International Centre for Allied Health Evidence

University of South Australia

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Systematic Review of the Literature

The Effectiveness of Lumbar Epidural Injection of Steroid with or without Local Anaesthetic

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Abbreviations

The following abbreviations are used in this report and are collated here for the reader's convenience.

Abbreviation		Abbreviation	
AI	Anaesthetic injection	**PGIC**	Patient Global Impression of Change
CI	Confidence Interval	**PLA2**	Phospholipase A2
CLESI	Caudal lumbar epidural steroid injections	**RCT**	Randomised Controlled trial
CSF	Cerebrospinal Fluid	**PRF**	Pulsed Radiofrequency
CT	Computer Tomography	**QALY**	Quality-adjusted life year
FG	Fluoroscopy Guided		
GP	General Practitioner	**RR**	Risk Ratio/Relative Risk
HNP	Herniated nucleus pulposis	**RMDQ**	Roland Morris Disability Questionnaire
iCAHE	International Centre for Allied Health Evidence	**SIGN**	Scottish Intercollegiate Guidelines Network
IL	Interlaminar	**SLNB**	Selective lumbar nerve root blocks
JOA	Japanese Orthopedic Association	**SPECT**	Single Photon Emission Computed Tomography
LESI	Lumbar Epidural Steroid Injection	**SR**	Systematic Review
L1-5	Lumbar levels 1 - 5	**TF**	Transforaminal
LBP	Low Back Pain	**TFLESI**	Transforaminal Lumbar Epidural Steroid Injection
LA	Local Anaesthesia	**TNF**	Tumour necrosis factor
LESI	Lumbar Epidural Steroid Injection	**USPSTF**	US Preventive Services Task Force
LRS	Lumbosacral radicular syndrome	**UK RCGP**	United Kingdom Royal College of General Practitioner
MA	Meta-analysis	**UG**	Ultrasound Guided
MRI	Magnetic Resonance Imaging	**VAS**	Visual Analogue Scale
MIL	Midline Interlaminar	**WMD**	Weighted Mean difference
MODQ	Modified Oswestry Disability Questionnaire		
NICE	The National Institute for Health and Care Excellence		
NRS	Numerical Rating Scale		
ODI	Oswestry Disability Index		
PIL	Parasagittal Interlaminar		
	Quality Ratings		
AQ	Acceptable Quality	**LQ**	Low Quality
CS	Can't say	**NA**	Not Applicable
HQ	High Quality	**R**	Reject (Unacceptable Quality)
QS	Quality of Study		

EXECUTIVE SUMMARY

Objective of the Review	The objective of this systematic review is to synthesise the evidence related to the effectiveness of injection of steroid with or without local anaesthetic to the lumbar epidural space as a form of interventional pain management. In order to review the evidence this review aims to answer the following research questions a) What is the evidence for the effectiveness of steroid injections into the lumbar epidural space with or without local anaesthetic in relieving pain and/or in improving functional outcomes in patients with pain? b) What is the evidence for the safety of steroid injections into the lumbar epidural space with or without local anaesthetic?
Evidence sourced	The search yielded 1,752 articles. After scrutiny, 1,647 articles were excluded as duplicates or failing to meet the inclusion criteria (shown in Figure 1), leaving 105 studies for inclusion in this review including 44 systematic reviews, 32 randomised controlled trials, 19 cohort studies and 10 case studies.
What is the evidence for the effectiveness of steroid injections into the lumbar epidural space with or without local anaesthetic in relieving pain and/or in improving functional outcomes in patients with pain?	**Lumbar Epidural Injections - General** 1. The evidence does not support the use of lumbar epidural steroid injections, as a broad intervention category, for the first line relief of pain or improving disability in patients with radicular symptoms or low back pain (Level A) 2. The evidence suggests that the use of lumbar epidural steroid injections, as a broad intervention category, for relief of pain or improving disability in patients with low back pain or radicular symptoms is effective in the short term, i.e. up to 6 weeks (Level A) 3. The evidence suggests that the use of lumbar epidural steroid injections, as a broad intervention category, for relief of pain or improving disability in patients with low back pain or radicular symptoms is not effective in the long term, i.e. greater than 6 weeks (Level A) 4. The evidence suggests that any benefit from the use of lumbar epidural steroid injections, as a broad intervention category, for relief of pain or improving disability in patients with back pain with or without radicular symptoms may be due to the volume of injectate or process of administration, not the steroid (Level A) **Lumbar Epidural Injections - Transforaminal** 5. The evidence suggests that the transforaminal approach is effective in reducing pain in patients with radiculopathy, particularly secondary to herniation of nucleus pulposus and particularly in the short term. (Level A) 6. The evidence suggests that the transforaminal approach is not effective in reducing disability and improving functional outcomes in patients with radiculopathy, particularly secondary to herniation of nucleus pulposus (Level B) **Lumbar Epidural Injections - Caudal** 7. The evidence suggests that lumbar epidural steroid injection, using a caudal approach, is effective in reducing pain and improving disability in patients

