 months) for ≥75% improvement in ODI scores in the short-term (3 months) or long-term (12 months).[13]
    - In addition, this trial reported that none of the following baseline characteristics impacted "response" (not defined) to ESI versus ENSI in the short- and long-term (i.e., 3 and 12 months), however no data were reported: anxiety scores; depression scores, SF-36; baseline Oswestry Disability Questionnaire; neurological abnormalities, previous episodes of sciatica, coexistent back pain, work status, and sex.

ESI versus disc decompression in patients with radiculopathy due to HNP:

Data from one trial[86] suggested that the following characteristic did not appear to modify treatment effect, the p-value for interaction was not reported:

- Duration of leg pain (<1 versus 1-3 versus >3 years) for reduction in leg pain VAS scores from baseline in the intermediate-term (6 months)

ESI versus ENSI in patients with stenosis:

In a separate report of the Friedly 2014 trial,[81] Turner et al. 2015[229] evaluated the predictive impact of 21 different baseline characteristics on six different outcomes measured at 1.5 months: RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, and Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores. This trial enrolled 400 patients with spinal stenosis and compared interlaminar or transforaminal ESI of triamcinolone (60-120 mg), betamethasone (6-12 mg), dexamethasone (8-10 mg), or methylprednisolone (60-120 mg) plus lidocaine to interlaminar or transforaminal ENSI with lidocaine alone; all injections were performed using fluoroscopic guidance.

- The following characteristics modified treatment effect of at least one short-term outcome evaluated: [229]
    - EQ-5D index score was evaluated as predictive continuous variable such that patients with lower baseline EQ-5D index scores had more improvement in buttock/hip/leg pain scores at 1.5 months when they had been randomized to ESI versus ENSI (interaction coefficient 2.95, 95% CI 0.11 to 5.76, p=0.04). This characteristic did not modify short-term treatment effect of any of the five other outcome measures assessed.
    - Employment (full-/part-time versus retired/not disabled versus retired/disabled versus other) modified short-term (1.5 month) Brief Pain Inventory scores such that patients with employment at baseline had lower scores in the ESI versus ENSI group while retired patients had better scores when treated with ESI versus ENSI (interaction p=0.02). This subgroup also modified treatment effect in terms of Swiss Spinal Stenosis Questionnaire physical subdomain scores at 1.5 months such that patients with employment classified as "other" had worse scores if they were in the ESI group than those in the ENSI group (interaction p=0.02).
    - Treatment expectation scores was evaluated as predictive continuous variable such that patients with lower baseline treatment expectations had better Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores at 1.5 months when randomized to ESI versus ENSI (interaction p=0.02).
- In the same trial,[229] none of the following characteristics modified treatment effect, with reported interaction p-values of at least 0.05:
    - Sex (male versus female) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
    - Race (Caucasian versus non-Caucasian) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
    - Ethnicity (Hispanic versus non-Hispanic) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
    - Education (high school or less versus some college versus college versus professional/graduate degree)for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
    - Employment (full-/part-time versus retired/not disabled versus retired/disabled versus other) for any of the following short-term outcomes (1.5 months): RMDQ scores,

buttock/hip/leg pain VAS scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.

- Smoking history (never/former smoker versus current smoker) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Diabetes (on insulin) status (no versus yes) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Duration of pain (<3 months versus 3-12 months versus 1-5 years versus >5 years) for any of the following short-term outcomes (1.5 months): RMDQ scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Stenosis severity (mild versus moderate versus severe) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Age (evaluated as a continuous variable and based on the treatment effect at the median, 25^{th}, and 75^{th} percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Body mass index (evaluated as a continuous variable and based on the treatment effect at the median, 25^{th}, and 75^{th} percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Treatment expectation scores (evaluated as a continuous variable and based on the treatment effect at the median, 25^{th}, and 75^{th} percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, or Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores.
- EQ-5D index scores (evaluated as a continuous variable and based on the treatment effect at the median, 25^{th}, and 75^{th} percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity

subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.

- EQ-5D pain scores (evaluated as a continuous variable and based on the treatment effect at the median, 25th, and 75th percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Patient Health Questionnaire-8 scores (evaluated as a continuous variable and based on the treatment effect at the median, 25th, and 75th percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Generalized Anxiety Disorder-7 scores (evaluated as a continuous variable and based on the treatment effect at the median, 25th, and 75th percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Pain Catastrophizing Scale total scores (evaluated as a continuous variable and based on the treatment effect at the median, 25th, and 75th percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Pain Catastrophizing Scale helplessness subscale scores (evaluated as a continuous variable and based on the treatment effect at the median, 25th, and 75th percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Pain Catastrophizing Scale rumination subscale scores (evaluated as a continuous variable and based on the treatment effect at the median, 25th, and 75th percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.
- Pain Catastrophizing Scale magnification subscale scores (evaluated as a continuous variable and based on the treatment effect at the median, 25th, and 75th percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.

- Fear-Avoidance Beliefs Questionnaire physical activities subscale scores (evaluated as a continuous variable and based on the treatment effect at the median, 25th, and 75th percentile) for any of the following short-term outcomes (1.5 months): RMDQ scores, buttock/hip/leg pain VAS scores, Brief Pain Inventory scores, Swiss Spinal Stenosis Questionnaire physical function subdomain scores, Swiss Spinal Stenosis Questionnaire symptom severity subdomain scores, or Swiss Spinal Stenosis Questionnaire treatment satisfaction subdomain scores.

- The following characteristics did not appear to modify treatment effect, however the p-value for interaction was not reported):
  - Injection approach (transforaminal versus interlaminar) for the following short-term (1.5 months) outcomes: patient satisfaction, change in leg pain VAS scores, change in RMDQ scores, and total adverse events (both major and minor). [81,226]

Cervical or Sacroiliac Spinal Injections

None of the included RCTs of cervical or sacroiliac spinal injections evaluated the differential efficacy or effectiveness of any subpopulation or characteristic (i.e., none reported stratified results for both treatment groups according to subgroups of interest or reported the results of a formal test for interaction).

4.4. Key Question 4: Cost effectiveness

4.4.1. Number of studies retained

This review focused on economic studies that evaluated, synthesized and compared costs and treatment outcomes for at least two treatment alternatives. Three studies met the inclusion criteria; two[116,204] of which were included in the 2011 HTA report and carried over here. In the updated search, four new studies were included for full-text review, one[230] of which met the inclusion criteria. All three included studies evaluated the cost effectiveness of lumbar ESI; no studies were identified that assessed the cost effectiveness of lumbar facet injections or of any included injection type in the cervical or sacroiliac spine.

4.4.2. Summary of included studies

Lumbar radiculopathy due to disc pathology: ESI versus ENSI

Karppinen et al. (2001) conducted a cost-effectiveness analysis[116] using costs collected alongside a double-blind randomized controlled trial[115] of fluoroscopically-guided ESI (methylprednisolone plus bupivacaine) versus ENSI (saline) injection in 160 patients with sciatica between one and six months' duration. Patients who had previously undergone lumbar surgery, were retired, or were clinically depressed were excluded from the trial. Additional information on this trial can be found in Appendix F. The perspective of this analysis was not stated; short-term (3 months) and long-term (12 months) cost-effectiveness was assessed.

Cost-effectiveness was reported as the cost per number of positive outcomes; a positive outcome was defined as 75% to 100% decrease in leg pain from baseline plus no surgery. Costs included study hospital charges, medications, and home health care; costs were estimated using the Finnish national insurance

registry based on data from the trial, medical records and study questionnaires. The cost of home help was calculated based on the average wage of a home helper. Sick leave was not valued. No discounting was performed. Although the study was conducted in Finland, it appeared that costs were reported in US dollars. The cost-effectiveness analysis was stratified based on subgroups of MRI-based classification of bulge, contained herniation, or extrusion. No sensitivity analysis was performed.

In the herniation subgroup (n=50), there was no statistically significant difference between ESI and ENSI groups in the percentage of patients who had a positive response at 3 months (24% vs. 29%) at 12 months, more ESI patients had achieved a positive response (44% vs. 21%), however the difference did not achieve statistical significance (p=0.09). The mean total cost per positive response was similar between groups at 3 months ($5850 vs. $6360). However, at 12 months, the mean cost per positive response was significantly lower in the ESI group ($4432 vs. $17,098, p=0.0073). The authors noted that considerably fewer ESI versus ENSI patients had undergone surgery by 12 months (20% vs. 42%); this difference contributed to the greater cost-effectiveness of ESI at 12 months due to the impact on effectiveness, sick leave, and cumulative costs.

In the extrusions subgroup (n=81), the study reported no statistical difference was found between ESI and ENSI treatment groups in the percentage of patients who had a positive response at 3 months (47% vs. 57%); at 12 months, fewer ESI patients achieved a positive response (36% vs. 59%) although the study reported the difference was not statistically significant. At 3 months, the mean cost per positive response was slightly (but not significantly) higher in the ESI group ($4081 vs. $2230); by 12 months, this difference was statistically meaningful ($7165 vs. $2484, p=0.0058). More ESI than ENSI patients received surgery through 12 months (32% vs. 13%); this difference contributed to the greater cost-effectiveness of ESI at 12 months due to the impact on effectiveness, and cumulative costs (no differences were seen in sick leave).

The percentage of patients in the bulge subgroup (n=29) with a positive response was not reported, although the study noted no significant differences between groups in any clinical outcome evaluated. There were no differences between groups in the average cost per positive response between ESI and ENSI groups at 3 months ($2640 vs. $2116) or 12 months ($3740 vs. $3629).

The authors noted that there were no statistically meaningful differences between ESI and ENSI groups in cost per improved outcome, however no data were reported for the entire population (i.e., not stratified by subgroups).

This is a relatively poorly conducted economic evaluation (QHES 49/100), with the lack of sensitivity analysis, long-term modeling, and statement of perspective as major limitations. However, a main strength of this study is that it provides real patient-level data from a randomized trial. The time horizon included (one year), relatively short term from an economic standpoint, suggests that over time the costs of ESI are similar to those in a saline ENSI group, but that stratifying future work according to MRI classification may be warranted.

Lumbar radiculopathy due to disc pathology: ESI versus NEI

Price et al. (2005)[204] performed a cost-utility analysis as part of a health technology assessment for the UK National Institute for Clinical Effectiveness (NICE). The cost utility analysis was based on trial data from a pragmatic multisite RCT,[13] which compared ESI (with triamcinolone acetonide, 1-3 injections) to placebo saline injections in 288 patients with unilateral subacute or chronic sciatica; use of imaging was not reported in this trial. Patients with spinal canal stenosis or a history of lumbar surgery, ESI,

depression, or current litigation were excluded from the trial. This study was conducted from both a provider's and a purchaser's perspective; short-term (3 months) cost-effectiveness was assessed.

Utility values were ultimately derived from SF-36 scores; these scores were converted into SF-6D scores, which were then used to calculate standard gamble scores which were then used to derive quality-adjusted life years (QALYs). For the provider perspective, costs included that of the intervention(s), physician and nurse time, and medications; although both treatment groups received conservative care (physiotherapy, education, medication), the costs were assumed not to differ between groups and thus were not measured. It was assumed that in the ESI group, 47%, 32%, and 21% would receive 3, 2, and 1 ESI (respectively). Costs were estimated from the NHS Trust and reported in 2002/2003 pounds sterling. For the purchaser perspective, the average cost to purchasers were included and were based on cumulative costs, including that of overheads. No discounting was performed; the authors stated this was due to the relatively short time horizon used. One-way sensitivity analyses of study variables were conducted.

When results were based on the trial protocol (i.e., up to 3 ESIs), the RCT reported an early benefit (3-6 weeks) with ESI versus NEI in standard gamble scores, but by the end of study follow-up (twelve weeks) the two arms were equivalent; the authors noted that the same trend was observed with other clinical outcomes such as pain relief and ODI scores. For the provider perspective, the incremental cost of 1-3 ESIs over NEI was £265, and the incremental QALY of 1-3 ESIs over NEI was 0.0059 (which was equivalent to 2.2 days of full health gained), resulting in a cost per QALY of £44,701. For the purchaser perspective, the cost per QALY was £354,172. The trial found no additional benefit to more than one injection; thus the authors recommended a management strategy of only one injection. Under this scenario (1 ESI only), the cost per QALY gained was lower than when up to three injections were provided, at £25,746 when based on the provider perspective and £167,145 based on the purchaser perspective. A sensitivity analysis was performed in which costs were varied; the maximum values of each cost was used and resulted in a doubling of costs for both treatment groups.

The authors concluded that the cost effectiveness ratios are higher than the implied thresholds used by NICE and therefore do not support coverage by the NHS. Further, given the high frequency with which epidural steroid injections are used in the NHS, a strategy of only one epidural steroid injection per patient would save the NHS £31 million. This was a reasonably well conducted study (QHES 78/100). Its strengths are in its use of clinical trial data and in its calculation of cost effectiveness estimates from a purchaser perspective; its limitations included a very short time horizon and no inclusion of potential harms in the analysis. Given the small, transient benefit of ESI in the trial, it is logical that cost effectiveness ratios would be relatively high, even for a moderately priced intervention.

Lumbar spinal stenosis: ESI versus disc or decompression procedures

Udeh et al.[230] conducted a cost utility analysis that compared epidural steroid injections to two different disc procedure comparators: minimally invasive decompression, and surgical lumbar decompression. The study was conducted from a Medicare payer perspective and used a two year time horizon. A decision tree model was used for the analysis; the patient population considered was symptomatic lumbar spinal stenosis refractory to conservative care. Serial epidural steroid injections was one treatment of interest; it was assumed that patients would receive six injections per year and that these would be done via the interlaminar (80%) or caudal (20%) approach. No assumptions regarding use of imaging guidance for ESI were stated. Note that the authors assumed epidural injections would only provide minimal relief: epidural injections were considered to be a form of conservative care, and only those who were unresponsive to conservative therapy were considered for inclusion. The two surgical

comparators of interest were minimally invasive decompression performed using the mild technique (Vertos Medical) and surgical lumbar decompression. Patients who received either surgical treatment and had a return of symptoms within two years postoperation were considered to be treatment failures and would proceed to a first or second surgical decompression, respectively.

Outcomes were measured in quality-adjusted life years (QALY), which were determined by calculating both QALY gains (based on quality of life) and QALY reductions (complications, including death, deep wound infections, post lumbar puncture headache, nerve root irritation, cord or cauda equine injury, nerve root injury, dural tear, or medical complications). QALY gains were calculated using data in the published literature. For ESI, calculated QALY gains were obtained from EQ-5D data published in a cost effectiveness study (Whynes; excluded from this report at full-text review due to its pre-post rather than comparative design) of patients with mild stenosis symptoms. The authors reduced the derived QALY values by 25% to account for the assumption that ESI was a form of conservative care and that patients had already failed conservative therapy. For minimally invasive decompression, published ODI data reported across four trials (total N=301) of patients with moderate to severe stenosis symptoms were obtained, converted to SF-6D data, which were then used to derive QALY values. For surgical decompression, QALY gains were obtained from EQ-5D or SF-6D data published in two cost-effectiveness studies of patients with severe stenosis; however, Udeh et al. assumed that the population of interest for their own study was not "at a level of lumbar spinal stenosis severity that requires surgery" and thus reduced QALY gains by 25%.

Costs included were those of the initial intervention, repeat or revision procedures, or any alternative treatments. Costs were obtained from the 2013 Medicare fee schedule and reported in 2013 US dollars. The authors noted that costs accrued due to complications were not included. Costs were discounted 3% annually.

Results of the base case analysis suggested that the cost per QALY was $81,518 for serial ESI, $43,760 for minimally invasive decompression, and $125,985 for surgical decompression. Thus, ESI was dominated by minimally invasive decompression but dominated surgical decompression. Additional details on the cost and QALY values are available in Appendix CC.

The conclusion that minimally invasive decompression dominated both other treatment options was challenged using one-way sensitivity analysis. All variables (e.g., cost, QALY gains, QALY reductions due to complications, incidence of complications, need for additional procedures) included in the base case model were varied, using their lowest and highest range values. ESI dominated minimally invasive decompression only when it was assumed that they would receive three or less injections per year (instead of the six assumed in the base case analysis). In all other scenarios, ESI remained dominated by minimally invasive decompression. It was unclear whether there was any scenario in which ESI was dominated by surgical decompression.

The authors concluded that that minimally invasive decompression was the most cost-effective treatment option for patients with symptomatic lumbar spinal stenosis refractory to conservative care. However, if the willingness to pay threshold was $40,500 or more, ESI maintained net monetary benefits. This was a reasonably well-conducted study (QHES 73/100) with a number of limitations. The published literature from which QALY values were derived for ESI was based only on patients with mild stenosis and for surgical decompression was based only on studies of severe stenosis. However, the population of interest was on patients with moderate or severe stenosis symptoms; the studies from which QALY values were derived for minimally invasive decompression surgery were based on the

correct population. Further, because of study assumptions, the QALY values obtained from the published literature for both ESI and surgical decompression were reduced by 25%; in contrast, the QALY values obtained from the literature for minimally invasive decompression were not reduced. As a result of this study design, it isn't surprising that minimally invasive decompression was be the most effective treatment option evaluated. Other limitations included reliance on the published literature; it did not appear that any of studies used to obtain QALY values directly compared any of the three included treatment options.

4.5. Comparison to Previous Report

The Body of Literature.

Our current report includes additional trials compared with our prior report. Of the 100 studies (across 123 citations) included in this updated report, a total of 39 studies (56 citations) were new. A total of 26 new trials were found that reported on the efficacy of ESI: 22 (35 citations) in the lumbar spine and four (9 citations) in the cervical spine. Of note, six lumbar trials and three cervical trials which were included in the previous report reported only preliminary results in a subset of patients. By the time of the re-review for this report, these trials had published longer-term follow-up studies in the entire study population (across 12 and 5 citations for the lumbar and cervical spine, respectively); these were not counted as new trials but as updates to previously included trials. For safety, 12 new studies were found, eight (2 cohorts, 6 case series) evaluating ESI in the lumbar spine, three case series of cervical ESI, and one case series of both lumbar and cervical ESI. In addition, a summary report of the FDA adverse events reporting database was included to evaluate rare but serious adverse events. For cost-effectiveness, one new study was found. Please see appendix CC, which identifies the studies in the previous and current report.

Methods.

Our earlier report relied on a previous systematic review by Chou et al (reference). It was a qualitative review which did not perform a meta-analysis. The current review conducted meta-analyses on several comparisons when two or more studies reported on the same outcome, had the same condition, and had similar controls (injections, conservative treatment, disc or decompression procedures). The update report added a long-term follow-up of ≥1 year which was not available in the earlier report.

The current review is consistent with the previous report in that there continues to be substantial heterogeneity (mixed results) in several of the pooled analyses. To address this, we used a random effects model to pool studies (Dersimonian-Laird (DL) random effects model). Given that the DL model in the presence of heterogeneity may result in overly small confidence intervals, we repeated the analyses using the profile likelihood method. The results in all cases were similar. We further explored heterogeneity using stratified analyses based on epidural approach, exclusion of outlier studies, the exclusion of poor-quality studies, and whether the control injection contained anesthetic or just saline. While statistical heterogeneity remained in a few analyses, the results for the rest were similar between the sensitivity and the primary analyses.

Results.

Lumbar radiculopathy due to disc and or foraminal narrowing, ESI versus control injections.

Our previous report (reference) found mixed evidence with respect to efficacy for lumbar epidural spinal injections vs. control injections for radiculopathy with some studies reporting no benefit or inferior results while others reported positive results in the short- and intermediate-term. The strength of evidence for those conclusions was LOW. That report did not perform meta-analysis, and based some conclusions on prior reviews. Our current report, as described above, performed meta-analysis when possible. Using meta-analysis for this report, we found, in the short-term, 30% more patients receiving ESI achieved a successful reduction in pain compared with a control injection, though there was no improvement in intermediate- or long-term pain success or short-, intermediate- or long-term change in function or function success. The strength of evidence for these results were mostly LOW. The risk of surgery following lumbar ESI is not reported in the last report. We found no difference in the risk of surgery comparing ESI with control injections in this report. The strength of evidence for this finding was LOW.

Lumbar radiculopathy due to disc and or foraminal narrowing, ESI versus disc or decompression. procedures.
The prior report noted one trial that demonstrated ESI resulted in poorer outcomes compared with discectomy in patients with disc prolapse. The current review adds one new study comparing ESI to discectomy with opposite results. Strength of evidence, INSUFFICIENT. In addition, two new studies not available in the previous review both report ESI performed poorer than radiofrequency nucleoplasty with respect to short- and long-term pain and function.

Lumbar radiculopathy due to disc and or foraminal narrowing, ESI versus conservative care.
One additional trial was added for this report to the single trial in the earlier review comparing ESI to conservative care. Due to risk of bias, inconsistent results and imprecision, the quality of evidence remains insufficient.

Lumbar radiculopathy due to disc and or foraminal narrowing, ESI versus other medication.
The previous report did not distinguish trials that included other medication. This review reports on 3 trials that do so; one demonstrated better improvement in functional but not pain or overall success with ESI versus etanercept injection in the short-term. A second trial reported better improvement in function with ESI versus clonidine injection in the short-term. A third trial found no difference between ESI and posterior ligament injection of saline combined with oral gabapentin in the short-term. The quality of evidence from these studies were rated LOW.

Lumbar radiculopathy due to multiple causes, ESI versus control injections.
The previous report did not distinguish trials that included patients with radiculopathy due to multiple causes in the same trial. This review reports on 3 studies that included patients with radiculopathy due to 2 or more of the following conditions: arachnoiditis, prolapsed or herniated disc, spinal stenosis, or prior back surgery. There were no differences in pain in the intermediate-term (2 trials) or long-term (1 trial) pain or risk of surgery (1 trial) comparing ESI to control injections.

Lumbar stenosis, ESI versus control injections.
Our previous report found low to moderate evidence of no benefit (pain and function) comparing ESI to control injections in the short- or intermediate-term. We added two new studies to this report that reinforced the results from the previous review: no differences in pain or functional scores in the short-term (quality of evidence, LOW), no difference in pain or function success in the short-term (quality of evidence, HIGH), no difference in the risk of surgery (quality of evidence, LOW).

Lumbar nonradicular axial pain, ESI vs. control injections.
The prior report concluded no difference in short-term pain and function compared with control injections; quality of evidence, MODERATE. The current report adds long-term follow-up data to two studies included in the prior report and concludes no difference in short-, intermediate- or long-term follow-up; quality of evidence, LOW. In the previous report, we did not reduce the quality of evidence due to imprecision or risk of bias, which resulted in a higher quality of evidence rating. Re-evaluating the methodology and the precision of the results led us to downgrade the quality to LOW.

Failed back surgery syndrome, ESI vs. control injections with and without other medication
The current report distinguishes ESI vs. control injections with and without other medications while the prior report considered the controls together. There was no difference between ESI and control injections with respect to pain and function in the prior report or in the current report. However, the

prior report rated the quality of evidence as MODERATE while the current report assessed the quality as LOW. In the previous report, we did not reduce the quality of evidence due to imprecision or risk of bias, which resulted in a higher quality of evidence rating. Re-evaluating the methodology and the precision of the results led us to downgrade the quality to LOW.

Lumbar facet joint pain, IASI vs. control injections.
No additional trials were identified; a total of three RCTs were included. While the new report assessed all three trials together as IASI versus control injections, the previous report divided these studies up into two comparisons: IASI vs. placebo (2 RCTs) and IASI vs. IAI with HA (1 RCT). Both reports concluded that there were no differences in pain or functional scores between groups in the short- and intermediate-term (quality of evidence, LOW).

Lumbar facet joint pain: EASI vs. control injections.
No additional trials were identified; a total of two trials (in three publications) were included. These studies were classified as lumbar medial branch (steroid) blocks versus medial branch sarapin injections. While the previous report concluded there was low strength of evidence of no difference between groups, the new reported evaluated the quality of evidence separately for different follow-up times and concluded that there was no difference between groups for pain or function scores in the short- or intermediate term based on low quality of evidence or in the long-term based on insufficient quality of evidence. Further, no differences were found between groups in pain or function success in the short-, intermediate-, or long-term based on low quality of evidence.
Cervicobrachialgia (neck pain ± radiculopathy and/or stenosis): ESI vs. Control injections.
One trial was included in both reports; no new trials were identified. The trial compared ESI to intramuscular steroid injections; the prior report referred to this comparison as ESI vs. non-placebo controls for neck pain with disc herniation and radiculitis. Both reports concluded that ESI was superior to control injections in terms of pain success in the long-term; the new report found the quality of evidence to be low while the old report considered it to be very low.

Cervical disc herniation with or without radiculopathy: ESI vs. Control injections.
The preliminary results from one trial were included in the prior report under the heading “neck pain with sciatica or radiculopathy”; this report included data on 70 patients. Since the prior HTA, two additional articles have been published and contain the results from the full trial of 120 patients. The new report concluded there were no differences between groups in: pain success (all timepoints), short- and long-term pain scores, intermediate- and long-term function scores, long-term function success, and intermediate- and long-term composite of pain and function success. However, there was significantly worse outcomes in the ESI group in the following: intermediate-term pain scores, short-term pain success, as well as short- and intermediate-term function. In all cases the new report found the quality of evidence to be low while the old report considered it to be very low.

Nonradicular neck pain: ESI vs. Control injections.
The preliminary results from one trial were included in the prior report under the heading “neck pain without sciatica or radiculopathy”; this report included data on 70 patients. Since the prior HTA, two additional articles have been published and contain the results from the full trial of 120 patients. The new report concluded there were no differences between groups in short-, intermediate- or long-term pain success, pain scores, function success, function scores, or in a composite of pain and function success (quality of evidence for all, LOW).

Cervical spinal stenosis: ESI vs. Control injections.

Preliminary results from one new trial were included in the updated report; this RCT was published subsequent to the prior HTA. The updated HTA concluded there were no differences between groups in short-, intermediate- or long-term pain success, pain scores, function success, function scores, or in a composite of pain and function success (quality of evidence for all, LOW).

Cervical failed surgery syndrome: ESI vs. Control injections.
The preliminary results from one new trial were included in the updated report; this RCT was published following the prior HTA. The new report found no differences between groups in short-, intermediate- or long-term pain success, pain scores, function success, function scores, or in a composite of pain and function success (quality of evidence for all, LOW).

Cervical facet pain: IASI (medial branch block) vs. control injection.
Two trials (in three publications) were included in the new report. While both trials were included in the prior report, the second publication (Manchikanti 2010, 2 year results) of one trial had erroneously been omitted from the prior HTA. For IASI versus control injections, both reports concluded there were no differences between groups in short-term pain success based on insufficient (or very low in the prior report) quality of evidence. For medial branch blocks versus control injections, long-term pain scores were significantly better in the ESI group than the control group, but there were otherwise no differences between groups in any outcomes, including: pain or function success in the intermediate- and long-term, pain scores in the short- and intermediate-term, and function scores in the short-, intermediate-, and long-term. In all cases, the quality of evidence was considered to be low in the new report (and very low in the prior report).

The following new categories were included in the updated report that were not in the prior report; the new categories are based on the addition of new literature published after the following report:

Lumbar facet joint pain, IASI vs. intramuscular steroid injections.
One trial was identified in the new report that compared IASI to intramuscular steroid injections; the trial was published after our previous report. There were significantly greater improvements in pain and functional scores with IASI in the short-term but no differences between groups in the intermediate-term (quality of evidence, MODERATE).

Lumbar facet joint pain, IASI vs. Radiofrequency denervation of the medial branch.
One new trial was identified for the updated report that compared IASI to radiofrequency denervation of the medial branch; this trial was published after our previous report. No differences between groups were found in pain or functional scores in the intermediate-term (quality of evidence, MODERATE).

Lumbar facet joint pain, EASI vs. Radiofrequency denervation of the medial branch.
One new trial was identified that was published subsequent to the previous report and compared EASI to radiofrequency denervation of the medial branch. The new report concluded that while there were no differences between groups in pain scores in the short-term, there was less improvement in pain scores with EASI in the intermediate- and long-term. In addition, significantly fewer EASI patients experienced pain success in the short-, intermediate-, or long-term. All conclusions were based on low quality of evidence.

Cervical radiculopathy due to disc and/or foraminal narrowing: ESI vs. Conservative Care (CC)

One new trial was identified and included in the updated report; this trial was published after the previous report. The new report concluded that there was low quality of evidence of the following: no difference between groups in short-term pain scores or surgery in the long-term; but worse intermediate-term pain scores as well as short- and intermediate-term function scores with ESI versus CC alone.

Cervical radiculopathy due to disc and/or foraminal narrowing: ESI + CC vs. Conservative Care (CC)
One trial was included in the new report; this trial was published after the previous report and was thus a new addition to the evidence base. The updated report found low quality of evidence for the following conclusions: greater improvement in short-term pain with ESI + CC but worse intermediate-term pain scores as well as short- and intermediate-term function scores with ESI + CC versus CC alone; no difference was found between groups in long-term surgery.

Myofascial pain syndrome: IASI vs. Conservative care (CC).
One new trial was published after our prior report and provided insufficient quality of evidence for all outcomes.

Safety
Both reports assessed all included RCTs for complications. A total of three cohort studies were included in the new report: from two recent cohort studies were added to the new report, and both reports included data from a cohort study on both cervical and lumbar injections. A total of 22 case series of lumbar and/or cervical injections were included in the new report, 10 of which were newly published since the prior report. While the prior HTA scanned published case reports for serious complications, the new HTA evaluated case reports of catastrophic adverse events using the report of the FDA Adverse Events Reporting Database. The new report concluded that catastrophic events were very rare but can occur following epidural steroid injections (quality of evidence, LOW). Both reports concluded that serious (or major) adverse events were rare and that non-serious (or minor) adverse events occurred relatively infrequently (moderate quality of evidence in new report and high strength of evidence in prior report).

5. Strength of Evidence (SoE) tables

The following summaries of evidence have been based on the highest quality of studies available. Additional information on lower quality studies is available in the report. A summary of the critical outcomes for each key question are provided in the tables below and are sorted by comparator. Only primary outcomes and/or time points reported by one or more trials for a given treatment comparison are included in the summary tables below. Details of these and other outcomes are available in the report.

7. Serious risk of bias: the majority of studies violated one or more of the criteria for good quality RCT related to the outcome reported (see Appendix for details)
8. Inconsistency: differing estimates of effects across trials
9. Imprecise effect estimate for a continuous outcome: wide (or unknown) confidence interval and/or small sample size
10. Imprecise effect estimate for a dichotomous outcome: small sample size and/or confidence interval includes both negligible effect and appreciable benefit or harm with TT
11. Imprecise effect estimate for a dichotomous outcome: small sample size, rare outcome
12. Serious risk of bias in evaluation of HTE: the subgroup variables were specified at randomization, however the hypothesized direction was not stated; the subgroup hypothesis was not one of a smaller number tested

5.1. Strength of Evidence Summary: Efficacy Results for Lumbar Spinal Injections

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
Lumbar radiculopathy due to disc and/or foraminal narrowing: ESI vs. Control Injections								
Δ Pain	Short-term: n=1696	15 RCTs[13,39,44,59,67,87,88,96,108,115,120,151,169-171,175,176,180,204,228] N=1748	Yes (-1)	Yes (-1)	No	No	WMD: -0.46 ~~(-0.97 to 0.05)~~ (-0.94 to 0.02) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	5 RCTs[88,115,151,169-171,175,176]	Yes (-1)	Yes (-1)	No	No	WMD: -0.15 (-1.17 to 0.86) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
		,180 N=587						
	Long-term	8 RCTs[13,39,88,108,115,151,169-171,175,176,180,204] N=905	Yes (-1)	Yes (-1)	No	No	WMD: -0.25 (-0.77 to 0.27) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain success	Short-term: N=1201	11 RCTs[13,59,67,72,87,88,151,169-171,175,176,180,204,213,228] N=1229	Yes (-1)	Yes (-1)	No	No	RR: ~~1.30 (1.06 to 1.58)~~ 1.27 (1.06 to 1.53) Conclusion: Greater proportion achieved pain success with ESI.	⊕⊕◯◯ LOW
	Intermediate-term	5 RCTs[59,88,151,169-171,175,176,180] N=487	Yes (-1)	Yes (-1)	No	No	RR: 1.14 (0.93 to 1.39) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	7 RCTs[13,65,74,88,151,169-171,175,176,180,204] N=726	Yes (-1)	No	No	Yes (-1)	RR: ~~1.10 (0.92 to 1.30)~~ 1.09 (0.95 to 1.26) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Δ Function	Short-term	11 RCTs[13,44	Yes (-1)	Yes (-1)	No	No	SMD: -0.21 (-0.56 to 0.14) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
		,59,88,108,115,151,169-171,175,176,180,204,217,228 N=1396						
	Intermediate-term	6 RCTs[88,115,151,169-171,175,176,180,217] N=740	Yes (-1)	Yes (-1)	No	No	SMD: -0.27 (-0.76 to 0.21) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	8 RCTs[13,88,108,115,151,169-171,175,176,180,204,217] N=1033	Yes (-1)	Yes (-1)	No	No	SMD: -0.09 (-0.46 to 0.28) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function success	Short-term	7 RCTs[13,44,67,151,169-171,175,176,180,204,228] N=988	Yes (-1)	Yes (-1)	No	No	RR: 1.04 (0.82 to 1.32) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	3 RCTs[151,169-171,175,176,180] N=360	Yes (-1)	Yes (-1)	No	Yes (-1)	RR: 1.09 (0.86 to 1.38) Conclusion: No difference between groups. Insufficient evidence prevents firm conclusion.	⊕◯◯◯ INSUFFICIENT

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
	Long-term	4 RCTs[13,151,169-171,175,176,180,204] N=588	Yes (-1)	No	No	No	RR: 1.07 (0.93 to 1.22) Conclusion: No difference between groups.	⊕⊕⊕○ MODERATE
Composite score success	Intermediate-term	3 RCTs[151,169-171,175,176,180] N=360	Yes (-1)	Yes (-1)	No	Yes (-1)	RR: 1.08 (0.86 to 1.35) Conclusion: No difference between groups. Insufficient evidence prevents firm conclusion.	⊕○○○ INSUFFICIENT
	Long-term	3 RCTs[151,169-171,175,176,180] N=360	Yes (-1)	No	No	Yes (-1)	RR: 1.04 (0.88 to 1.23) Conclusion: No difference between groups.	⊕⊕○○ LOW
Risk of Surgery	Not specified	16 RCTs[13,39,59,65,67,72,74,87,108,115,120,204,210,213,217,221,228] N=1705	Yes (-1)	No	No	Yes (-1)	RR: ~~0.82 (0.63 to 1.07)~~ 0.83 (0.66 to 1.04) Conclusion: No difference between groups.	⊕⊕○○ LOW
Lumbar radiculopathy due to disc and/or foraminal narrowing: ESI vs. Control injections with other medications								
Δ Pain & function **Pain & function success**	Short-term	1 RCT[59] n=84	Yes (-1)	Unknown	No	Yes (-1)	ESI superior to etanercept on the ODI, MD: −16.2 (95% CI −26.0, −6.27). No differences in change in pain, proportions with successful outcomes, or risks of surgery.	⊕⊕○○ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
Risk of surgery								
Δ Function	Short-term	1 RCT[38] n=26	Yes (-1)	Unknown	No	Yes (-1)	ESI superior to clonidine on the RMDQ, MD: -5.67 (95% CI: -10.12, -1.22).	⊕⊕◯◯ LOW
Δ Pain & function **Pain success**	Short-term	1 RCT[57] N=145	Yes (-1)	Unknown	No	Yes (-1)	No difference between ESI + oral placebo pills versus posterior ligament injection of saline + oral gabapentin in pain or function, or the likelihood of achieving pain success.	⊕⊕◯◯ LOW
Lumbar radiculopathy due to disc and/or foraminal narrowing: ESI vs. Disc or decompression procedures								
Δ Pain & function	Short-, intermediate- and long-term	2 RCTs[15,41] N=150	Yes (-1)	Yes (-1)	No	Yes (-1)	Insufficient evidence to determine the effects of ESI versus discectomy.	⊕◯◯◯ INSUFFICIENT
Δ Pain & function **Pain and function success** **Risk of surgery**	Short-, intermediate- and long-term	2 RCTs[86,240] N=169	Yes (-1)	No	No	Yes (-1)	ESI consistently performed poorer than radiofrequency nucleoplasty with respect to improvement in VAS pain and ODI function in the short-term (2 RCTs), intermediate-term (1 RCT), and long-term (1 RCT); and pain and function success in the intermediate- and long-term (1 RCT). There was no difference in risk of undergoing surgery in one trial.	⊕⊕◯◯ LOW
Lumbar radiculopathy due to disc and/or foraminal narrowing: ESI vs. Conservative Care								
Δ Pain & function	Short- and intermediate-term	2 RCTs[37,188] N=136	Yes (-1)	Yes (-1)	No	Yes (-1)	Insufficient evidence to determine effects of ESI versus conservative care.	⊕◯◯◯ INSUFFICIENT
Lumbar radiculopathy due to multiple causes: ESI vs. Control injections								
Pain success	Intermediate-term	1 RCT[34] N=35	Yes (-1)	Unknown	No	Yes (-1)	No difference between ESI versus epidural saline in pain relief. Diagnosis: arachnoiditis, prolapsed disc, no radiographic	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
							abnormalities or inconclusive findings	
Δ Pain & function	Short- and Intermediate-term	1 RCT[22] N=84	Yes (-1)	Unknown	No	Yes (-1)	No difference between ESI versus autologous conditioned serum administered via the interlaminar approach in pain or ODI scores. Diagnosis: Herniated nucleus pulposus or scarring after previous surgery.	⊕⊕◯◯ LOW
Δ Pain **Risk of surgery**	Short- and long-term	1 RCT[239] N=92	Yes (-1)	Unknown	No	Yes (-1)	ESI was associated with greater short-term pain relief (data NR; p<0.004) compared with intramuscular or interspinous ligament steroid injection. No difference in long-term pain relief or risk of surgery. Diagnosis: Disc prolapse or spinal stenosis	⊕⊕◯◯ LOW
Lumbar spinal stenosis: ESI vs. Control Injections								
Δ Pain	Short-term	4 RCTs[81,136,137,139,143,144,191] N=642	Yes (-1)	Yes (-1)	No	No	WMD: -0.17 (-0.62 to 0.29) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain success	Short-term	3 RCTs[81,136,137,139,143,144] N=606	No	No	No	No	RR: 1.03 (0.91 to 1.18) Conclusion: No difference between groups.	⊕⊕⊕⊕ HIGH
	Long-term	4 RCTs[65,74,136,137,139,143,144] N=287	Yes (-1)	No	No	Yes (-1)	RR: 1.04 (0.86 to 1.26) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Δ Function	Short-term	4 RCTs[81,136,137,139,1	Yes (-1)	Yes (-1)	No	No	SMD: ~~-0.47 (-1.08 to 0.14)~~ **-2.15 (-5.83 to 1.52)** Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
		[43,144,191] N=642					~~Insufficient evidence prevents firm conclusion.~~	
Function success	Short-term	3 RCTs[81,136,137,139,143,144] N=606	No	No	No	No	RR: 0.98 (0.84 to 1.15) Conclusion: No difference between groups.	⊕⊕⊕⊕ HIGH
Composite score success	Short-term	3 RCTs[136,137,139,143,144,191] N=256	Yes (-1)	Yes (-1)	No	Yes (-1)	RR: 1.07 (0.77 to 1.48) Conclusion: No difference between groups. Insufficient evidence prevents firm conclusion.	⊕◯◯◯ INSUFFICIENT
Risk of surgery	Not specified	3 RCTs[65,74,191] N=103	Yes (-1)	No	No	Yes (-1)	RR: 0.86 (0.48 to 1.52) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Lumbar spinal stenosis: ESI vs. Control injections with other medication								
Δ Pain and function	Short-term	1 RCT[196] N=80	Yes (-1)	Unknown	No	Yes (-1)	ESI was associated with less pain relief compared with etanercept injection (-2.3 ± 1.5 vs. -4.4 ± 1.4; p=0.03). No difference in ODI.	⊕⊕◯◯ LOW
Lumbar spinal stenosis: ESI vs. Decompression procedures								
Δ Pain and function **Pain success**	Short-term	1 RCT[36] N=38	Yes (-1)	Unknown	No	Yes (-1)	ESI was associated with a lower likelihood of pain success (≥2-point improvement on VAS) compared with the MILD procedure: 35% vs. 76%, RR 0.5 (0.2 to 0.9). No difference in VAS pain scores or ODI improvement.	⊕⊕◯◯ LOW
Lumbar spinal stenosis: ESI vs. Conservative care								
Δ Pain and	Short- and	1 RCT[122]	Yes (-1)	Unknown	No	Yes (-1)	No differences between groups in pain and	⊕⊕◯◯

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
function	intermediate-term	(N=29)					function (RMDQ) improvement.	LOW
Lumbar nonradicular axial pain: ESI vs. Control injections								
Δ Pain	Short term	2 RCTs[138,140-142,145,146] N=240	Yes (-1)	Yes (-1)	No	Yes (-1)	No consistent differences between groups. Insufficient evidence prevents firm conclusion.	⊕◯◯◯ INSUFFICIENT
	Intermediate and long term	2 RCTs[138,140-142,145,146] N=240	Yes (-1)	No	No	Yes (-1)	No differences between groups. MD at 6 months -0.3 (-0.68, 0.08) and 0 (-0.25 to 0.25); and at 24 months -0.3 (-0.73, 0.13) and 0 (-0.30 to 0.3.0)	⊕⊕◯◯ LOW
Pain and Function success	Short, intermediate and long term	2 RCTs[138,140-142,145,146] N=240	Yes (-1)	No	No	Yes (-1)	No differences between groups pain success or function success at any time-point.	⊕⊕◯◯ LOW
Δ Function	Short, intermediate and long term	2 RCTs[138,140-142,145,146] N=240	Yes (-1)	Yes (-1)	No	Yes (-1)	No consistent differences between groups. Insufficient evidence prevents firm conclusion.	⊕◯◯◯ INSUFFICIENT
Composite score success	Short, intermediate and long term	2 RCTs[138,140-142,145,146] N=240	Yes (-1)	No	No	Yes (-1)	No differences between groups.	⊕⊕◯◯ LOW
Lumbar nonradicular axial pain: Intradiscal steroid injections vs. Intradiscal control injections								
Δ Pain and Function	Short and intermediate	1 RCT[43] N=80	Yes (-1)	Unknown	No	Yes (-1)	Greater improvement in both pain and function (ODI) with intradiscal injection of	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
	term						betamethasone versus saline at 3 months (MD -5.05, 95% CI -5.52 to -4.58; and MD -23.2, 95% CI -27.7 to -18.7, respectively) and 6 months (MD -4.55, 95% CI -5.0 to -4.1; and MD -23.3; 95% CI -27.8 to -18.9).	
	Long term	1 RCT[118] N=120	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups for pain or function improvement	⊕⊕◯◯ LOW
Pain and function success	Short term	1 RCT[220] N=25	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups in pain or function success in the short term.	⊕⊕◯◯ LOW
Risk of surgery	Cumulative	1 RCT[118] N=120	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups in cumulative risk of surgery over 12 months.	⊕⊕◯◯ LOW
Lumbar nonradicular axial pain: Intradiscal non-steroid injections vs. Intradiscal control injections								
Δ Pain and Function	Intermediate and long term	1 RCT[200] N=72	Yes (-1)	Unknown	No	Yes (-1)	Greater improvement in pain and function (ODI) with intradiscal injection of methylene blue versus lidocaine at 6 months (MD -4.36, 95% CI -4.78 to -3.94; and MD -31.5, 95% CI -34.7 to -28.4, respectively) and 24 months (MD -4.56, 95% CI -4.98 to -4.14; and MD -33.9, 95% CI -37.5 to -30.4, respectively).	⊕⊕◯◯ LOW
Lumbar nonradicular axial pain: Discography plus intradiscal steroid injection vs. Discography alone								
Δ Pain and Function; and Risk of Surgery	Short, intermediate and long term	1 RCT[40] N=171	Yes (-1)	Unknown	No	Yes (-2)[1]	No differences between groups. No firm conclusions can be made regarding improvement in pain and function in the short, intermediate or long-term, and for cumulative risk of surgery due to insufficient evidence.	⊕◯◯◯ INSUFFICIENT
Failed back surgery syndrome: ESI vs. Control injections								
Δ Pain and	Short,	1	Yes	Unknown	No	Yes	No difference between groups for pain or	⊕⊕◯◯

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
Function; Function and composite score success	intermediate and long term	RCT[172-174] N=140	(-1)			(-1)	function improvement, function success or composite outcome success.	LOW
Failed back surgery syndrome: ESI vs. Control injections with other substances								
Δ Pain	Short and intermediate term	2 RCTs[186,212] N=69	Yes (-1)	No	No	Yes (-1)	No difference between groups for ESI compared with forceful saline or morphine.	⊕⊕◯◯ LOW
Pain success	Short, intermediate and long term	3 RCTs[69,186,212] N=129	Yes (-1)	No	No	Yes (-1)	No difference between groups for ESI compared with forceful saline, morphine or hyaluronidase.	⊕⊕◯◯ LOW
Δ Function	Short and intermediate term	1 RCT[186] N=47	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups for improvement in function (Dallas ADL score) for ESI compared with forceful saline.	⊕⊕◯◯ LOW
Facet joint pain: Intra-articular steroid injection vs. Intra-articular control injection								
Δ Pain	Short and intermediate term	3 RCTs[45,83,126] N=227	Yes (-1)	No	No	Yes (-1)	No difference between groups.	⊕⊕◯◯ LOW
Δ Function	Short and intermediate term	1 RCT[83] N=60	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups.	⊕⊕◯◯ LOW
Facet joint pain: Intra-articular steroid injection vs. Intramuscular steroid injection								
Δ Pain	Short and intermediate term	1 RCT[208] N=60	No	Unknown	No	Yes (-1)	Significantly greater improvement following intra-articular versus intramuscular steroid injections in the short-term (MD -1.6; 95% CI -2.62 to -0.58); no difference between	⊕⊕⊕◯ MODERATE

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
							groups in the intermediate term.	
Δ Function	Short and intermediate term	1 RCT[208] N=60	No	Unknown	No	Yes (-1)	Significantly greater improvement following intra-articular versus intramuscular steroid injections in the short-term (MD -2.7; 95% CI -4.71 to -0.69); no difference between groups in the intermediate term.	⊕⊕⊕○ MODERATE
Facet joint pain: Intra-articular steroid injection vs. Radiofrequency denervation of the medial branch								
Δ Pain and Function	Intermediate term	1 RCT[123] N=52	No	Unknown	No	Yes (-1)	No differences between groups in pain or function improvement.	⊕⊕⊕○ MODERATE
Facet joint pain: Extra-articular steroid injection vs. Extra-articular control injection								
Δ Pain and function	Short and intermediate term	1 RCT[178,179] N=120	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups for pain or function improvement.	⊕⊕○○ LOW
	Long term	2 RCTs[166,178,179] N=204	Yes (-1)	Yes (-1)	No	Yes (-1)	No difference between groups for improvement in pain or function. Insufficient evidence prevents firm conclusion.	⊕○○○ INSUFFICIENT
Pain success	Short, intermediate and long term	2 RCTs[166,178,179] N=204	Yes (-1)	No	No	Yes (-1)	No difference between groups.	⊕⊕○○ LOW
Function success	Short, intermediate and long term	1 RCT[178,179] N=120	Yes (-1)	Unknown	No	Yes (-1)	No differences between groups.	⊕⊕○○ LOW
Facet joint pain: Extra-articular steroid injection vs. Radiofrequency denervation of the medial branch								
Δ Pain and Pain success	Short, intermediate and long term	1 RCT[53] N=100	Yes (-1)	Unknown	No	Yes (-1)	Significantly less improvement in pain with methylprednisolone 40 mg plus lidocaine vs. radiofrequency denervation at intermediate	⊕⊕○○ LOW

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Effect Size (95% CI) Conclusion	Quality
							(MD 1.6; 95% CI 1.27 to 1.93) and long-term (MD 2.0; 95% CI 1.79 to 2.21) follow-up; no difference between groups at short-term follow-up. Significantly fewer patients who received steroid injections reported pain success at all timepoints: short term, 80% vs. 100% (RR 0.80; 95% CI 0.70 to 0.92); intermediate term, 68% vs. 90% (RR 0.76; 95% CI 0.61 to 0.93); and long term, 62% vs. 88% (RR 0.70; 95% CI 0.55 to 0.90).	
Sacroiliac joint pain: Intraarticular steroid injection vs. Conservative treatment								
Δ Pain and function; Pain success; Composite score success	Short term	1 RCT[235] (N=51)	Yes (-1)	Unknown	No	Yes (-1)	No difference between groups in pain improvement, pain success, and composite score success. Significantly less improvement in function (RAND-36) with steroid injection versus physiotherapy and manual therapy, respectively: MD -31.2 (-44.1 to -18.2) and MD -37.9 (-46.2 to -29.7)	⊕⊕◯◯ LOW
Sacroiliac joint pain: Extraarticular steroid injection vs. Extraarticular control injection								
Δ Pain	Short term	1 RCT[128] (N=24)	Yes (-1)	Unknown	No	Yes (-1)	Greater improvement in pain with steroid vs. anesthetic injection: median -4.0 (range, -5.7 to -0.1) vs. -1.3 (range, -6.4 to 4.3); p=0.046	⊕⊕◯◯ LOW

CI: confidence interval; ESI: epidural steroid injection; MD: mean difference; ODI: Oswestry Disability Index; RCT: randomized controlled trial; RMDQ: Roland Morris Disability Questionnaire; RR: risk ratio; SMD: standardized mean difference; WMD: weighted mean difference.

2. Imprecise effect estimate: unknown confidence interval (all data estimated from graphs)

5.2. Strength of Evidence Summary: Efficacy Results for Cervical Spinal Injections

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
Cervical radiculopathy due to disc and/or foraminal narrowing: ESI vs. Conservative Care (CC)								
Arm pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[58] N=105	Yes (-1)	Unknown	No	Yes (-1)	ESI -3.2 ± 1.3, CC -2.8 ± 1.8 MD -0.4 (-1.0 to 0.2) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[58] N=104	Yes (-1)	Unknown	No	Yes (-1)	ESI -3.8 ± 1.3, CC -4.9 ± 1.8 MD 1.1 (0.5 to 1.7) Conclusion: Less improvement in arm pain with ESI versus CC.	⊕⊕◯◯ LOW
Function: NDI scores (0-100) (mean ± SD)	**Short-term**	1 RCT[58] N=105	Yes (-1)	Unknown	No	Yes (-1)	ESI 15.8 ± 2.9, CC 14.1 ± 2.7 MD 1.7 (0.6 to 2.8) Conclusion: Worse function with ESI versus CC.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[58] N=105	Yes (-1)	Unknown	No	Yes (-1)	ESI 11.0 ± 2.4, CC 5.4 ± 2.4 MD 5.6 (4.7 to 6.5) Conclusion: Worse function with ESI versus CC.	⊕⊕◯◯ LOW
Surgery	**Long-term**	1 RCT[58] N=114	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC 6%, CC 7% RR 0.80 (0.19 to 3.43) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Cervical radiculopathy due to disc and/or foraminal narrowing: ESI plus Conservative Care (CC) vs. Conservative Care (CC) alone								
Arm pain: ΔNRS scores (0-10) (mean ± SD (% improvement))	**Short-term**	1 RCT[58] N=107	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC -4.1 ± 1.5 (64%) CC -2.8 ± 1.8 (46%) MD -1.3 (-1.9 to -0.7) Conclusion: Greater improvement in arm pain with ESI+CC versus CC.	⊕⊕◯◯ LOW
	Intermediate-	1 RCT[58]	Yes	Unknown	No	Yes	ESI+CC -4.4 ± 1.6 (69%), CC -4.9 ± 1.8	⊕⊕◯◯

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
	term	N=105	(-1)			(-1)	(80%) MD 0.5 (-0.2 to 1.2) Conclusion: Less improvement in arm pain with ESI+CC versus CC.	LOW
Function: NDI scores (0-100) (mean ± SD)	**Short-term**	1 RCT[58] N=107	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC 18.1 ± 3.0, CC 14.1 ± 2.7 MD 4.0 (2.9 to 5.1) Conclusion: Worse function with ESI+CC versus CC.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[58] N=105	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC 15.0 ± 2.5, CC 5.4 ± 2.4 MD 9.6 (8.7 to 10.5) Conclusion: Worse function with ESI+CC versus CC.	⊕⊕◯◯ LOW
Surgery	**Long-term**	1 RCT[58] N=114	Yes (-1)	Unknown	No	Yes (-1)	ESI+CC 6%, CC 7% RR 0.80 (0.19 to 3.43) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Cervicobrachialgia (neck pain ± radiculopathy and/or stenosis): ESI versus Control Injections								
Pain: ≥50% improvement in NRS scores (% patients)	**Long-term**	1 RCT[223] N=42	Yes (-1)	Unknown	No	Yes (-1)	ESI 68%, NEI 12% RR 5.78 (1.53 to 21.84) Conclusion: More ESI patients achieved ≥50% improvement in pain than did NEI patients.	⊕⊕◯◯ LOW
Cervical disc herniation with or without radiculopathy: ESI versus Control Injections								
Pain: ≥50% improvement in NRS scores (% patients)	**Short-term**	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 75%, ENSI 85% RR 0.88 (0.74 to 1.06) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 73%, ENSI 83% RR 0.88 (0.73 to 1.06) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
	Long-term	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 68%, ENSI 72% RR 0.95 (0.75 to 1.21) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.1 ± 0.9, ENSI -4.2 ± 0.8 MD 0.1 (-0.2 to 0.4) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.0 ± 0.9, ENSI -4.4 ± 0.8 MD 0.4 (0.1 to 0.7) Conclusion: Slightly less improvement in ~~NDI~~ NRS scores with ESI vs. ENSI.	⊕⊕◯◯ LOW
	Long-term	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.1 ± 1.1, ENSI -4.1 ± 1.0 MD 0.0 (-0.4 to 0.4) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ≥50% improvement in NDI scores (% patients)	**Short-term**	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 85% RR 0.82 (0.68 to 1.00) Conclusion: Slightly fewer ESI patients achieved ≥50% improvement in pain than did ENSI patients.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 73%, ENSI 83% RR 0.88 (0.73 to 1.06) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 73% RR 0.95 (0.76 to 1.20) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function:	**Short-term**	1 RCT[157,158]	Yes	Unknown	No	Yes	ESI -13.6 ± 3.9, ENSI -14.9 ± 3.4	⊕⊕◯◯

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
ΔNDI scores (0-100) (mean ± SD)		N=120	(-1)			(-1)	MD 1.3 (-0.02 to 2.6) Conclusion: Slightly less improvement in NDI scores with ESI than ENSI.	LOW
	Intermediate-term	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -13.9 ± 4.2, ENSI -15.8 ± 3.4 MD 1.9 (0.5 to 3.3) Conclusion: Slightly less improvement in NDI scores with ESI vs. ENSI.	⊕⊕◯◯ LOW
	Long-term	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.9 ± 4.2, ENSI -15.9 ± 3.5 MD 1.0 (-0.4 to 2.5) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
NRS & NDI scores (% patients)	**Intermediate-term**	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 73%, ENSI 82% RR 0.90 (0.74 to 1.09) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[157,158] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 68%, ENSI 72% RR 1.12 (0.91 to 1.37) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Nonradicular neck pain: ESI versus Control Injection								
Pain: ≥50% improvement in NRS scores (% patients)	**Short-term**	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 85%, ENSI 73% RR 1.16 (0.96 to 1.40) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 77%, ENSI 78% RR 0.98 (0.81 to 1.19) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 75%, ENSI 75% RR 1.00 (0.81 to 1.23) Conclusion: No difference between	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
							groups.	
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.3 ± 0.6, ENSI -4.2 ± 0.9 MD -0.1 (-0.4 to 0.2) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.1 ± 0.8, ENSI -4.3 ± 0.9 MD 0.2 (-0.1 to 0.5) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.1 ± 0.9, ENSI -4.2 ± 1.0 MD 0.1 (-0.2 to 0.4) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ≥50% improvement in NDI scores (% patients)	**Short-term**	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 78%, ENSI 70% RR 1.12 (0.90 to 1.38) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 73%, ENSI 68% RR 1.07 (0.85 to 1.35) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 75% RR 0.93 (0.75 to 1.16) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ΔNDI scores (0-100) (mean ± SD)	**Short-term**	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.9 ± 4.3, ENSI -14.7 ± 3.6 MD -0.2 (-1.6 to 1.2) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-	1 RCT[152,153]	Yes	Unknown	No	Yes	ESI -14.4 ± 4.3, ENSI -15.2 ± 3.4	⊕⊕◯◯

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
	term	N=120	(-1)			(-1)	MD 0.8 (-0.6 to 2.2) Conclusion: No difference between groups.	LOW
	Long-term	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.8 ± 4.4, ENSI -16.1 ± 3.4 MD 1.3 (-0.1 to 2.7) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain + Function: ≥50% improvement in NRS & NDI scores (% patients)	**Short-term**	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 78%, ENSI 70% RR 1.12 (0.90 to 1.38) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 73%, ENSI 68% RR 1.07 (0.85 to 1.35) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[152,153] N=120	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 75% RR 0.93 (0.75 to 1.16) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Spinal stenosis: ESI versus Control Injection								
Pain: ≥50% improvement in NRS scores (% patients)	**Short-term**	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 87%, ENSI 87% RR 1.00 (0.82 to 1.22) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 80%, ENSI 90% RR 0.89 (0.72 to 1.10) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
	Long-term	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 73% RR 0.95 (0.69 to 1.31) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.5 ± 0.6, ENSI -4.2 ± 0.7 MD -0.3 (-0.6 to 0.04) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.3 ± 0.6, ENSI -4.5 ± 0.6 MD 0.2 (-0.1 to 0.5) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.2 ± 0.7, ENSI -4.3 ± 0.7 MD 0.1 (-0.3 to 0.5) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ≥50% improvement in NDI scores (% patients)	**Short-term**	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 87%, ENSI 77% RR 1.13 (0.89 to 1.44) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 83%, ENSI 87% RR 0.96 (0.78 to 1.19) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 77% RR 0.91 (0.67 to 1.24) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ΔNDI scores (0-100)	**Short-term**	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -15.6 ± 3.6, ENSI -14.1 ± 3.5 MD -1.5 (-3.3 to 0.3) Conclusion: No difference between	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
(mean ± SD)							groups.	
	Intermediate-term	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -15.7 ± 3.5, ENSI -16.0 ± 3.2 MD 0.3 (-1.4 to 2.0) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI -15.3 ± 3.5, ENSI -16.0 ± 3.4 MD 0.7 (-1.1 to 2.5) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain + Function: ≥50% improvement in NRS & NDI scores (% patients)	**Short-term**	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 87%, ENSI 77% RR 1.13 (0.89 to 1.44) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 80%, ENSI 87% RR 0.92 (0.74 to 1.16) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[163] N=60	Yes (-1)	Unknown	No	Yes (-1)	ESI 70%, ENSI 73% RR 0.95 (0.69 to 1.31) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Failed surgery syndrome: ESI versus Control Injections								
Pain: ≥50% improvement in NRS scores (% patients)	**Short-term**	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 71%, ENSI 79% RR 0.91 (0.67 to 1.23) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 75%, ENSI 71% RR 1.05 (0.76 to 1.44)	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
							Conclusion: No difference between groups.	
	Long-term	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 68%, ENSI 71% RR 0.95 (0.67 to 1.34) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -3.8 ± 0.7, ENSI -4.3 ± 0.8 MD 0.5 (0.1 to 0.9) Conclusion: Less improvement in pain with ESI versus ENSI.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -4.0 ± 0.7, ENSI -4.3 ± 0.7 MD 0.3 (-0.1 to 0.7) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -3.9 ± 0.9, ENSI -4.3 ± 0.7 MD 0.4 (-0.03 to 0.8) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ≥50% improvement in NDI scores (% patients)	**Short-term**	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 75%, ENSI 71% RR 1.05 (0.76 to 1.44) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 75%, ENSI 68% RR 1.11 (0.79 to 1.54) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 64%, ENSI 71% RR 0.90 (0.63 to 1.29) Conclusion: No difference between groups.	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
Function: ΔNDI scores (0-100) (mean ± SD)	**Short-term**	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.0 ± 3.5, ENSI -14.1 ± 3.3 MD 0.1 (-1.7 to 1.9) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -14.2 ± 3.5, ENSI -14.7 ± 3.2 MD 0.5 (-1.3 to 2.3) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI -13.8 ± 3.4, ENSI -15.0 ± 3.1 MD 1.2 (-0.5 to 2.9) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain + Function: ≥50% improvement in NRS & NDI scores (% patients)	**Short-term**	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 68%, ENSI 68% RR 1.00 (0.70 to 1.43) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 71%, ENSI 64% RR 1.11 (0.77 to 1.60) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[162] N=56	Yes (-1)	Unknown	No	Yes (-1)	ESI 64%, ENSI 71% RR 0.90 (0.63 to 1.29) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Facet pain: IASI versus Intra-articular control injection								
Pain: ≥50% improvement in NRS scores (% patients)	**Short-term**	1 RCT[21] N=41	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~10%, IANSI ~11% RR ~0.9 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
	Intermediate-term	1 RCT[177,181] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI 95%, IANSI 87% RR 1.10 (0.98 to 1.23) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[177,181] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI 93%, IANSI 85% RR 1.10 (0.97 to 1.25) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[177,181] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -4.5 ± 0.7, IANSI -4.4 ± 0.6 MD -0.1 (-0.3 to 0.1) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Intermediate-term	1 RCT[177,181] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -4.8 ± 0.7, IANSI -4.6 ± 0.7 MD -0.2 (-0.5 to 0.1) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[177,181] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -5.0 ± 0.7, IANSI -4.7 ± 0.7 MD -0.3 (-0.6 to -0.05) Conclusion: More improvement in pain with IASI versus IANSI.	⊕⊕◯◯ LOW
Function: ≥50% improvement in NDI scores (% patients)	**Intermediate-term**	1 RCT[177,181] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI 65%, IANSI 60% RR 1.08 (0.82 to 1.43) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[177,181] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI 75%, IANSI 70% RR 1.07 (0.86 to 1.34) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Function: ΔNDI scores (0-100)	**Short-term**	1 RCT[177,181] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -12.9 ± 3.1, IANSI -13.4 ± 3.5 MD 0.5 (-0.7 to 1.7) Conclusion: No difference between	⊕⊕◯◯ LOW

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
(mean ± SD)							groups.	
	Intermediate-term	1 RCT[177,181] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -13.5 ± 3.0, IANSI -13.4 ± 3.6 MD -0.1 (-1.3 to 1.1) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
	Long-term	1 RCT[177,181] N=120	Yes (-1)	Unknown	No	Yes (-1)	IASI -14.1 ± 3.1, IANSI -13.8 ± 3.4 MD -0.3 (-1.5 to 0.9) Conclusion: No difference between groups.	⊕⊕◯◯ LOW
Myofascial pain syndrome: IASI versus Conservative Care								
Tension headache (% patients)	**Short-term**	1 RCT[199] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~16%, CC ~24% RR ~0.7 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
	Intermediate-term	1 RCT[199] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~9%, CC ~21% RR ~0.4 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
	Long-term	1 RCT[199] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~3%, CC ~19% RR ~0.2 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
Pain: ΔNRS scores (0-10) (mean ± SD)	**Short-term**	1 RCT[199] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~-3.7, IANSI ~-1.4 MD ~-2.3 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
	Intermediate-term	1 RCT[199] N=306	Yes (-1)	Unknown	No	Yes (-2)[1]	IASI ~-3.9, IANSI ~-1.6 MD ~-2.3 (NC) Conclusion: No firm conclusions can be made.	⊕◯◯◯ INSUFFICIENT
	Long-term	1 RCT[199]	Yes	Unknown	No	Yes	IASI ~-4.0, IANSI ~-1.6	⊕◯◯◯

Outcome	Follow-up	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
		N=306	(-1)			(-2)[1]	MD ~-2.4 (NC) Conclusion: No firm conclusions can be made.	INSUFFICIENT

CI: confidence interval; ESI: epidural steroid injection; ENSI: epidural non-steroid injection; CC: conservative care; IANSI: intraarticular non-steroid injection; IASI: intraarticular steroid injection; MD: mean difference; NC: not calculable; NEI: non-epidural injection; RCT: randomized controlled trial; RR: risk ratio.

~ indicates data estimated from graph; f/u: follow-up; MD: mean difference; NC: not calculable; RR: relative risk

2. Imprecise effect estimate: unknown confidence interval

5.3. Strength of Evidence Summary: Harms

Catastrophic adverse events: non-transient paralysis (tetraplegia, paraplegia), blindness; as well as death, arachnoiditis, stroke, cardiac arrest, spinal cord infarction, spinal cord injury, and meningitis

Serious adverse events: epidural hematoma, deep infection, respiratory failure, spinal nerve injury, fever or infection attributed to the injection, hematoma, intravascular injection of steroid with neurologic sequelae, nerve root injury, retroperitoneal hematoma, subarachnoid injection, seroma, neurovascular complications, surgery or hospitalization necessary due to adverse events attributed to the procedure, and angina attributed to the procedure.

Non-serious adverse events: all other adverse events; note that the following were considered non-serious unless sufficient detail was reported to suggest that symptoms did not remit easily or were more severe: cerebrospinal fluid tap, dural pucture or tears, new neurological symptoms, sensory deficits, paresthesia and numbness in lower extremity, excessive pain, procedural bleeding, and procedural hypotension

Outcome	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
Catastrophic adverse events	60 RCTs* N=6290 1 report of FDA Adverse Events Reporting Database[78]	Yes (-1)	No	No	Yes (-1)[1]	Across all RCTs of epidural, facet joint and intradiscal injections in the lumbar or cervical spine that reported any adverse events, no catastrophic adverse events were reported to occur. Observational studies (3 cohort studies and 22 case series) were consistent with trials in reporting no instances of catastrophic events. One recent analysis of the FDA Adverse Events Reporting Database found a total of 131 major neurologic adverse events, which included five deaths (including suicide in two patients with arachnoiditis) and 41 cases of arachnoiditis; other events included (but aren't limited to) brainstem stroke, motor-incomplete tetraplegia, paraplegia, paralysis, spinal cord infarction, cardiac arrest, blindness, and meningitis, although total numbers of each event were unclear. In the majority of cases, the injection approach was unavailable, and the report did not attribute any major adverse events to any particular injection approach or imaging utilization; further, a	⊕⊕◯◯ LOW

Outcome	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Absolute Risk Effect Size (95% CI) Conclusion	Quality
						causal relationship between particulate steroid injections and major adverse events has not been established.	
Serious adverse events	60 RCTs* N=6290 1 report of FDA Adverse Events Reporting Database[78]	Yes (-1)	No	No	No	Across all RCTs of epidural, facet joint and intradiscal injections in the lumbar or cervical spine that reported any adverse events, serious adverse events were rare, and no differences between treatment groups were detected. Aside from the following events, which were reported to occur in at least one patient, no serious adverse events were reported in the RCTs. Lumbar EI (with or without steroid): retroperitoneal hematoma (1%), subarachnoid entry or injection (0%-3%), hospitalization and/or surgery (2.0%-2.5%). Cervical EI (with or without steroid): subarachnoid puncture (0.3%-0.9%). Lumbar ESI vs. disc or decompression procedure: paresthesia and numbness in lower extremity for 3-4 days (4% (1/24) vs. 12% (3/26), p=0.34), seroma (0% vs. 1%) Observational studies were consistent with trials in finding low rates of serious adverse events.	⊕⊕⊕○ MODERATE
Non-serious adverse events	60 RCTs* N=6290 1 report of FDA Adverse Events Reporting Database[78]	Yes (-1)	No	No	No	Across all RCTs of epidural, facet joint and intradiscal injections in the lumbar or cervical spine that reported any adverse events, reported that the majority of non-serious adverse events occurred infrequently. However, methods for assessing adverse events were not well reported. Observational studies were consistent with the randomized trials.	⊕⊕⊕○ MODERATE

*All RCTs that reported on any harm was included in the study count based on the assumption that that study evaluated and reported any adverse event that occurred: the RCT count included 51 lumbar RCTs (N=5094) and 9 cervical RCTs (N=1196).

1. Imprecise effect estimate: rare outcomes

5.4. Strength of Evidence Summary: Differential Efficacy and Harms

Subgroup	Outcome	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Conclusion	Quality
Lumbar radiculopathy: ESI vs. Control injections								
Disc prolapse vs. foraminal narrowing	Short-term pain, function	1 RCT[228] N=124	Yes (-2)[1]	Yes (-1)	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias, inconsistency and imprecision to determine if the effect of ESI varies depending on reason for radiculopathy (disc prolapse or foraminal narrowing).	⊕◯◯◯ INSUFFICIENT
Disc herniation vs extrusion	≥75% improvement in leg pain, function quality of life, and risk of surgery in the long-term	1 RCT[116] N=128	Yes (-2)[1]	Yes (-1)	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias, inconsistency and imprecision to determine if the effect of ESI varies depending on reason for radiculopathy (disc herniation or disc extrusion).	⊕◯◯◯ INSUFFICIENT
Disc herniation vs disc degeneration	Risk of surgery, short-term	1 RCT[217] N=183	Yes (-2)[1]	Unknown	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias and imprecision to determine if the effect of ESI varies depending on reason for radiculopathy (disc herniation or disc degeneration).	⊕◯◯◯ INSUFFICIENT
Symptom duration (<3 or 4 vs ≥3 or 4 months)	≥50% improvement in pain, short-term; or ≥75% improvement in function, short- and long-term	2 RCTs[13,87] N=378	Yes (-2)[1]	No	No	Yes (-1)	There was insufficient evidence from 2 trials based on serious risk of bias and imprecision to determine if the effect of ESI varies depending on symptom duration (<3 or 4 vs ≥3 or 4 months)	⊕◯◯◯ INSUFFICIENT
Baseline scores for anxiety or depression, SF-36, ODI, neurological	"Response" (not defined), short- and long-term	1 RCT[13] N=228	Yes (-2)[1]	Unknown	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias and imprecision to determine if the effect of ESI varies depending on baseline characteristics.	⊕◯◯◯ INSUFFICIENT

Subgroup	Outcome	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Conclusion	Quality
abnormalities, prior episodes of sciatica, coexistent back pain, work status, or sex								
Lumbar radiculopathy: ESI vs. Disc decompression								
Symptom duration (<1 vs 1-3 vs >3 years)	Reduction in leg pain, intermediate-term (6 months)	1 RCT[86] N=90	Yes (-2)[1]	Unknown	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias and imprecision to determine if the effect of ESI varies depending on symptom duration (<1 vs 1-3 vs >3 years)	⊕◯◯◯ INSUFFICIENT
Lumbar stenosis: ESI vs. Control Injections Stenosis								
EQ-5D index score, employment status, treatment expectation, sex, race, ethnicity, education, smoking history, diabetes status, pain duration, stenosis severity, age, body mass index, EQ-5D pain scores, Patient Health Questionnaire-	Short-term pain, function, quality of life, patient satisfaction	1 RCT[229] N=400	Yes (-1)[2]	Yes (-1)	No	Yes (-1)	There was insufficient evidence from 1 trial based on serious risk of bias, inconsistency and imprecision to determine if the effect of ESI versus ENSI varies depending on any of several baseline characteristics or injection approach (tranforaminal vs. interlaminar)	⊕◯◯◯ INSUFFICIENT

Subgroup	Outcome	Studies N	Serious Risk Of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Conclusion	Quality
8 scores, Generalized Anxiety Disorder-7 scores, Pain Catastrophizing Scale (total scores; helplessness, rumination, and magnification subscale scores), Fear-Avoidance Beliefs Questionnaire physical activities subscale scores, injection approach								

ESI: epidural steroid injection; RCT: randomized controlled trial;

1. Serious risk of bias in evaluation of HTE: unclear whether the subgroup variables were specified a priori; the hypothesized impact of subgroup on treatment effect was not stated
2. Serious risk of bias in evaluation of HTE: large number of subgroups tested (i.e., subgroup hypothesis not one of a smaller number tested); was unclear whether any of the subgroup variables were specified a priori; the hypothesized impact of subgroup on treatment effect was not stated

5.5. Strength of Evidence Summary: Cost Effectiveness

For lumbar radiculopathy due to disc pathology, two economic studies were included:

- One poorly conducted (QHES 49/100) cost-effectiveness study[116] conducted alongside an RCT[115] of fluoroscopically-guided ESI versus ENSI reported the cost per positive response (≥75% improvement in leg pain and absence of surgery); results were stratified based on MRI classification of disc herniation, extrusion, and bulge. For the disc herniation subgroup, ESI had a lower cost per positive response at 12 months compared with ENSI ($4432 vs. $17,098, p=0.0073); this difference was not observed at 3 months. In the extrusions subgroup, the opposite was true, with a significantly higher cost per positive response in the ESI versus ENSI group at 12 months ($7165 vs. $2484, p=0.0058); the difference was smaller and not significant at 3 months. In the bulge subgroup, there were no differences between groups in the cost per positive response at either 3 or 12 months. The analysis had major limitations, including a relatively short time horizon, lack of sensitivity analysis, long-term modeling, and statement of perspective. Further, results were only presented based on subgroups but not for the population as a whole. The authors stated that future work should be done to assess the impact of the cost-effectiveness of ESI versus ENSI when stratified based on MRI classification.
- One reasonably well-conducted (QHES 78/100) cost utility analysis[204] was performed using RCT[13] data that compared ESI (1-3 injections) to NEI (interligamentous saline injections); use of imaging was not reported in this trial. Utility values were derived from SF-36 scores through 12 weeks. The study found that based on 12-week data, the incremental cost per QALY of up to three ESIs (over NEI) was high, ranging from £44,701 to £354,172 for the provider and purchaser perspectives, respectively. Based on the same timeframe, the incremental cost per QALY of a single ESI (over NEI) was somewhat lower but remained high, ranging from £25,746 to £167,145 for the provider and purchaser perspectives, respectively. The authors concluded that the cost-effectiveness ratios are higher than the NICE thresholds and did not support NHS coverage. The main limitation of this study was its very short time horizon.

For lumbar spinal stenosis, one economic study was included:

- This cost utility analysis was relatively well-conducted (QHES 73/100) and compared serial ESI (i.e., 6 injections) to two different procedures (minimally invasive decompression and surgical decompression) in patients with moderate to severe symptomatic lumbar stenosis refractory to conservative care.[230] All data were derived from the literature, and all comparisons were indirect. No assumptions regarding use of imaging guidance for ESI were stated. Utility values were derived from EQ-5D, SF-6D, or ODI data. The study found that ESI was dominated by minimally invasive decompression, with cost per QALYs of $81,518 and $43,760, respectively. ESI dominated surgical decompression, which had a cost per QALY of $125,985. One-way sensitivity analysis showed that when three or less ESI were performed per year it dominated minimally invasive decompression; in no other scenario was it found to dominate minimally invasive decompression. The authors concluded that minimally invasive decompression was the most cost-effective treatment option in this patient population. However, the study made a number of assumptions that increase the risk of bias of their conclusions, including the assumption that patients had already failed ESI, which impacted the QALY values for this group. Other limitations included reliance on the published literature, and basing ESI QALY values on patients with mild stenosis rather than moderate to severe stenosis.

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Tables

Table 8. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Pain improvement (VAS or NRS, 0-10) for epidural steroid injection (ESI) vs. control injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Pain score Mean ± SD		Δ from base-line		Mean difference A vs. B* (95% CI)
						Group A	Group B	Group A	Group B	
Short term (≤3 mos.)	Datta 2011	Methylprednisolone 80 mg + bupivacaine 0.125% No imaging	Bupivacaine 0.125%	Caudal	3 mos.	4.9 ± 1.29 (n=39)	6.2 ± 0.79 (n=42)	-2.5 ± 0.78	-1.0 ± 0.5	-1.5 (-1.79 to -1.21)
		Triamcinolone 80 mg + bupivacaine 0.125% No imaging	Bupivacaine 0.125%	Caudal	3 mos.	4.8 ± 0.92 (n=40)	6.2 ± 0.79 (n=42)	-2.6 ± 0.58	-1.0 ± 0.5	-1.6 (-1.83 to -1.37)
		Dexamethasone 15 mg + bupivacaine 0.125% No imaging	Bupivacaine 0.125%	Caudal	3 mos.	5.2 ± 1.59 (n=42)	6.2 ± 0.79 (n=42)	-2.1 ± 1.14	-1.0 ± 0.5	-1.1 (-1.48 to -0.72)
	Manchikanti 2012,2011, 2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	3.4 ± 1.7 (n=60)	4.1 ± 1.8 (n=60)	-4.4 ± 1.12	-4.0 ± 1.21	-0.40 (-0.82 to 0.02)
	Ghai 2015	Methylprednisolone 80 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	3 mos.	3.1 (n=35)	4.5 (n=34)	-4.9 ± 2.73	-3.5 ± 2.68	-1.40 (-2.68 to -0.12)
	Klenerman 1984	Methylprednisolone 80 mg + saline Imaging NR	Bupivacaine 0.25%	Inter-laminar	2 mos.	2.5 ± 1.79† (n=19)	1.9 ± 1.55† (n=16)	-2.3 ± 1.13	-3.4 ± 0.98	1.1 (0.4 to 1.8)
	Manchikanti 2014,2013, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	3 mos.	3.5 ± 1.0 (n=60)	3.9 ± 1.6 (n=60)	-4.5 ± 0.63	-4.3 ± 1.01	-0.20 (-0.50 to 0.10)
	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water	Bupivacaine 0.5% + water	Trans-foraminal	1 mo.	Unadjusted 2.14 ± 1.99 (n=28)	Unadjusted: 3.83 ± 3.57 (n=30)	-3.57 ± 1.24	-2.48 ± 2.3	Unadjusted: -1.09 (-2.03 to -0.15)

Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Pain score Mean ± SD Group A	Pain score Mean ± SD Group B	Δ from base-line Group A	Δ from base-line Group B	Mean difference A vs. B* (95% CI)
	Fluoroscopy				Adjusted: 2.54 (95% CI, 1.36 to 3.69)‡ (n=28)	Adjusted: 3.78 (95% CI, 2.72 to 4.85)‡ (n=30)			Adjusted: -1.26 (-2.79 to 0.27)‡
Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Bupivacaine 0.5%	Trans-foraminal	1 mo.	4.1 ± 3.0 (n=28)	6.7 ± 2.8 (n=27)	-2.9 ± 1.93	-0.7 ± 1.69	-2.2 (-3.16 to -1.24)
Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	3 mos.	4.0 ± 1.5 (n=60)	4.1 ± 1.8 (n=60)	-4.2 ± 0.95	-4.2 ± 1.21	0.00 (-0.39 to 0.39)
Tafazal 2009/Ng 2005	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Bupivacaine 0.25%	Trans-foraminal	3 mos.	NR (n=65)	NR (n=59)	-2.45 ± 0.36	-2.26 ± 0.41	-0.19 (-0.33 to -0.05)
Bush 1991	Triamcinolone 80 mg + procaine hydrochloride 0.5% + saline	Saline (25 ml)	Caudal	1 mo.	1.6 (n=12)	4.5 (n=11)	-2.26 ± 0.96	-0.42 ± 0.9	-1.83 (-2.59 to -1.07)
Iversen 2011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	3 mos.	4.1† (n=34)	3.4† (n=35)	-0.91 ± 0.94	1.95 ± 0.98	1.04 (0.59 to 1.49)
Carette 1997	Methylprednisolone 80 mg + saline Imaging NR	Saline	Inter-laminar	3 mos.	3.89 (n=77)	3.95 (n=79)	-2.67 ± 3.6	-2.2 ± 3.44 3.	-0.47 (-1.58 to 0.64)
Klenerman 1984	Methylprednisolone 80 mg + saline Imaging NR	Saline	Inter-laminar	2 mos.	2.5 ± 1.79† (n=19)	2.0 ± 1.55† (n=16)	-2.3 ± 1.13	-4.5 ± 0.98	2.2 (1.5 to 2.9)
Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline	Trans-foraminal	1 mo.	4.1 ± 3.0 (n=28)	5.5 ± 2.6 (n=37)	-2.9 ± 1.93	-1.1 ± 1.56	-1.8 (-2.68 to -0.92)

Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Pain score Mean ± SD Group A	Pain score Mean ± SD Group B	Δ from base-line Group A	Δ from base-line Group B	Mean difference A vs. B* (95% CI)
Karppinen 2001	Methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline 0.9%	Trans-foraminal	3 mos.	3.13 (n=79)	3.43 (n=79)	-3.97 ± 1.3	-4.09 ± 1.5	Unadjusted: 0.12 (-0.32, 0.56) Adjusted: 0.05 (-1.1 to 1.2)§
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	3 mos.	4.1‡ (n=34)	2.9‡ (n=36)	-0.91 ± 2.94	-1.93 ± 2.89	Un-adjusted: 1.04 (0.59 to 1.49) Adjusted: 1.12 (−0.10 to 2.34)** Adjusted: 1.00 (−0.22 to 2.23)††
Arden 2005/Price 2005	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	Soft tissue injection of saline (2 ml) into interspinous ligament	Inter-laminar	3 mos.	NR (n=120)	NR (n=108)	-1.3 ± 3.3	-1.8 ± 3.3	0.50 (-0.36 to 1.36)
Helliwell 1985	Methylprednisolone 80 mg + saline Imaging NR	Interspinous ligament injection of saline (5 ml)	Inter-laminar	3 mos.	NR (n=20)	NR (n=19)	-2.7 ± 2.94†	-0.4 ± 2.94†	-2.30 (-4.15 to -0.45)
Klenerman 1984	Methylprednisolone 80 mg + saline Imaging NR	Interspinous ligament needling without injection	Inter-laminar	2 mos.	2.5‡ (n=19)	3.0‡ (n=12)	-2.3 ± 2.94	-3.5 ± 2.89	1.20 (-0.90 to 3.30)
Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Intramuscular injection of triamcinolone 40 mg	Trans-foraminal	1 mo.	4.1 ± 3.0 (n=28)	5.9 ± 3.4 (n=28)	-2.9 ± 1.93	-1.7 ± 2.16	-1.20 (-2.27 to -0.13)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Pain score Mean ± SD Group A	Pain score Mean ± SD Group B	Δ from base-line Group A	Δ from base-line Group B	Mean difference A vs. B* (95% CI)
	Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Intramuscular injection of saline (2 ml)	Trans-foraminal	1 mo.	4.1 ± 3.0 (n=28)	6.0 ± 2.5 (n=30)	-2.9 ± 1.93	-1.0 ± 1.58	-1.90 (-2.81 to -0.99)
Inter-mediate (>3 to <12 mos.)	Manchikanti 2012,2011, 2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	3.5 ± 1.7 (n=60)	3.9 ± 1.8 (n=60)	-4.3 ± 1.12	-4.2 ± 1.21	-0.10 (-0.52 to 0.32)
	Ghai 2015	Methylprednisolone 80 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	9 mos.	2.7 (n=35)	4.6 (n=34)	-5.3 ± 0.63	-3.4 ± 1.01	-1.90 (-2.30 to -1.50)
	Manchikanti 2014,2013,2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	6 mos.	3.5 ± 1.0 (n=60)	4.1 ± 1.6 (n=60)	-4.5 ± 0.63	-4.1 ± 1.01	-0.40 (-0.70 to -0.10)
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	6 mos.	4.1 ± 1.7 (n=60)	3.9 ± 1.5 (n=60)	-4.1 ± 1.12	-4.4 ± 0.95	0.30 (-0.07 to 0.67)
	Karppinen 2001	Methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline 0.9%	Trans-foraminal	6 mos.	3.07 (n=78)	2.16 (n=80)	-4.03 ± 1.12	-5.36 ± 0.95	Unadjusted: 1.33 (1.01 to 1.65) Adjusted: 1.62 (0.56 to 2.68)§
Long-term (≥12 mos.)	Manchikanti 2012,2011, 2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	3.6 ± 1.8 (n=60)	4.2 ± 1.8 (n=60)	-4.2 ± 1.21	-3.9 ± 1.21	-0.30 (-0.73 to 0.13)
	Ghai 2015	Methylprednisolone 80 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	12 mos.	2.6 (n=35)	4.4 (n=34)	-5.4 ± 0.85	-3.6 ± 1.05	-1.80 (-2.25 to -1.35)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Pain score Mean ± SD Group A	Pain score Mean ± SD Group B	Δ from base-line Group A	Δ from base-line Group B	Mean difference A vs. B* (95% CI)
	Manchikanti 2014,2013, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	24 mos.	3.7 ± 1.4 (n=60)	4.1 ± 1.7 (n=60)	-4.3 ± 0.85	-4.1 ± 1.05	-0.20 (-0.54 to 0.14)
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	24 mos.	4.2 ± 1.6 (n=60)	4.0 ± 1.6 (n=60)	-4.0 ± 1.03	-4.3 ± 1.03	0.30 (-0.07 to 0.67)
	Bush 1991	Triamcinolone 80 mg + procaine hydrochloride 0.5% + saline	Saline (25 ml)	Caudal	12 mos.	1.42 (n=12)	2.96 (n=11)	-2.43	-1.96	-0.47
	Iversen 2011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	12 mos.	2.2† (n=34)	2.7† (n=33)	-2.81 ± 1.21	-2.65 ± 1.21	-0.16 (-0.74 to 0.42)
	Karppinen 2001	Methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline 0.9%	Trans-foraminal	12 mos.	2.39 (n=78)	2.42 (n=80)	-4.71 ± 1.03	-5.1 ± 1.03	Unadjusted: 0.39 (0.07 to 0.71) Adjusted: 0.53 (-0.50 to 1.57)§
	Iversen 2011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%, subcutaneous injection superficial to the sacral hiatus and outside spinal canal	Caudal	12 mos.	2.2 ± 2.36† (n=34)	2.0 ± 2.76† (n=32)	-2.81 ± 1.49	-2.83 ± 1.75	Un-adjusted: 0.02 (-0.77 to 0.81); Adjusted: −0.02 (−1.29 to 1.25)**; Adjusted: −0.14 (−1.41 to 1.14)††
	Arden 2005/Price 2005	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	Saline (2 ml) soft tissue injection into interspinous ligament	Inter-laminar	12 mos.	NR (n=120)	NR (n=108)	-1.7 ± 3.6	-2.0 ± 3.4	0.3 (-0.61 to 1.21)

CI: confidence interval; NR: not reported; NRS: numerical rating scale; SD: standard deviation; VAS: visual analog scale.
*A negative score favors the intervention and a positive score favors the control.
†Means were estimated from graph in article.
‡Adjusted for study site, sex, duration of pain, opiod use, and baseline outcome score.
§Difference ANCOVA adjusted for level of symptomatic disc and days on sick leave.
**Adjusted for baseline values.
††Further adjusted for duration of leg pain, back pain, and sick leave.
Manchikanti et al., caudal: (1) 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;11:801-15; (2) 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; (3) 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.
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Manchikanti et al., transforaminal: Transforaminal epidural injections in chronic lumbar disc herniation: a randomized, double-blind, active-control trial. Pain Physician 2014;17:E489-501.