with radiculopathy, spinal stenosis or low back pain independent of steroid or imaging (Level A)

8. The evidence suggests that lumbar epidural steroid injection with anaesthetic, using a caudal approach, is more effective in reducing pain and improving disability in patients with radiculopathy, spinal stenosis or low back pain than steroid alone. (Level A/Level B)

Lumbar Epidural Injections - Interlaminar

9. The evidence suggests that lumbar epidural steroid injection, using an interlaminar approach, is effective in reducing pain and improving disability in patients with radiculopathy, spinal stenosis or discogenic low back pain in the short term (Level A)
    a. The parasagittal approach is more effective than the midline approach
    b. The effectiveness is better in the short term

Lumbar Conditions – Post-operative

10. The evidence suggests that lumbar epidural steroid injections are of benefit during surgery for post-operative outcomes of pain in the short-term, but not long-term (Level A)

Lumbar Conditions - Radiculopathy

11. The transforaminal approach is more effective in reducing pain but not improving functional outcomes in patients with radiculopathy (Level A)
12. For radiculopathy of non-specific causes, the evidence suggests that the optimal approaches for reducing pain and improving functional outcomes are the transforaminal or interlaminar approaches in the short or long term. (Level B)

Lumbar Conditions – Axial Low Back Pain

13. For axial low back pain, the evidence suggests that the optimal approaches for reducing pain and improving functional outcomes are the caudal sacral or the Interlaminar approaches in the short term (up to 3 months). (Level B)
14. For axial low back pain, the evidence suggests that neither approach is better at achieving long-term improvements in pain or functional outcomes (> 3 months). (Level B)

Lumbar Conditions – Herniated Disc

15. For radiculopathy secondary to herniated disc the evidence suggests that the optimal approach for reducing pain and improving functional outcomes is the transforaminal approach in the short or long term. (Level B)
16. For pain due to a herniated disc, the evidence suggests that all approaches are equally effective in the short-term for reducing pain and improving functional outcomes, with possibly slightly better long term effects with the transforaminal approach. (Level B)

Lumbar Conditions – Spinal Stenosis

17. For pain due to spinal stenosis, the evidence suggests that the optimal approaches for reducing pain and improving functional outcomes are the caudal/sacral and interlaminar approach in the short or long term. (Level B)

	Economic Analysis 18. The evidence suggests that lumbar epidural steroid injections may present a cost-effective intervention in the short term through reducing other health expenditure, reducing the need for expensive surgery and reducing sick days. Any significant cost effectiveness associated with lumbar epidural steroid injections is dependent on repeat injections on an as needed basis. (Level C)
What is the evidence for the safety of steroid injections into the lumbar epidural space with or without local anaesthetic?	1. Minor complications associated with lumbar epidural steroid injections are not uncommon, but rarely require significant medical attention (Level B) 2. Major complications associated with lumbar epidural steroid injections are rare (Level B) 3. Transforaminal lumbar epidural steroid injections are associated with a higher incidence of major complications (Level B)

1. Background

1.1 Objective of this Review

The objective of this systematic review is to synthesise the evidence related to the effectiveness of injection of steroid with or without local anaesthetic to the lumbar epidural space as a form of interventional pain management.