Table 9. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Pain success for epidural steroid injection (ESI) vs. control injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of Pain success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Short term (≤3 mos.)	Datta 2011	Methylprednisolone 80 mg + bupivacaine 0.125% No imaging used	Bupivacaine 0.125%	Caudal	complete pain relief (<6 diclofenac tablets/wk)	3 mos.	43.5% (17/39)	26.2% (11/42)	1.66 (0.89 to 3.1)
		Triamcinolone 80 mg + bupivacaine 0.125% No imaging used	Bupivacaine 0.125%	Caudal	complete pain relief (<6 diclofenac tablets/wk)	3 mos.	42.9% (18/42)	26.2% (11/42)	1.64 (0.88 to 3.03)
		Dexamethasone 15 mg + bupivacaine 0.125% No imaging used	Bupivacaine 0.125%	Caudal	complete pain relief (<6 diclofenac tablets/wk)	3 mos.	37.5% (15/40)	26.2% (11/42)	1.43 (0.75 to 2.73)
	Manchikanti 2012,2011, 2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in pain on NRS	3 mos.	80.0% (48/60)	76.7% (46/60)	1.04 (0.86 to 1.26)
	el Zahaar 1991	Hydrocortisone 5 ml + carbocaine 4% + saline Imaging NR	Carbocaine 4% + saline	Caudal	≥75% subjective improvement in baseline back, leg and thigh symptoms	>24 hrs.	73.6% (14/19 herniated disc subgroup)	71.4% (10/14 herniated disc subgroup)	1.03 (0.67 to 1.58)
	Cuckler 1985	Methylprednisolone 80 mg + procaine 1% Imaging NR	Procaine 1% + saline	Inter-laminar	≥75% subjective improvement in baseline symptoms	>24 hrs.	31.8% (7/22 herniated disc subgroup)	35.7% (5/14 herniated disc subgroup)	0.89 (0.35 to 2.26)
	Ghai 2015	Methylprednisolone 80 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in pain on NRS	3 mos.	86% (30/35)	50% (17/34)	1.71 (1.19 to 2.46)
	Manchikanti 2014,2013,2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in pain on NRS	3 mos.	88% (53/60)	78% (47/60)	1.13 (0.96 to 1.33)
	Rogers 1992	Methylprednisolone 80 mg + lignocaine 2% +	Lignocaine 2% + saline	Inter-laminar	Subjective assessment of	1 mo.	20% (3/15)	6.7% (1/15)	3.00 (0.35 to 25.68)

Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of Pain success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
	saline Imaging NR			"complete pain relief"				
Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Bupivacaine 0.5%	Trans-foraminal	Improvement of ≥50% from baseline in pain on NRS	1 mo.	53.6% (95% CI 36% to 72%) (15/28)	7.4% (95% CI 0% to 17%) (2/27)	7.23 (1.82 to 28.67)
Ng 2005/ Tafazal 2009	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Bupivacaine 0.25%	Trans-foraminal	Improvement of ≥20% from baseline in pain on VAS	3 mos.	41.5% (18/43)	47.5% (20/43)	0.9 (0.56 to 1.45)
Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	Improvement of ≥50% from baseline in pain on NRS	3 mos.	73% (44/60)	77% (46/60)	0.96 (0.78 to 1.18)
Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Bupivacaine 0.5% + water	Trans-foraminal	Improvement of ≥50% from baseline in leg pain and positive GPE obviating the need for further intervention	3 mo.	50% (14/28)	43% (13/30)	1.15 (0.66 to 2.00)
Snoek 1977	Methylprednisolone 80 mg Imaging NR	Saline	Inter-laminar	Subjective relief of radiating pain (i.e., no pain or did not extend as far after injection)	Mean 48 ± 24 hrs.	25.9% (7/27)	12.5% (3/24)	2.07 (0.6 to 7.14)
Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline	Trans-foraminal	Improvement of ≥50% from baseline in pain on NRS	1 mo.	53.6% (95% CI 36% to 72%) (15/28)	18.9% (95% CI, 6% to 32%) (7/37)	2.83 (1.34 to 6.00)
Arden 2005/ Price 2005	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	Saline (2 ml) soft tissue injection into interspinous ligament	Inter-laminar	Improvement of ≥50% from baseline in VAS	3 mos.	43% (52/120)	46% (50/108)	1.12 (0.85 to 1.48)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of Pain success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
	Dilke 1973	Methylprednisolone 80 mg + saline (10 ml) Imaging NR	Saline (1 ml) interspinous ligament injection	Inter-laminar	Patient assessment of pain (“none”)	3 mos.	36% (16/44)	21% (8/38)	1.73 (0.83 to 3.58)
	Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Intramuscular injection of triamcinolone 40 mg or saline (2 ml)	Trans-foraminal	Improvement of ≥50% from baseline in VAS	1 mo.	54% (15/28)	17.2% (10/58)	3.11 (1.60 to 6.02)
	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept + Bupivacaine 0.5% + water	Trans-foraminal	Improvement of ≥50% from baseline in leg pain and positive GPE obviating the need for further intervention	3 mo.	50% (14/28)	42% (11/26)	1.18 (0.66 to 2.11)
	Cohen 2015	Methylprednisolone 60 mg + bupivacaine 0.25% + saline + oral placebo medication	Posterior ligament injection of saline (3 ml) + oral gabapentin 300 mg	Inter-laminar or trans-foraminal	>2 point decrease in average leg pain coupled with positive GPE without additional procedural or non-rescue pharma-cological interventions	3 mos.	37% (27/73)	29% (21/72)	1.27 (0.79 to 2.03)
Inter-mediate (>3 to <12 mos.)	Manchikanti 2012,2011,2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in pain on NRS	6 mos.	82% (49/60)	77% (46/60)	1.07 (0.89 to 1.28)
	Ghai 2015	Methylprednisolone 80 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in pain on NRS	9 mos.	89% (31/35)	53% (18/34)	1.67 (1.19 to 2.35)
	Manchikanti 2014,2013,20	Betamethasone 6 mg + lidocaine 0.5%	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from	6 mos.	88% (53/60)	70% (42/60)	1.26 (1.04 to 1.53)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of Pain success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
	10	Fluoroscopy			baseline in pain on NRS				
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	Improvement of ≥50% from baseline in pain on NRS	6 mos.	68% (41/60)	73% (44/60)	0.93 (0.74 to 1.17)
	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Bupivacaine 0.5% + water	Trans-foraminal	Improvement of ≥50% from baseline in leg pain and positive GPE obviating the need for further intervention	6 mo.	29% (8/28)	40% (12/30)	0.71 (0.34 to 1.48)
	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept + Bupivacaine 0.5% + water	Trans-foraminal	Improvement of ≥50% from baseline in leg pain and positive GPE obviating the need for further intervention	6 mo.	29% (8/28)	38% (10/26)	0.74 (0.35 to 1.59)
Long-term (≥12 mos.)	Manchikanti 2012,2011, 2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in pain on NRS	24 mos.	68% (41/60)	63% (38/60)	1.08 (0.83 to 1.40)
	el Zahaar 1991	Hydrocortisone 5 ml + carbocaine 4% + saline Imaging NR	Carbocaine 4% + saline	Caudal	≥75% subjective improvement in baseline back, leg and thigh symptoms	Mean 20.9 (13-36) mos.	57.8% (11/19 herniated disc subgroup)	64.2% (9/14 herniated disc subgroup)	0.90 (0.52 to 1.56)
	Cuckler 1985	Methylprednisolone 80 mg + procaine 1% Imaging NR	Procaine 1% + saline	Inter-laminar	≥75% subjective improvement in baseline symptoms	Mean 20.5 (13 to 30) mos.	26.1% (6/23 herniated disc subgroup)	15.4% (2/13 herniated disc subgroup)	1.70 (0.40 to 7.22)
	Ghai 2015	Methylprednisolone 80	Lidocaine 0.5%	Inter-	Improvement of	12	89% (31/35)	59% (20/34)	1.51 (1.11 to

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of Pain success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
		mg + lidocaine 0.5% Fluoroscopy		laminar	≥50% from baseline in pain on NRS	mos.			2.04)
	Manchikanti 2014,2013, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in pain on NRS	24 mos.	70.0% (42/60)	63.3% (38/60)	1.11 (0.86 to 1.42)
	Manchikanti 2014 24 months	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	Improvement of ≥50% from baseline in pain on NRS	24 mos.	58% (35/60)	67% (40/60)	0.88 (0.66 to 1.16)
	Arden 2005/ Price 2005	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	Saline (2 ml) soft tissue injection into interspinous ligament	Inter-laminar	Improvement of ≥50% from baseline in VAS	12 mos.	48% (58/120)	44% (48/108)	1.09 (0.82 to 1.44)

CI: confidence interval; NR: not reported; NRS: numerical rating scale; VAS: visual analog scale.

Manchikanti et al., caudal: (1) 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;11:801-15; (2) 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; (3) 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.

Manchikanti et al., interlaminar: (1) 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; (2) 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; (3) A randomized, double-blind, active-control trial of the effectiveness of lumbar interlaminar epidural injections in disc herniation. Pain Physician 2014;17:E61-74.

Manchikanti et al., transforaminal: Transforaminal epidural injections in chronic lumbar disc herniation: a randomized, double-blind, active-control trial. Pain Physician 2014;17:E489-501.

Table 10. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Function improvement for epidural steroid injection (ESI) vs. control injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Function score Mean ± SD Group A	Function score Mean ± SD Group B	Δ from baseline Group A	Δ from baseline Group B	Mean difference A vs. B* (95% CI)
Oswestry Disability Index (ODI)										
Short term (≤3 mos.)	Manchikanti 2012,2011,2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	(0-50 scale) 13.6 ± 6.5 (n=60)	(0-50 scale) 16.5 ± 7.2 (n=60)	-28.6 ± 7.84	-25.4 ± 8.95	-3.20 (-6.21 to -0.19)
	Sayegh 2009	Betamethasone 7 mg + xylocaine 2% No imaging used	Xylocaine 2% + water	Caudal	1 mo.	(scale NR) 8.7 ± 11.9 (n=89)	(scale NR) 23.5 ± 9.6 (n=85)	-29.8 ± 9.92	-15 ± 7.61	-14.80 (-17.42 to -12.18)
	Ghai 2015	Methylprednisolone 80 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	3 mos.	(scale NR) 21 (n=35)	(scale NR) 27 (n=34)	-25.8 ± 16	-22.6 ± 19.88	-3.20 (-11.73 to 5.33)
	Manchikanti 2014,2013,2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	3 mos.	(0-50 scale) 14.0 ± 4.2 (n=60)	(0-50 scale) 15.8 ± 6.3 (n=60)	-31.2 ± 6.24	-29 ± 7.59	-2.20 (-4.69 to 0.29)
	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Bupivacaine 0.5% + water	Trans-foraminal	1 mo.	(0-100 scale) Unadjusted: 22.43 ± 16.72 (n=28) Adjusted: 24.1 (16.6 to 31.6)† (n=28)	(0-100 scale) Unadjusted: 28.80 ± 21.22 (n=30) Adjusted: 30.0 (23.2 to 36.7)† (n=30)	-20.47 ± 10.28 NR	-12.1 ± 12.74 NR	Un-adjusted: -8.37 (-14.31 to -2.43) Adjusted: -5.87 (-15.6 to 3.85)†
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	3 mos.	(0-50 scale) 14.7 ± 16.4 (n=60)	(0-50 scale) 16.5 ± 17.2 (n=60)	-26.6 ± 7.69	-26.8 ± 8.85	0.20 (-2.77 to 3.17)
	Tafazal	Methylprednisolone	Bupivacaine	Trans-	3 mos.	(0-100 scale)	(0-100 scale)	-9.3 ± 2.3	-10.7 ± 2.6	0.57

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Function score Mean ± SD Group A	Function score Mean ± SD Group B	Δ from baseline Group A	Δ from baseline Group B	Mean difference A vs. B* (95% CI)
	2009/Ng 2005	40 mg + bupivacaine 0.25% Fluoroscopy	0.25%	foraminal		NR (n=65)	NR (n=59)			(0.21 to 0.93)
	Iversen 2011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	3 mos.	(0-100 scale) 25‡ (n=34)	(0-100 scale) 21.5‡ (n=35)	-7.5 ± 9.14	4. - 9.9 ± 8.19	2.40 (-1.70 to 6.50)
	Carette 1997	Methylprednisolone 80 mg + saline Imaging NR	Saline	Inter-laminar	3 mos.	(0-100 scale) 32.2 (n=77)	(0-100 scale) 34.6 (n=79)	-17.3 ± 20.6	5. - 15.4 ± 25.5	-1.90 (-9.17 to 5.37)
	Karppinen 2001	Methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline 0.9%	Trans-foraminal	3 mos.	(0-100 scale) 22.9 (n=79)	(0-100 scale) 22.6 (n=79)	-20 ± 7.31	-20.9 ± 9.03	Un-adjusted: 0.90 (-1.66 to 3.46); Adjusted: 1.3 (95% CI -6.1 to 8.6)§
	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	3 mos.	(0-100 scale) 25 ± 12.1‡ (n=34)	(0-100 scale) 17.5 ± 12.1‡ (n=36)	-7.5 ± 7.65	-8.8 ± 8.35	Un-adjusted: 1.3 (-2.45 to 5.05); Adjusted: 4.0 (−1.9 to 9.9)**; Adjusted: 3.7 (−2.3 to 9.7)††
	Arden 2005/ Price 2005	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	Interspinous ligament of saline (2 ml)	Inter-laminar	3 mos.	(0-100 scale) NR (n=120)	(0-100 scale) NR (n=108)	-12 ± 19	-12 ± 21	0 (-5.22 to 5.22)
Inter-	Manchikanti	Methylprednisolone	Lidocaine 0.5%	Caudal	6 mos.	(0-50 scale)	(0-50 scale)	-28.4 ±	-27.4 ± 9.1	-1.00 (-4.16

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Function score Mean ± SD Group A	Function score Mean ± SD Group B	Δ from baseline Group A	Δ from baseline Group B	Mean difference A vs. B* (95% CI)
mediate (>3 to <12 mos.)	2012,2011,2008	40 mg + lidocaine 0.5% Fluoroscopy				13.7 ± 7.0 (n=60)	15.5 ± 7.3 (n=60)	8.55		to 2.16)
	Sayegh 2009	Betamethasone 7 mg + xylocaine 2% No imaging used	Xylocaine 2% + water	Caudal	6 mos.	(scale NR) 5.8 ± 8.6 (n=83)	(scale NR) 13.6 ± 10.5 (n=70)	-32.7 ± 6.68	-24.9 ± 8.5	-7.80 (-10.26 to -5.34)
	Ghai 2015	Methylprednisolone 80 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	9 mos.	(scale NR) 18 (n=35)	(scale NR) 26 (n=34)	-28.8 ± 6.24	-23.6 ± 8	-5.20 (-8.59 to -1.81)
	Manchikanti 2014,2013,2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	6 mos.	(0-50 scale) 13.5 ± 4.2 (n=60)	(0-50 scale) 16.1 ± 6.6 (n=60)	-32.2 ± 6.24	-28.4 ± 8	-3.80 (-6.37 to -1.23)
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	6 mos.	(0-50 scale) 14.3 ± 6.6 (n=60)	(0-50 scale) 15.2 ± 16.7 (n=60)	-27.4 ± 7.92	-29.4 ± 8.12	2.00 (-0.87 to 4.87)
	Karppinen 2001	Methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline 0.9%	Trans-foraminal	6 mos.	(0-100 scale) 18.9 (n=78)	(0-100 scale) 15.8 (n=80)	-24 ± 7.92	-27.7 ± 8.12	Un-adjusted: 3.70 (1.20 to 6.20); Adjusted: 5.9 (95% CI, -0.7 to 12.4)§
Long-term (≥12 mos.)	Manchikanti 2012,2011,2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	(0-50 scale) 13.5 ± 7.2 (n=60)	(0-50 scale) 15.6 ± 7.3 (n=60)	-28.8 ± 8.85	-27.2 ± 9.1	-1.60 (-4.81 to 1.61)
	Sayegh 2009	Betamethasone 7 mg + xylocaine 2%	Xylocaine 2% + water	Caudal	12 mos.	(scale NR) 4.9 ± 7.1	(scale NR) 13.0 ± 10.1	-33.6 ± 5.23	-25.5 ± 8.1	-8.10 (-10.31 to -

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Function score Mean ± SD Group A	Function score Mean ± SD Group B	Δ from baseline Group A	Δ from baseline Group B	Mean difference A vs. B* (95% CI)
		No imaging used				(n=81)	(n=70)			5.89)
	Ghai 2015	Methylprednisolone 80 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	12 mos.	(scale NR) 19 (n=35)	(scale NR) 27 (n=34)	-27.8 ± 6.37	-32.6 ± 8.29	4.80 (1.30, 8.30)
	Manchikanti 2014,2013,2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	24 mos.	(0-50 scale) 13.5 ± 4.8 (n=60)	(0-50 scale) 16.1 ± 6.8 (n=60)	-32.2 ± 6.37	-28.4 ± 8.29	-3.80 (-6.45, -1.15)
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	24 mos.	(0-50 scale) 14.1 ± 6.5 (n=60)	(0-50 scale) 14.9 ± 6.9 (n=60)	-27.8 ± 7.8	-30 ± 8.4	2.20 (-0.70, 5.10)
	Iversen 2011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	12 mos.	(0-100 scale) 19‡ (n=34)	(0-100 scale) 14.5‡ (n=33)	-13.5 ± 7	-16.9 ± 8.58	3.40 (-0.36 to 7.16)
	Karppinen 2001	Methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline 0.9%	Trans-foraminal	12 mos.	(0-100 scale) 15.9 (n=78)	(0-100 scale) 16.3 (n=80)	-27 ± 7.8	-27.2 ± 8.4	Un-adjusted: 0.20 (-2.33 to 2.73) Adjusted: 0.4 (95% CI, -6.2 to 7.0)§
	Iversen (011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Subcutaneous injection of saline 0.9% superficial to the sacral hiatus and outside spinal canal	Caudal	12 mos.	(0-100 scale) 19 ± 12.1† (n=34)	13 ± 12.1† (n=32)	-13.5 ± 7.65	-13.3 ± 8.35	Un-adjusted: -0.2 (-4.07 to 3.67); Adjusted: 1.9 (−4.2 to 8.0)**; Adjusted: 1.7 (−4.5 to 7.8)††

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Function score Mean ± SD Group A	Function score Mean ± SD Group B	Δ from baseline Group A	Δ from baseline Group B	Mean difference A vs. B* (95% CI)
	Arden 2005/ Price 2005	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	interspinous ligament injection of salinen (2 ml)	Inter-laminar	3 mos.	(0-100 scale) NR (n=120)	(0-100 scale) NR (n=108)	-16 ± 23	-14 ± 24	-2.0 (-8.12 to 4.12)
Patient Specified Functional Outcome Scale (PSFOS) (0-12 scale)‡‡										
Short-term (≤3 mos.)	Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Bupivacaine 0.5%	Trans-foraminal	1 mo.	median 8 (IQR 6 to 9) (n=28)	median 6 (IQR 2 to 12) (n=27)	NR	NR	NR
			Saline	Trans-foraminal	1 mo.	median 8 (IQR 6 to 9) (n=28)	median 6 (IQR 4 to 9) (n=37)	NR	NR	NR
		Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Intramuscular injection of saline (2 ml)	Trans-foraminal	1 mo.	median 8 (IQR 6 to 9) (n=28)	median 10 (IQR 6 to 12) (n=30)	NR	NR	NR
			Intramuscular injection of triamcinolone 40 mg	Trans-foraminal	1 mo.	median 8 (IQR 6 to 9) (n=28)	median 10 (IQR 6 to 12) (n=28)	NR	NR	NR

CI: confidence interval; IQR: interquartile range; NR: not reported; SD: standard deviation.
*A negative score favors the intervention and a positive score favors the control.
†Adjusted for study site, sex, duration of pain, opiod use, baseline outcome score
‡Estimated from graph in article.
§ Difference ANCOVA adjusted for level of symptomatic disc and days on sick leave
**Adjusted for baseline values.
††Further adjusted for duration of leg pain, back pain, and sick leave.
‡‡ Minimum possible improvement = 0; maximum = 12.
Manchikanti et al., caudal: (1) 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;11:801-15; (2) 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; (3) 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.
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Table 11. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Function Success for epidural steroid injection (ESI) vs. control injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of function success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Oswestry Disability Index (ODI)									
Short term (≤3 mos.)	Manchikanti 2012,2011, 2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in ODI	3 mos.	73.3% (44/60)	61.7% (37/60)	1.19 (0.93 to 1.53)
	Manchikanti 2014,2013, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in ODI	3 mos.	81.7% (49/60)	73.3% (44/60)	1.11 (0.92 to 1.35)
	Ng 2005/ Tafazal 2009	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Bupivacaine 0.25%	Trans-foraminal	Improvement of ≥10% from baseline in pain on ODI	3 mos.	35% (14/40)	55% (23/41)	0.62 (0.38 to 1.03)
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	Improvement of ≥50% from baseline in ODI	3 mos.	68.3% (41/60)	75.0% (45/60)	0.91 (0.73 to 1.14)
	Carette 1997	Methylprednisolone 80 mg + saline Imaging NR	Saline	Inter-laminar	ODI score ≤ 20 (0-50)	3 mos.	37.7% (29/77)	41.8% (33/79)	0.90 (0.61 to 1.33)
	Arden 2005/ Price 2005	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	Saline (2 ml) soft tissue injection into interspinous ligament	Inter-laminar	Improvement of ≥75% from baseline in ODI	3 mos.	17% (20/120)	23% (25/108)	0.72 (0.42 to 1.22)
Inter-mediate (>3 to <12 mos.)	Manchikanti 2012,2011, 2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in ODI	6 mos.	73.3% (44/60)	71.7% (43/60)	1.02 (0.82 to 1.28)
	Manchikanti 2014,2013, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in ODI	6 mos.	86.7% (52/60)	63.3% (38/60)	1.37 (1.10 to 1.70)
	Manchikanti (2014)	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	Improvement of ≥50% from baseline in ODI	6 mos.	70.0% (42/60)	76.7% (46/60)	0.91 (0.74 to 1.13)
Long-term (≥12 mos.)	Manchikanti 2012,2011,	Methylprednisolone 40 mg + lidocaine 0.5%	Lidocaine 0.5%	Caudal	Improvement of ≥50% from	24 mos.	70.0% (42/60)	60.0% (36/60)	1.17 (0.90 to 1.52)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of function success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
	2008	Fluoroscopy			baseline in ODI				
	Manchikanti 2014,2013, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in ODI	24 mos.	73.3% (44/60)	63.3% (38/60)	1.16 (0.91 to 1.48)
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	Improvement of ≥50% from baseline in ODI	24 mos.	65.0% (39/60)	71.7% (43/60)	0.91 (0.71 to 1.16)
	Arden 2005/ Price 2005	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	Saline (2 ml) soft tissue injection into interspinous ligament	Inter-laminar	Improvement of ≥75% from baseline in ODI	12 mos.	32.5% (38/120)	29.6% (32/108)	1.07 (0.72 to 1.58)
Roland Morris Disability Questionnaire (RMDQ)									
Short term (≤3 mos.)	Datta 2011	Methylprednisolone 80 mg + bupivacaine 0.125% No imaging used	Bupivacaine 0.125%	Caudal	Improvement of >5 points from baseline in RMDQ	3 mos.	69% (27/39)	23.8% (10/42)	2.91 (1.63 to 5.19)
		Triamcinolone 80 mg + bupivacaine 0.125% No imaging used	Bupivacaine 0.125%	Caudal	Improvement of >5 points from baseline in RMDQ	3 mos.	71% (30/42)	23.8% (10/42)	3 (1.69 to 5.33)
		Dexamethasone 15 mg + bupivacaine 0.125% No imaging used	Bupivacaine 0.125%	Caudal	Improvement of >5 points from baseline in RMDQ	3 mos.	62% (25/40)	23.8% (10/42)	2.63 (1.45 to 4.74)
Protocol-defined success (various)									
Short term (≤3 mos.)	Rogers 1992	Methylprednisolone 80 mg + lignocaine 2% + saline Imaging NR	Lignocaine 2% + saline	Inter-laminar	Full ability to work	1 mo.	53.3% (8/15)	33.3% (5/15)	1.6 (0.68 to 3.77)
	Snoek 1977	Methylprednisolone 80 mg Imaging NR	Saline	Inter-laminar	Physio-therapist assessment of improved ability to perform physical	Mean 48 ± 24 hrs.	70.0% (19/27)	42.8% (10/24)	1.69 (0.99 to 2.88)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of function success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
					activities				
					Subjective patient assessment of improved ability to perform physical activities	Mean 48 ± 24 hrs.	66.7% (18/27)	41.7% (10/24)	1.6 (0.93 to 2.75)

CI: confidence interval; NR: not reported.
Manchikanti et al., caudal: (1) 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;11:801-15; (2) 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; (3) 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.
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Manchikanti et al., transforaminal: Transforaminal epidural injections in chronic lumbar disc herniation: a randomized, double-blind, active-control trial. Pain Physician 2014;17:E489-501.

Table 12. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Composite score success for epidural steroid injection (ESI) vs. Control Injections

Timepoint	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Improvement of ≥50% from baseline in both pain on numerical rating scale (NRS) and function on Oswestry Disability Index (ODI)								
Short term (≤3 mos.)	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	3 mos.	67% (40/60)	75% (45/60)	0.89 (0.71 to 1.12)
Intermediate (>3 to <12 mos.)	Manchikanti 2012,2011,2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	73.3% (44/60)	71.7% (43/60)	1.02 (0.82 to 1.28)
	Manchikanti 2014,2013,2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	6 mos.	85.0% (51/60)	63.3% (38/60)	1.34 (1.08 to 1.67)
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	6 mos.	67% (40/60)	73% (44/60)	0.91 (0.72 to 1.15)
Long-term (> 12 mos.)	Manchikanti 2012,2011,2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	65.0% (39/60)	60.0% (36/60)	1.08 (0.82 to 1.43)
	Manchikanti 2014,2013,2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	24 mos.	70.0% (42/60)	60.0% (36/60)	1.17 (0.90 to 1.52)
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	24 mos.	57% (34/60)	65% (39/60)	0.87 (0.65 to 1.16)

Manchikanti et al., caudal: (1) 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;11:801-15; (2) 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; (3) 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.

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Table 13. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Risk of Surgery for epidural steroid injection (ESI) vs. control injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Short term (≤3 mos.)	Datta (2011)	Methylprednisolone 80 mg or Triamcinolone 80 mg or Dexamethasone 15 mg + bupivacaine 0.125% No imaging used	Bupivacaine 0.125%	Caudal	3 mos.	6.6% (10/152)	16.4% (9/55)	0.40 (0.17 to 0.94)
	Klenerman 1984	Methylprednisolone 80 mg + saline Imaging NR	Bupivacaine or saline 0.25%	Inter-laminar	2 mos.	0% (0/19)	6.3% (2/16)	0.21 (0.01 to 4.34)
		Methylprednisolone 80 mg + saline Imaging NR	Saline 0.25%	Inter-laminar	2 mos.	0% (0/19)	0% (0/16)	Not estimable
	Dilke 1973	Methylprednisolone 80 mg + saline (10 ml) Imaging NR	Saline (1 ml) interspinous ligament injection	Inter-laminar	3 mos.	14% (7/51)	21% (10/48)	0.66 (0.27 to 1.59)
	Klenerman 1984	Methylprednisolone 80 mg + saline Imaging NR	Interspinous ligament needling without injection	Inter-laminar	2 mos.	0% (0/19)	0% (0/12)	Not estimable
	Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Intramuscular injection of triamcinolone 40 mg or saline (2 ml)	Trans-foraminal	1 mo.	35.7% (10/28)	25.9% (15/58)	1.38 (0.71 to 2.67)
Long-term (> 12 mos.)	Sayegh 2009	Betamethasone 7 mg + xylocaine 2% No imaging used	Xylocaine 2% + water	Caudal	12 mos.	12.9% (12/93)*	22.2% (20/90)*	0.58 (0.30 to 1.12)
	el Zahaar 1991	Hydrocortisone 5 ml + carbocaine 4% + saline Imaging NR	Carbocaine 4% + saline	Caudal	Mean 20.9 (13-36) mos.	26.3% (5/19 herniated disc subgroup)	21.4% (3/14 herniated disc subgroup)	1.23 (0.35 to 4.30)
	Cuckler 1985	Methylprednisolone 80 mg + procaine 1% Imaging NR	Procaine 1% + saline	Inter-laminar	Mean 20.5 (13 to 30) mos.	45.5% (10/22 herniated disc subgroup)	21.4% (3/14 herniated disc subgroup)	2.12 (0.70 to 6.39)
	Rogers 1992	Methylprednisolone 80 mg + lignocaine 2% + saline Imaging NR	Lignocaine 2% + saline	Inter-laminar	20-21 mos.	26.7% (4/15)	26.7% (4/15)	1.00 (0.31 to 3.28)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
	Riew 2006/ 2000	Betamethasone 6 mg + bupivacaine 0.25% Fluoroscopy	Bupivacaine 0.25%	Trans-forminal	60 mos.	39% (11/28)	70% (19/27)	0.56 (0.33 to 0.94)
	Tafazal 2009/Ng 2005	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Bupivacaine 0.25%	Trans-foraminal	12 mos.	14.1% (9/64)	21.5% (14/65)	0.65 (0.3 to 1.4)
	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Bupivacaine 0.5% + water	Trans-foraminal	12 mos.	21.4% (6/28)	16.7% (5/30)	1.20 (0.65 to 2.21)
	Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Bupivacaine 0.5% or saline	Trans-foraminal	12 mos.	35.7% (10/28)	26% (7/27)	1.38 (0.61 to 3.09)
	Bush 1991	Triamcinolone 80 mg + procaine hydrochloride 0.5% + saline	Saline (25 ml)	Caudal	12 mos.	8.3% (1/12)	18.2% (2/11)	0.46 [0.05 to 4.38]
	Iversen 2011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	12 mos.	2.7% (1/37)	15% (6/39)	0.18 (0.02 to 1.39)
	Carette 1997	Methylprednisolone 80 mg + saline Imaging NR	Saline	Inter-laminar	12 mos.†	25.8%† (n=77)	24.8%† (n=79)	N/A†
	Snoek 1977	Methylprednisolone 80 mg Imaging NR	Saline	Inter-laminar	Range 8-20 mos. (mean NR)	51.9% (14/27)	58.3% (14/24)	0.89 (0.54 to 1.46)
	Ghahreman 2010	Triamcinolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline	Trans-foraminal	12 mos.	35.7% (10/28)	19% (7/37)	1.89 (0.82 to 4.34)
	Karppinen 2001	Methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Saline 0.9%	Trans-foraminal	12 mos.	22.5% (18/80)	18.8% (15/80)	1.29 (0.44 to 3.75)
	Iversen 2011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%, subcutaneous injection superficial to the sacral hiatus and outside	Caudal	12 mos.	2.7% (1/37)	20.0% (8/40)	0.14 (0.02 to 1.03)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
			spinal canal					
	Arden 2005/Price 2005	Triamcinolone 80 mg + bupivacaine 0.125% Imaging NR	Saline (2 ml) soft tissue injection into interspinous ligament	Inter-laminar	12 mos.	12.5% (15/120)	13.0% (14/108)	0.96 (0.49 to 1.90)

CI: confidence interval; NR: not reported;
*4.3% (4/93) vs. 5.6% (5/90) at 1 month; 6.5% (6/93) vs. 16.7% (15/90) at 6 months; and 2.2% (2/93) vs. 0% (0/90) at 12 months.
†Cumulative probability (Kaplan-Meier survival analysis) of undergoing surgery in 12 month post-randomization.

Table 14. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Opioid success for ESI vs. Control Injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of opioid success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Short term (≤3 mos.)	Iversen 2011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	Cessation of morphine use	6 wks	16.2% (6/37)	2.9% (1/35)	5.68 (0.72 to 44.8)
			Subcutaneous injection of saline 0.9% superficial to the sacral hiatus and outside spinal canal	Caudal	Cessation of morphine	6 wks	16.2% (6/37)	5.4% (2/37)	3.0 (0.65 to 13.91)
	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Bupivacaine 0.5% + water	Trans-foraminal	Cessation of nonopioid analgesic or ≥20% decrease in opioid use	1 mo.	63% (17/28)	50% (14/30)	1.30 (0.8 to 2.11) adjusted OR: 1.67 (0.48 to 5.77)*
Inter-mediate (>3 to <12 mos)	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Bupivacaine 0.5% + water	Trans-foraminal	Cessation of nonopioid analgesic or ≥20% decrease in opioid use	6 mo.	92% (11/12)	75% (9/12)	1.22 (0.85 to 1.77)

CI: confidence interval; OR: odds ratio
*adjusted for study site, sex, duration of pain, opioid use, and baseline leg pain.

Table 15. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Improvement (reduction) in opioid usage for epidural steroid injection (ESI) vs. control injections

						Opioid usage* Mean ± SD		Δ from baseline		Mean difference A vs. B† (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Short term (≤3 mos.)	Manchikanti 2012,2011, 2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	30.1 ± 31.8 (n=60)	32.8 ± 31.6 (n=60)	-14.9 ± 37.57	-19 ± 38.34	4.1 (-9.48 to 17.68)
	Manchikanti 2014,2013, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	3 mos.	42.4 ± 39.9 (n=60)	34.3 ± 25.2 (n=60)	-4.7 ± 24.4	-15.3 ± 24.39	10.6 (1.87 to 19.33)
	Manchikanti 2014	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	3 mos.	40.8 ± 31.8 (n=60)	48.6 ± 45.1 (n=60)	-28.1 ± 32.62	-14.3 ± 30.12	-13.8 (-25.03 to -2.57)
Inter-mediate (>3 to < 12 mos.)	Manchikanti 2012,2011, 2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	31.1 ± 37.5 (n=60)	32.9 ± 31.6 (n=60)	-13.9 ± 35.76	-18.9 ± 38.34	5.0 (-8.27 to 18.27)
	Manchikanti 2014,2013, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	6 mos.	36.5 ± 27.6 (n=60)	37.3 ± 43.3 (n=60)	-10.6 ± 17.33	-12.3 ± 26.39	1.7 (-6.29 to 9.69)
	Manchikanti 2014)	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	6 mos.	39.3 ± 32.2 (n=60)	45.3 ± 42.4 (n=60)	-29.6 ± 32.5	-17.6 ± 29.73	-12.0 (-23.15 to -0.85)
Long-term (≥12 mos.)	Manchikanti 2012,2011, 2008	Methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	31.1 ± 37.5 (n=60)	32.8 ± 31.6 (n=60)	-13.9 ± 35.76	-19 ± 38.34	5.1 (-8.17 to 18.37)
	Manchikanti 2014,2013,20 10	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	24 mos.	36.6 ± 27.6 (n=60)	36.2 ± 43.7 (n=60)	-10.5 ± 17.33	-13.4 ± 26.58	2.9 (-5.13 to 10.93)

						Opioid usage* Mean ± SD		Δ from baseline		Mean difference A vs. B† (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
	Manchikanti 2014)	Betamethasone 3 mg + lidocaine 1% Fluoroscopy	Lidocaine 1% + saline	Trans-foraminal	24 mos.	36.6 ± 32.4 (n=60)	42.9 ± 37.5 (n=60)	-32.3 ± 32.45	-20 ± 29.64	-12.3 (-23.42 to -1.18)

CI: confidence interval; SD: standard deviation
*Morphine equivalents in milligrams per day.
†A positive score favors the intervention and a negative score favors the control.
Manchikanti et al., caudal: (1) 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;11:801-15; (2) 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; (3) 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.
Manchikanti et al., interlaminar: (1) 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; (2) 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; (3) A randomized, double-blind, active-control trial of the effectiveness of lumbar interlaminar epidural injections in disc herniation. Pain Physician 2014;17:E61-74.
Manchikanti et al., transforaminal: Transforaminal epidural injections in chronic lumbar disc herniation: a randomized, double-blind, active-control trial. Pain Physician 2014;17:E489-501.