In order to review the evidence this review aims to answer the following research questions

a) What is the evidence for the effectiveness of steroid injections into the lumbar epidural space with or without local anaesthetic in relieving pain and/or in improving functional outcomes in patients with pain?
b) What is the evidence for the safety of steroid injections into the lumbar epidural space with or without local anaesthetic?

1.2 Description of the Intervention

Epidural injections are one of the most commonly performed procedures in interventional pain medicine (Cohen et al 2013). Epidural injections for pain management have most commonly included local anaesthetics or steroids. Recently there has been a trend towards the use of other injectates to attempt to augment the effect of the epidural injections, including O_2, N_2O (Turan et al 2015) and Hyaluronidase (Rahimzadeh et al 2014).

The first therapeutic epidural injection was performed in 1885 by neurologist James Leonard Corning, who injected a local anesthetic between the lower lumbar spinous processes in a healthy man to treat ''seminal incontinence''. Since then the use of caudal and lumbar epidural injections for the treatment of low back pain has continued to evolve. The initial injectates used up to the 1950s to treat low back pain involved a mixture of local anesthetic and saline. The use of corticosteroids to manage low back pain was first recorded in 1953 by Lievre et al, with the first modern controlled trial evaluating epidural steroid injections performed in 1970 by Swerdlow and Sayle-Creer.

Steroids - Rationale

Pure mechanical compression of nerves has been shown to induce painless neurologic deficits such as altered sensation (paraesthesia) and motor weakness (Macnab 1971). The generation of pain in the low back, particularly related to radiculopathy, is multifactorial, and local inflammation is considered to be a potential factor. In 1951 Lindahl and Rexed (1951) found histologic evidence of inflammation in nerve root biopsies obtained at surgery from patients suffering from sciatica due to proven disc herniation. Nachemson (1988) noted a fibrinous reaction in the epidural and perineural tissues of some patients undergoing surgery for radicular pain suggesting local inflammation (Nachemson 1988).

Experimental evidence suggests a biochemical source of neural injury in lumbar disc disease. Annular damage (fissures, tears, and herniations) leads to the escape of nuclear material, which causes an inflammatory reaction, local nociceptor stimulation, potential nerve injury, and subsequently pain. When this occurs by fissures reaching the outer disc annulus, which is innervated, it may serve to explain back pain and somatic referred pain into the lower limb. When the fissure extends through the annulus, the inflammatory process leads to radicular limb pain. This process may explain those instances of severe radicular pain occurring in the absence of gross neural compression (Cannon and Aprill 2000).

Locally, corticosteroids act to inhibit the inflammatory response induced by mechanical, chemical, or immunologic agents. This inhibition occurs in specific leukocyte functions, including leukocyte aggregation at inflammatory sites, prevention of degranulation of granulocytes, mast cells, and macrophages, and stabilization of lysosomal and other membranes (Di Rosa et al 1986). Steroids also inhibit PLA2 activity, therefore interrupting the arachidonic acid cascade. It has also been shown that local application of cortisone blocks transmission in normal nociceptive C-fibres, potentially blocking nociceptive nerves in the manner of local anaesthetics.

Several different steroid preparations may be used, with or without local anaesthetic or normal saline to increase the volume of the injectate. Typical steroids used include methylprednisolone acetate, betamethasone acetate/propionate, and triamcinolone acetate. The benefits of adding a local anaesthetic include potential immediate pain relief for the patient, which provides feedback to the practitioner that the steroid solution is near the presumed site of pathology.

Techniques

Lumbar epidural steroid injections (LESI) aim to deliver a steroid preparation into the epidural and perineural spaces of the lumbar spine, and can be achieved through three separate routes.