Table 16. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Quality of life improvement for epidural steroid injection (ESI) vs. control injections

						Function score Mean ± SD		Δ from baseline		Mean difference A vs. B (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
European Quality of Life 5 Dimensions Questionnaire (EQ5D) (-0.594 to 1 scale)*										
Short term (≤3 mos.)	Iversen 2011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	3 mos.	0.60† (n=34)	0.64† (n=35)	0.06 ± 0.16	0.18 ± 0.2	-0.12 (-0.21 to -0.03)
			Subcutaneous injection of saline 0.9% superficial to the sacral hiatus and outside spinal canal	Caudal	3 mos.	NR	NR	NR	NR	Adjusted: −0.12 (−0.23 to −0.00)‡ Adjusted: −0.11 (0.22 to 0.00)§
Long-term (≥12 mos.)	Iversen 2011	Triamcinolone 40 mg + saline 0.9% Ultrasound	Saline 0.9%	Caudal	12 mos.	0.74† (n=34)	0.77† (n=33)	0.16 ± 0.16	0.31 ± 0.2	-0.15 (-0.24 to -0.06)
			Subcutaneous injection of saline 0.9% superficial to the sacral hiatus and outside spinal canal	Caudal	12 mos.	NR	NR	NR	NR	Adjusted: −0.05 (−0.17 to 0.06)‡ Adjusted: −0.05 (−1.6 to 0.07)§
Sickness Impact Profile (SIP)										
Short term (≤3 mos.)	Carette 1997	Methylprednisolone 80 mg + saline Imaging NR	Saline	Inter-laminar	3 mos.	Overall: 12.4 Physical: 9.9 Psycho-social: 8.7 (n=77)	Overall: 13.2 Physical: 9.4 Psycho-social: 12.1 (n=79)	Overall: -9.2 ± 10.8 Physical: -8.8 ± 11.6 Psycho-social:	Overall: -8.0 ± 14.1 Physical: -8.2 ± 14.3 Psycho-social:	Overall: -1.2 (-5.2 to 2.8) Physical: -0.6 (-4.7 to 3.6)

						Function score Mean ± SD		Δ from baseline		Mean difference A vs. B (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
								-7.2 ± 10.7	-5.3 ± 14.9	Psycho-social: -1.9 (-6.1 to 2.2)
Lifestyle/Function Questionnaire (scale, 6-18)**										
Short-term (≤3 mos.)	Bush (1991)	Triamcinolone 80 mg + procaine hydrochloride 0.5% + saline	Saline (25 ml)	Caudal	1 mo.	15.8 (n=12)	13.7 (n=11)	2.4	0.8	1.6
Long-term (≥12 mos.)					12 mos.	16.6 (n=12)	15.6 (n=11)	3.2	2.7	0.5

CI: confidence interval; NR: not reported; SD: standard deviation.
*For the European Quality of Life 5 Dimensions Questionnaire and Lifestyle/Function questionnaire, a positive score favors the intervention and a negative score favors the control; for the Sickness Impact Profile, a negative score favors the intervention and a positive score favors the control.
†Estimated from graph in article.
‡Adjusted for baseline scores
§Further adjusted for duration of leg pain, back pain, and sick leave.
**Specific symptomatology questionnaire designed by Grogono and Woodgate to determine any effects on the patient's lifestyle; 6 = worst and 18 = best

Table 17. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Pain and Function Improvement for epidural steroid injection (ESI) vs. control injections with other medications

						Pain score Mean ± SD		Δ from base-line		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Pain improvement on visual analog scale (VAS) or numerical rating scale (NRS) (0-10 scale)										
Short term (≤3 mos.)	Burgher 2011	Triamcinolone 40 or 80 mg + lidocaine 2% Fluoroscopy	Clonidine 200 or 400 mg + lidocaine 2%	Trans-foraminal	1 mo.	NR (n=14)	NR (n=9)	NR	NR	-1.54 ± 1.05 (-3.6 to 0.52)
	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept 4 mg + bupivacaine 0.5% + water	Trans-foraminal	1 mo.	Unadjusted: 2.14 ± 1.99 (n=28) Adjusted: 2.54 (95% CI, 1.36 to 3.69)† (n=28)	Unadjusted: 3.63 ± 3.10 (n=26) Adjusted 3.56 (95% CI, 2.35 to 4.72)† (n=26)	-3.57 ± 1.24	-2.99 ± 2.03	Unadjusted: -0.58 (-1.49 to 0.33) Adjusted: -1.01 (-2.60 to 0.58)†
	Cohen 2015	Methylprednisolone 60 mg + bupivacaine 0.25% + saline + oral placebo medication	Posterior ligament injection of saline (3 ml) + oral gabapentin 300 mg	Inter-laminar or trans-foraminal	3 mos.	3.4 ± 2.7 (n=73)	3.7 ± 2.8 (n=72)	-2.0 ± 2.6	-1.6 ± 2.7	Un-adjusted: -0.4 (-1.26 to 0.46) Adjusted: −0.3 (−1.2 to 0.5)‡
Oswestry Disability Index (ODI)										
Short term (≤3 mos.)	Burgher 2011	Triamcinolone 40 or 80 mg + lidocaine 2% Fluoroscopy	Clonidine 200 or 400 mg + lidocaine 2%	Trans-foraminal	1 mo.	(scale NR) (n=14)	(scale NR) (n=9)	NR	NR	-7.04 ± 3.17 (-13.25 to -0.83); p=0.04
	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept 4 mg + bupivacaine 0.5% + water	Trans-foraminal	1 mo.	(0-100 scale) Unadjusted: 22.43 ± 16.72 (n=28)	(0-100 scale) Unadjusted: 38.27 ± 24.69 (n=26)	-20.47 ± 10.28	-2.83 ± 14.88	-17.64 (-0.56 to 3.36)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Pain score Mean ± SD Group A	Pain score Mean ± SD Group B	Δ from base-line Group A	Δ from base-line Group B	Mean difference A vs. B* (95% CI)
						Adjusted: 24.1 (16.6 to 31.6)† (n=28)	Adjusted: 40.3 (32.91 to 47.61)† (n=26)	NR	NR	-16.2 (-26.0 to -6.27)†
	Cohen 2015	Methylprednisolone 60 mg + bupivacaine 0.25% + saline + oral placebo medication	Posterior ligament injection of saline (3 ml) + oral gabapentin 300 mg	Inter-laminar or trans-foraminal	3 mos.	(scale NR) 33.6 ± 19.4 (n=73)	(scale NR) 29.6 ± 16.3 (n=72)	-6.2± 15.8	-10.2 ± 16.7	Un-adjusted: 4.0 (-1.29 to 9.29); Adjusted: 3.9 (−1.1 to 9.0)‡
Roland Morris Disability Questionnaire (RMDQ) (0-24 scale)										
Short term (≤3 mos.)	Burgher 2011	Triamcinolone 40 or 80 mg + lidocaine 2% Fluoroscopy	Clonidine 200 or 400 mg + lidocaine 2%	Trans-foraminal	1 mo.	NR (n=14)	NR (n=9)	NR	NR	-5.67 ± 2.27 (-10.12 to -1.22)

CI: confidence interval; NR: not reported; SD: standard deviation.
*A negative score favors the intervention and a positive score favors the control.
†Adjusted for study site, sex, duration of pain, opiod use, and baseline outcome score.
‡Adjusted for baseline values.

Table 18. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Pain, function, and opioid success, overall success and risk of surgery for epidural steroid injection (ESI) vs. control injections with other mediations

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk ratio (95% CI)
Pain Success									
Short term (≤3 mos.)	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept + Bupivacaine 0.5% + water	Trans-foraminal	Improvement of ≥50% from baseline in leg pain and positive GPE obviating the need for further intervention	3 mo.	50% (14/28)	42% (11/26)	1.18 (0.66 to 2.11)
	Cohen 2015	Methylprednisolone 60 mg + bupivacaine 0.25% + saline + oral placebo medication	Posterior ligament injection of saline (3 ml) + oral gabapentin 300 mg	Inter-laminar or trans-foraminal	>2 point decrease in average leg pain coupled with positive GPE without additional procedural or non-rescue pharma-cological interventions	3 mos.	37% (27/73)	29% (21/72)	1.27 (0.79 to 2.03)
Inter-mediate (>3 mos. to <12 mos)	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept + Bupivacaine 0.5% + water	Trans-foraminal	Improvement of ≥50% from baseline in leg pain and positive GPE obviating the need for further intervention	6 mo.	29% (8/28)	38% (10/26)	0.74 (0.35 to 1.59)
Global Perceived Effect (GPE)*									
Short term (≤3 mos.)	Cohen (2015)	Methylprednisolone 60 mg + bupivacaine 0.25% + saline + oral placebo medication	Posterior ligament injection of saline (3 ml) + oral gabapentin 300 mg	Inter-laminar or trans-foraminal	Not requiring further non-rescue interventions plus self-	3 mos.	45% (33/73)	33% (24/72)	1.36 (0.9 to 2.05)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk ratio (95% CI)
					reported pain improvement and satisfaction with treatment				
Risk of Surgery									
Short term (≤3 mos.)	Cohen (2015)	Methylprednisolone 60 mg + bupivacaine 0.25% + saline + oral placebo medication	Posterior ligament injection of saline (3 ml) + oral gabapentin 300 mg	Inter-laminar or trans-foraminal	Cumulative risk of surgery	3 mos.	13% (9/72)	14% (10/69)	0.86 (0.37 to 1.99)
Inter-mediate (>3 mos. to <12 mos.)	Burgher (2011)	Triamcinolone 40 or 80 mg + lidocaine 2% Fluoroscopy	Clonidine 200 or 400 mg + lidocaine 2%	Trans-foraminal	Cumulative risk of surgery	6 mos.	6.7% (1/15)	27.3% (3/11)	0.24 (0.03 to 2.05)
Long-term (≥12 mos.)	Cohen (2012)	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept 4 mg + bupivacaine 0.5% + water	Trans-foraminal	Cumulative risk of surgery	12 mos.	21.4% (6/28)	23.1% (6/26)	0.93 (0.34 to 2.52)
Opioid Success									
Short term (≤3 mos.)	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept + Bupivacaine 0.5% + water	Trans-foraminal	Cessation of nonopioid analgesic or ≥20% decrease in opioid use	1 mo.	63% (17/28)	36% (9/26)	unadjusted RR 1.75 (0.96 to 3.22) adjusted OR 3.0 (0.83 to 10.8)*
	Cohen 2015	Methylprednisolone 60 mg + bupivacaine 0.25% + saline + oral placebo medication	Posterior ligament injection of saline (3 ml) + oral gabapentin 300 mg	Inter-laminar or trans-foraminal	>20% reduction in opioid use or complete cessation of non-opioid analgesics	3 mos.	58% (23/40)	47% (14/30)	1.23 (0.77 to 1.96)
Inter-mediate (>3 mos. to <12 mos.)	Cohen 2012	Methylprednisolone 60 mg + bupivacaine 0.5% + water Fluoroscopy	Etanercept + Bupivacaine 0.5% + water	Trans-foraminal	Cessation of nonopioid analgesic or ≥20% decrease in opioid use	6 mo.	92% (11/12)	65% (7/11)	1.44 (0.89 to 2.32)

CI: confidence interval; GPE: global perceived effect.
*adjusted for study site, sex, duration of pain, opioid use, and baseline leg pain.

Table 19. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Pain and Function Improvement for epidural steroid injection (ESI) vs. disc or decompression procedure

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Pain score Mean ± SD		Δ from base-line		Mean difference A vs. B* (95% CI)
						Group A	Group B	Group A	Group B	
Pain improvement on visual analog scale (VAS) or numerical rating scale (NRS) (0-10 scale)										
Short term (≤3 mos.)	Butterman 2004	Betamethasone 10-15 mg Fluoroscopy in 76% of pts	Discectomy Imaging NR	Inter-laminar	3 mos.	4.1† (n=50)	1.4† (n=50)	-3.3 ± 0.61	-5.6 ± 0.61	2.3 (2.06 to 2.54)
	Aronsohn 2010	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Percutaneous micro-discectomy Fluoroscopy	Approach NR	6 wks.	2.0 (n=24)	7.1 (n=26)	-7.3 ± 0.61	-2.0 ± 0.61	-5.3 (-5.64 to -4.96)
	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone Fluoroscopy	Plasma disc decompression with coblation Fluoroscopy	Trans-formanial	3 mos.	NR (n=40)	NR (n=45)	-2.3 ± 0.5‡	-4.6 ± 0.4‡	2.3 (2.1 to 2.5)
	Wu 2015	Betamethasone mg NR + lidocaine 1% Fluoroscopy	Nucleoplasty + nerve root injection of betamethasone and lidocaine Fluoroscopy	Trans-formanial	3 mos.	3.3 ± 0.8 (n=29)	2.3 ± 0.6 (n=35)	-4.0 ± 0.6	-5.0 ± 0.63	1.0 (0.7 to 1.3)
			Nucleoplasty only using radiofrequency Fluoroscopy	Trans-formanial	3 mos.	3.3 ± 0.8 (n=29)	2.3 ± 0.8 (n=33)	-4.0 ± 0.6	-4.9 ± 0.74	0.9 (0.57 to 1.23)
Inter-mediate (>3 to <12 mos)	Butterman 2004	Betamethasone 10-15 mg Fluoroscopy in 76% of pts	Discectomy Imaging NR	Inter-laminar	6 mos.	2.7† (n=27)	1.2† (n=50)	-4.7 ± 0.61	-5.8 ± 0.61	1.1 (0.82 to 1.38)
	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone	Plasma disc decompression with coblation	Trans-formanial	6 mos.	NR (n=40)	NR (n=45)	-2.1 ± 0.5‡	-4.7± 0.6‡	2.6 (2.36 to 2.84)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Pain score Mean ± SD		Δ from base-line		Mean difference A vs. B* (95% CI)
						Group A	Group B	Group A	Group B	
		Fluoroscopy	Fluoroscopy							
Long term (≥12 mos.)	Butterman 2004	Betamethasone 10-15 mg Fluoroscopy in 76% of pts	Discectomy Imaging NR	Inter-laminar	36 mos.	0.8† (n=23)	1.5† (n=50)	-6.6 ± 0.61	-5.5 ± 0.61	-1.1 (-1.4 to -0.8)
	Wu 2015	Betamethasone mg NR + lidocaine 1% Fluoroscopy	Nucleoplasty + nerve root injection of betamethasone and lidocaine Fluoroscopy	Trans-formanial	3 mos.	3.4 ± 0.6 (n=29)	2.1 ± 0.7 (n=35)	-3.9 ± 0.63	-5.2 ± 0.61	1.3 (0.99 to 1.61)
			Nucleoplasty only using radiofrequency Fluoroscopy	Trans-formanial	3 mos.	3.4 ± 0.6 (n=29)	2.3 ± 0.6 (n=33)	-3.9 ± 0.63	-4.9 ± 0.8	1.0 (0.65 to 1.35)
Oswestry Disability Index (0-100)										
Short term (≤3 mos.)	Butterman 2004	Betamethasone 10-15 mg Fluoroscopy in 76% of pts	Discectomy Imaging NR	Inter-laminar	3 mos.	34† (n=50)	22† (n=50)	-13 ± 4.33	-26 ± 4.32	13 (11.3 to 14.7)
	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone Fluoroscopy	Plasma disc decompression with coblation Fluoroscopy	Trans-formanial	3 mos.	NR (n=40)	NR (n=45)	–2 ± 2‡	–11 ± 3‡	9.0 (7.93 to 10.07)
	Wu 2015	Betamethasone mg NR + lidocaine 1% Fluoroscopy	Nucleoplasty + nerve root injection of betamethasone and lidocaine Fluoroscopy	Trans-formanial	3 mos.	30.5 ± 5.6 (n=29)	24.3 ± 6.3 (n=35)	-17.6 ± 7.6	-23.4 ± 7.66	5.8 (2.05 to 9.55)
			Nucleoplasty only using radiofrequency	Trans-formanial	3 mos.	30.5 ± 5.6 (n=29)	25.3 ± 6.5 (n=33)	-17.6 ± 7.6	-22.4 ± 6.42	4.8 (1.27 to 8.33)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Pain score Mean ± SD		Δ from base-line		Mean difference A vs. B* (95% CI)
						Group A	Group B	Group A	Group B	
			Fluoroscopy							
Inter-mediate (>3 to <12 mos)	Butterman 2004	Betamethasone 10-15 mg Fluoroscopy in 76% of pts	Discectomy Imaging NR	Inter-laminar	6 mos.	15† (n=27)	16† (n=50)	-32 ± 4.33	-32 ± 4.32	0 (-2.03 to 2.03)
	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone Fluoroscopy	Plasma disc decompression with coblation Fluoroscopy	Trans-formanial	6 mos.	NR (n=40)	NR (n=45)	–4 ± 2‡	–14 ± 4‡	10 (8.29 to 11.71)
Long term (≥12 mos.)	Butterman 2004	Betamethasone 10-15 mg Fluoroscopy in 76% of pts	Discectomy Imaging NR	Inter-laminar	36 mos.	8† (n=27)	16† (n=50)	-39 ± 4.33	-32 ± 4.32	-7.0 (-9.03 to -4.97)
	Wu 2015	Betamethasone mg NR + lidocaine 1% Fluoroscopy	Nucleoplasty + nerve root injection of betamethasone and lidocaine Fluoroscopy	Trans-formanial	12 mos.	27.8 ± 4.9 (n=29)	22.9 ± 5.3 (n=35)	-20.3 ± 7.94	-24.8 ± 8.11	4.5 (0.55 to 8.45)
	Wu 2015	Betamethasone mg NR + lidocaine 1% Fluoroscopy	Nucleoplasty only using radiofrequency Fluoroscopy	Trans-formanial	12 mos.	ODI (0-100) 27.8 ± 4.9 (n=29)	ODI (0-100) 22.7 ± 6.3 (n=33)	-20.3 ± 7.94	-25.0 ± 6.48	4.7 (1.06 to 8.34)
Improvement in Quality of Life on the SF-36 Physical Component Score										
Inter-mediate (>3 to <12 mos)	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone Fluoroscopy	Plasma disc decompression with coblation Fluoroscopy	Trans-formanial	6 mos.	35.5 ± 7† (n=39)	43.5 ± 7† (n=43)	3.5 ± 4.43	11.5 ± 4.43	-8.0 (-9.92 to -6.08)
Improvement in Quality of Life on the SF-36 Mental Component Score										
Inter-mediate (>3 to <12 mos)	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone	Plasma disc decompression with coblation	Trans-formanial	6 mos.	47.5 ± 10† (n=39)	47.5 ± 14† (n=43)	1.5 ± 6.32	4.5 ± 8.49	-3.0 (-6.22 to 0.22)

		Fluoroscopy	Fluoroscopy							
Improvement in Medication Usage (tablets/week)										
Short term (≤3 mos.)	Aronsohn 2010	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Percutaneous micro-discectomy Fluoroscopy	Approach NR	6 wks.	2.2 ± 1 (n=24)	2.1 ± 2 (n=26)	-3.8 ± 3.26	-2.9 ± 1.84	-0.9 (-2.38 to 0.58)

CI: confidence interval; NR: not reported; SD: standard deviation; SF-36: Short Form 36 questionnaire

*A negative score favors the intervention and a positive score favors the control.

†Estimated from graph in article.

‡Change scores calculated using the Generalized Estimating Equations model adjusted for baseline back pain VAS scores, preprocedure duration of leg pain, and clinical center enrollment.

Table 20. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Pain, function, and opioid success, overall success and risk of surgery for epidural steroid injection (ESI) vs. disc or decompression procedure

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Pain Success									
Inter-mediate	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone Fluoroscopy	Plasma disc decompression with coblation Fluoroscopy	Trans-formanial	Improvement of ≥2.5 points from baseline in VAS	6 mos.	21% (8/39)	49% (21/43)	0.42 (0.21 to 0.84)
Long term						24 mos.	21% (8/39)	42% (18/43)	0.49 (0.24 to 1.0)
Function Success									
Inter-mediate	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone Fluoroscopy	Plasma disc decompression with coblation Fluoroscopy	Trans-formanial	Improvement of ≥13 points from baseline in ODI	6 mos.	15% (6/40)	32% (14/44)	0.47 (0.2 to 1.11)
Long term						24 mos.	10% (4/40)	30% (13/44)	0.34 (0.12 to 0.95)
Quality of Life Success									
Inter-mediate	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone Fluoroscopy	Plasma disc decompression with coblation Fluoroscopy	Trans-formanial	Improvement of ≥5 points from baseline in SF-36	6 mos.	21% (8/39)	37% (16/43)	0.55 (0.27 to 1.14)
Long term						24 mos.	13% (5/39)	33% (14/43)	0.39 (0.16 to 0.99)
Patient Satisfaction									
Short term	Aronsohn 2010	Methylprednisolone 40 mg + bupivacaine 0.25% Fluoroscopy	Percutaneous micro-discectomy (single level) Fluoroscopy	Approach NR	Not defined	6 wks.	42% (10/24)	79% (20/26)	0.54 (0.32 to 0.91)
Intermedia te term	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone Fluoroscopy	Plasma disc decompression with coblation Fluoroscopy	Trans-formanial	Extremely satisfied Extremely/ very satisfied	6 mos.	15% (6/39) 39% (15/39)	38% (16/43) 56% (23/43)	0.41 (0.18 to 0.95) 0.72 (0.44 to 1.17)
Risk of Surgery									

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
	Gertzen 2010	Methylprednisolone or betamethasone or triamcinolone Fluoroscopy	Plasma disc decompression with coblation Fluoroscopy	Trans-formanial	Cumulative risk of surgery	24 mos.	10.0% (4/40)†	15.6% (7/45)†	0.64 (0.2 to 2.03)
	Wu 2015	Betamethasone mg NR + lidocaine 1% Fluoroscopy	Nucleoplasty + nerve root injection of betamethasone and lidocaine Fluoroscopy	Trans-formanial	Cumulative risk of surgery	12 mos.	13% (5/39)	3% (1/36)	4.62 (0.57 to 37.64)
			Nucleoplasty only using radiofrequency Fluoroscopy	Trans-formanial	Cumulative risk of surgery	12 mos.	13% (5/39)	6% (2/35)	2.24 (0.46 to 10.84)
Opioid success									
Short term	Butterman 2004	Betamethasone 10-15 mg Fluoroscopy in 76% of patients	Discectomy Imaging NR	Inter-laminar	Proportion of patients using narcotics	3 mos.	24% (12/50)	14% (7/50)	1.71 (0.74 to 3.99)
Long term						36 mos.	0% (0/23)	2% (1/47)	1.02 (0.04 to 29.36)

CI: confidence interval; ODI: Oswestry Disability Index; NR: not reported; SF-36: Short-Form 36 questionnaire; VAS: visual analog scale.
*adjusted for study site, sex, duration of pain, opioid use, and baseline leg pain.
†Not including additional steroid injection (5 and 13 pts, for group A and B, respective

Table 21. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Pain and Function Improvement for epidural steroid injection (ESI) vs. conservative care

					Pain score Mean ± SD		Δ from base-line		Mean difference A vs. B* (95% CI)
Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Pain improvement on visual analog scale (VAS) or numerical rating scale (NRS) (0-10 scale)									

						Pain score Mean ± SD		Δ from base-line		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Short term	Buchner 2000	Methylprednisolone 100 mg + bupivacaine + conservative treatment Imaging not reported	Bed rest + medication + Graded rehabilitation†	Inter-laminar	6 wks.	3.29 (range, 0-8.5) (n=17)	3.81 (range, 0-10.0) (n=19)	-5.15 ± 7.92	-4.29 ± 6.7	-0.86 (-5.68 to 3.96)
Inter-mediate	Murakibhavi 2011	Triamcinolone 80 mg + lidocaine 2% + saline Fluoroscopy	Medication + physiotherapy‡	Caudal	6 mos.	2.7 ± 0.8 (n=50)	6.1 ± 0.5 (n=50)	-5.4 ± 0.6	-2.0 ± 0.85	-3.4 (-3.69 to -3.11)
	Buchner 2000	Methylprednisolone 100 mg + bupivacaine + conservative treatment Imaging not reported	Bed rest + medication + Graded rehabilitation†	Inter-laminar	6 mos.	3.29 (range, 0-8.5) (n=17)	3.92 (range, 0-10.0) (n=19)	-5.15 ± 6.43	-4.18 ± 6.68	-0.97 (-5.26 to 3.32)
Function Improvement on the Oswestry Disability Index (ODI) (0-100)										
Inter-mediate	Murakibhavi 2011	Triamcinolone 80 mg + lidocaine 2% + saline Fluoroscopy	Medication + physiotherapy‡	Caudal	6 mos.	12.3 ± 2.6 (n=50)	24.9 ± 1.5 (n=50)	-23.7 ± 1.56	-11 ± 1.66	-12.7 (-13.33 to -12.07)
Function Improvement on the Hannover Functional Ability Questionnaire (HFAQ) (0-100)										
Short term	Buchner 2000	Methylprednisolone 100 mg + bupivacaine + conservative treatment Imaging NR	Bed rest + medication + Graded rehabilitation†	Inter-laminar	6 wks.	61.5 (range, 25-88) (n=17)	58.3 (range, 13-100) (n=19)	23 ± 40.97	18.4 ± 59.91	4.6 (-28.64 to 37.84)
Inter-mediate term					6 mos.	61.8 (range, 25-83) (n=17)	57.2 (range, 17-83) (n=19)	23.3 ± 39.26	17.3 ± 55.38	6.0 (-25.12 to 37.12)
Improvement in Depression on the Beck Depression Inventory (BDI) (0-64 scale)										
Inter-mediate	Murakibhavi 2011	Triamcinolone 80 mg + lidocaine 2% + saline Fluoroscopy	Medication + physiotherapy‡	Caudal	6 mos.	8.6 ± 2.2 (n=50)	13.3 ± 1.7 (n=50)	-9.4 ± 1.62	-5.6 ± 2.1	-3.8 (-4.54 to -3.06)

CI: confidence interval; NR: not reported; SD: standard deviation.
*For the VAS/NRS, ODI, and BDI a negative score favors the intervention and a positive score favors the control; for the HFAQ, a positive score favors the intervention and a negative score favors the control.
†To include analgesics; NSAIDS or tramadol; graded rehabilitation including hydrotherapy, electroanalgesia, and spinal mobilization physiotherapy.
‡To include tizanidine 6-12 mg/d, diclofenac 50-100 mg/d, amitriptyline 10-50 mg qhs, bilateral skin traction, physiotherapy including TENS, short-wave diathermy, and back extension exercises

Table 22. Lumbar radiculopathy due to disc pathology and/or foraminal narrowing: Pain, function, and opioid success, overall success and risk of surgery for epidural steroid injection (ESI) vs conservative care

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Pain Success									
Short term	Murakibhavi 2011	Triamcinolone 80 mg + lidocaine 2% + saline Fluoroscopy	Medication + physiotherapy*	Caudal	Patient assessment of "complete pain relief"	3 wks.	92% (46/50)	32% (16/50)	0.16 (0.04 to 0.56)
Inter-mediate						6 mos.	86% (43/50)	24% (12/50)	0.29 (0.09 to 0.9)
Risk of Surgery									
Inter-mediate	Murakibhavi 2011	Triamcinolone 80 mg + lidocaine 2% + saline Fluoroscopy	Medication + physiotherapy*	Caudal	Cumulative risk of surgery	6 mos.	2.0% (1/50)	0% (0/50)	2 (0.07 to 58.28)
	Buchner 2000	Methylprednisolone 100 mg + bupivacaine + conservative treatment Imaging not reported	Bed rest + medication + Graded rehabilitation†	Inter-laminar	Cumulative risk of surgery	6 mos.	12% (2/17)	21% (4/19)	1.82 (0.63 to 5.24)

CI: confidence interval.
*To include tizanidine 6-12 mg/d, diclofenac 50-100 mg/d, amitriptyline 10-50 mg qhs, bilateral skin traction, physiotherapy including TENS, short-wave diathermy, and back extension exercises
†To include analgesics; NSAIDS or tramadol; graded rehabilitation including hydrotherapy, electroanalgesia, and spinal mobilization physiotherapy.

Table 23. Lumbar radiculopathy attributed to multiple causes: Pain and Function Improvement for epidural steroid injection (ESI) vs. control injections

						Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Pain improvement on visual analog scale (VAS) (0-10 scale)										
Short-term	Becker 2007	Triamcinolone 5 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	2.5 mos.	2.7† (n=27)	1.8† (n=32)	-5.49 ± 0.55	-5.98 ± 1.04	0.49 (0.07 to 0.91)
		Triamcinolone 10 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	2.5 mos.	3.0† (n=25)	1.8† (n=32)	-5.19 ± 0.75	-5.98 ± 1.04	0.79 (0.33 to 1.25)
Inter-mediate term		Triamcinolone 5 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	5.5 mos.	3.68 ± 2.83 (n=27)	2.33 ± 2.48 (n=32)	-4.51 ± 2.2	-5.45 ± 1.53	0.94 (-0.04 to 1.92)
		Triamcinolone 10 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	5.5 mos.	3.26 ± 2.82 (n=24)	2.33 ± 2.48 (n=32)	-4.93 ± 2.2	-5.45 ± 1.53	0.52 (-0.51 to 1.55)
Function Improvement on the Oswestry Disability Index (ODI) (0-150)										
Short-term	Becker 2007	Triamcinolone 5 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	2.5 mos.	12.4 ± 9.0 (n=27)	11.2 ± 10.2 (n=32)	-8.2 ± 5.47	-10.8 ± 6.12	2.6 (-0.36 to 5.56)
		Triamcinolone 10 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	2.5 mos.	11.0 ± 10.2 (n=25)	11.2 ± 10.2 (n=32)	-8.4 ± 6.36	-10.8 ± 6.12	2.4 (-0.87 to 5.67)
Inter-mediate		Triamcinolone 5 mg + anesthetic (1 ml) (type	IL-1Ra-enriched, autologous	Inter-laminar	5.5 mos.	11.1 ± 7.1 (n=27)	11.7 ± 9.2 (n=32)	-9.5 ± 4.9	-10.3 ± 5.6	0.8 (-1.88 to

						Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
term		NR) Fluoroscopy	conditioned serum (1 ml)							3.48)
		Triamcinolone 10 mg + anesthetic (1 ml) (type NR) Fluoroscopy	IL-1Ra-enriched, autologous conditioned serum (1 ml)	Inter-laminar	5.5 mos.	11.4 ± 10.3 (n=24)	11.7 ± 9.2 (n=32)	-8 ± 6.4	-10.3 ± 5.6	2.3 (-0.91 to 5.51)

IL-1Ra: Interleukin-1 receptor antagonist.
*A negative score favors the intervention and a positive score favors the control.
†Estimated from graph in article.

Table 24. Lumbar radiculopathy attributed to multiple causes: Pain, function, and opioid success, overall success and risk of surgery for epidural steroid injection (ESI) vs. control injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Pain Success									
Inter-mediate term	Breivik 1976	Methylprednisolone 80 mg + bupivacaine 0.25% Imaging NR	Bupivacaine 0.25%	Caudal	Patient assessment of "considerable" pain relief: reduction of pain and/or paresis to enable return to work or rehabilitation for other work	Mean 9.4 mos.	56.3% (9/16)	26% (5/19)	2.14 (0.9 to 5.09)
Risk of Surgery									
Long-term	Wilson-MacDonald 2005	Methylprednisolone 80 mg + bupivacaine (0.5%) 40 mg	Intramuscular/ interspinous ligament injection with methylprednisolone 80 mg + bupivacaine (0.5%) 40 mg	Inter-laminar	Cumulative risk of surgery	12 mos.	41% (18/44)	31% (15/48)	1.31 (0.76 to 2.27)

CI: confidence interval.

Table 25. Spinal Stenosis: Pain improvement (VAS or NRS, 0-10) for ESI vs. Control Injections

						Pain score Mean ± SD		Δ from base-line		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Short term	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	4.1 ± 1.9 (n=50)	4.1 ± 1.8 (n=50)	-3.5 ± 1.3	-3.8 ± 1.2	0.30 (-0.20 to 0.80)
	Manchikanti 2012,2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	3 mos.	3.7 ± 1.5 (n=60)	3.7 ± 1.3 (n=60)	-4.3 ± 0.9	-4.3 ± 0.9	0.00 (-0.32 to 0.32)
	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1% Fluoroscopy	Lidocaine 0.25-1%	Inter-laminar	1.5 mos.	4.2 ± 3.0 (n=136)	4.5 ± 2.9 (n=136)	-3.1 ± 3.3	-2.8 ± 3.1	Unadjusted: -0.20 (-0.96 to 0.56) Adjusted: -0.3 (95% CI, -1.0 to 0.4; p=0.37)†
	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1% Fluoroscopy	Lidocaine 0.25-1%	Trans-foraminal	1.5 mos.	4.9 ± 2.6 (n=57)	4.9 ± 2.7 (n=57)	-2.0 ± 2.6	-2.0 ± 2.8	Unadjusted: 0.00 (-0.99 to 0.99) Adjusted:0.1 (95% CI, -0.9 to 1.0; p=0.89)†
	Nam 2011	Triamcinolone 20 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Trans-foraminal	3 mos.	3.83 (n=17)	4.73 (n=19)	-3.5 ± 0.5	-2.7 ± 0.6	-0.81 (-1.19 to 0.43)
Inter-mediate	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	4.2 ± 1.9 (n=50)	4.1 ± 1.7 (n=50)	-3.4 ± 1.35	-3.8 ± 1.12	0.4 (-0.09 to 0.89)
	Manchikanti 2012,2015	Betamethasone (1 ml) + lidocaine 0.5%	Lidocaine 0.5%	Inter-laminar	6 mos.	3.8 ± 1.7 (n=60)	3.6 ± 1.5 (n=60)	-4.2 ± 1.08	-4.4 ± 1.03	0.2 (-0.18 to 0.58)

						Pain score Mean ± SD		Δ from base-line		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
		Fluoroscopy								
Long-term	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	4.7 ± 2.2 (n=50)	4.6 ± 1.8 (n=50)	-2.9 ± 1.63	-3.3 ± 1.21	0.4 (-0.11 to 0.91)
	Manchikanti 2012, 2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	24 mos.	3.6 ± 1.7 (n=60)	3.8 ± 1.8 (n=60)	-4.4 ± 1.08	-4.2 ± 1.31	-0.2 (-0.63 to 0.23)

CI: confidence interval; NRS: numerical rating scale; VAS: visual analog scale; SD: standard deviation.
*A negative score favors the intervention and a positive score favors the control.
†Adjusted for baseline outcome values and recruitment site.
Manchikanti et al., caudal: (1) 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; (2) 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; (3) 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.
Manchikanti et al., interlaminar: (1) Lumbar interlaminar epidural injections in central spinal stenosis: preliminary results of a randomized, double-blind, active control trial. Pain Physician 2012;15:51-63; (2) 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.

Table 26. Spinal stenosis: Pain success for epidural steroid injection (ESI) vs. control injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of Pain success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Short term	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in pain on NRS	3 mos.	62% (31/50)	66% (33/50)	0.94 (0.70 to 1.26)
	Manchikanti 2012, 2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in pain on NRS	3 mos.	83% (50/60)	77% (46/60)	1.09 (0.91 to 1.30)
	el Zahaar 1991	Hydrocortisone 5 ml + carbocaine 4% + saline Imaging NR	Carbocaine 4% + saline	Caudal	≥75% subjective improvement in baseline back, leg and thigh pain	>24 hrs.	55.5% (10/18 stenosis subgroup)	50.0% (6/12 stenosis subgroup)	1.11 (0.55 to 2.24)
	Cuckler 1985	Methylprednisolone 80 mg + procaine 1% Imaging NR	Procaine 1% + saline	Inter-laminar	≥75% subjective improvement in baseline back, leg and thigh pain	>24 hrs.	25.0% (5/20 stenosis subgroup)	17.6% (3/17 stenosis subgroup)	1.42 (0.4 to 5.08)
	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1% Fluoroscopy	Lidocaine 0.25-1%	Inter-laminar or Trans-foraminal*	Improvement of ≥30% from baseline in pain on NRS	1.5 mos.	49.2% (96/193)	49.7% (96/193)	1.00 (0.81 to 1.22)
	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1% Fluoroscopy	Lidocaine 0.25-1%	Inter-laminar or Trans-foraminal*	Improvement of ≥50% from baseline in pain on NRS	1.5 mos.	38.3% (74/193)	38.3% (74/193)	1.00 (0.78 to 1.29)
Inter-mediate	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in pain on NRS	6 mos.	56% (28/50)	58% (29/50)	0.97 (0.69 to 1.36)
	Manchikanti 2012, 2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in pain on NRS	6 mos.	80% (48/60)	75% (45/60)	1.07 (0.88 to 1.29)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of Pain success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Long-term	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in pain on NRS	24 mos.	44% (22/50)	42% (21/50)	1.05 (0.67 to 1.65)
	Manchikanti2 012, 2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in pain on NRS	24 mos.	73% (44/60)	72% (43/60)	1.02 (0.82 to 1.28)
	el Zahaar 1991	Hydrocortisone 5 ml + carbocaine 4% + saline Imaging NR	Carbocaine 4% + saline	Caudal	≥75% subjective improvement in baseline back, leg and thigh pain	Mean 20.9 (13-36) mos.	38.9% (7/18 stenosis subgroup)	33.3% (4/12 stenosis subgroup)	1.17 (0.43 to 3.13)
	Cuckler 1985	Methylprednisolone 80 mg + procaine 1% Imaging NR	Procaine 1% + saline	Inter-laminar	≥75% subjective improvement in baseline back, leg and thigh pain	Mean 20.5 (13 to 30) mos.	22% (5/23 stenosis subgroup)	14% (2/14 stenosis subgroup)	1.52 (0.34 to 6.81)

CI: confidence interval; NR: not reported; NRS: numerical rating scale.
*Pain success not reported stratified by approach.
Manchikanti et al., caudal: (1) 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; (2) 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; (3) 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.
Manchikanti et al., interlaminar: (1) Lumbar interlaminar epidural injections in central spinal stenosis: preliminary results of a randomized, double-blind, active control trial. Pain Physician 2012;15:51-63; (2) 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.

Table 27. Spinal Stenosis: Function improvement for epidural steroid injection (ESI) vs. control injections

					Function score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Oswestry Disability Index (ODI)										

						Function score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Short term	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	(0-50 scale) 16.8 ± 7.9 (n=50)	(0-50 scale) 17.2 ± 6.8 (n=50)	-11.3 ± 5.0	-12.6 ± 4.3	1.3 (-0.53 to 3.13)
	Manchikanti 2012, 2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	3 mos.	(0-50 scale) 15.2 ± 6.2 (n=60)	(0-50 scale) 15.3 ± 5.3 (n=60)	-15.3 ± 5.1	-15.7 ± 3.8	0.4 (-0.2 to 2.0)
	Nam 2011	Triamcinolone 20 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Trans-foraminal	3 mos.	(0-100 scale) 37.2 (n=17)	(0-100 scale) 48.6 (n=19)	-25.8 ± 2.7	-14.4 ± 3.5	-11.4 (-13.4 to 9.4)
Inter-mediate	Manchikanti 2012,2012,2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	(0-50 scale) 16.9 ± 8.2 (n=50)	(0-50 scale) 17.2 ± 7.3 (n=50)	-11.2 ± 5.3	-12.6 ± 4.68	1.4 (-0.56 to 3.36)
	Manchikanti 2012, 2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	6 mos.	(0-50 scale) 14.8 ± 6.4 (n=60)	(0-50 scale) 15.1 ± 5.9 (n=60)	-15.7 ± 5.05	-15.9 ± 3.88	0.2 (-1.41 to 1.81)
Long-term	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	(0-50 scale) 17.0 ± 7.6 (n=50)	(0-50 scale) 17.5 ± 7.3 (n=50)	-11.1 ± 4.79	-12.3 ± 4.68	1.2 (-0.66 to 3.06)
	Manchikanti 2012, 2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	24 mos.	(0-50 scale) 13.7 ± 6.4 (n=60)	(0-50 scale) 15.1 ± 7.2 (n=60)	-16.8 ± 5.05	-15.9 ± 4.35	-0.9 (-2.59 to 0.79)
Roland Morris Disability Questionniare (scale 0-24)										
Short-term	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine	Lidocaine 0.25-1%	Inter-laminar	1.5 mos.	11.8 ± 6.5 (n=136)	12.6 ± 6.3 (n=136)	-4.8 ± 6.0	-3.3 ± 5.3	Adjusted: -1.4 (-2.8 to -0.1, p=0.04)†

						Function score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
		0.25-1% Fluoroscopy								
	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1% Fluoroscopy	Lidocaine 0.25-1%	Trans-foraminal	1.5 mos.	12.0 ± 5.6 (n=57)	12.1 ± 6.6 (n=57)	-2.4 ± 4.7	-2.6 ± 5.3	Adjusted: 0.3 (-1.9 to 1.8)†
SSSQ Physical Function Subscale (scale 1-4)										
Short-term	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1% Fluoroscopy	Lidocaine 0.25-1%	Inter-laminar or Trans-foraminal‡	1.5 mos.	2.3 ± 0.7 (n=193)	2.2 ± 0.6 (n=193)	-0.2 ± 0.42	-0.3 ± 0.36	Un-adjusted: 0.1 (0.02 to 0.18) Adjusted 0.1 (–0.1 to 0.2)†

CI: confidence interval; SD: standard deviation; SSSQ: Swiss Spinal Stenosis Questionnaire
*A negative score favors the intervention and a positive score favors the control.
†Adjusted for baseline outcome values and recruitment site.
‡SSSQ scores not reported stratified by approach.
Manchikanti et al., caudal: (1) 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; (2) 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; (3) 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.
Manchikanti et al., interlaminar: (1) Lumbar interlaminar epidural injections in central spinal stenosis: preliminary results of a randomized, double-blind, active control trial. Pain Physician 2012;15:51-63; (2) 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.

Table 28. Spinal Stenosis: Function Success for epidural steroid injection (ESI) vs. control injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of function success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Oswestry Disability Index (ODI)									
Short term	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in ODI	3 mos.	49% (24/50)	58% (29/50)	0.83 (0.57 to 1.20)
	Manchikanti 2012, 2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in ODI	3 mos.	77% (46/60)	78% (47/60)	0.98 (0.81 to 1.19)
Inter-mediate	Manchikanti2 012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in ODI	6 mos.	50% (25/50)	54% (27/50)	0.93 (0.63 to 1.35)
	Manchikanti 2012,2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in ODI	6 mos.	78% (47/60)	73% (44/60)	1.07 (0.87 to 1.31)
Long-term	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in ODI	24 mos.	46% (23/50)	42% (21/50)	1.1 (0.7 to 1.71)
	Manchikanti 2012,2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in ODI	24 mos.	75% (45/60)	75% (45/60)	1.0 (0.81 to 1.23)
Roland Morris Disability Questionnaire (RMDQ)									
Short term	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1% Fluoroscopy	Lidocaine 0.25-1%	Inter-laminar or Trans-foraminal*	Improvement of ≥30% from baseline in pain on RMDQ	1.5 mos.	37.3% (72/193)	31.6% (61/193)	1.18 (0.90 to 1.56)
	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-	Lidocaine 0.25-1%	Inter-laminar or Trans-foraminal*	Improvement of ≥50% from baseline in pain on EMDQ	1.5 mos.	23.8% (46/193)	20.2% (39/193),	1.18 (0.81 to 1.72)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of function success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
		1% Fluoroscopy							
	Ohtori 2012	Dexamethasone 15 mg + bupivacaine 0.125% No imaging used	Bupivacaine 0.125%	Caudal	Improvement of >5 points from baseline in RMDQ	3 mos.	62% (25/40)	23.8% (10/42)	2.63 (1.45 to 4.74)
Other outcomes									
Short term	Fukusaki 1998	Methylprednisolone 40 mg and mepivacaine 1% No imaging used	Mepivacaine 1%	Inter-laminar	Excellent results: ability to walk a mean of 100m Good results: ability to walk a mean of 20 to 100m	3 mos.	0% (0/19) 5.3% (1/19)	0% (0/18) 5.6% (1/18)	Not calculable 0.95 (0.06 to 14.04)
	Fukusaki 1998	Methylprednisolone 40 mg and mepivacaine 1% No imaging used	Saline	Inter-laminar	Excellent results: ability to walk a mean of 100m Good results: ability to walk a mean of 20 to 100m	3 mos.	0% (0/19) 5.3% (1/19)	0% (0/16) 6.3% (1/16)	Not calculable 0.84 (0.06 to 12.42)

*Function success not reported stratified by approach.
Manchikanti et al., caudal: (1) 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; (2) 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; (3) 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.
Manchikanti et al., interlaminar: (1) Lumbar interlaminar epidural injections in central spinal stenosis: preliminary results of a randomized, double-blind, active control trial. Pain Physician 2012;15:51-63; (2) 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.