The caudal approach involves placing a needle into the sacral epidural space through the sacral hiatus. This approach is the relatively easiest approach, however, as the sacral epidural space must be filled before solutions can be delivered into the lumbar region, larger volumes of injectate are required to reach the lumbar epidural space.

The translaminar or interlaminar approach is technically more demanding, but delivers injectate directly into the lumbar epidural space closer to the source of pain. However, the medication is placed posteriorly without any guarantee that it will flow to the ventral epidural space where the disc-nerve root pathology is occurring.

Whilst traditionally these procedures are performed using palpation for guidance during needle placement, fluoroscopy and contrast have been increasingly promoted to maximize the chance of a favourable response.

The transforaminal approach delivers injectate into the epidural space to a specific nerve root and the ventral epidural space, using fluoroscopic guidance for precise needle placement.

Cannon and Aprill (2000) suggest that if fluoroscopy was not available, the caudal route was preferable for disc pathology at the L5/S 1 level. As solutions usually flow cephalad in the epidural space, and most persons have an insufficient posterior epidural space at L5/S1, there is an increased risk of a dural puncture with the interlaminar route.

For disc levels above L5/S 1, the interlaminar route is usually preferred because it is closer to the pathologic level, and given the tendency of solutions injected via

the caudal route to not flow above the L4/5 level.

If fluoroscopy is available, and the patient has unilateral signs and symptoms, then the transforaminal route is usually employed. For central and posterolateral disc herniations, the injection is usually performed one level below. For foraminal and extraforaminal disc herniations or for foraminal stenosis, the injection is placed at that level.

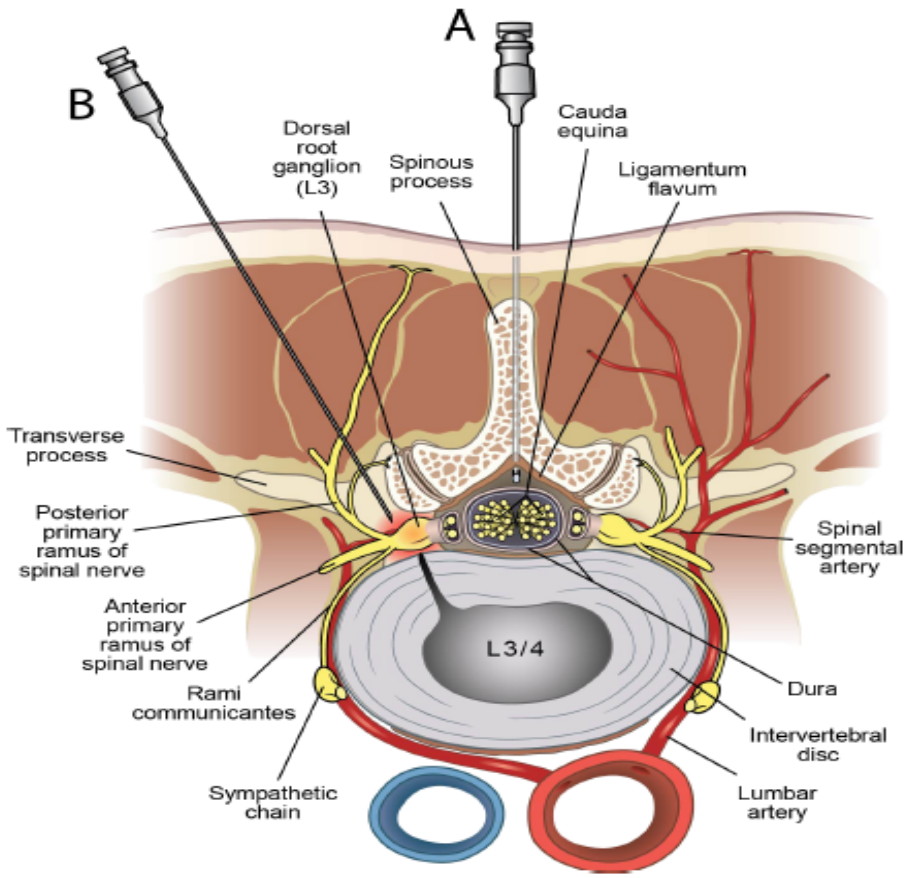

Figure 1: A: Interlaminar approach, B: Transforaminal Approach
(Adapted from Cohen et al 2013)