Table 29. Spinal Stenosis: Composite score success for epidural steroid injection (ESI) vs. control injections

Time-point	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Short term	Manchikanti 2012,2012,2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in both pain and ODI	3 mos.	48% (24/50)	58% (29/50)	0.83 (0.57 to 1.20)
	Manchikanti 2012,2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in both pain and ODI	3 mos.	77% (46/60)	75% (45/60)	1.02 (0.84 to 1.25)
	Nam 2011	Triamcinolone 20 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Trans-foraminal	Improvement of >40% from baseline in both pain and ODI and patient satisfaction good or excellent*	3 mos.	76% (13/17)	42% (8/19)	1.82 (1.01 to 3.27)
Inter-mediate	Manchikanti 2012,2012,2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in both pain and ODI	6 mos.	50% (25/50)	54% (27/50)	0.93 (0.63 to 1.35)
	Manchikanti 2012,2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in both pain and ODI	6 mos.	77% (46/60)	72% (43/60)	1.07 (0.87 to 1.32)
Long-term	Manchikanti 2012,2012,2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	Improvement of ≥50% from baseline in both pain and ODI	24 mos.	44% (22/50)	38% (19/50)	1.16 (0.72 to 1.86)
	Manchikanti 2012,2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	Improvement of ≥50% from baseline in both pain and ODI	24 mos.	73% (44/60)	72% (43/60)	1.02 (0.82 to 1.28)

CI: confidence interval; ODI: Oswestry Disability Index.

*For patient satisfaction: "no residual pain (excellent)" or "improvement of pain symptoms by more than 50% (good)"

Manchikanti et al., caudal: (1) 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; (2) 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; (3) 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.

Manchikanti et al., interlaminar: (1) Lumbar interlaminar epidural injections in central spinal stenosis: preliminary results of a randomized, double-blind, active control trial. Pain Physician 2012;15:51-63; (2) 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.

Table 30. Spinal Stenosis: Risk of Surgery for epidural steroid injection (ESI) vs. control injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Short term	Nam 2011	Triamcinolone 20 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Trans-foraminal	3 mos.	12% (2/17)	5.3% (1/19)	2.24 (0.22 to 22.5)
Long-term	el Zahaar 1991	Hydrocortisone 5 ml + carbocaine 4% + saline Imaging NR	Carbocaine 4% + saline	Caudal	Mean 20.9 (13-36) mos.	44.4% (8/18 stenosis subgroup)	58.3% (7/12 stenosis subgroup)	0.76 (0.38 to 1.54)
	Cuckler 1985	Methylprednisolone 80 mg + procaine 1% Imaging NR	Procaine 1% + saline	Inter-laminar	Mean 20.5 (13-30) mos.	26% (6/23 stenosis subgroup)	29% (4/14 stenosis subgroup)	0.91 (0.31 to 2.66)

CI: confidence interval; NR: not reported.

Table 31. Spinal Stenosis: Improvement (reduction) in opioid usage and quality of life for epidural steroid injection (ESI) vs. control injections

						Opioid usage Mean ± SD		Δ from baseline		Mean difference A vs. B (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Improvement in Opioid usage*										
Short term	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	33.1 ± 27.5 (n=50)	33.3 ± 35.7 (n=50)	-16.1 ± 26.08	-12.4 ± 32.5	-3.7 (-15.25 to 7.85)
	Manchikanti 2012,2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	3 mos.	42.8 ± 40.8 (n=60)	44.0 ± 40.4 (n=60)	-28.2 ± 64.49	-16.5 ± 34.31	-11.7 (-30.2 to 6.78)
Inter-mediate	Manchikanti 2012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	33.7 ± 34.7 (n=50)	34.4 ± 43.0 (n=50)	-15.5 ± 25.34	-11.3 ± 31.81	-4.2 (-15.47 to 7.07)
	Manchikanti 2012,2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	6 mos.	40.2 ± 36.2 (n=60)	40.2 ± 40.6 (n=60)	-30.8 ± 66.96	-20.3 ± 34.28	-10.5 (-29.5 to 8.53)
Long-term	Manchikanti2 012,2012, 2008	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	32.5 ± 34.8 (n=50)	35.7 ± 43.3 (n=50)	-16.7 ± 25.34	-10 ± 31.81	-6.7 (-17.97 to 4.57)
	Manchikanti 2012,2015	Betamethasone (1 ml) + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	24 mos.	33.4 ± 29.5 (n=60)	37.9 ± 38.3 (n=60)	-37.6 ± 70.94	-22.6 ± 34.67	-15 (-34.98 to 4.98)
European Quality of Life 5 Dimensions Questionnaire (EQ5D) (-0.594 to 1 scale)†										
Short term	Friedly 2014	Triamcinolone 60-120 mg or Betamethasone 8-10 mg or Methylprednisolone 60 to 120 mg + lidocaine 0.25-1% Fluoroscopy	Lidocaine 0.25-1%	Inter-laminar or Trans-foraminal	1.5 mos.	0.70 ± 0.20 (n=193)	0.68 ± 0.19 (n=193)	0.13 ± 0.13	0.09 ± 0.12	0.04 (0.02, 0.06)

CI: confidence interval.
*A negative score favors the intervention and a positive score favors the control; morphine equivalents in milligrams per day.
†A positive score favors the intervention and a negative score favors the control.
Manchikanti et al., caudal: (1) 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; (2) 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; (3) 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.
Manchikanti et al., interlaminar: (1) Lumbar interlaminar epidural injections in central spinal stenosis: preliminary results of a randomized, double-blind, active control trial. Pain Physician 2012;15:51-63; (2) 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.

Table 32. Spinal Stenosis: Patient Satisfaction for epidural stenosis injection (ESI) vs. control injections

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of reduction in medication	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Short term	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 or Trans-foraminal*	SSSQ satisfaction scale (% of patients reporting very or somewhat satisfied)	1.5 mos.	67% (129/193)	54% (104/193)	1.24 (1.05 to 1.46)

CI: confidence interval; SSSQ: Swiss Spinal Stenosis Questionnaire
*Not reported stratified by approach.

Table 33. Spinal Stenosis: Pain and Function Improvement for ESI vs. control Injections with other medication, disc or decompression procedures, and conservative care.

						Outcome score Mean ± SD		Δ from base-line		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Pain improvement on visual analog scale (VAS) or numerical rating scale (NRS) (0-10 scale)										
Short term	Ohtori 2012	Dexamethasone 3.3 mg + lidocaine 1% Fluoroscopy	Etanercept + lidocaine 1%	Trans-foraminal	1 mo.	5.2 ± 0.7 (n=40)	3.5 ± 0.8 (n=40)	-2.3 ± 1.5	-4.4 ± 1.44	2.1 (1.46 to 2.74)
	Brown 2012	Triamcinolone 80 mg (40 mg in diabetics) + saline Fluoroscopy	Minimally invasive lumbar decompression Fluoroscopy	Inter-laminar	1.5 mos.	6.3 ± 1.4 (n=17)	3.8 ± 1.3 (n=21)	-0.1 ± 0.85	-2.5 ± 0.85	2.4 (1.86 to 2.94)
	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	3 mos.	2.3 (n=10)	2.4 (n=10)	-3.1	-3.1	0
			Home exercises + diclofenac 75 mg	Inter-laminar	3 mos.	2.3 (n=10)	3.8 (n=9)	3.0	2.0	1.0
Inter-mediate	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	6 mos.	2.6 (n=10)	2.2 (n=10)	-2.7	-3.3	-0.6
			Home exercises + diclofenac 75 mg	Inter-laminar	6 mos.	2.6 (n=10)	3.3 (n=9)	-2.7	-2.5	-0.2
Oswestry Disability Index (ODI) (0-100)										
Short term	Ohtori 2012	Dexamethasone 3.3 mg + lidocaine 1% Fluoroscopy	Etanercept + lidocaine 1%	Trans-foraminal	1 mo.	30 ± 6.0 (n=40)	28 ± 6.2 (n=40)	-10 ± 4.22	-10 ± 4.93	0 (-2.01 to 2.01)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Outcome score Mean ± SD Group A	Outcome score Mean ± SD Group B	Δ from base-line Group A	Δ from base-line Group B	Mean difference A vs. B* (95% CI)
	Brown 2012	Triamcinolone 80 mg (40 mg in diabetics) + saline Fluoroscopy	Minimally invasive lumbar decompression Fluoroscopy	Inter-laminar	1.5 mos.	34.8 ± 8.2 (n=17)	27.4 ± 7.0 (n=21)	-5.7 ± 4.96	-11.4 ± 4.43	5.7 (2.67 to 8.73)
Roland Morris Disability Index (RMDQ) (0-24)										
Short term	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	3 mos.	11 (n=10)	11 (n=10)	-7	-8	1.0
			Home exercises + diclofenac 75 mg	Inter-laminar	3 mos.	11 (n=10)	10 (n=9)	-7	-5	-2.0
Inter-mediate	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	6 mos.	13 (n=10)	12 (n=10)	-5	-7	2.0
			Home exercises + diclofenac 75 mg	Inter-laminar	6 mos.	13 (n=10)	9 (n=9)	-5	-6	1.0

CI: confidence interval.
*A negative score favors the intervention and a positive score favors the control.
†Including ultrasound for 10 mins, hot pack for 20 mins, and TENS for 20 mins.

Table 34. Spinal Stenosis: Pain success and patient satisfaction for epidural spinal injection (ESI) vs. disc or decompression procedures

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Definition of success	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Pain Success									
Short term	Brown 2012	Triamcinolone 80 mg (40 mg in diabetics) + saline Fluoroscopy	Minimally invasive lumbar decompression Fluoroscopy	Inter-laminar	Improvement of ≥2 points from baseline in VAS	1.5 mos.	35.3% (6/17)	76.2% (16/21)	0.46 (0.23 to 0.92)
Patient Satisfaction									
Short term	Brown 2012	Triamcinolone 80 mg (40 mg in diabetics) + saline Fluoroscopy	Minimally invasive lumbar decompression Fluoroscopy	Inter-laminar	% of patients with a score ≤2.5 on the ZCQ patient satisfaction domain	1.5 mos.	41.2% (7/17	58.8% (12/21)	0.72 (0.37 to 1.42)

CI: confidence interval; VAS: visual analog scale; ZCQ: Zurich Claudication Questionnaire.

Table 35. Lumbar nonradicular axial pain: Improvement in pain, function, and opioid use for epidural steroid injection (ESI) vs. control injection

						Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Pain improvement on VAS (0-10)										
Short term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	3.6 ± 1.4 (n=60)	4.2 ± 1.8 (n=60)	-4.3 ± 0.85	-3.8 ± 1.21	-0.5 (-0.87 to -0.13)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	3 mos.	3.5 ± 1.2 (n=60)	3.6 ± 0.9 (n=60)	-4.2 ± 0.72	-4.4 ± 0.61	0.2 (-0.04 to 0.44)
Inter-mediate term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	3.7 ± 1.5 (n=60)	4.1 ± 1.8 (n=60)	-4.2 ± 0.92	-3.9 ± 1.21	-0.3 (-0.68 to 0.08)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	6 mos.	3.6 ± 1.2 (n=60)	3.9 ± 1.1 (n=60)	-4.1 ± 0.72	-4.1 ± 0.67	0 (-0.25 to 0.25)
Long-term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	4.0 ± 1.7 (n=60)	4.4 ± 1.9 (n=60)	-3.9 ± 1.08	-3.6 ± 1.3	-0.3 (-0.73 to 0.13)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	24 mos.	3.6 ± 1.4 (n=60)	3.9 ± 1.3 (n=60)	-4.1 ± 0.87	-4.1 ± 0.78	0 (-0.3 to 0.3)
Function improvement on ODI (0-50)										
Short term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	14.5 ± 5.5 (n=60)	16.3 ± 7.2 (n=60)	-13.9 ± 3.31	-12 ± 4.4	-1.9 (-3.29 to -0.51)

						Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	3 mos.	14.6 ± 5.1 (n=60)	14.9 ± 4.3 (n=60)	-14.6 ± 3.26	-15.8 ± 2.79	1.2 (0.11 to 2.29)
Inter-mediate term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	14.3 ± 5.9 (n=60)	16.4 ± 7.4 (n=60)	-14.1 ± 3.54	-11.9 ± 4.56	-2.2 (-3.66 to -0.74)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	6 mos.	14.4 ± 5.2 (n=60)	15.4 ± 4.8 (n=60)	-14.8 ± 3.29	-15.3 ± 2.95	0.5 (-0.62 to 1.62)
Long term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	14.9 ± 6.4 (n=60)	16.5 ± 7.7 (n=60)	-13.5 ± 3.86	-11.8 ± 4.79	-1.7 (-3.26 to -0.14)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	24 mos.	14.6 ± 6.1 (n=60)	14.9 ± 5.1 (n=60)	-14.6 ± 3.67	-15.8 ± 3.09	1.2 (-0.01 to 2.41)
Improvement in opioid use (morphine equivalents, mg/day)										
Short term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	29.9 ± 19.9	28.7 ± 27.1	-6.3 ± 12.55	-5.8 ± 20.22	-0.5 (-6.52 to 5.52)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	3 mos.	40.3 ± 35.7	35.5 ± 24.2	-13.1 ± 33.1	-21.7 ± 44.48	8.6 (-5.43 to 22.63)
Inter-mediate term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	31.0 ± 19.9	31.5 ± 38.4	-5.2 ± 12.55	-3.0 ± 23.23	-2.2 (-8.88 to 4.48)

						Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	6 mos.	41.8 ± 37.3	36.1 ± 27.0	-11.6 ± 32.79	-21.1 ± 42.97	9.5 (-4.18 to 23.18)
Long-term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	29.8 ± 20.3	31.0 ± 38.4	-6.4 ± 12.69	-3.5 ± 23.23	-2.9 (-9.6 to 3.8)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	24 mos.	41.8 ± 37.3	36.3 ± 27.0	-11.6 ± 32.79	-20.9 ± 42.97	9.3 (-4.38 to 22.98)

CI: confidence interval.
*A negative score favors the intervention and a positive score favors the control.
†Numerical rating scale of 0-100 mm was converted to a 0-10 mm scale.
Manchikanti et al., caudal: (1) 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; (2) 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; (3) 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.
Manchikanti et al., interlaminar: (1) 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; (2) Fluoroscopic lumbar interlaminar epidural injections in managing chronic lumbar axial or discogenic pain. J Pain Res 2012;5:301-11; (3) A randomized, double-blind, active-controlled trial of fluoroscopic lumbar interlaminar epidural injections in chronic axial or discogenic low back pain: results of 2-year follow-up. Pain Physician 2013;16:E491-504.

Table 36. Lumbar nonradicular axial pain: Success in pain, function, and composite outcome of pain and function for epidural steroid injections (ESI) vs. control injection

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Pain success (improvement of ≥50% from baseline in pain on NRS)								
Short term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	80% (48/60)	68% (41/60)	1.17 (0.95 to 1.45)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	3 mos.	83% (50/60)	88% (53/60)	0.94 (0.82 to 1.09)
Inter-mediate	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	80% (48/60)	68% (41/60)	1.17 (0.95 to 1.45)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	6 mos.	82% (49/60)	77% (46/60)	1.07 (0.89 to 1.28)
Long-term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	65% (39/60)	57% (34/60)	1.15 (0.86 to 1.53)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	24 mos.	72% (43/60)	73% (44/60)	0.98 (0.78 to 1.22)
Function success (improvement of ≥50% from baseline on ODI)								
Short term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	3 mos.	75% (45/60)	60% (36/60)	1.25 (0.97 to 1.61)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	3 mos.	78% (47/60)	83% (50/60)	0.94 (0.79 to 1.12)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Inter-mediate	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	75% (45/60)	62% (37/60)	1.22 (0.95 to 1.56)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	6 mos.	77% (46/60)	73% (44/60)	1.05 (0.85 to 1.29)
Long-term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	63% (38/60)	56% (34/60)	1.12 (0.83 to 1.5)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Inter-laminar	24 mos.	70% (42/60)	72% (43/60)	0.98 (0.78 to 1.23)
Overall success (composite outcome of improvement of ≥50% from baseline on NRS and ODI)								
Short term	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	3 mos.	77% (46/60)	83% (50/60)	0.92 (0.77 to 1.1)
Inter-mediate	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	6 mos.	72% (43/60)	62% (37/60)	1.16 (0.9 to 1.5)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	6 mos.	75% (45/60)	72% (43/60)	1.05 (0.84 to 1.3)
Long-term	Manchikanti 2012, 2011, 2008	Betamethasone 6 mg OR methylprednisolone 40 mg + lidocaine 0.5% Fluoroscopy	Lidocaine 0.5%	Caudal	24 mos.	60% (36/60)	54% (32/60)	1.13 (0.82 to 1.54)
	Manchikanti 2013, 2012, 2010	Betamethasone 6 mg + lidocaine 0.5% Fluoroscopic	Lidocaine 0.5%	Inter-laminar	24 mos.	67% (40/60)	72% (43/60)	0.93 (0.73 to 1.18)

CI: confidence interval; NRS: numerical rating scale; ODI: Oswestry Disability Index.

Manchikanti et al., caudal: (1) 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; (2) 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; (3) 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.
Manchikanti et al., interlaminar: (1) 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; (2) Fluoroscopic lumbar interlaminar epidural injections in managing chronic lumbar axial or discogenic pain. J Pain Res 2012;5:301-11; (3) A randomized, double-blind, active-controlled trial of fluoroscopic lumbar interlaminar epidural injections in chronic axial or discogenic low back pain: results of 2-year follow-up. Pain Physician 2013;16:E491-504.

Table 37. Lumbar nonradicular axial pain: Pain and function improvement for intradiscal injections (with or without steroid) vs. intradiscal control injection or discography

						Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Pain improvement on VAS (0-10)										
Short term	Cao (2011)†	Betamethasone (dose NR) Guidance NR	Saline	Intradiscal	3 mos.	1.7 ± 0.89 (n=40)	6.9 ± 1.3 (n=40)	-4.95 ± 0.69	0.1 ± 0.81	-5.05 (-5.52 to -4.58)
	Butterman (2004)	Discography + betamethasone (mean 9.7 mg)	Discography alone	Intradiscal	3 mos.	4.2‡ (n=86)	6.5‡ (n=85)	-1.2	0	-1.2
Inter-mediate term	Cao (2011)†	Betamethasone (dose NR) Guidance NR	Saline	Intradiscal	6 mos.	2.2 ± 0.95 (n=40)	6.9 ± 1.07 (n=40)	-4.45 ± 0.69	0.1 ± 0.75	-4.55 (-5.0 to -4.1)
	Peng (2010)	Methylene blue (10 mg) + lidocaine 2% Fluoroscopic guidance	Isotonic saline + lidocaine 2%	Intradiscal	6 mos.	2.49 ± 1.74 (n=36)	6.35 ± 1.17 (n=35)	-4.74 ± 1.06	-0.38 ± 0.73	-4.36 (-4.78 to -3.94)
	Butterman (2004)	Discography + betamethasone (mean 9.7 mg)	Discography alone	Intradiscal	6 mos.	4.0‡ (n=86)	6.0‡ (n=85)	-1.4	-0.5	-0.9
Long term	Khot 2004	Methylprednisolone 40 mg Fluoroscopic guidance	Saline	Intradiscal	12 mos.	NR (n=46)	NR (n=52)	Median (IQR) 0 (-1 to 1)	Median (IQR) 0 (-0.25 to 1)	Median difference: 0
	Peng (2010)	Methylene blue (10 mg) + lidocaine 2% Fluoroscopic guidance	Isotonic saline + lidocaine 2%	Intradiscal	24 mos.	1.98 ± 1.60 (n=36)	6.04 ± 1.41 (n=35)	-5.25 ± 0.96	-0.69 ± 0.85	-4.56 (-4.98 to -4.14)
	Butterman (2004)	Discography + betamethasone (mean 9.7 mg)	Discography alone	Intradiscal	24 mos.	4.5‡ (n=86)	5.9‡ (n=85)	-0.9	-0.6	-0.4
Function improvement on ODI (0-100)										
Short term	Cao (2011)†	Betamethasone (dose NR) Guidance NR	Saline	Intradiscal	3 mos.	12.9 ± 2.14 (n=40)	37.65 ± 11.9 (n=40)	-20.7 ± 6.91	2.5 ± 7.61	-23.2 (-27.7 to -18.7)
	Butterman	Discography + betamethasone	Discography	Intradiscal	3 mos.	46.5‡	54.1‡	-5.3	2.0	-7.3

						Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
	(2004)	(mean 9.7 mg)	alone			(n=86)	(n=85)			
Inter-mediate term	Cao (2011)†	Betamethasone (dose NR) Guidance NR	Saline	Intradiscal	6 mos.	14.25 ± 2.6 (n=40)	39.1 ± 12.2 (n=40)	-19.35 ± 6.61	3.95 ± 7.7	-23.3 (-27.75 to -18.85)
	Peng (2010)	Methylene blue (10 mg) + lidocaine 2% Fluoroscopic guidance	Isotonic saline + lidocaine 2%	Intradiscal	6 mos.	16.00 ± 11.91 (n=36)	48.40 ± 7.77 (n=35)	-32.47 ± 8.39	-0.97 ± 4.7	-31.5 (-34.65 to -28.35)
	Butterman (2004)	Discography + betamethasone (mean 9.7 mg)	Discography alone	Intradiscal	6 mos.	44.2‡ (n=86)	49.4‡ (n=85)	-7.5	-2.7	-4.9
Long term	Khot 2004	Methylprednisolone 40 mg Fluoroscopic guidance	Saline	Intradiscal	12 mos.	NR (n=46)	NR (n=52)	-2.28 ± 2.49	-3.42 ± 1.79	1.14 (0.27 to 2.01)
	Peng (2010)	Methylene blue (10 mg) + lidocaine 2% Fluoroscopic guidance	Isotonic saline + lidocaine 2%	Intradiscal	24 mos.	12.89 ± 11.95 (n=36)	47.69 ± 10.92 (n=35)	-35.58 ± 8.39	-1.68 ± 6.82	-33.9 (-37.45 to -30.35)
	Butterman (2004)	Discography + betamethasone (mean 9.7 mg)	Discography alone	Intradiscal	24 mos.	41.4‡ (n=86)	44.6‡ (n=85)	-10.3	2.5	-12.8

CI: confidence interval; IQR: interquartile range; ODI: Oswestry Disability Index; SD: standard deviation; VAS: visual analog scale.
*A negative score favors the intervention and a postivie score favors the control.
†Patients with Modic Type I and Modic Type II changes were pooled to create one intervention group and one control group.
‡Data estimated from graphs.

Table 38. Lumbar nonradicular axial pain: Success in pain, function and overall improvement, and satisfaction, opioid use, and risk of surgery for intradiscal injections (with or without steroid) vs. intradiscal control injection or discography

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Outcome definition	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Pain success									
Short term	Simmons (1992)	Methylprednisolone 80 mg Fluoroscopic guidance	Bupivacaine 0.5%	Intra-discal	10-14 days	Improvement on VAS (details NR)	43% (6/14)	36% (4/11)	1.18 (0.44 to 3.17)
Inter-mediate term	Peng (2010)	Methylene blue (10 mg) + lidocaine 2% Fluoroscopy	Isotonic saline + lidocaine 2%	Intra-discal	6 mos.	"Complete relief" (NRS = 0-10)	19% (7/36)	NR*	Not estimable
						"Dramatic improvement" (NRS = 0-20)	28% (10/36)	NR*	Not estimable
						"Obvious improvement" (reduction of NRS of at least 20 points)	42% (15/36)	NR*	Not estimable
Function success									
Short term	Simmons (1992)	Methylprednisolone 80 mg Fluoroscopic guidance	Bupivacaine 0.5%	Intra-discal	10-14 days	Improvement on ODI (details NR)	36% (5/14)	27% (3/11)	1.31 (0.4 to 4.32)
Overall success									
Short term	Simmons (1992)	Methylprednisolone 80 mg Fluoroscopic guidance	Bupivacaine 0.5%	Intra-discal	10-14 days	Self-reported overall improvement (details NR)	21% (3/14)	9% (1/11)	2.36 (0.28 to 19.66)
	Butterman (2004)	Discography + betamethasone (mean 9.7 mg)	Discography alone	Intra-discal	1-3 mos.	Self-reported success in treatment of symptoms	40.7% (35/86)	0% (0/85)	Not estimable
Inter-mediate term	Butterman (2004)	Discography + betamethasone (mean 9.7 mg)	Discography alone	Intra-discal	7-12 mos.	Self-reported success in treatment of symptoms	22.1% (19/86)	0% (0/85)	Not estimable
Long-term	Butterman (2004)	Discography + betamethasone (mean 9.7 mg)	Discography alone	Intra-discal	12-24 mos.	Self-reported success in treatment of symptoms symptoms	17.4% (15/86)	1.2 (1/85)	14.8 (2.0 to 109.8)
Surgery									
Long-term	Khot 2004	Methylprednisolone 40 mg Fluoroscopic guidance	Saline	Intra-discal	12 mos.	Risk of surgery	10% (6/60)	6.7% (4/60)	1.5 (0.45 to 5.05)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Outcome definition	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
	Butterman (2004)	Discography + betamethasone (mean 9.7 mg)	Discography alone	Intra-discal	24 mos.	Underwent fusion	65% (56/86)	83% (71/85)	0.77 (0.65 to 0.93)
Patient satisfaction									
Long term	Peng (2010)	Methylene blue (10 mg) + lidocaine 2% Fluoroscopic guidance	Isotonic saline + lidocaine 2%	Intra-discal	24 mos.	Completely satisfied or satisfied	91.7% (33/36)	14.3% (5/35)	6.42 (2.83 to 14.53)
Opioid or NSAID use									
Long term	Peng (2010)	Methylene blue (10 mg) + lidocaine 2% Fluoroscopic guidance	Isotonic saline + lidocaine 2%	Intra-discal	24 mos.	No use OR occasional use of opioids or NSAIDs	91.7% (33/36)	57.1% (20/35)	1.6 (1.18 to 2.17)
						No use of any medications	83.3% (30/36)	5.7% (2/35)	14.58 (3.77 to 56.46)
						Occasional use of NSAIDs or opioids	8.3% (3/36)	51.4% (18/35)	0.16 (0.05 to 0.5)
						Regular use of NSAIDs or opioids	8.3% (3/36)	42.9% (15/35)	0.19 (0.06 to 0.61)
	Butterman (2004)	Discography + betamethasone (mean 9.7 mg)	Discography alone	Intra-discal	24 mos.	Less/much less use of narcotics or NSAIDs	19.7% (17/86)	3.5% (3/85)	5.6 (1.7 to 18.4)

CI: confidence interval; NR: not reported; NRS: numerical rating scale; NSAIDs: nonsteroidal anti-inflammatory drugs; VAS: visual analog scale.

Table 39. Failed Back Surgery Syndrome: Pain and function improvement and opioid use for epidural steroid injection (ESI) vs. control injection or control injection with other medication

						Score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Pain improvement on VAS (0-10)										
Short term	Manchikanti 2012, 2010, 2008	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	3 mos.	4.1 ± 1.7 (n=70)	4.2 ± 1.8 (n=70)	-3.7 ± 1.12	-3.6 ± 1.17	-0.1 (-0.48 to 0.28)
	Meadeb 2001	Predisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	2 mos.	5.30 ± 2.47 (n=16)	6.16 ± 2.44 (n=16)	-0.24 ± 1.57	-0.86 ± 1.49	0.62 (-0.44 to 1.68)
		Forceful injection, prednisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	2 mos.	5.25 ± 2.25 (n=15)	6.16 ± 2.44 (n=16)	-0.7 ± 1.33	-0.86 ± 1.49	0.16 (-0.83 to 1.15)
Inter-mediate term	Manchikanti 2012, 2010, 2008	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	6 mos.	4.1 ± 1.7 (n=70)	4.3 ± 1.9 (n=70)	-3.7 ± 1.12	-3.5 ± 1.25	-0.2 (-0.59 to 0.19)
	Rocco 1989	Triamcinolone diacetate 75 mg + lidocaine 5% and saline Imaging NR	Morphine 8 mg + lidocaine 5%	NR	6 mos.	4.2 (n=8)	5.7 (n=7)	-2.2 ± 1.34	1.7 ± 1.38	-3.9 (-5.28 to -2.52)
		Triamcinolone diacetate 75 mg + morphine 8 mg + lidocaine 5% Imaging NR	Morphine 8 mg + lidocaine 5%	NR	6 mos.	5.8 (n=7)	5.7 (n=7)	0.8 ± 1.34	1.7 ± 1.38	-0.9 (-2.32 to 0.52)
	Meadeb 2001	Predisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	4 mos.	4.53 ± 2.40 (n=16)	5.95 ± 2.42 (n=16)	-1.01 ± 1.57	-1.07 ± 1.49	0.06 (-1.0 to 1.12)
		Forceful injection, prednisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	4 mos.	5.76 ± 2.47 (n=15)	5.95 ± 2.42 (n=16)	-0.19 ± 1.44	-1.07 ± 1.49	0.88 (-0.15 to 1.91)
Long term	Manchikanti 2012, 2010, 2008	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	24 mos.	4.2 ± 1.8 (n=70)	4.4 ± 1.9 (n=70)	-3.6 ± 1.21	-3.4 ± 1.25	-0.2 (-0.61 to 0.21)
Function improvement on ODI (0-50)										
Short term	Manchikanti 2012, 2010,	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9%	Lidocaine 0.5% + saline 0.9%	Caudal	3 mos.	(ODI 0-50) 16.8 ± 6.8	(ODI 0-50) 17.6 ± 6.3	-12.3 ± 4.19	-12.7 ± 3.82	0.4 (-0.93

						Score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
	2008	Fluoroscopy				(n=70)	(n=70)			to 1.73)
Intermediate term					6 mos.	(ODI 0-50) 16.3 ± 7.0 (n=70)	(ODI 0-50) 17.6 ± 6.9 (n=70)	-12.8 ± 4.34	-12.7 ± 4.26	-0.1 (-1.53 to 1.33)
Long term					24 mos.	(ODI 0-50) 16.6 ± 7.0 (n=70)	(ODI 0-50) 17.8 ± 7.2 (n=70)	-12.5 ± 4.34	-12.5 ± 4.5	0 (-1.46 to 1.46)
Function improvement on Dallas ADLs domain										
Short-term	Meadeb 2001	Predisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	2 mos.	60.3 ± 23.4 (n=16)	68.0 ± 14.6 (n=16)	-5.3 ± 14.78	-3 ± 8.81	-2.3 (-10.73 to 6.13)
		Forceful injection of prednisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	2 mos.	59.6 ± 16.5 (n=15)	68.0 ± 14.6 (n=16)	-1.2 ± 10.4	-3 ± 8.81	1.8 (-5.01 to 8.61)
Intermediate term	Meadeb 2001	Predisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	4 mos.	58.4 ± 22.8 (n=16)	67.3 ± 18.9 (n=16)	-7.2 ± 14.29	-3.7 ± 11.62	-3.5 (-12.52 to 5.52)
		Forceful injection of prednisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	4 mos.	65.3 ± 18.5 (n=15)	67.3 ± 18.9 (n=16)	4.5 ± 11.21	-3.7 ± 11.62	8.2 (0.16 to 16.24)
Opioid use (morphine equivalents, mg/day)										
Short term	Manchikanti 2012, 2010, 2008	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	3 mos.	39 ± 35.8 (n=70)	40 ± 47.5 (n=70)	-8 ± 25.14	-9 ± 32.54	1 (-8.63 to 10.63)
Intermediate term					6 mos.	39 ± 35.6 (n=70)	38 ± 43.4 (n=70)	-8 ± 25.12	-11 ± 32.22	3 (-6.57 to 12.57)
Long-term					12 mos.	40 ± 35.5 (n=70)	38 ± 43.2 (n=70)	-7 ± 25.11	-11 ± 32.22	4 (-5.57 to 13.57)

ADLs: activities of daily living; CI: confidence interval; ODI: Oswestry Disability Index; VAS: visual analog scale.

*A negative score favors the intervention and a postivie score favors the control.

Manchikanti et al., caudal: (1) 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; (2) 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; (3) 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.

Table 40. Failed Back Surgery Syndrome: Success in pain and function and overall success for epidural steroid injection (ESI) vs. control injection or control injection with other medication

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Outcome definition	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Pain success									
Short term	Manchikanti 2012, 2010, 2008	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	3 mos.	≥50% improvement from baseline on NRS	43% (6/14)	36% (4/11)	1.18 (0.44 to 3.17)
	Devulder 1999	Nerve root sleeve injection, methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Nerve root sleeve injection, bupivacaine 0.5% + 1500 U hyaluronidase	Trans-foraminal	3 mos.	≥50% improvement on the (verbal pain rating scale	40% (8/20)	25% (5/20)	1.6 (0.63 to 4.05)
						Any temporary pain relief	40% (8/20)	25% (5/20)	1.6 (0.63 to 4.05)
		Nerve root sleeve injection, methylprednisolone 40 mg + bupivacaine 0.5% + 1500 U hyaluronidase Fluoroscopy	Nerve root sleeve injection, bupivacaine 0.5% + 1500 U hyaluronidase	Trans-foraminal	3 mos.	≥50% improvement on the (verbal pain rating scale	25% (5/20)	25% (5/20)	1.0 (0.34 to 2.93)
						Any temporary pain relief	30% (6/20)	25% (7/20)	0.86 (0.35 to 2.1)
Inter-mediate term	Manchikanti 2012, 2010, 2008	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	6 mos.	≥50% improvement from baseline on NRS	66% (46/70)	60% (42/70)	1.1 (0.85 to 1.41)
	Rocco 1989	Triamcinolone diacetate 75 mg + lidocaine 5% and saline Imaging NR	Morphine 8 mg + lidocaine 5%	NR	6 mos.	Pain relief: self-reporting of pain as “better”	12% (1/8)	0% (0/7)	1.75 (0.07 to 44.67)
		Triamcinolone diacetate 75 mg + morphine 8 mg + lidocaine 5% Imaging NR	Morphine 8 mg + lidocaine 5%	NR	6 mos.	Pain relief: self-reporting of pain as “better”	0% (0/7)	0% (0/7)	1.0 (0.02 to 43.7)
	Devulder 1999	Nerve root sleeve injection, methylprednisolone 40 mg + bupivacaine 0.5% Fluoroscopy	Nerve root sleeve injection, bupivacaine 0.5% + 1500 U	Trans-foraminal	6 mos.	≥50% improvement on the (verbal pain rating scale	35% (7/20)	25% (5/20)	1.4 (0.53 to 3.68)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Outcome definition	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
			hyaluronidase						
						Any temporary pain relief	35% (7/20))	25% (5/20)	1.4 (0.53 to 3.68)
		Nerve root sleeve injection, methylprednisolone 40 mg + bupivacaine 0.5% + 1500 U hyaluronidase Fluoroscopy	Nerve root sleeve injection, bupivacaine 0.5% + 1500 U hyaluronidase	Trans-foraminal	6mos.	≥50% improvement on the (verbal pain rating scale	20% (4/20)	25% (5/20)	0.8 (0.25 to 2.55)
						Any temporary pain relief	35% (7/20))	25% (5/20)	1.4 (0.53 to 3.68)
	Meadeb 2001	Predisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	4 mos.	Pain improved ≥15% on VAS	25% (4/16)	43.8% (7/16)	0.57 (0.21 to 1.58)
		Forceful injection, prednisolone acetate 125 mg Fluoroscopy	Forceful saline 20 mL	Caudal	4 mos.	Pain improved ≥15% on VAS	20% (3/15)	43.8% (7/16)	0.46 (0.14 to 1.45)
Long-term	Manchikanti 2012, 2010, 2008	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	24 mos.	≥50% improvement from baseline on NRS	56% (39/70)	49% (34/70)	1.15 (0.83 to 1.58)
Function success									
Short term	Manchikanti 2012, 2010, 2008	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9% Fluoroscopy	Lidocaine 0.5% + saline 0.9%	Caudal	3 mos.	≥50% improvement from baseline on ODI	57% (40/70)	56% (39/70)	1.03 (0.77 to 1.37)
Inter-mediate term					6 mos.	≥50% improvement from baseline on ODI	63% (44/70)	56% (39/70)	1.13 (0.86 to 1.49)
Long-term					24 mos.	≥50% improvement from baseline on ODI	56% (39/70)	49% (34/70)	1.15 (0.83 to 1.58)
Overall success									
Inter-mediate	Manchikanti 2012, 2010,	Betamethasone 6 mg + lidocaine 0.5% + saline 0.9%	Lidocaine 0.5% + saline 0.9%	Caudal	6 mos.	Pain relief ≥50% and ODI	61% (43/70)	56% (39/70)	1.1 (0.83 to 1.46)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Outcome definition	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
term	2008	Fluoroscopy				improved ≥50%			
Long-term					24 mos.	Pain relief ≥50% and ODI improved ≥50%	58% (41/70)	47% (33/70)	1.24 (0.91 to 1.71)

CI: confidence interval; NRS: numerical rating scale; ODI: Oswestry disability index; VAS: visual analog scale.
Manchikanti et al., caudal: (1) 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; (2) 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; (3) 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.

Table 41. Facet joint pain: Improvement in pain, function, quality of life and opioid use for intra- and extra-articular steroid injections vs. intra- or extra-articular control injection, extra-articular steroid injection, or radiofrequency denervation.

					Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A	Group B	Group A	Group B	
Pain improvement on VAS (0-10)									
Short term	Civelek 2012	Extra-articular injection of methylprednisolone 40 mg + lidocaine 1% Fluoroscopy	Radio-frequency denervation (medial branch)	1 mo.	3.4 ± 1.1 (n=50)	2.2 ± 1.3 (n=50)	-5.1 ± 0.68	-6 ± 0.9	0.9 (0.59 to 1.21)
	Manchikanti 2010, 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	3 mos.	3.5 ± 1.1 (n=60)	3.8 ± 1.3 (n=60)	-4.4 ± 0.67	-4.4 ± 0.82	0 (-0.27 to 0.27)
	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg and lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	3 mos.	4.7 ±3.12 (n=31)	6.1 ± 2.75 (n=29)	-2.3 ± 2.23	-0.7 ± 1.79	-1.6 (-2.62 to -0.58)
	Lilius 1989	Intra-articular injection of methylprednisolone acetate 80 mg + bupivacaine 30 mg Fluoroscopy	Intra-articular injection of saline	3 mos.	4.4 ± 2.8† (n=28)	4.3 ± 2.6† (n=42)	-0.1 ± 1.98	-0.9 ± 1.7	0.8 (-0.09 to 1.69)
	Carette 1991	Intra-articular injection of methylprednisolone acetate 20 mg + isotonic saline Fluoroscopy	Intra-articular injection of isotonic saline	1 mo.	4.5 ± 2.8 (n=48)	4.7 ± 2.6 (n=48)	-1.8 ± 1.98	-1.5 ± 1.7	-0.3 (-1.04 to 0.44)
	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg	Intra-articular injection of sodium hyaluronate 10 mg	1 mo.	3.01 ± 2.33 (n=30)	4.08 ± 2.56 (n=30)	-3.86 ± 1.57	-2.84 ± 1.66	-1.02 (-1.84 to -0.2)

					Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A	Group B	Group A	Group B	
		CT fluoroscopy							
Inter-mediate term	Civelek 2012	Extra-articular injection of methylprednisolone 40 mg + lidocaine 1% Fluoroscopy	Radio-frequency denervation (medial branch)	6 mos.	4.4 ± 0.8 (n=50)	2.5 ± 1.5 (n=50)	-4.1 ± 0.48	-5.7 ± 1.08	1.6 (1.27 to 1.93)
	Manchikanti 2010, 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	6 mos.	3.3 ± 0.8 (n=60)	3.6 ± 1.5 (n=60)	-4.6 ± 0.6	-4.6 ± 0.98	0 (-0.29 to 0.29)
	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg and lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	6 mos.	5.3 ± 2.85 (n=31)	5.8 ±3.3 (n=29)	-1.7 ± 1.98	-1 ± 2.28	-0.7 (-1.78 to 0.38)
	Carette 1991	Intra-articular injection of methylprednisolone acetate 20 mg + isotonic saline Fluoroscopy	Intra-articular injection of isotonic saline	6 mos.	4.0 ± 2.5 (n=48)	5.0 ± 2.7 (n=47)	-2.3 ± 1.7	-1.2 ± 1.79	-1.1 (-1.8 to -0.4)
	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg CT fluoroscopy	Intra-articular injection of sodium hyaluronate 10 mg	6 mos.	3.34 ± 2.07 (n=30)	3.80 ± 2.65 (n=30)	-3.53 ± 1.34	-3.12 ± 1.74	-0.41 (-1.2 to 0.38)
	Lakemeier 2013	Intra-articular injection of betamethasone 3 mg + bupivacaine 0.5% + sham denervation Fluoroscopy	Radiofrequency denervation of the medial branch + bupivacaine 0.5%	6 mos.	5.4 ± 2.1 (n=26)	4.7 ± 2.4 (n=26)	-1.6 ± 2.5	-1.9 ± 3	0.3 (-1.2 to 1.8)
Long-term	Civelek 2012	Extra-articular injection of methylprednisolone	Radio-frequency denervation (medial	12 mos.	4.9 ± 0.6 (n=50)	2.6 ± 1.0 (n=50)	-3.6 ± 0.42	-5.6 ± 0.63	2.0 (1.79 to

					Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A	Group B	Group A	Group B	
		40 mg + lidocaine 1% Fluoroscopy	branch)						2.21)
	Manchikanti 2010, 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	24 mos.	3.2 ± 0.9 (n=60)	3.5 ± 1.5 (n=60)	-4.7 ± 0.61	-4.7 ± 0.98	0 (-0.29 to 0.29)
	Manchikanti 2001	Extra-articular injection of methylprednisolone 40 and bupivacaine 0.25% or lidocaine 0.5% + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or lidocaine 0.5% + Sarapin	Post-treat-ment, tim-ing un-clear (up to 30 mos.)	3.3 ± 0.2 (n=42)	3.5 ± 0.3 (n=42)	-4.4 ± 0.13	-4.1 ± 0.23	-0.3 (-0.38 to -0.22)
Improvement in pain on McGill Pain Questionnaire, pain rating index									
Short term	Carette 1991	Intra-articular injection of methylprednisolone acetate 20 mg + isotonic saline Fluoroscopy	Intra-articular injection of isotonic saline	1 mo.	19.0 (n=48)	22.8 (n=48)	NR	NR	-3.8 (-9.4 to 1.9)
Inter-mediate term				6 mos.	17.1 (n=48)	21.6 (n=47)	NR	NR	-4.5 (-9.7 to 0.7)
Improvement in function on ODI									
Short term	Manchikanti 2010 to 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	3 mos.	13.5 ± 5.6 (n=60)	12.7 ± 4.7 (n=60)	-12.4 ± 3.4	-13.9 ± 2.94	1.5 (0.36 to 2.64)
	Fuchs 2005	Intra-articular injection	Intra-articular	1 mo.	12.3 ± 7.5	14.2 ± 10.7	-6.1 ± 4.5	-6.5 ± 6.42	0.4 (-2.41 to

					Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A	Group B	Group A	Group B	
		of triamcinolone acetonide 10 mg CT fluoroscopy	injection of sodium hyaluronate 10 mg		(n=30)	(n=30)			3.21)
Inter-mediate term	Manchikanti 2010, 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	6 mos.	12.2 ± 5.0 (n=60)	12.7 ± 4.7 (n=60)	-13.7 ± 3.16	-13.9 ± 2.94	0.2 (-0.89 to 1.29)
	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg CT fluoroscopy	Intra-articular injection of sodium hyaluronate 10 mg	6 mos.	13.0 ± 7.1 (n=30)	12.6 ± 9.7 (n=30)	-5.4 ± 4.29	-8.1 ± 5.87	2.7 (0.1 to 5.3)
	Lakemeier 2013	Intra-articular injection of betamethasone 3 mg + bupivacaine 0.5% + sham denervation Fluoroscopy	Radiofrequency denervation of the medial branch + bupivacaine 0.5%	6 mos.	33.0 ± 17.4 (n=26)	28.0 ± 20.0 (n=26)	5.7 ± 20.9	12.8 ± 24.8	-7.1 (-19.57 to 5.37)
Long term	Manchikanti 2010, 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	24 mos.	11.0 ± 4.8 (n=60)	12.0 ± 4.9 (n=60)	-14.9 ± 3.1	-14.6 ± 3.02	-0.2 (-0.89 to 1.29)
Improvement in function on NRS (0-10)									
Long term	Manchikanti 2001	Extra-articular injection of methylprednisolone 40 and bupivacaine 0.25% or lidocaine 0.5% + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or lidocaine 0.5% + Sarapin	Post-treat-ment, tim-ing un-clear (up to 30 mos.)	5.7 ± 0.2 (n=42)	5.3 ± 0.2 (n=42)	2 ± 0.13	1.7 ± 0.13	0.3 (0.25 to 0.35)

					Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A	Group B	Group A	Group B	
Improvement in function on RMDQ (0-24)									
Short term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg and lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	3 mos.	10.6 ± 6.68 (n=31)	14.7 ± 6.32 (n=29)	-4.4 ± 4.01	-1.7 ± 3.92	-2.7 (-4.71 to -0.69)
	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg CT fluoroscopy	Intra-articular injection of sodium hyaluronate 10 mg	1 mo.	7.2 ± 5.1 (n=30)	8.4 ± 5.4 (n=30)	-5.3 ± 3.08	-4.1 ± 3.29	-1.2 (-2.81 to 0.41)
Inter-mediate term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg and lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	6 mos.	10.9 ± 7.53 (n=31)	13.4 ± 7.01 (n=29)	5.7 ± 20.9	12.8 ± 24.8	-7.1 (-19.57 to 5.37)
	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg CT fluoroscopy	Intra-articular injection of sodium hyaluronate 10 mg	6 mos.	8.3 ± 4.8 (n=30)	7.1 ± 5.4 (n=30)	-4.2 ± 2.93	-5.4 ± 3.29	1.2 (-0.38 to 2.78)
	Lakemeier 2013	Intra-articular injection of betamethasone 3 mg + bupivacaine 0.5% + sham denervation Fluoroscopy	Radiofrequency denervation of the medial branch + bupivacaine 0.5%	6 mos.	9.0 ± 6.4 (n=26)	9.1 ± 6.0 (n=26)	4.2 ± 7.0	3.7 ± 6.9	
SF-36 physical function									
Short term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and	3 mos.	45† (n=31)	40† (n=29)	13	8	5

					Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A	Group B	Group A	Group B	
			lidocaine						
	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg CT fluoroscopy	Intra-articular injection of sodium hyaluronate 10 mg	1 mo.	55† (n=30)	55† (n=30)	15	16	-1
Inter-mediate term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	6 mos.	45† (n=31)	40† (n=29)	13	8	5
	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg CT fluoroscopy	Intra-articular injection of sodium hyaluronate 10 mg	6 mos.	55† (n=30)	58† (n=30)	15	19	-4
SF-36 Role Physical									
Short term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	3 mos.	49† (n=31)	27† (n=29)	28	16	12
Inter-mediate term				6 mos.	46† (n=31)	27† (n=29)	25	16	9
SF-36 General Health									
Short term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	3 mos.	58† (n=31)	60† (n=29)	0	9	-9

					Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A	Group B	Group A	Group B	
Inter-mediate term				6 mos.	60† (n=31)	56† (n=29)	2	5	-3
SF-36 Bodily Pain									
Short term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	3 mos.	44† (n=31)	36† (n=29)	11	5	6
Inter-mediate term				6 mos.	43† (n=31)	36† (n=29)	10	5	5
SF-36 Vitality									
Short term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	3 mos.	53† (n=31)	53† (n=29)	4	11	-7
Inter-mediate term				6 mos.	55† (n=31)	50† (n=29)	6	8	-2
SF-36 Social functioning									
Short term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	3 mos.	67† (n=31)	57† (n=29)	10	2	12
Inter-mediate				6 mos.	67† (n=31)	53† (n=29)	10	-2	14

					Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A	Group B	Group A	Group B	
term									
SF-36 Mental health									
Short term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	3 mos.	63† (n=31)	67† (n=29)	7	16	-9
Inter-mediate term				6 mos.	65† (n=31)	65† (n=29)	9	14	-5
SF-36 Role emotional									
Short term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	3 mos.	70† (n=31)	53† (n=29)	4	5	-1
Inter-mediate term				6 mos.	72† (n=31)	73† (n=29)	6	25	-19
SF-36 functional limitations									
Short term	Fuchs 2005	Intra-articular injection of triamcinolone acetonide 10 mg CT fluoroscopy	Intra-articular injection of sodium hyaluronate 10 mg	3 mos.	Due to physical: 35† Due to emotional: 60† (n=30)	Due to physical: 33† Due to emotional: 50† (n=30)	Due to physical: 23 Due to emotional: 9	Due to physical: 27 Due to emotional: -1	Due to physical: -4 Due to emotional: 10
Inter-mediate				6 mos.	Due to physical:	Due to physical:	Due to physical:	Due to physical:	Due to physical:

					Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A	Group B	Group A	Group B	
term					36† Due to emotional: 75† (n=30)	43† Due to emotional: 70† (n=30)	24 Due to emotional: 24	37 Due to emotional: 19	-13 Due to emotional: 5
Improvement in QOL on the EQ5D (5-15)									
Short term	Civelek 2012	Extra-articular injection of methylprednisolone 40 mg + lidocaine 1% Fluoroscopy	Radio-frequency denervation (medial branch)	1 mo.	6.0 (n=50)	5.6 (n=50)	-9.0	-8.4	-0.6
Inter-mediate term				6 mos.	7.2 (n=50)	6.5 (n=50)	-7.8	-7.5	-0.3
Long term				12 mos.	8.0 (n=50)	6.7 (n=50)	-7.0	-7.3	0.3
Improvement in QOL on the Sickness Impact Profile (0-100)									
Short term	Carette 1991	Intra-articular injection of methylprednisolone acetate 20 mg + isotonic saline Fluoroscopy	Intra-articular injection of isotonic saline	1 mo.	Overall: 9.3 Physical: 5.2 Psycho-social: 8.2 (n=48)	Overall: 9.8 Physical: 6.3 Psycho-social: 9.0 (n=48)	Overall: -2.1 Physical: 1.0 Psycho-social: -2.5	Overall: -3.6 Physical: -0.6 Psycho-social: -3.3	Overall: 1.5 Physical: 1.6 Psycho-social: 0.8
Inter-mediate term				6 mos.	Overall: 7.8 Physical: 4.3 Psycho-social: 7.7 (n=48)	Overall: 10.8 Physical: 7.9 Psycho-social: 9.0 (n=47)	Overall: -3.6 Physical: 0.1 Psycho-social: -3.0	Overall: -2.6 Physical: 1.0 Psycho-social: -3.3	Overall: -1.0 Physical: -0.9 Psycho-social: 0.3

					Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A	Group B	Group A	Group B	
Patient satisfaction on the NASS (1-4)									
Short term	Civelek 2012	Extra-articular injection of methylprednisolone 40 mg + lidocaine 1% Fluoroscopy	Radio-frequency denervation (medial branch)	1 mo.	1.3 (n=50)	1.3 (n=50)	N/A	N/A	N/A
Inter-mediate term				6 mos.	1.7 (n=50)	1.4 (n=50)	N/A	N/A	N/A
Long term				12 mos.	2.0 (n=50)	1.5 (n=50)	N/A	N/A	N/A
Change in opioid use (morphine equivalents mg/day)									
Long term	Manchikanti 2010, 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	24 mos.	30 ± 27.1 (n=60)	27 ± 23.8 (n=60)	-7 ± 24.8	-4 ± 15.55	-3 (-10.41 to 4.41)

CI: confidence interval; N/A: not applicable; ODI: Oswestry Disability Index; NASS: North American spine Society questionnaire; QOL: quality of life; RMDQ: Roland Morris Diabiliy Questionnaire; SD: standard deviation; SF-36: Short-Form 36; VAS: Visual Analog Scale.
*A negative score favors the intervention and a positive score favors the control with the exception of the SF-36 scores for which a positive score favors the intervention and a negative score favors the control.
†Estimated from graphs in articles.

Table 42. Facet joint pain: Success in pain, function and composite outcome of pain and function, and opioid use and anxiety/depression for intra- and extra-articular steroid injections vs. intra- or extra-articular control injection, extra-articular steroid injection, or radiofrequency denervation.

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Pain success (improvement of ≥50% from baseline in pain on VAS or NRS)							
Short term	Civelek 2012	Extra-articular injection of methylprednisolone 40 mg + lidocaine 1% Fluoroscopy	Radio-frequency denervation (medial branch)	1 mo.	80% (40/50)	100% (50/50)	0.8 (0.7 to 0.92)
	Manchikanti 2010, 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	3 mos.	82% (49/60)	83% (50/60)	0.98 (0.83 to 1.16)
	Manchikanti 2001	Extra-articular injection of methylprednisolone 40 and bupivacaine 0.25% or lidocaine 0.5% + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or lidocaine 0.5% + Sarapin	3 mos.	100% (41/41)	100% (32/32)	1 (1 to 1)
Inter-mediate	Civelek 2012	Extra-articular injection of methylprednisolone 40 mg + lidocaine 1% Fluoroscopy	Radio-frequency denervation (medial branch)	6 mo.	68% (34/50)	90% (45/50)	0.76 (0.61 to 0.93)
	Manchikanti 2010, 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	6 mos.	93% (56/60)	83% (50/60)	1.12 (0.98 to 1.28)
	Manchikanti 2001	Extra-articular injection of methylprednisolone 40 and bupivacaine 0.25% or lidocaine 0.5% + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or lidocaine 0.5% + Sarapin	4-6 mos. 7-12 mos.	88% (36/41) 17% (7/41)	75% (24/32) 25% (8/32)	1.17 (0.93 to 1.47) 0.68 (0.28 to 1.68)
Long-term	Civelek 2012	Extra-articular injection of methylprednisolone 40 mg + lidocaine 1% Fluoroscopy	Radio-frequency denervation (medial branch)	12 mos.	62% (31/50)	88% (44/50)	0.7 (0.55 to 0.9)
	Manchikanti 2010, 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	24 mos.	90% (54/60)	85% (51/60)	1.06 (0.92 to 1.21)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
		Fluoroscopy					
	Manchikanti 2001	Extra-articular injection of methylprednisolone 40 and bupivacaine 0.25% or lidocaine 0.5% + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or lidocaine 0.5% + Sarapin	>12 mos.	5% (2/41)	16% (5/32)	0.31 (0.06 to 1.51)
Function success (≥40% improvement from baseline on ODI)							
Short term	Manchikanti 2010 to 2008	Extra-articular injection of betamethasone + bupivacaine 0.25% or bupivacaine + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or bupivacaine + Sarapin	3 mos.	72% (43/60)	82% (49/60)	0.88 (0.72 to 1.07)
Inter-mediate				6 mos.	78% (47/60)	83% (50/60)	0.94 (0.79 to 1.12)
Long-term				24 mos.	88% (53/60)	87% (52/60)	1.02 (0.89 to 1.17)
QOL success (EQ5D score <9)							
Short term	Civelek 2012	Extra-articular injection of methylprednisolone 40 mg + lidocaine 1% Fluoroscopy	Radio-frequency denervation (medial branch)	1 mos.	77% (46/60)	83% (50/60)	0.92 (0.77 to 1.1)
Inter-mediate				6 mos.	72% (43/60)	62% (37/60)	1.16 (0.9 to 1.5)
Long-term				12 mos.	60% (36/60)	54% (32/60)	1.13 (0.82 to 1.54)
Global Improvement*							
Short term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine Fluoroscopy	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide and lidocaine	3 mos.	77.4% (24/31)	72.4% (21/29)	1.07 (0.8 to 1.43)
	Carette 1991	Intra-articular injection of methylprednisolone acetate 20 mg + isotonic saline Fluoroscopy	Intra-articular injection of isotonic saline	1 mo.	42% (20/48)	33% (16/48)	1.25 (0.74 to 2.11)
Inter-mediate term	Ribeiro 2013	Intra-articular injection of triamcinolone hexacetonide 20 mg + lidocaine	Intramuscular (to paravertebral) injections of 20 mg triamcinolone hexacetonide	6 mos.	77.4% (24/31)	69.0% (20/29)	1.12 (0.82 to 1.53)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
		Fluoroscopy	and lidocaine				
	Carette 1991	Intra-articular injection of methylprednisolone acetate 20 mg + isotonic saline Fluoroscopy	Intra-articular injection of isotonic saline	6 mos.	46% (22/48)	15% (7/47)	3.08 (1.45 to 6.51)
Patient satisfaction success (NASS score 1 or 2)							
Short term	Civelek 2012	Extra-articular injection of methylprednisolone 40 mg + lidocaine 1% Fluoroscopy	Radio-frequency denervation (medial branch)	1 mos.	88% (44/50)	100% (50/50)	0.88 (0.79 to 0.97)
Inter-mediate				6 mos.	75% (38/50)	90% (45/50)	0.84 (0.7 to 1.01)
Long-term				12 mos.	66% (33/50)	88% (44/50)	0.75 (0.6 to 0.94)
Opioid use (use of schedule II opioids)							
Long-term	Manchikanti 2001	Extra-articular injection of methylprednisolone 40 and bupivacaine 0.25% or lidocaine 0.5% + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or lidocaine 0.5% + Sarapin	Post-treat-ment, timing unclear (up to 30 mos.)	15% (6/41)	19% (6/32)	0.78 (0.28 to 2.19)
Opioid use (change in narcotic use)†							
Long-term	Manchikanti 2001	Extra-articular injection of methylprednisolone 40 and bupivacaine 0.25% or lidocaine 0.5% + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or lidocaine 0.5% + Sarapin	Post-treat-ment, timing unclear (up to 30 mos.)	None: 19% (8/41) Mild: 32% (13/41) Moderate: 34% (14/41) Heavy: 15% (6/41)	None: 25% (8/32) Mild: 22% (7/32) Moderate: 34% (11/32) Heavy: 19% (6/32)	None: 0.78 (0.33 to 1.85) Mild: 1.45 (0.66 to 3.21) Moderate: 0.99 (0.52 to 1.88) Heavy: 0.78 (0.28 to 2.19)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Time-point	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Generalized Anxiety Disorder – MCMI-II							
Long-term	Manchikanti 2001	Extra-articular injection of methylprednisolone 40 and bupivacaine 0.25% or lidocaine 0.5% + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or lidocaine 0.5% + Sarapin	Post-treat-ment, timing unclear (up to 30 mos.)	61% (25/41)	63% (20/32)	0.98 (0.68 to 1.40)
Depression – BDI							
Long-term	Manchikanti 2001	Extra-articular injection of methylprednisolone 40 and bupivacaine 0.25% or lidocaine 0.5% + Sarapin Fluoroscopy	Extra-articular injection of bupivacaine 0.25% or lidocaine 0.5% + Sarapin	Post-treat-ment, timing unclear (up to 30 mos.)	58% (24/41)	72% (23/32)	0.81 (0.58 to 1.14)

BDI: Beck Depression Inventory; CI: confidence interval; EQ5D: European Quality of Life 5 Dimensions; MCMI-II: Millon Clinical Multiaxial Inventory II; ODI: Oswestry Disability Index; NASS: North American spine Society questionnaire; SD: standard deviation; VAS: Visual Analog Scale.

*For Ribeiro 2013, global improvement was defined as the percentage of patients self-rated as "better" or "much better"; for Carette 1991, global improvement was defined as the percentage of patients self-rated as having "very marked" or "marked" improvement.

† Narcotic intake classified as follows: "intake of class IV narcotics… up to a maximum of four times to or hydrocodone twice or less per day to 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 et al. 2010, 2008: (1) 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; (2) Evaluation of lumbar facet joint nerve blocks in managing chronic low back pain: a randomized, double-blind, controlled trial with a 2-year follow-up. Int J Med Sci 2010;7:124-35.

Machikanti et al. 2001: Effectiveness of lumbar facet joint nerve blocks in chronic low back pain: a randomized clinical trial. Pain Physician 2001;4:101-17.

Table 43. Sacroiliac joint pain: Improvement in pain, function, and quality of life for intra- or extra-articular steroid injection vs. extra-articular control injection or conservative treatment.

						Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
Pain improvement on VAS (0-10)										
Short term	Luukkainen 2002	Extra-articular; Methylprednisolone 60 mg + lidocaine 20 mg	lidocaine 20 mg	Peri-articular	1 mo.	NR (n=13)	NR (n=11)	median -4.0 (range, -5.7 to -1.0)	median -1.3 (range, -6.4 to 4.3)	-2.7 (NC); p=0.046
	Visser 2013	Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	3 mos.	5.0 ± 1.9 (n=18)	3.9 ± 1.4 (n=15)	-0.7 ± 1.15	-0.4 ± 0.84	-0.3 (-0.98 to 0.38)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	5.0 ± 1.9 (n=18)	3.3 ± 2.3 (n=18)	-0.7 ± 1.15	-1.9 ± 1.45	1.2 (0.34 to 2.06)
RAND-36 physical function										
Short term	Visser 2013	Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	3 mos.	37.9 ± 15.4 (n=18)	51.25 ± 28.7 (n=15)	-7.4 ± 10.27	23.75 ± 23.82	-31.15 (-44.11 to -18.19)
		Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	37.9 ± 15.4 (n=18)	60.5 ± 24.3 (n=18)	-7.4 ± 10.27	30.5 ± 14.6	-37.9 (-46.15 to -29.65)
RAND-36 social functioning										
Short term	Visser 2013	Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	3 mos.	55.8 ± 25.3 (n=18)	47.0 ± 21.3 (n=15)	7.8 ± 15.71	6.2 ± 12.91	1.6 (-8.17 to 11.37)
		Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	55.8 ± 25.3 (n=18)	70.2 ± 28.5 (n=18)	7.8 ± 15.71	29.9 ± 17.12	-22.1 (-32.84 to -11.36)
RAND-36 role limitations (physical)										
Short term	Visser 2013	Intra-articular; Kenacort 20 mg and	Physiotherapy	Intra-articular	3 mos.	25.0 ± 42.5 (n=18)	25.0 ± 20.4 (n=15)	10 ± 27.32	12.5 ±	-2.5 (-17.23 to

						Pain score Mean ± SD		Δ from baseline		Mean difference A vs. B* (95% CI)
	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Group A	Group B	Group A	Group B	
		lidocaine 30 mg							15.01	12.23)
		Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	25.0 ± 42.5 (n=18)	45.0 ± 49.7 (n=18)	10 ± 27.32	42.5 ± 43.57	-32.5 (-56.26 to -8.74)
RAND-36 Role limitations (emotional)										
Short term	Visser 2013	Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	3 mos.	60.0 ± 51.6 (n=18)	58.3 ± 50.1 (n=15)	6.7 ± 32.22	-25 ± 30.77	31.7 (10.16 to 53.24)
		Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	60.0 ± 51.6 (n=18)	63.0 ± 48.4 (n=18)	6.7 ± 32.22	44.4 ± 29.06	-37.7 (-57.74 to -17.66)
RAND-36 Mental health										
Short term	Visser 2013	Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	3 mos.	65.2 ± 23.7 (n=18)	69.0 ± 22.9 (n=15)	2.0 ± 15.15	4.0 ± 14.1	-2.0 (-12 to 8.0)
		Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	65.2 ± 23.7 (n=18)	73.3 ± 17.6 (n=18)	2.0 ± 15.15	22.6 ± 12.57	-20.6 (-29.7 to -11.5)
RAND-36 Vitality										
Short term	Visser 2013	Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	3 mos.	49.5 ± 17.7 (n=18)	61.3 ± 15.5 (n=15)	6.0 ± 12.63	6.3 ± 11.18	-0.3 (-8.43 to 7.83)
		Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	49.5 ± 17.7 (n=18)	55.8 ± 18.5 (n=18)	6.0 ± 12.63	22.5 ± 11.45	-16.5 (-24.38 to -8.62)
RAND-36 Pain										
Short term	Visser 2013	Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	3 mos.	43.8 ± 20.6 (n=18)	44.5 ± 9.0 (n=15)	11.3 ± 12.63	17 ± 9.49	-5.7 (-13.25 to 1.85)

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Pain score Mean ± SD Group A	Pain score Mean ± SD Group B	Δ from baseline Group A	Δ from baseline Group B	Mean difference A vs. B* (95% CI)
		Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	43.8 ± 20.6 (n=18)	57.0 ± 23.7 (n=18)	11.3 ± 12.63	33.3 ± 14.5	-22 (-30.88 to -13.12)
RAND-36 Health perception										
Short term	Visser 2013	Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	3 mos.	57.3 ± 17.8 (n=18)	51.3 ± 14.9 (n=15)	6 ± 13.81	2.5 ± 17.19	3.5 (-7.29 to 14.29)
		Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	57.3 ± 17.8 (n=18)	59.5 ± 26.2 (n=18)	6 ± 13.81	0.5 ± 15.77	5.5 (-4.19 to 15.19)
RAND-36 Health change										
Short term	Visser 2013	Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	3 mos.	45.5 ± 21.8 (n=18)	56.3 ± 31.5 (n=15)	4.6 ± 13.95	6.3 ± 19.5	-1.7 (-13.49 to 10.09)
		Intra-articular; Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	57.3 ± 17.8 (n=18)	44.4 ± 27.3 (n=18)	16.4 ± 10.81	16.6 ± 17	-0.2 (-9.51 to 9.11)

CI: confidence interval; VA: visual analog scale.

*For the VAS, a negative score favors the intervention and a positive score favors the control; for the RAND-36, a positive score favors the intervention and a negative score favors the control.

Table 44. Sacroiliac Joint Pain: Success in pain and overall success for intra-articular steroid injection vs. conservative care

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Outcome definition	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
Pain success									
Short term	Visser 2013	Kenacort 20 mg and lidocaine 30 mg	Physiotherapy	Intra-articular	3 mos.	Improvement of ≥2 points on VAS	28% (5/18)	20% (3/15)	1.39 (0.40 to 4.89)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	Improvement of ≥2 points on VAS	28% (5/18)	56% (10/18)	0.50 (0.21 to 1.17)
Overall treatment success									
Short	Visser 2013	Kenacort 20 mg and	Physiotherapy	Intra-	3 mos.	Complete relief of	50% (9/18)	20% (3/15)	2.5 (0.82 to

	Author (year)	Intervention (A) Steroid used Imaging guidance	Comparator (B) Substance used	Approach	Time-point	Outcome definition	Group A % (n/N)	Group B % (n/N)	Risk Ratio (95% CI)
term		lidocaine 30 mg		articular		complaints at 6 weeks or 3 months, or 3 month average VAS pain score < baseline VAS score			7.61)
		Kenacort 20 mg and lidocaine 30 mg	Manual therapy	Intra-articular	3 mos.	Complete relief of complaints at 6 weeks or 3 months, or 3 month average VAS pain score < baseline VAS score	50% (9/18)	72% (13/18)	0.69 (0.40 to 1.19)

CI: confidence interval; VAS: visual analog scale.

Table 45. Interlaminar ESI* (± conservative care) versus conservative care* for cervical radiculopathy based on imaging: NRS arm pain scores

		NRS (0-10) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI vs. ΔCC	
Author (year)	Time point	ESI	CC	ΔESI	ΔCC	Mean Difference (95% CI)†	p-value†
Cohen 2014	3 months	3.0 ± 0.6 (n = 49)	3.3 ± 0.5 (n = 56)	-3.2 ± 1.3	-2.8 ± 1.8	-0.4 (-1.0 to 0.2)	0.200
	6 months	2.4 ± 0.5 (n = 49)	1.2 ± 0.5 (n = 55)	-3.8 ± 1.3	-4.9 ± 1.8	1.1 (0.5 to 1.7)	0.001
		NRS (0-10) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI+CC vs. ΔCC	
Author (year)	Time point	ESI + CC	CC	ΔESI+CC	ΔCC	Mean Difference (95% CI)†	p-value†
Cohen 2014	3 months	2.3 ± 0.5 (n = 51)	3.3 ± 0.5 (n = 56)	-4.1 ± 1.5	-2.8 ± 1.8	-1.3 (-1.9 to -0.7)	<0.001
	6 months	2.0 ± 0.4 (n = 50)	1.2 ± 0.5 (n = 55)	-4.4 ± 1.6	-4.9 ± 1.8	0.5 (-0.2 to 1.2)	0.137

CC: conservative care; CI: confidence interval; ESI: epidural steroid injection; NRS: numerical rating scale; SD: standard deviation.
*Treatment details: ESI injectate: depo-methylprednisolone 60 mg + saline (3 ml total); ESI=ESI alone (continuation of medical therapy was permitted); CC: conservative care consisting of pain medication, muscle relaxants, and physical therapy; ESI + CC= ESI + conservative care; no additional co-interventions were given
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 46. Interlaminar ESI* (± conservative care) versus conservative care* for cervical radiculopathy based on imaging: NRS neck pain scores

		NRS (0-10) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI vs. ΔCC	
Author (year)	Time point	ESI	CC	ΔESI	ΔCC	Mean Difference (95% CI)†	p-value†
Cohen 2014	3 months	3.0 ± 0.5 (n = 49)	4.0 ± 0.5 (n = 56)	-2.8 ± 1.9	-1.9 ± 1.7	-0.9 (-1.6 to -0.2)	0.012
	6 months	3.3 ± 0.5 (n = 47)	1.8 ± 0.6 (n = 55)	-2.5 ± 1.9	-4.1 ± 1.7	1.6 (0.9 to 2.3)	<0.001
		NRS (0-10) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI+CC vs. ΔCC	
Author (year)	Time point	ESI + CC	CC	ΔESI+CC	ΔCC	Mean Difference (95% CI)†	p-value†
Cohen 2014	3 months	2.8 ± 0.5 (n = 51)	4.0 ± 0.5 (n = 56)	-2.8 ± 2.0	-1.9 ± 1.7	-0.9 (-1.6 to -0.2)	0.013
	6 months	2.8 ± 0.4 (n = 50)	1.8 ± 0.6 (n = 55)	-2.8 ± 2.1	-4.1 ± 1.7	1.3 (0.6 to 2.0)	0.001

CC: conservative care; CI: confidence interval; ESI: epidural steroid injection; NRS: numerical rating scale; SD: standard deviation.

*Treatment details: ESI injectate: depo-methylprednisolone 60 mg + saline (3 ml total); ESI=ESI alone (continuation of medical therapy was permitted); CC: conservative care consisting of pain medication, muscle relaxants, and physical therapy; ESI + CC= ESI + conservative care; no additional co-interventions were given

†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 47. Interlaminar ESI* (± conservative care) versus conservative care* for cervical radiculopathy based on imaging: NDI scores

		NDI (0-100) scores (mean ± SD)		ESI+ CC vs. CC	
Author (year)	**Time point**	**ESI**	**CC**	**Mean Difference (95% CI)†‡**	**p-value†**
Cohen 2014	**3 months**	15.8 ± 2.9 (n = 49)	14.1 ± 2.7 (n = 56)	1.7 (0.6 to 2.8)	0.002
	6 months	11.0 ± 2.4 (n = 49)	5.4 ± 2.4 (n = 55)	5.6 (4.7 to 6.5)	<0.001
		NDI (0-100) scores (mean ± SD)		**ESI+ CC vs. CC**	
Author (year)	**Time point**	**ESI + CC**	**CC**	**Mean Difference (95% CI)†‡**	**p-value†**
Cohen 2014	**3 months**	18.1 ± 3.0 (n = 51)	14.1 ± 2.7 (n = 56)	4.0 (2.9 to 5.1)	<0.001
	6 months	15.0 ± 2.5 (n = 50)	5.4 ± 2.4 (n = 55)	9.6 (8.7 to 10.5)	<0.001

CC: conservative care; CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index; SD: standard deviation.
*Treatment details: ESI injectate: depo-methylprednisolone 60 mg + saline (3 ml total); ESI=ESI alone (continuation of medical therapy was permitted); CC: conservative care consisting of pain medication, muscle relaxants, and physical therapy; ESI + CC= ESI + conservative care; no additional co-interventions were given
†calculated values (MD calculated as intervention minus control)
‡Change from baseline scores could not be calculated, as baseline scores were reported as median (IQR) while follow-up scores were reported as mean ± SD. Baseline scores for NDI (median (IQR) for ESI vs. CC were 38.0 (30.0 to 50.0) (n = 55) vs. 34.0 (28.0 to 52.0) (n = 59), while those for ESI + CC vs. CC were 38.0 (28.0 to 48.0) (n = 55) vs. 34.0 (28.0 to 52.0) (n = 59).

Table 48. Interlaminar ESI* versus interlaminar control injection* for chronic cervical disc herniation with or without radiculopathy: Secondary outcomes

Outcome	Time point	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Positive GPE‡	**1 month**	61% (33/54)	60% (35/58)	1.01 (0.75 to 1.36)	0.934
Positive Categorical Outcome§	**1 month**	54% (29/54)	52% (30/58)	1.04 (0.73 to 1.47)	0.835
Positive outcome**	**3 months**	37% (18/49)	27% (15/56)	1.37 (0.78 to 2.42)	0.276
	6 months	26% (12/47)	24% (13/55)	1.08 (0.55 to 2.13)	0.825
Medication reduction	**1 month**	35% (15/43)	36% (16/45)	0.98 (0.56 to 1.73)	0.948
Surgery	**12 months**	6% (3/55)	7% (4/59)	0.80 (0.19 to 3.43)	0.769
Outcome	**Time point**	**ESI + CC % (n/N)**	**Control injection % (n/N)**	**Risk Ratio (95% CI)†**	**p-value†**
Positive GPE‡	**1 month**	73% (37/51)	60% (35/58)	1.20 (0.92 to 1.57)	0.181
Positive Categorical Outcome§	**1 month**	65% (33/51)	52% (30/58)	1.25 (0.91 to 1.72)	0.173
Positive outcome**	**3 months**	57% (29/51)	27% (15/56)	2.12 (1.29 to 3.48)	0.002
	6 months	44% (22/50)	24% (13/55)	1.86 (1.05 to 3.29)	0.028
Medication reduction	**1 month**	55% (23/42)	36% (16/45)	1.54 (0.95 to 2.49)	0.074
Surgery	**12 months**	6% (3/55)	7% (4/59)	0.80 (0.19 to 3.43)	0.769

CC: conservative care; CI: confidence interval; ESI: epidural steroid injection; GPE: global perceived effect; SD: standard deviation.
*Treatment details: ESI injectate: depo-methylprednisolone 60 mg + saline (3 ml total); ESI=ESI alone (continuation of medical therapy was permitted); CC: conservative care consisting of pain medication, muscle relaxants, and physical therapy; ESI + CC= ESI + conservative care; no additional co-interventions were given
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)
‡Positive GPE: pain improved since previous visit, satisfied with treatment, and would recommend the treatment to others.
§ Positive categorical outcome: positive GPE and ≥50% decrease in NRS arm pain score
**Positive outcome: Positive GPE, ≥2-point decrease in NRS arm pain score, without additional procedural interventions
††Medication reduction: ≥20% reduction in opioid use or cessation of non-opioid analgesics

Table 49. ESI* versus control injection (intramuscular steroid + local anesthetic injection)* for chronic cervicobrachialgia with or without radiculopathy and/or stenosis: improvement in VAS pain from baseline

Author (year)	Time point	% VAS pain improvement from baseline	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Stav (1993)	**12 months**	≥50%	68% (17/25)	12% (2/17)	5.78 (1.53 to 21.84)	0.0004
		≥75%	56% (14/25)	6% (1/17)	9.52 (1.38 to 65.78)	0.0010
		50-74%	12% (3/25)	6% (1/17)	2.04 (0.23 to 18.00)	0.513
		31-49%	20% (5/25)	18% (3/17)	1.13 (0.31 to 4.13)	0.851
		0-30%	4% (1/25)	59% (10/17)	0.07 (0.01 to 0.48)	0.0001
		≤0%	8% (2/25)	12% (2/17)	0.68 (0.11 to 4.37)	0.687

CI: confidence interval; ESI: epidural steroid injection; NEI: non-epidural steroid injection; VAS: visual analog scale.
*Treatment details; injectate in both groups: 80 mg methylprednisolone + 1% lidocaine; co-interventions available to both groups (continuation of medication)
†calculated values (intervention versus control)
‡ Authors report p-value to be statistically significant (p=0.0377); it is unclear what accounts for the discrepancy between the reported and calculated p-values.

Table 50. Interlaminar ESI* versus interlaminar control injection* for chronic cervical disc herniation with or without radiculopathy: ≥50% improvement in NRS pain scores from baseline

		≥50% NRS pain improvement		ΔESI vs. ΔControl	
Author (year)	Time point	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Manchikanti (2013)	**3 months**	75% (45/60)	85% (51/60)	0.88 (0.74 to 1.06)	0.173
	6 months	73% (44/60)	83% (50/60)	0.88 (0.73 to 1.06)	0.186
	24 months	68% (41/60)	72% (43/60)	0.95 (0.75 to 1.21)	0.692

CI: confidence interval; ESI: epidural steroid injection; NRS: numerical rating scale.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (RR = intervention/control); co-interventions received by both groups (exercise and medication)

Table 51. Interlaminar ESI* versus interlaminar control injection* for chronic cervical disc herniation with or without radiculopathy: NRS pain scores

		NRS (0-10) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI vs. ΔControl injection	
Author (year)	Time point	ESI	Control	ΔESI	ΔControl	Mean Difference (95% CI)†	p-value†
Manchikanti (2013)	**3 months**	3.8 ± 1.4 (n = 60)	3.7 ± 1.4 (n = 60)	-4.1 ± 0.9	-4.2 ± 0.8	0.1 (-0.2 to 0.4)	0.521
	6 months	3.9 ± 1.5 (n = 60)	3.5 ± 1.4 (n = 60)	-4.0 ± 0.9	-4.4 ± 0.8	0.4 (0.1 to 0.7)	0.011
	24 months	3.8 ± 1.7 (n = 60)	3.8 ± 1.6 (n = 60)	-4.1 ± 1.1	-4.1 ± 1.0	0.0 (-0.4 to 0.4)	1.000

CI: confidence interval; ESI: epidural steroid injection; NRS: numerical rating scale; SD: standard deviation.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 52. Interlaminar ESI* versus interlaminar control injection* for chronic cervical disc herniation with or without radiculopathy: ≥50% improvement in NDI scores from baseline

		≥50% NDI improvement			
Author (year)	Time point	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Manchikanti (2013)	**3 months**	70% (42/60)	85% (51/60)	0.82 (0.68 to 1.00)	0.050
	6 months	73% (44/60)	83% (50/60)	0.88 (0.73 to 1.06)	0.186
	24 months	70% (42/60)	73% (44/60)	0.95 (0.76 to 1.20)	0.687

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (RR = intervention/control)

Table 53. Interlaminar ESI* versus interlaminar control injecton* for chronic cervical disc herniation with or without radiculopathy: NDI scores

		NDI (0-100) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI vs. ΔControl injection	
	Time point	ESI	Control	ΔESI	ΔControl	Mean Difference (95% CI)†	p-value†
Manchikanti (2013)	**3 months**	15.6 ± 6.3 (n = 60)	14.7 ± 5.5 (n = 60)	-13.6 ± 3.9	-14.9 ± 3.4	1.3 (-0.02 to 2.6)	0.054
	6 months	15.3 ± 7.0 (n = 60)	13.8 ± 5.4 (n = 60)	-13.9 ± 4.2	-15.8 ± 3.4	1.9 (0.5 to 3.3)	0.007
	24 months	14.3 ± 6.9 (n = 60)	13.7 ± 5.7 (n = 60)	-14.9 ± 4.2	-15.9 ± 3.5	1.0 (-0.4 to 2.5)	0.159

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index; SD: standard deviation.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol).

Table 54. Interlaminar ESI* versus control injection* for chronic cervical disc herniation with or without radiculopathy: ≥50% improvement in both NRS pain and NDI scores from baseline

		≥50% NRS and NDI improvement			
Author (year)	Time point	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Manchikanti (2013)	**3 months**	NR	NR	NR	NR
	6 months	73% (44/60)	82% (49/60)	0.90 (0.74 to 1.09)	0.276
	24 months	68% (48/60)	72% (43/60)	1.12 (0.91 to 1.37)	0.288

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index; NRS: numerical rating scale.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (RR = intervention/control)

Table 55. Interlaminar ESI* versus control injection* for chronic nonradicular neck pain: ≥50% improvement in NRS pain scores from baseline

≥50% NRS pain improvement					
Author (year)	Time point	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Manchikanti (2014)	**3 months**	85% (51/60)	73% (44/60)	1.16 (0.96 to 1.40)	0.117
	6 months	77% (46/60)	78% (47/60)	0.98 (0.81 to 1.19)	0.828
	24 months	75% (45/60)	75% (45/60)	1.00 (0.81 to 1.23)	1.00

CI: confidence interval; ESI: epidural steroid injection; NRS: numerical rating scale
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions received by both groups (structured exercise program and medication)
†calculated values (RR = intervention/control)

Table 56. Interlaminar ESI* versus control injection* for chronic nonradicular neck pain: NRS pain scores

		NRS (0-10) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI vs. ΔControl injection	
Author (year)	Time point	ESI	Control	ΔESI	ΔControl	Mean Difference (95% CI)†	p-value†
Manchikanti (2014)	**3 months**	3.3 ± 1.0 (n=60)	3.7 ± 1.4 (n=60)	-4.3 ± 0.6	-4.2 ± 0.9	-0.1 (-0.4 to 0.2)	0.475
	6 months	3.5 ± 1.3 (n=60)	3.6 ± 1.4 (n=60)	-4.1 ± 0.8	-4.3 ± 0.9	0.2 (-0.1 to 0.5)	0.201
	24 months	3.5 ± 1.4 (n=60)	3.7 ± 1.6 (n=60)	-4.1 ± 0.9	-4.2 ± 1.0	0.1 (-0.2 to 0.4)	0.566

CI: confidence interval; ESI: epidural steroid injection; NRS: numerical rating scale; SD: standard deviation.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions received by both groups (structured exercise program and medication)
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 57. Interlaminar ESI* versus interlaminar control injection* for chronic nonradicular neck pain: ≥50% improvement in NDI scores from baseline

		≥50% NDI improvement			
Author (year)	Time point	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Manchikanti (2014)	**3 months**	78% (47/60)	70% (42/60)	1.12 (0.90 to 1.38)	0.299
	6 months	73% (44/60)	68% (41/60)	1.07 (0.85 to 1.35)	0.549
	24 months	70% (42/60)	75% (45/60)	0.93 (0.75 to 1.16)	0.541

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index.

*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions received by both groups (structured exercise program and medication)

†calculated values (RR = intervention/control)

Table 58. Interlaminar ESI* versus interlaminar control injection* for chronic nonradicular neck pain: NDI scores

		NDI (0-100) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI vs. ΔControl injection	
Author (year)	Time point	ESI	Control	ΔESI	ΔControl	Mean Difference (95% CI)†	p-value†
Manchikanti (2014)	**3 months**	13.7 ± 5.4 (n=60)	15.5 ± 6.0 (n=60)	-14.9 ± 4.3	-14.7 ± 3.6	-0.2 (-1.6 to 1.2)	0.783
	6 months	14.2 ± 6.1 (n=60)	15.0 ± 5.6 (n=60)	-14.4 ± 4.3	-15.2 ± 3.4	0.8 (-0.6 to 2.2)	0.261
	24 months	13.8 ± 6.5 (n=60)	14.1 ± 5.7 (n=60)	-14.8 ± 4.4	-16.1 ± 3.4	1.3 (-0.1 to 2.7)	0.073

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index; SD: standard deviation.