Optimal volume

Epidurography is a method of documenting epidural injectate spread and involves fluoroscopy with radiopaque contrast agents. Burn et al (1973) employed the technique with large volumes of injectate (20ml vs. 40ml) in both the caudal and translaminar approaches. They reported that the two most important factors determining the spread of solutions in the epidural space were the volume used and the route of entry. Larger volumes usually spread to more spinal levels, and the translaminar lumbar route was more likely to reach upper lumbar levels than the caudal route. They reported that solutions primarily flow cephalad in the epidural space (half of translaminar injections placed at the L3/4 level did not spread below the L5 level), they take the path of least resistance (going around adhesions and sometimes preferentially staying on the side they are placed on), and that it was impossible to predict what level a given volume would reach in any individual. Given that the rationale for using an epidural injection is to deposit the

steroid as close to the pathology as possible, many practitioners use fluoroscopy with radiopaque contrast to not only document where the injectate will go but also modify the position or volume of injectate in an attempt to ensure that the steroid solution reaches the target site. Bryan et al (1999) using epidurography with caudal epidural injections showed that with needle advancement to the S2/3 level, 85% of injections using 8ml of contrast reached the L4/5 disc level.

However, even with the use of fluoroscopy and contrast along with traditional injection routes, there is no guarantee that the medication will reach the pathologic site. Bryan et al (1999) performed a series of 100 caudal LESI using fluoroscopy and contrast and showed that 31% of the injections spread to the dorsal epidural space only (i.e., no ventral flow). Similar problems can occur with the interlaminar approach, which places the medication dorsally without any guarantee that it will flow ventrally or even bilaterally in the epidural space.

For the transforaminal approach, there is less variation in the volume of medication needed to reach the pathologic site. If the needle is placed in the ventral aspect of the root canal, the contrast (and therefore medication) usually flows in the ventral epidural space (Cannon and Aprill 2000).

Indications

Conditions

LESI are done for the relief of pain thought to arise as a result of inflammation that affects the neural elements in the epidural and perineural spaces of the spine. Cannon and Aprill (2000) suggested that LESI were most commonly used in patients with radicular pain rather than in those with low back or somatic referred pain.

Radicular pain is characteristic in its quality. It is shooting or lancinating pain that travels down the affected limb in characteristic patterns reminiscent of dermatomes. It is often associated with altered sensation, typically paraesthesia, in a similar distribution and is commonly associated with low back pain or a history of recurring low back pain. The clinical diagnosis is supported by physical findings suggesting nerve root tension.

Somatic referred pain is deep and aching in character and less clearly defined in its distribution. It usually arises from a primary spinal pain generator such as injury or pathology affecting the disc, facet joint or spinal ligaments. The coexistence of radicular and somatic referred limb pain can confound the diagnostic process and make it harder to predict which patient will have a successful response.

A few studies have looked at which patient characteristics predict a less favourable response to an epidural steroid injection. LESI are usually prescribed in patients with radiculopathy caused by discopathy or degenerative stenosis of the spinal canal (D'Orazio et al 2015). They have also been used in patients with back pain secondary to spondylosis with or without significant associated radiculopathy. Patients referring an axial pain not irradiating to a specific territory, myofascial pain, or neurogenic claudication and severe or worsening neurological deficit respond less to treatment (D'Orazio et al 2015).