*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions received by both groups (structured exercise program and medication)

†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 59. Interlaminar ESI* versus interlaminar control injection* for chronic nonradicular neck pain: ≥50% improvement in both NRS pain and NDI scores from baseline

≥50% NDI improvement					
Author (year)	**Time point**	**ESI % (n/N)**	**Control injection % (n/N)**	**Risk Ratio (95% CI)†**	**p-value†**
Manchikanti (2014)	**3 months**	78% (47/60)	70% (42/60)	1.12 (0.90 to 1.38)	0.299
	6 months	73% (44/60)	68% (41/60)	1.07 (0.85 to 1.35)	0.549
	24 months	70% (42/60)	75% (45/60)	0.93 (0.75 to 1.16)	0.541

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index;
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions received by both groups (structured exercise program and medication)
†calculated values (RR = intervention/control)

Table 60. Interlaminar ESI* versus interlaminar control injection* for chronic spinal stenosis neck pain: ≥50% improvement in NRS pain scores from baseline

≥50% NRS pain improvement					
Author (year)	**Time point**	**ESI % (n/N)**	**Control injection % (n/N)**	**Risk Ratio (95% CI)†**	**p-value†**
Manchikanti (2012)	3 months	87% (26/30)	87% (26/30)	1.00 (0.82 to 1.22)	1.000
	6 months	80% (24/30)	90% (27/30)	0.89 (0.72 to 1.10)	0.282
	12 months	70% (21/30)	73% (22/30)	0.95 (0.69 to 1.31)	0.776

CI: confidence interval; ESI: epidural steroid injection; NRS: numerical rating scale.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (RR = intervention/control)

Table 61. Interlaminar ESI* versus interlaminar control injection* for chronic spinal stenosis neck pain: NRS pain scores

		NRS (0-10) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI vs. ΔControl injection	
Author (year)	Time point	ESI	Control	ΔESI	ΔControl	Mean Difference (95% CI)†	p-value†
Manchikanti (2012)	3 months	3.5 ± 0.9 (n = 30)	3.7 ± 1.2 (n = 30)	-4.5 ± 0.6	-4.2 ± 0.7	-0.3 (-0.6 to 0.04)	0.080
	6 months	3.7 ± 1.0 (n = 30)	3.4 ± 0.9 (n = 30)	-4.3 ± 0.6	-4.5 ± 0.6	0.2 (-0.1 to 0.5)	0.202
	12 months	3.8 ± 1.2 (n = 30)	3.6 ± 1.1 (n = 30)	-4.2 ± 0.7	-4.3 ± 0.7	0.1 (-0.3 to 0.5)	0.582

CI: confidence interval; ESI: epidural steroid injection; NRS: numerical rating scale; SD: standard deviation.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 62. Interlaminar ESI* versus interlaminar control injection* for chronic spinal stenosis neck pain: ≥50% improvement in NDI scores from baseline

		≥50% NDI improvement		ΔESI vs. ΔControl injection	
Author (year)	Time point	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Manchikanti (2012)	**3 months**	87% (26/30)	77% (23/30)	1.13 (0.89 to 1.44)	0.321
	6 months	83% (25/30)	87% (26/30)	0.96 (0.78 to 1.19)	0.720
	12 months	70% (21/30)	77% (23/30)	0.91 (0.67 to 1.24)	0.563

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (RR = intervention/control)

Table 63. Interlaminar ESI* versus interlaminar control injection* for chronic spinal stenosis neck pain: NDI scores

		NDI (0-100) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI vs. ΔControl injection	
Author (year)	Time point	ESI	Control	ΔESI	ΔControl	Mean Difference (95% CI)†	p-value†
Manchikanti (2012)	**3 months**	13.6 ± 3.8 (n = 30)	15.1 ± 5.8 (n = 30)	-15.6 ± 3.6	-14.1 ± 3.5	-1.5 (-3.3 to 0.3)	0.107
	6 months	13.5 ± 4.6 (n = 30)	13.2 ± 4.8 (n = 30)	-15.7 ± 3.5	-16.0 ± 3.2	0.3 (-1.4 to 2.0)	0.730
	12 months	13.9 ± 4.5 (n = 30)	13.2 ± 5.4 (n = 30)	-15.3 ± 3.5	-16.0 ± 3.4	0.7 (-1.1 to 2.5)	0.435

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index; SD: standard deviation.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 64. Interlaminar ESI* versus interlaminar control injection* for chronic spinal stenosis neck pain: ≥50% improvement in both NRS pain and NDI scores from baseline

		≥50% NDI improvement			
Author (year)	Time point	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Manchikanti (2012)	**3 months**	87% (26/30)	77% (23/30)	1.13 (0.89 to 1.44)	0.321
	6 months	80% (24/30)	87% (26/30)	0.92 (0.74 to 1.16)	0.492
	12 months	70% (21/30)	73% (22/30)	0.95 (0.69 to 1.31)	0.776

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (RR = intervention/control)

Table 65. Interlaminar ESI* versus interlaminar control injection* for failed cervical surgery syndrome: ≥50% improvement in NRS pain scores from baseline

		≥50% NRS pain improvement			
Author (year)	Time point	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Manchikanti (2012)	**3 months**	71% (20/28)	79% (22/28)	0.91 (0.67 to 1.23)	0.541
	6 months	75% (21/28)	71% (20/28)	1.05 (0.76 to 1.44)	0.765
	12 months	68% (19/28)	71% (20/28)	0.95 (0.67 to 1.34)	0.773

CI: confidence interval; ESI: epidural steroid injection; NRS: numerical rating scale.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (RR = intervention/control)

Table 66. Interlaminar ESI* versus interlaminar control injection* for failed cervical surgery syndrome: NRS pain scores

		NRS (0-10) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI vs. ΔControl injection	
Author (year)	Time point	ESI	Control	ΔESI	ΔControl	Mean Difference (95% CI)†	p-value†
Manchikanti (2012)	**3 months**	4.0 ± 1.2 (n = 28)	3.7 ± 1.2 (n = 28)	-3.8 ± 0.7	-4.3 ± 0.8	0.5 (0.1 to 0.9)	0.016
	6 months	3.8 ± 1.1 (n = 28)	3.7 ± 1.1 (n = 28)	-4.0 ± 0.7	-4.3 ± 0.7	0.3 (-0.1 to 0.7)	0.115
	12 months	3.9 ± 1.4 (n = 28)	3.6 ± 1.1 (n = 28)	-3.9 ± 0.9	-4.3 ± 0.7	0.4 (-0.03 to 0.8)	0.069

CI: confidence interval; ESI: epidural steroid injection; NRS: numerical rating scale; SD: standard deviation.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 67. Interlaminar ESI* versus interlaminar control injection* for failed cervical surgery syndrome: ≥50% improvement in NDI scores from baseline

		≥50% NDI improvement			
Author (year)	Time point	ESI % (n/N)	Control injection % (n/N)	Risk Ratio (95% CI)†	p-value†
Manchikanti (2012)	**3 months**	75% (21/28)	71% (20/28)	1.05 (0.76 to 1.44)	0.765
	6 months	75% (21/28)	68% (19/28)	1.11 (0.79 to 1.54)	0.558
	12 months	64% (18/28)	71% (20/28)	0.90 (0.63 to 1.29)	0.571

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index; SD: standard deviation.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (RR = intervention/control)

Table 68. Interlaminar ESI* versus interlaminar control injection* for failed cervical surgery syndrome: NDI scores

		NDI (0-100) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔESI vs. ΔControl injection	
Author (year)	Time point	ESI	Control	ΔESI	ΔControl	Mean Difference (95% CI)†	p-value†
Manchikanti (2012)	**3 months**	14.8 ± 5.7 (n = 28)	15.9 ± 5.3 (n = 28)	-14.0 ± 3.5	-14.1 ± 3.3	0.1 (-1.7 to 1.9)	0.913
	6 months	14.6 ± 5.8 (n = 28)	15.3 ± 5.0 (n = 28)	-14.2 ± 3.5	-14.7 ± 3.2	0.5 (-1.3 to 2.3)	0.579
	12 months	15.0 ± 5.6 (n = 28)	15.0 ± 4.7 (n = 28)	-13.8 ± 3.4	-15.0 ± 3.1	1.2 (-0.5 to 2.9)	0.173

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index; SD: standard deviation.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 69. Interlaminar ESI* versus interlaminar control injection* for failed cervical surgery syndrome: ≥50% improvement in both NRS pain and NDI scores from baseline

≥50% NDI improvement					
Author (year)	**Time point**	**ESI % (n/N)**	**Control injection % (n/N)**	**Risk Ratio (95% CI)†**	**p-value†**
Manchikanti (2012)	**3 months**	68% (19/28)	68% (19/28)	1.00 (0.70 to 1.43)	1.000
	6 months	71% (20/28)	64% (18/28)	1.11 (0.77 to 1.60)	0.571
	12 months	64% (18/28)	71% (20/28)	0.90 (0.63 to 1.29)	0.571

CI: confidence interval; ESI: epidural steroid injection; NDI: neck disability index.
*Treatment details: ESI injectate: "non-particulate" betamethasone 6 mg + 0.5% lidocaine; ENSI injectate: 0.5% lidocaine; co-interventions available to both groups (continuation of exercise and medication)
†calculated values (RR = intervention/control)

Table 70. Intra-articular (medial branch) steroid injection* versus non-steroidal intra-articular (medial branch) injection* for facet joint pain: ≥50% improvement in NRS pain scores from baseline

≥50% NRS/VAS pain improvement					
Author (year)	**Time point**	**IASI % (n/N)**	**IANSI % (n/N)**	**Risk Ratio (95% CI)†**	**p-value†**
Barnsley (1994)	**2.7 months**	~10% (NR)‡	~11% (NR)‡	~0.9 (NC)	NR
Manchikanti (2010, 2008)	**3 months**	NR	NR	NR	NR
	6 months	95% (57/60)	87% (52/60)	1.10 (0.98 to 1.23)	0.115
	24 months	93% (56/60)	85% (51/60)	1.10 (0.97 to 1.25)	0.144

CI: confidence interval; IASI: Intra-articular steroid injection; IANSI: intra-articular non-steroidal injection; NC: not calculable; NR: not reported; NRS: numerical rating scale; VAS: visual analog scale.
*Treatment details: Steroid group injectate: 5.7 mg betamethasone (Barnsley), "non-particulate" betamethasone 0.15 mg + 0.25% bupivacaine ± Sarapin (Manchikanti); Non-steroid group injectate: 0.5% bupivacaine (Barnsley), 0.25% bupivacaine ± Sarapin (Manchikanti); co-interventions received by both groups (exercise and medication)
†calculated values: (RR = intervention/control)
‡ Data estimated from graph

Table 71. Intra-articular (medial branch) steroid injection* versus non-steroidal intra-articular (medial branch) injection* for facet joint pain: NRS pain scores

		NRS (0-10) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔIASI vs. ΔIANSI	
Author (year)	Time point	IASI	IANSI	ΔIASI	ΔIANSI	Mean Difference (95% CI)†	p-value†
Manchikanti (2010, 2008)	**3 months**	3.7 ± 0.9 (n = 60)	3.8 ± 1.0 (n = 60)	-4.5 ± 0.7	-4.4 ± 0.6	-0.1 (-0.3 to 0.1)	0.403
	6 months	3.4 ± 0.7 (n = 60)	3.6 ± 1.1 (n = 60)	-4.8 ± 0.7	-4.6 ± 0.7	-0.2 (-0.5 to 0.1)	0.120
	24 months	3.2 ± 1.0 (n = 60)	3.5 ± 1.1 (n = 60)	-5.0 ± 0.7	-4.7 ± 0.7	-0.3 (-0.6 to -0.05)	0.021

CI: confidence interval; IASI: Intra-articular steroid injection; IANSI: intra-articular non-steroidal injection; NRS: numerical rating scale; SD: standard deviation.
*Treatment details: Steroid group injectate: 5.7 mg betamethasone (Barnsley), "non-particulate" betamethasone 0.15 mg + 0.25% bupivacaine ± Sarapin (Manchikanti); Non-steroid group injectate: 0.5% bupivacaine (Barnsley), 0.25% bupivacaine ± Sarapin (Manchikanti); co-interventions available to both groups (continuation of exercise and medication)
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 72. Intra-articular (medial branch) steroid injection* versus non-steroidal intra-articular (medial branch) injection* for facet joint pain: ≥50% improvement in NDI scores from baseline

		≥50% NDI improvement			
Author (year)	Time point	IASI % (n/N)	IANSI % (n/N)	Risk Ratio (95% CI)†	p-value†
Manchikanti (2010, 2008)	**3 months**	NR	NR	NR	NR
	6 months	65% (39/60)	60% (36/60)	1.08 (0.82 to 1.43)	0.573
	24 months	75% (45/60)	70% (42/60)	1.07 (0.86 to 1.34)	0.541

CI: confidence interval; IASI: Intra-articular steroid injection; IANSI: intra-articular non-steroidal injection; NC: not calculable; NDI: neck disability index; NR: not reported.
*Treatment details: Steroid group injectate: 5.7 mg betamethasone (Barnsley), "non-particulate" betamethasone 0.15 mg + 0.25% bupivacaine ± Sarapin (Manchikanti); Non-steroid group injectate: 0.5% bupivacaine (Barnsley), 0.25% bupivacaine ± Sarapin (Manchikanti); co-interventions available to both groups (continuation of exercise and medication)
†calculated values (RR = intervention/control)

Table 73. Intra-articular (medial branch) steroid injection* versus non-steroidal intra-articular (medial branch) injection* for facet joint pain: NDI scores

		NDI (0-100) scores (mean ± SD)		Δ from baseline (mean ± SD)†		ΔIASI vs. ΔIANSI	
Author (year)	Time point	IASI	IANSI	ΔIASI	ΔIANSI	Mean Difference (95% CI)†	p-value†
Manchikanti (2010, 2008)	**3 months**	12.2 ± 4.6 (n = 60)	12.0 ± 5.2 (n = 60)	-12.9 ± 3.1	-13.4 ± 3.5	0.5 (-0.7 to 1.7)	0.429
	6 months	11.6 ± 4.2 (n = 60)	12.0 ± 5.6 (n = 60)	-13.5 ± 3.0	-13.4 ± 3.6	-0.1 (-1.3 to 1.1)	0.869
	24 months	11.0 ± 4.7 (n = 60)	11.6 ± 4.4 (n = 60)	-14.1 ± 3.1	-13.8 ± 3.4	-0.3 (-1.5 to 0.9)	0.615

CI: confidence interval; IASI: Intra-articular steroid injection; IANSI: intra-articular non-steroidal injection; NDI: neck disability index; SD: standard deviation.

*Treatment details: Steroid group injectate: 5.7 mg betamethasone (Barnsley), "non-particulate" betamethasone 0.15 mg + 0.25% bupivacaine ± Sarapin (Manchikanti); Non-steroid group injectate: 0.5% bupivacaine (Barnsley), 0.25% bupivacaine ± Sarapin (Manchikanti); co-interventions available to both groups (continuation of exercise and medication)

†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

Table 74. Intra-articular (medial branch) steroid injection* versus no injection* for myofascial pain syndrome: Tension type headache

		Tension headache			
Author (year)	Time point	IASI % (n/N)	No injection % (n/N)	Risk Ratio (95% CI)†	p-value‡
Park (2012)§	**Baseline**	~35%	~30%	~1.2 (NC)	NR
	3 months	~16%	~24%	~0.7 (NC)	<0.05
	6 months	~9%	~21%	~0.4 (NC)	<0.05
	12 months	~3%	~19%	~0.2 (NC)	<0.05

CI: confidence interval; IASI: Intra-articular steroid injection; NC: not calculable.

*Treatment details: Steroid group injectate: 5 mg triamcinolone + 187.5 IU hyaluronidase + 1% lidocaine; No injection: no treatment except the co-interventions received by both groups (exercise and medication)

†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

‡p-values reported by the study and represent the difference between the groups at 3, 6, and 12 months

§Data estimated from graphs

Table 75. Intra-articular (medial branch) steroid injection* versus no injection* for myofascial pain syndrome: NRS pain scores

		NRS (0-10) scores (mean ± SD)			Δ from baseline (mean ± SD)†		ΔIASI vs. Δ No Injection	
Author (year)	Time point	IASI	No Injection	p-value‡	ΔIASI	ΔNo Injection	Mean Difference (95% CI)†	p-value†
Park (2012)§	**3 months**	~2.9 (n=155)	~5.0 (n=151)	<0.05	~-3.7	~-1.4	~-2.3 (NC)	NC
	6 months	~2.7 (n=155)	~4.8 (n=151)	<0.05	~-3.9	~-1.6	~-2.3 (NC)	NC
	12 months	~2.6 (n=155)	~4.8 (n=151)	<0.05	~-4.0	~-1.6	~-2.4 (NC)	NC

CI: confidence interval; IASI: Intra-articular steroid injection; IANSI: intra-articular non-steroidal injection; NC: not calculable; NRS: numerical rating scale; SD: standard deviation.

*Treatment details: Steroid group injectate: 5 mg triamcinolone + 187.5 IU hyaluronidase + 1% lidocaine; no injection: no treatment except the co-interventions received by both groups (exercise and medication)

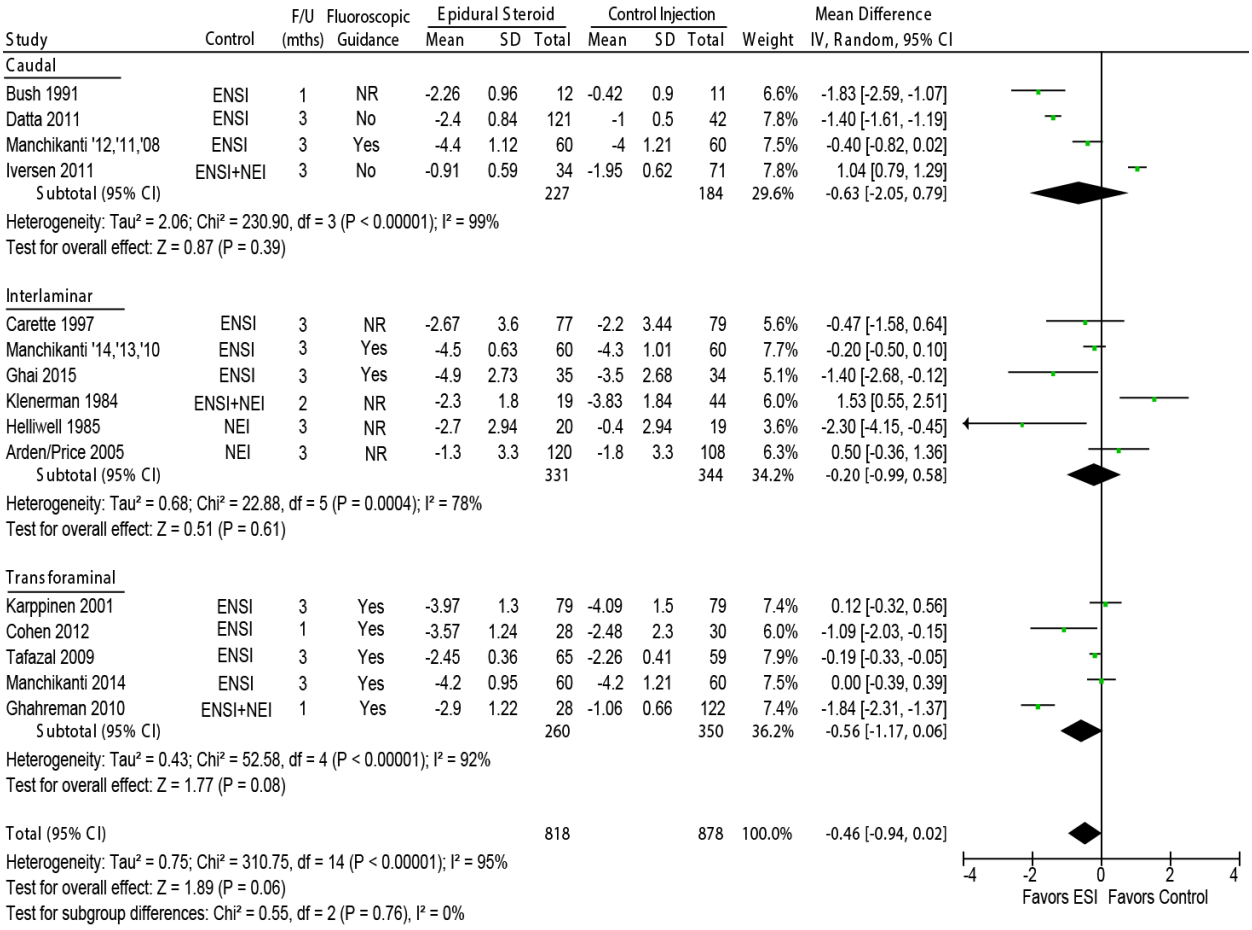
†calculated values (change from baseline calculated as follow-up score minus baseline score; MD calculated as Δintervention minus Δcontrol)

‡p-values reported by the study and represent the difference between the groups at 3, 6, and 12 months

§Data estimated from graphs

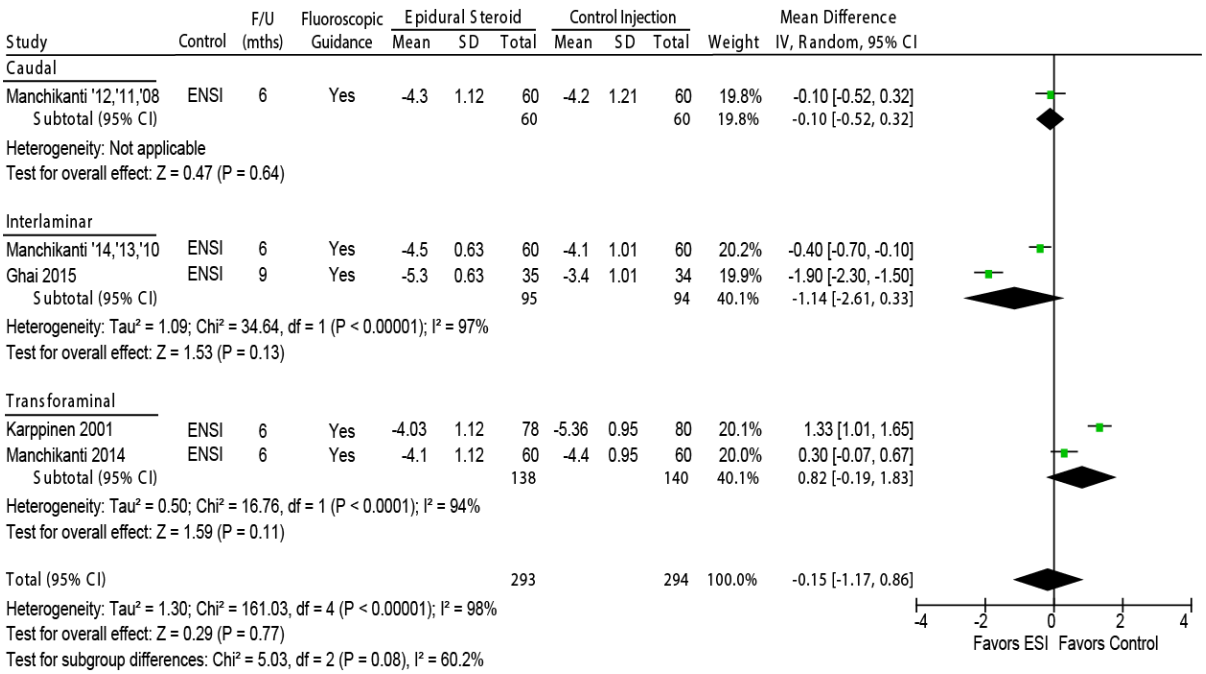
Figures

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



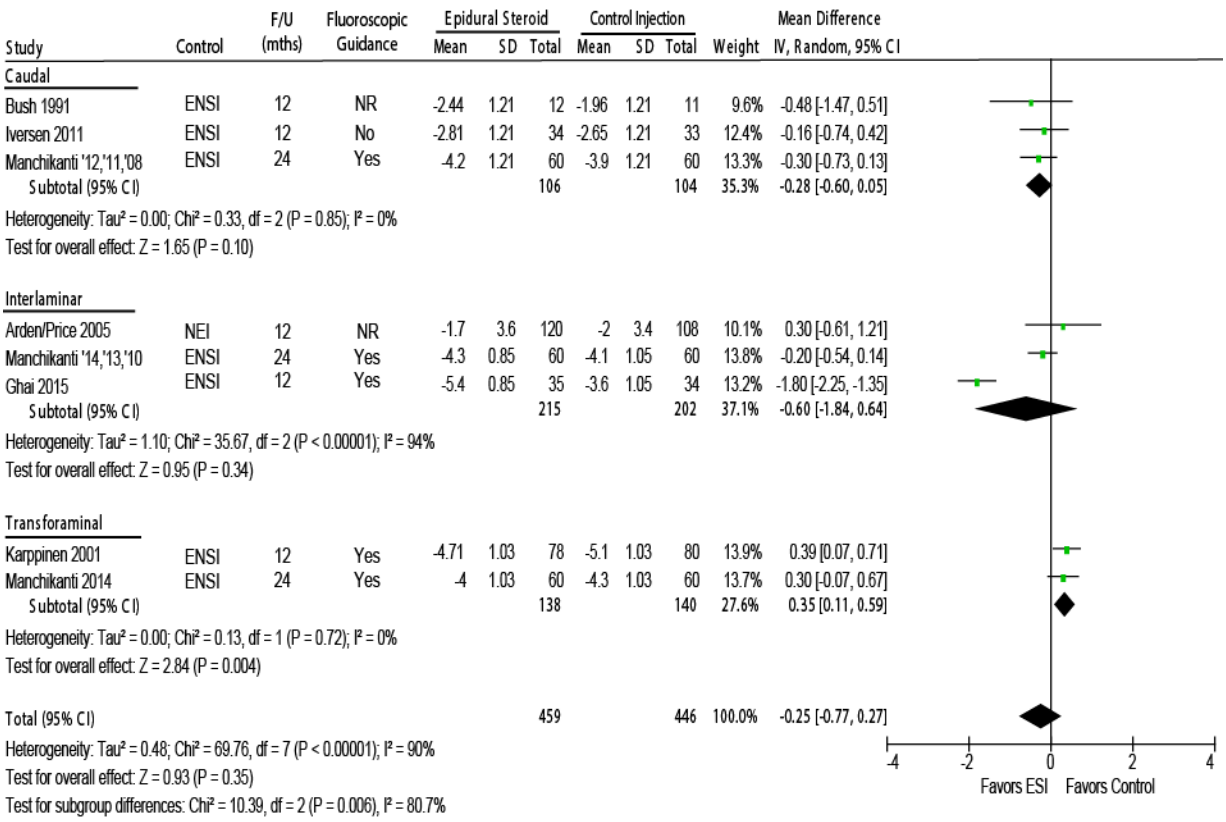
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 4. Epidural steroid injections vs. control injections for due to disc pathology and/or foraminal narrowing: IMPROVED PAIN, INTERMEDIATE FOLLOW-UP



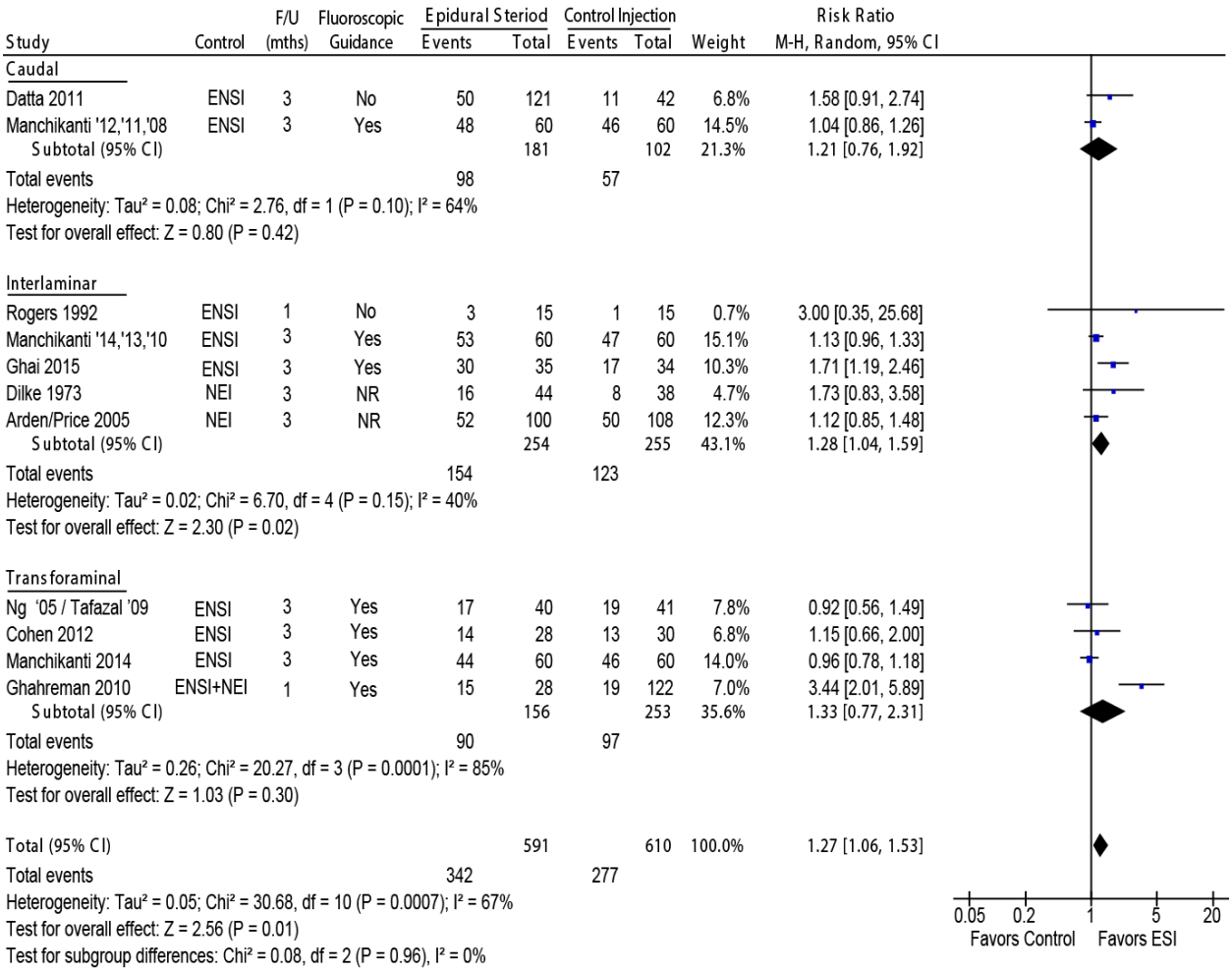
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

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



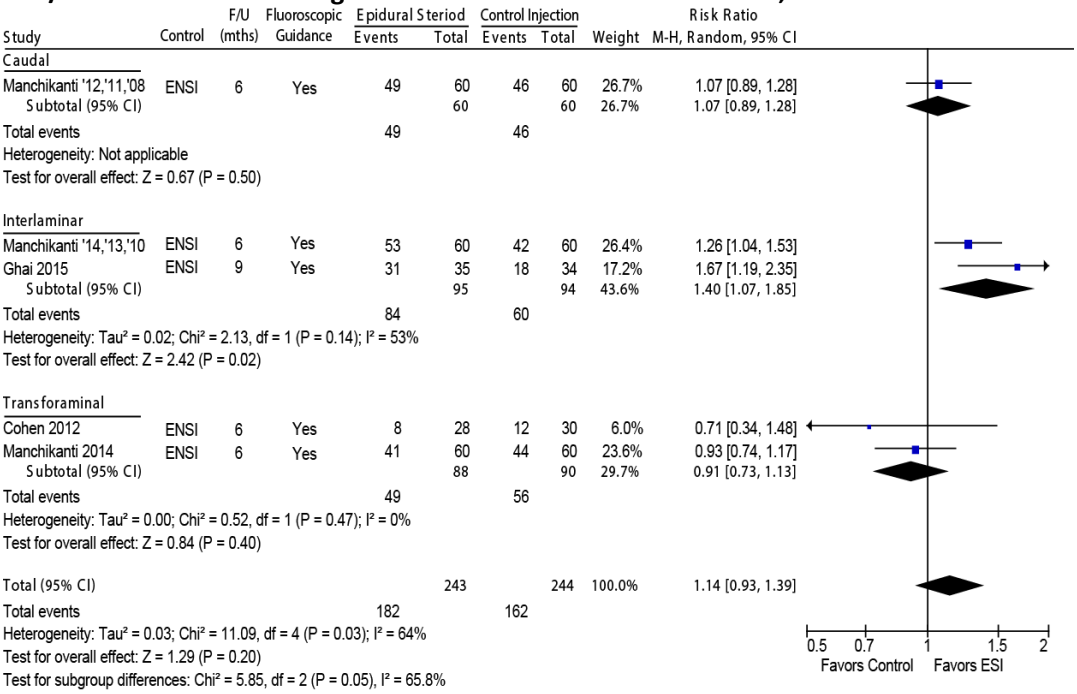
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

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



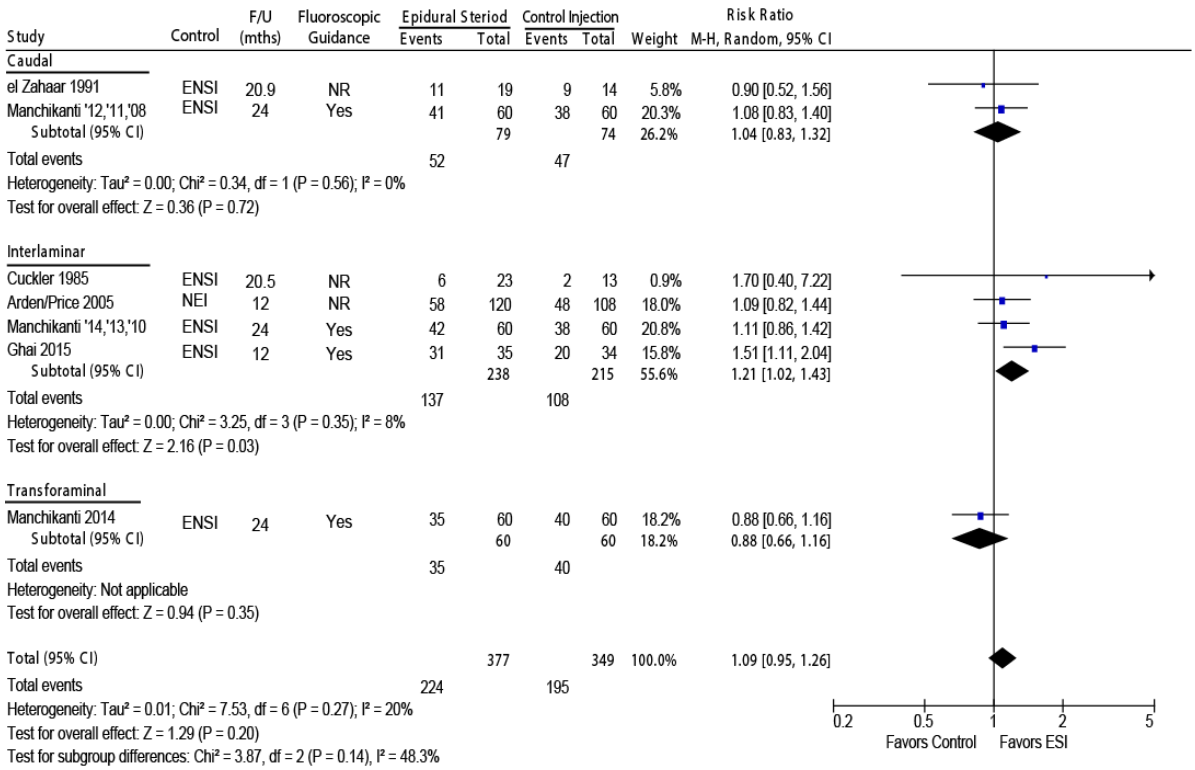
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 7. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH PAIN SUCCESS, INTERMEDIATE FOLLOW-UP



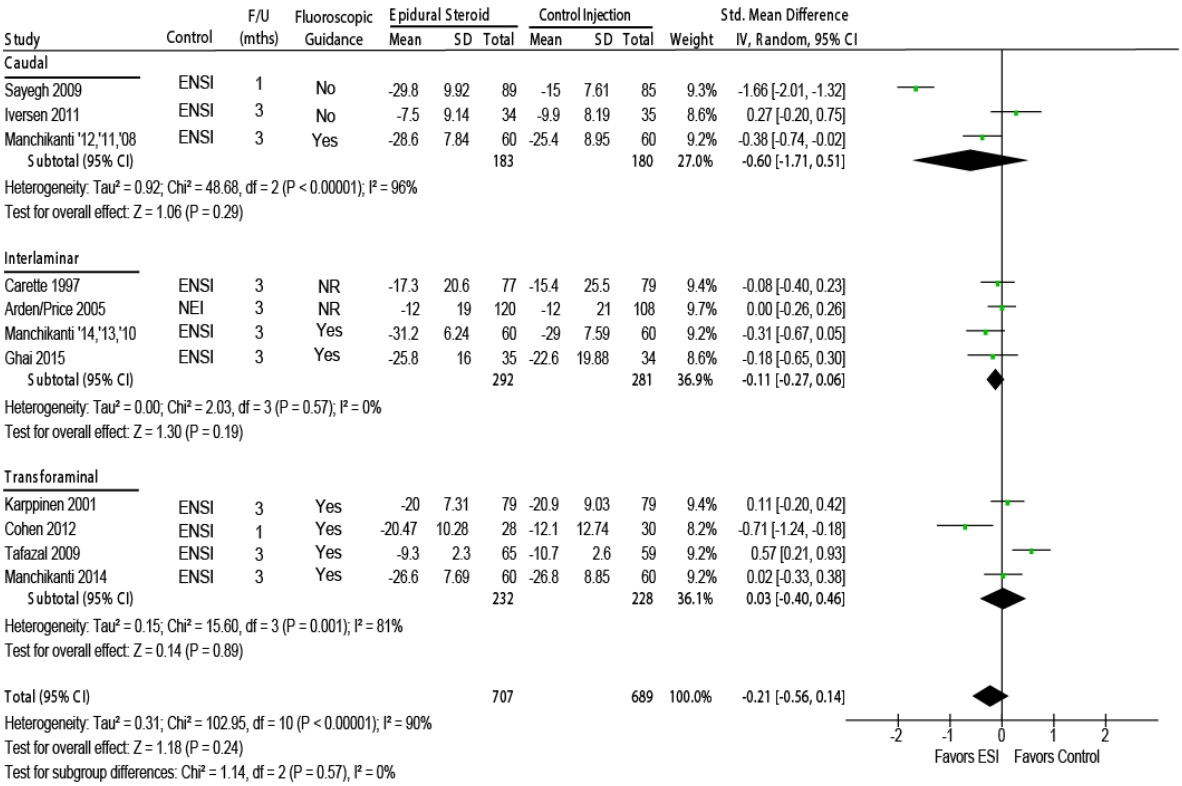
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

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



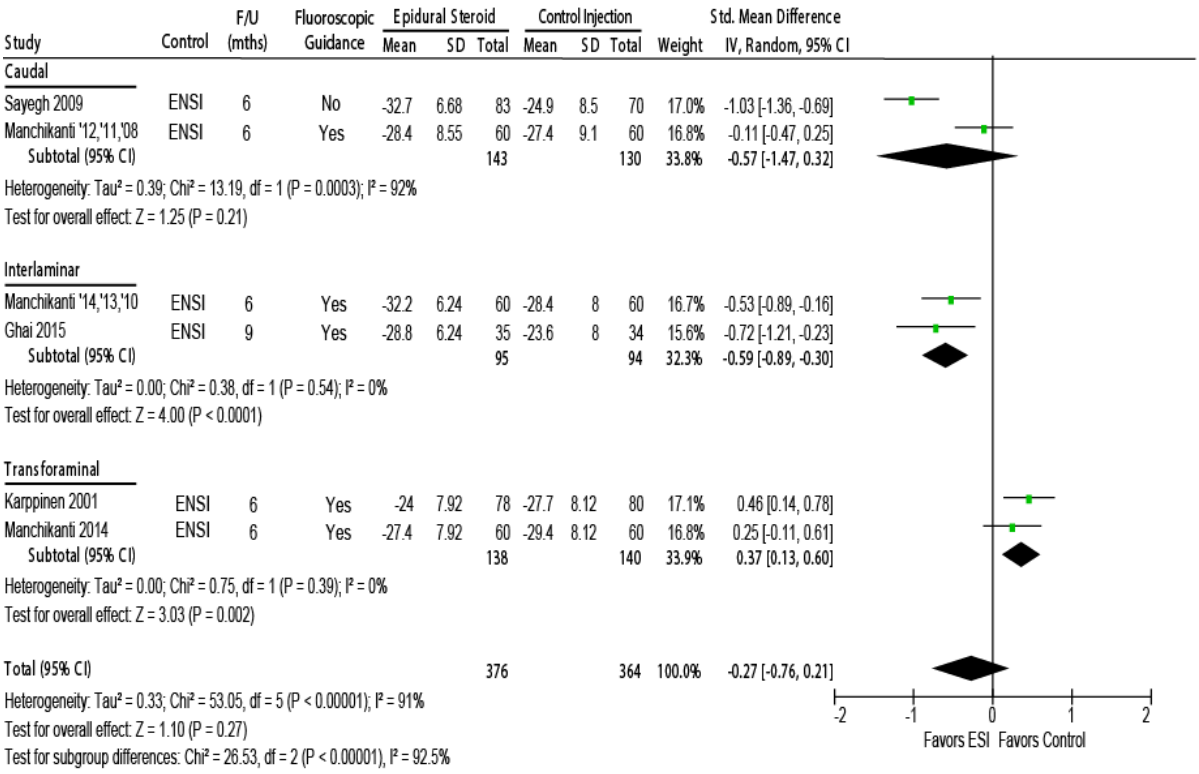
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

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



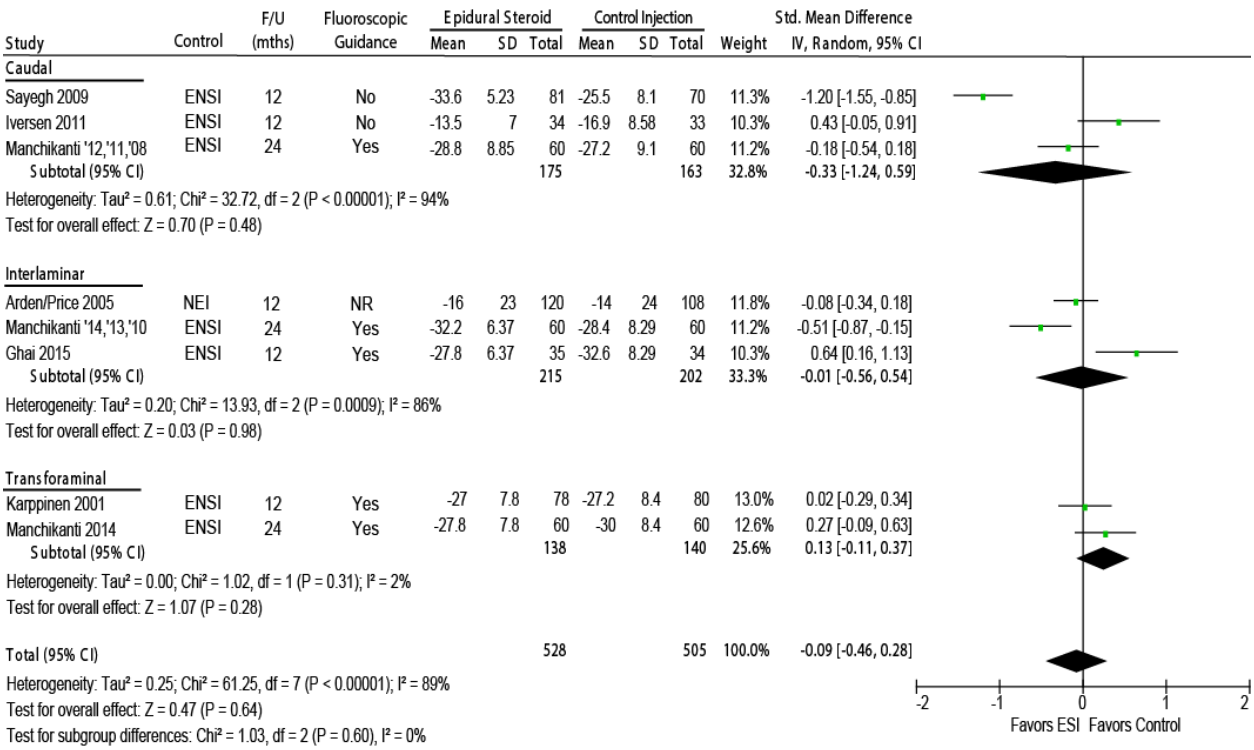
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