	Acuteness The optimal time frame for use of LESI is also a concern. Most patients have had some type of conservative treatment prior to injection. This may have consisted of analgesics, oral steroids, physical therapy, manual medicine or other modalities. Usually, failure to improve with conservative treatment or severity of symptoms dictates when to intervene. Response to treatment may depend on the acuteness of the presentation, for example, an injection performed early in the treatment process in a patient with an acute radiculopathy that impairs functional activities and sleep may reduce local inflammation and help prevent epidural and perineural fibrosis, which can occur early and may lead to permanent damage and symptoms.

2. Methodology

2.1 Review question

What is the effectiveness of injection of steroid into the lumbar epidural space with or without local anaesthetic as a form of interventional pain management?

2.2 Methods

A systematic review of the published research literature was undertaken to provide a synthesis of the available research evidence related to the effectiveness of lumbar epidural steroid injection with or without local anaesthetic as a form of interventional pain management. All published and accessible research evidence was sought through a systematic and rigorous search strategy. The evidence base for this review included research evidence from existing systematic reviews, meta-analyses, and high-level primary research (randomised controlled trials, prospective cohort studies). Where no systematic reviews, randomised controlled trials or prospective cohort studies were located then other primary study designs (excluding commentary /expert opinion) were considered.

2.3 Search strategy

The search was developed using a standard PICO structure (see Table 1). Only English articles published, using human participants, which were accessible in full text were included.

Table 1 Criteria for considering studies in the review

Population	Humans
Intervention	Injection of steroid with or without local anaesthetic to the lumbar epidural space
Comparator	Any active treatment or placebo.
Outcomes	• Pain-related primary outcome; • Functional outcomes (range of motion, reduction of disability, return to work, quality of life) • Safety and risk • Relationship to imaging • Best practice recommendations • Cost effectiveness

A combination of search terms (Table 2) was used to identify and retrieve articles in the following databases:

- OVID
  - EMBASE,
  - MEDLINE,
  - AMED,
- ICONDA,
- CINAHL,
- PubMed,
- Pre-Medline,
- The Cochrane Library,
- Scopus,
- TRIP database

Table 2 Search terms for the review

Search terms 1	Search terms 2	Search terms 2	Search terms 3
• Pain • Risk • Complication* • Adverse events	• Injections, • Epidural • Spinal .	• Lumbar • Low back Sciatica Lumbar Radiculopathy	• Steroid • Betamethasone • Dexamethasone • Fluocortolone • Methylprednisolone • Paramethasone • Prednisolone • Prednisone • Triamcinolone • Hydrocortisone • Cortisone • Methandrostenolone • Stanozolol • Methenolone • Oxymetholone • Oxandrolone • Nandrolone • Diflucortolone • Fluprednisolone

The titles and abstracts identified from the above search strategy were assessed for eligibility by the *i*CAHE researchers. Full-text copies of eligible articles were retrieved for full examination. Reference lists of included full-text articles were searched for relevant literature not located through database searching.

2.4 Study Selection

Inclusion Criteria

- Study types: systematic reviews, all primary research designs - randomised controlled trials (RCTs), cohort studies (prospective or retrospective), case studies, case series
- Participants: patients with lumbar (low back) pain with or without lumbar radiculopathy
- Intervention: steroid injections with or without local anaesthetic to the lumbar epidural space
- Controls: any active treatment or placebo, or no-intervention control
- Outcomes: pain relief (primary), functional outcomes, safety and risk (secondary)
- Publication criteria – English language, full text available, in peer reviewed journal

Exclusion criteria

- Studies only available in abstract form e.g. conference presentations
- Grey literature and no-English language material
- Studies involving healthy volunteers or experimentally induced pain
- Studies on interventions involving other spinal levels (thoracic or cervical), where the data for lumbar cannot be extracted

2.5 Critical Appraisal

The SIGN (Scottish Intercollegiate Guidelines Network) checklists specific to the study designs of the included studies were used to assess their methodological quality. The SIGN checklists ask a number of questions with 'yes' (Y), 'no' (N), 'can't say' (CS) or 'not applicable' (NA) as responses. The appraiser then assigns an overall rating of quality, based on responses to the questions, of either high quality (HQ ++), acceptable quality (A+), low quality (LQ-) or unacceptable.