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



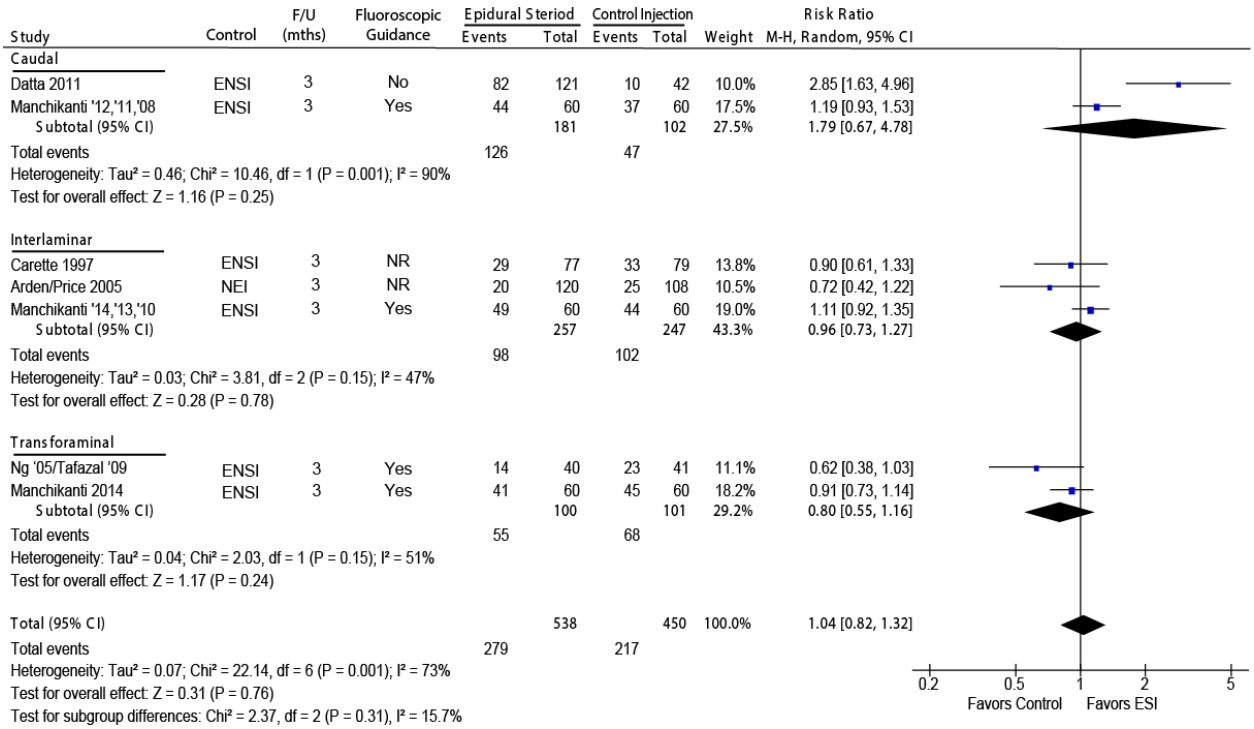
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

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



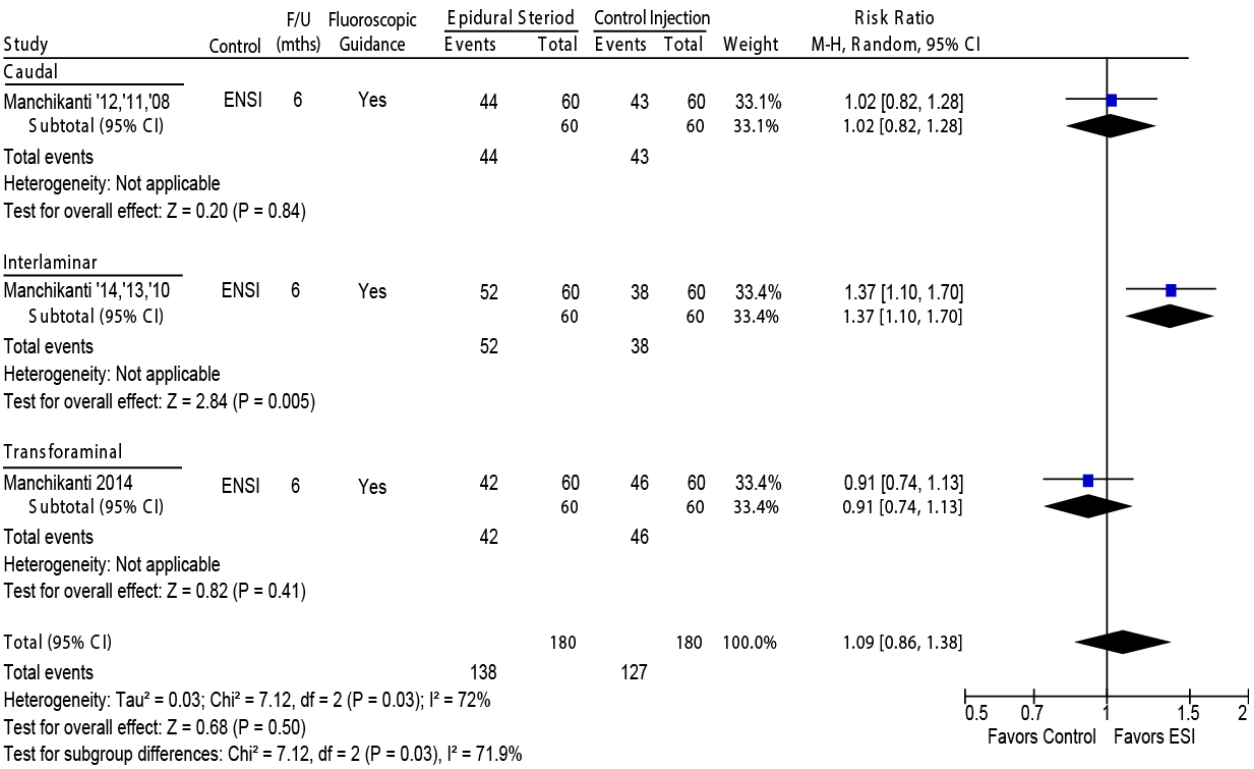
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

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



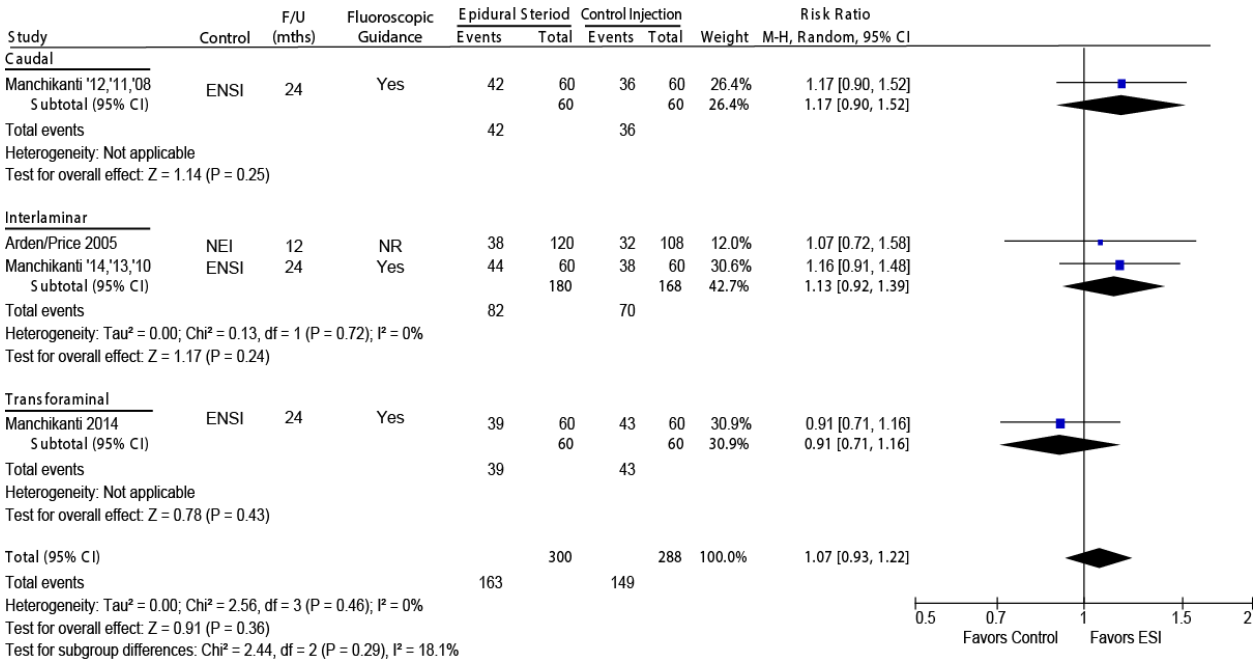
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 13. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH FUNCTION SUCCESS, INTERMEDIATE FOLLOW-UP



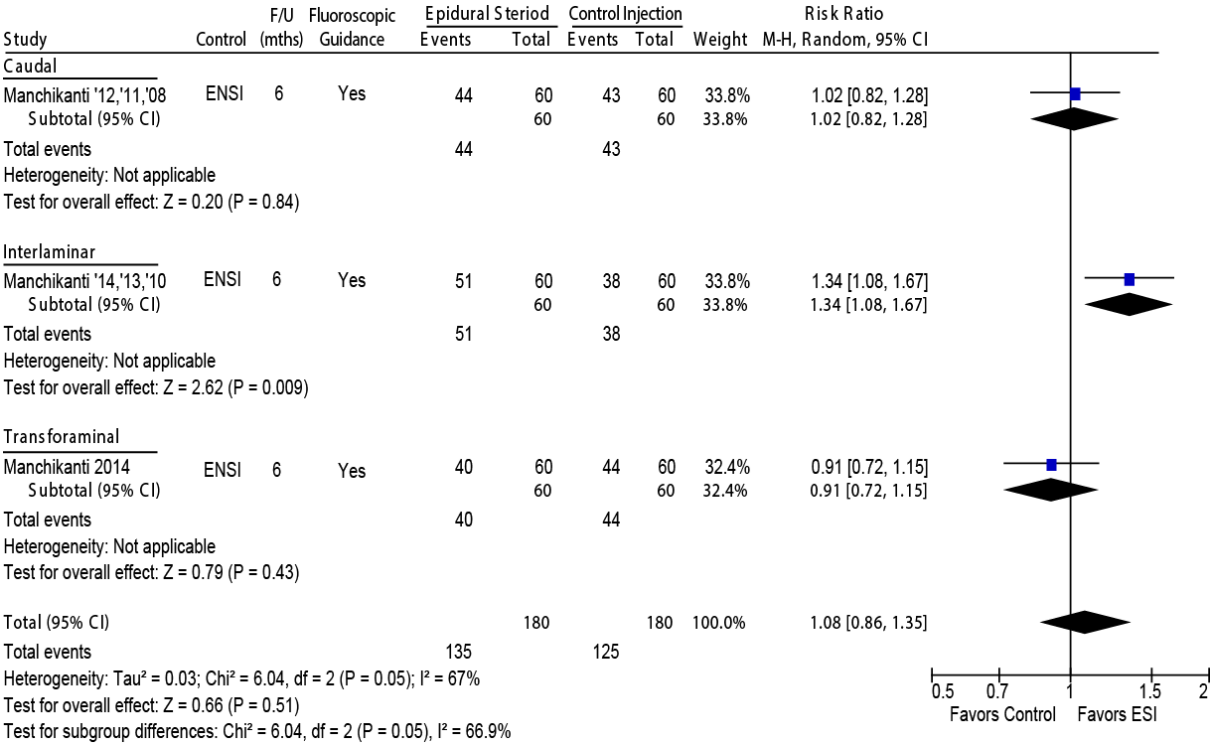
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 14. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH FUNCTION SUCCESS, LONG-TERM FOLLOW-UP



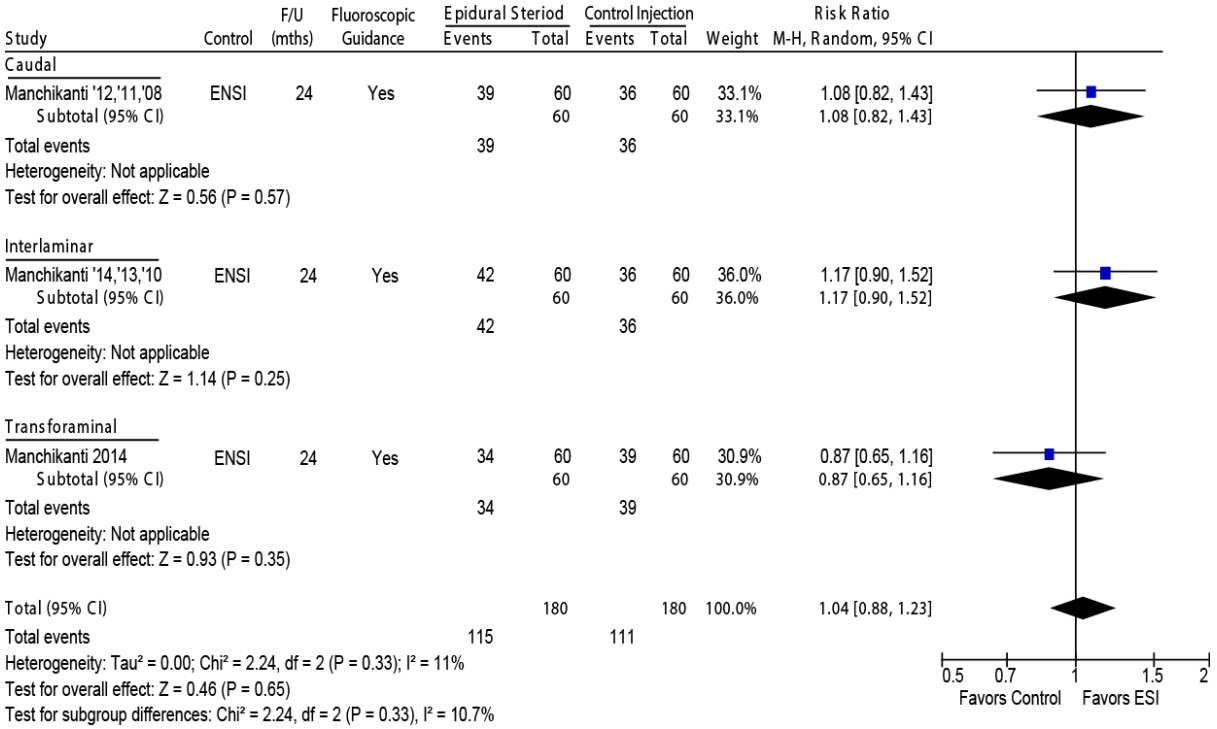
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 15. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH COMPOSITE SCORE SUCCESS, INTERMEDIATE FOLLOW-UP



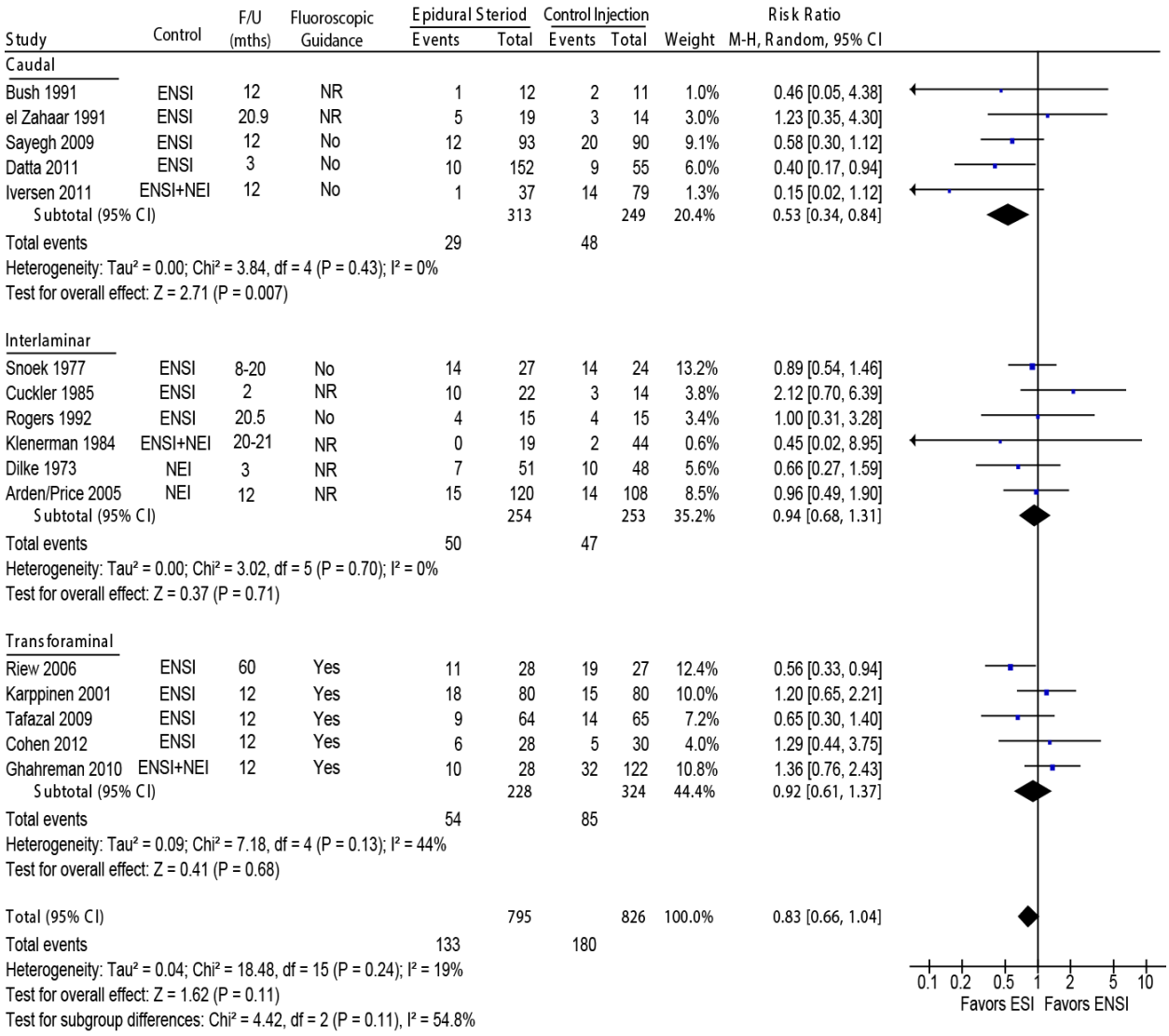
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 16. Epidural steroid injections vs. control injections for radiculopathy due to disc pathology and/or foraminal narrowing: PROPORTION WITH COMPOSITE SCORE SUCCESS, LONG-TERM FOLLOW-UP



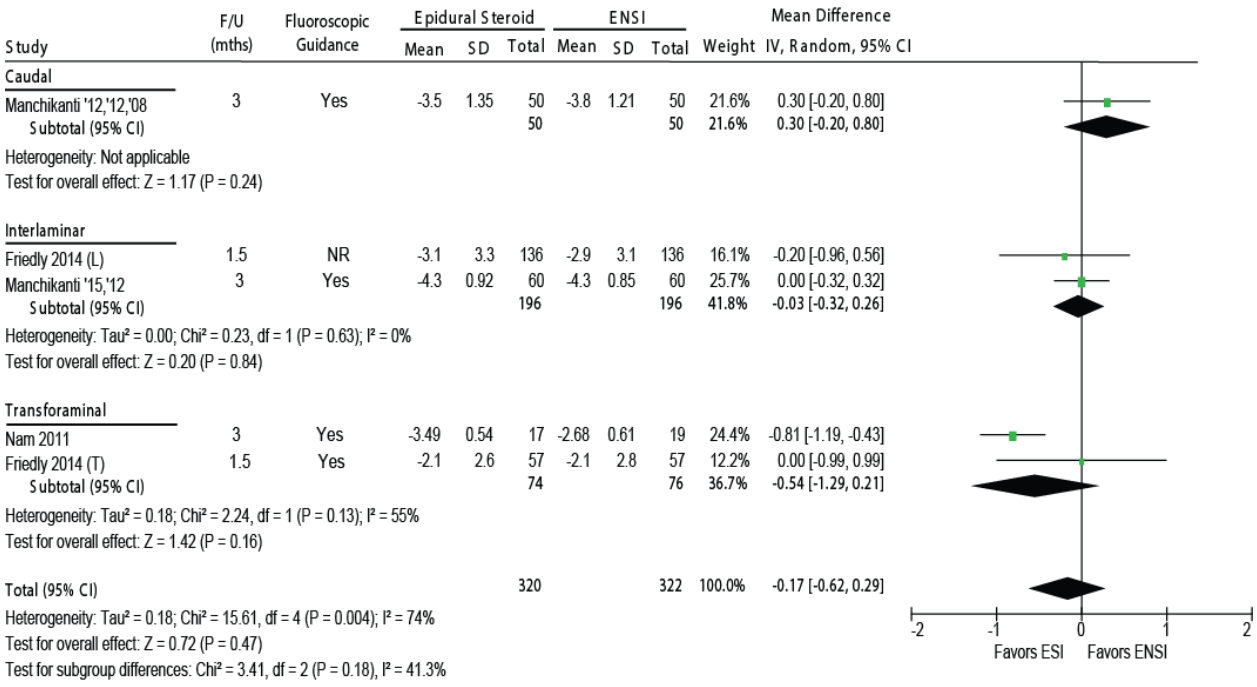
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

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



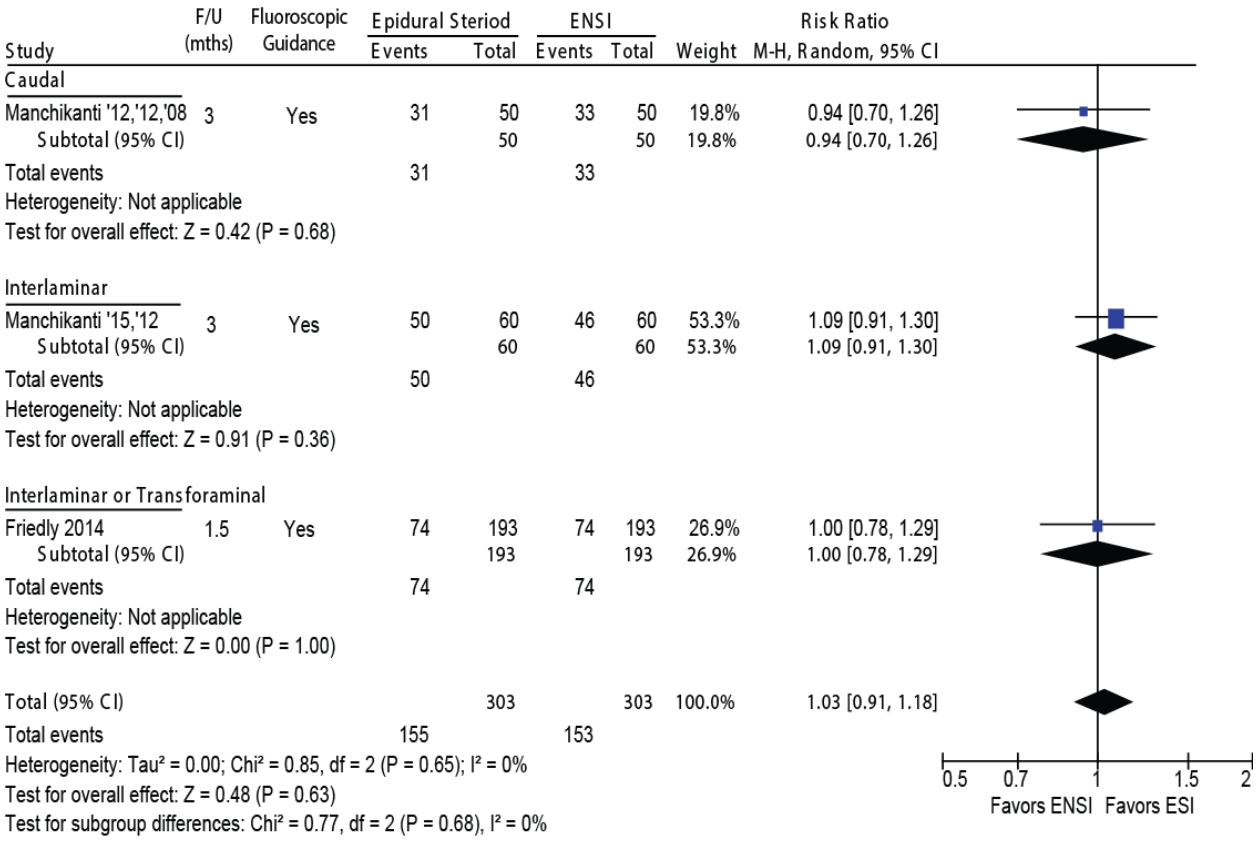
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 18. Epidural steroid injections (ESI) vs. control injections for spinal stenosis: IMPROVED PAIN, SHORT-TERM FOLLOW-UP



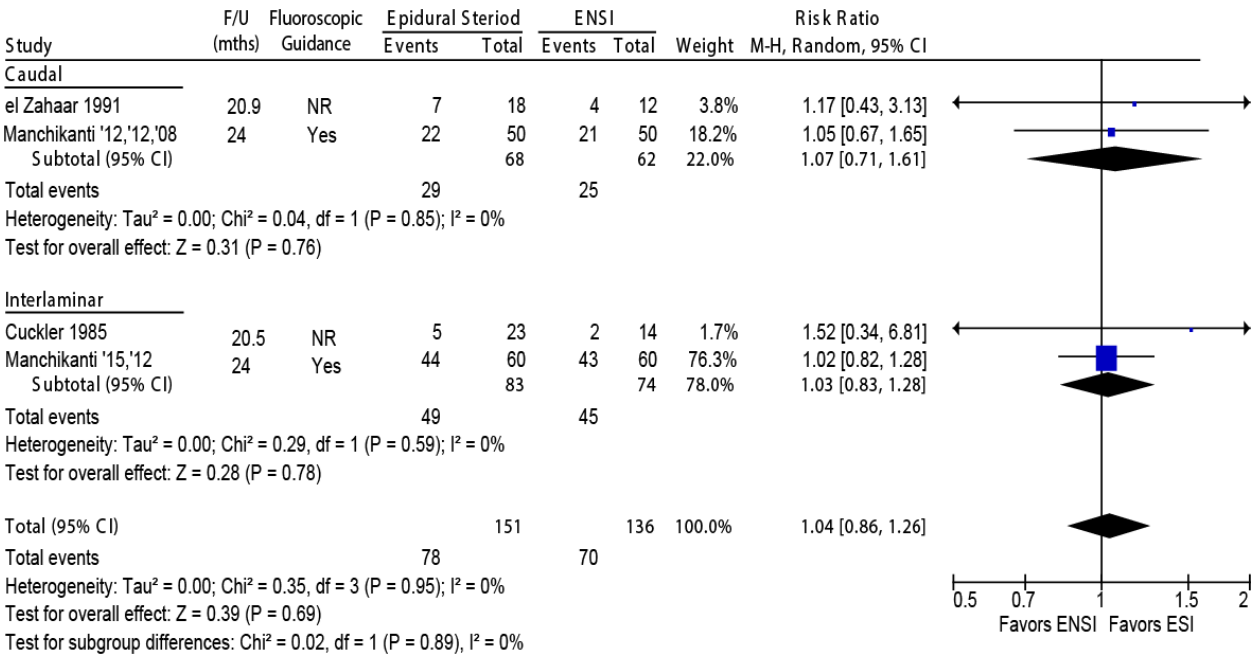
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 19. Epidural steroid injections (ESI) vs. control injections for spinal stenosis: PROPORTION WITH PAIN SUCCESS, SHORT-TERM FOLLOW-UP



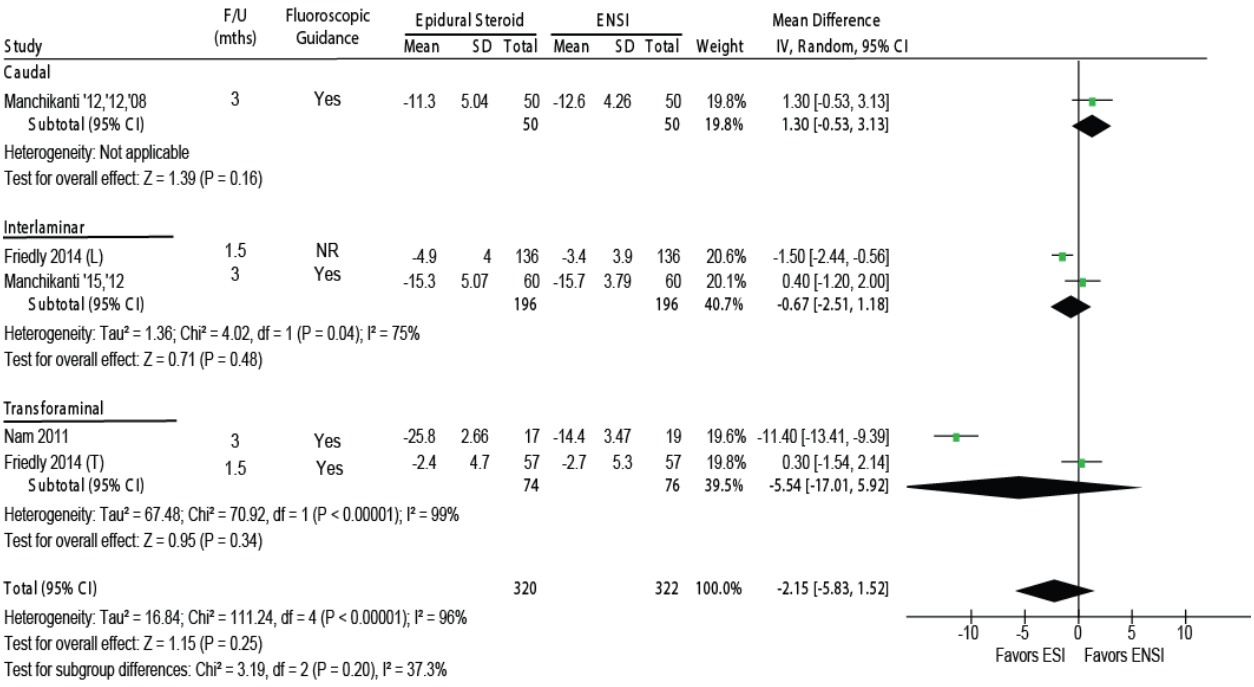
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

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



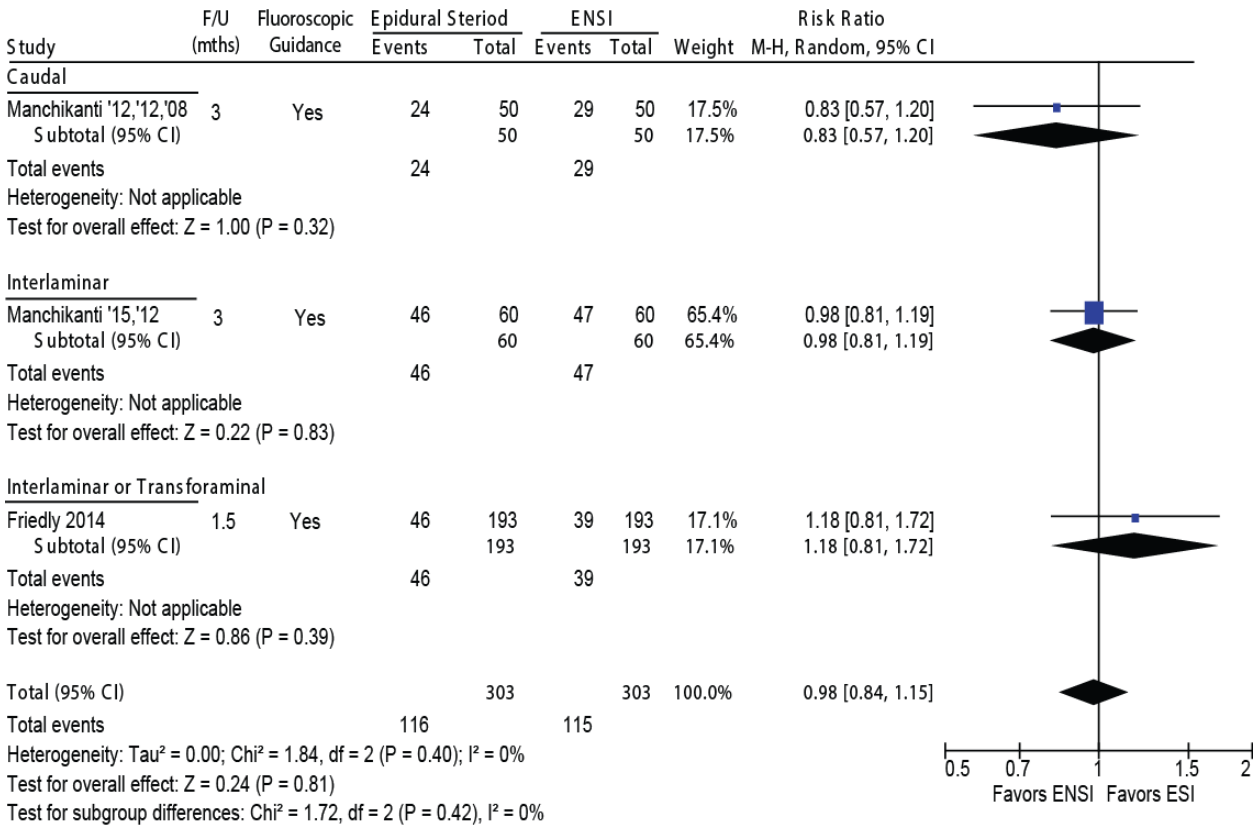
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

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



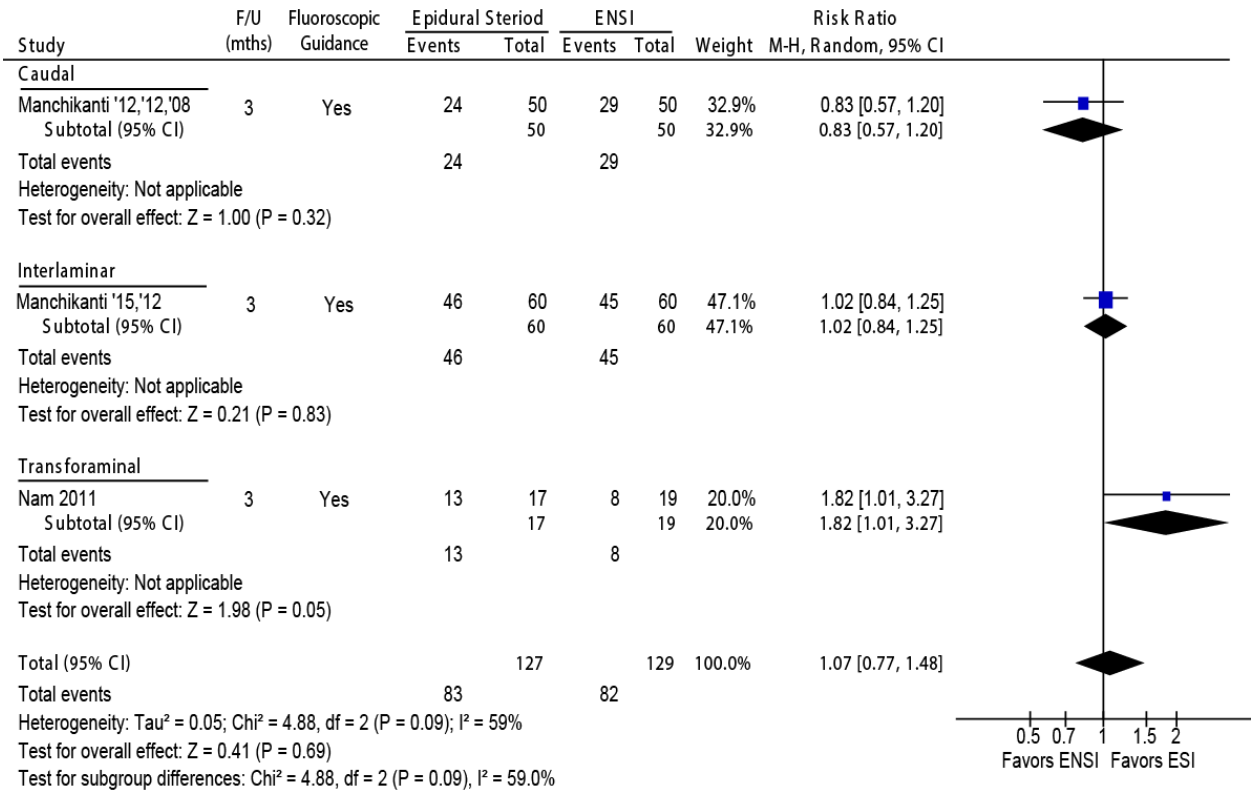
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 22. Epidural steroid injections (ESI) vs. control injections for spinal stenosis: PROPORTION WITH FUNCTION SUCCESS, SHORT-TERM FOLLOW-UP



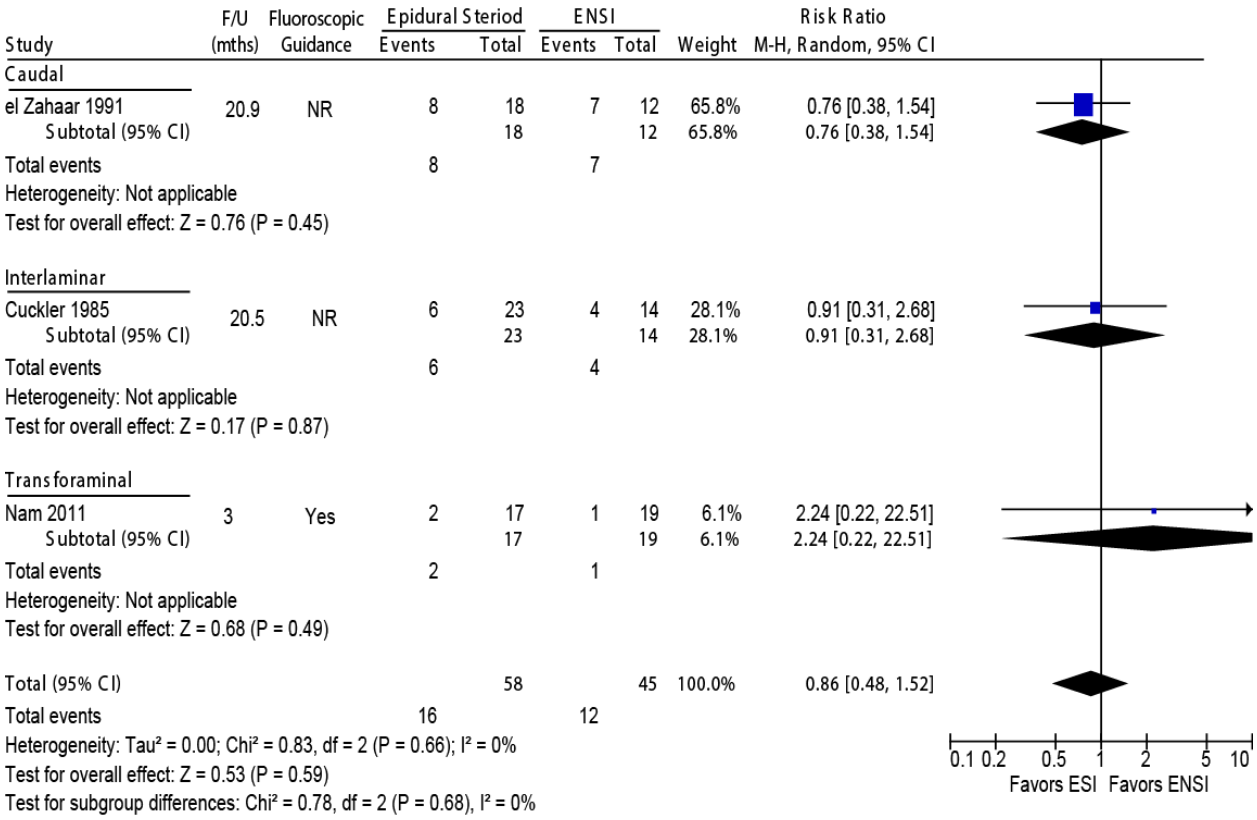
CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 23. Epidural steroid injections (ESI) vs. control injections for spinal stenosis: PROPORTION WITH COMPOSITE SCORE SUCCESS, SHORT-TERM FOLLOW-UP



CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.

Figure 24. Epidural steroid injections (ESI) vs. control injections for spinal stenosis: RISK OF SURGERY



CI: confidence interval; ENSI: epidural non-steroid injection; ESI: epidural steroid injection; F/U: follow-up; NEI: non-epidural injection; NR: not reported; SD: standard deviation.