Copies of the SIGN checklist are provided in Appendix 1.

2.6 Data Extraction

Data were extracted from the identified publications using a data extraction tool which was specifically developed for this review. The following information was extracted from individual studies:

- Evidence source (Author, date, country)
- Study design
- Level of evidence
- Characteristics of participants
- Interventions
  - Epidural approach
  - Steroid used
  - Use of imaging
- Outcome measures
  - Pain
  - Functional outcomes
  - Safety and Risk
- Results

2.7 Data Synthesis

As described, for this review each study was graded for overall methodological quality using the SIGN checklist specific to its study design.

Recommendations from the literature were made and scored according to a modification of the SIGN Evidence Grading Matrix (see Table 3). The modification was to add levels 1 and 2 to differentiate between the 1+ and 1- and 2+ and 2- levels of evidence.

Table 3: Modified SIGN Evidence Grading Matrix

Levels of scientific evidence	
1++	High-quality meta-analyses, high-quality systematic reviews of clinical trials with very little risk of bias
1+	Well-conducted meta-analyses, systematic review of clinical trials or well-conducted clinical trials with low risk of bias

1	Meta-analyses, systematic review of clinical trials or clinical trials with a moderate (acceptable) level risk of bias.
1-	Meta-analyses, systematic reviews of clinical trials or clinical trials with high risk of bias.
2++	High-quality systematic reviews of cohort or case and control studies; cohort or case and control studies with very low risk of bias and high probability of establishing a causal relationship
2+	Well-conducted cohort or case and control studies with low risk of bias and moderate probability of establishing a causal relationship
2	Cohort or case and control studies with moderate risk of bias and potential risk that the relationship is not causal.
2-	Cohort or case and control studies with high risk of bias and significant risk that the relationship is not causal.
3	Non-analytical studies, such as case reports and case series.
4	Expert opinion.

To standardise the strengths of recommendations from the extensive literature used for this review, a structured system was developed to incorporate a number of quality measures. Four measures were selected as important variables for the assessment of strength of recommendations from the primary and secondary research sources. These were:

a) Combination of data via meta-analysis
b) Quality of systematic review/trials
c) Number of RCTs
d) Consistency of the evidence

A scoring system was developed, based on a 0 and 1 score for each of these variables:

1. Combination of data via meta-analysis: Yes = 1, No = 0
2. Quality of systematic review: HQ/Acc (+) =1, LQ(0)/R = 0
3. Number of RCTs: ≥ 5RCTs = 1, < 5=0
4. Consistency: ≥ 75% agreement = 1, < 75% agreement = 0

This allowed for a maximum potential score of 4 and a minimum score of 0, which reflected a measure of the evidence strength across a range of studies. The resultant score was transferred to the SIGN Evidence Grading Matrix:

Total Score	SIGN Evidence Grading Matrix score
4	1++
3	1+
2	1
1/0	1-

Final recommendations were graded according to the Scottish Intercollegiate Guidelines Network (SIGN) Grades of Recommendations (Table 4).

Table 4: Scottish Intercollegiate Guidelines Network (SIGN) Grades of Recommendations

Grades of Recommendations	
A	At least one meta-analysis, systematic review or clinical trial classified as 1++ and directly applicable to the target population of the guideline, or a volume of scientific evidence comprising studies classified as 1+ and which are highly consistent with each other.
B	A body of scientific evidence comprising studies classified as 2++, directly applicable to the target population of the guideline and highly consistent with each other, or scientific evidence extrapolated from studies classified as 1++ or 1+.
C	A body of scientific evidence comprising studies classified as 2+, directly applicable to the target population of the guideline and highly consistent with each other, or scientific evidence extrapolated from studies classified as 2++.
D	Level 3 or 4 scientific evidence, or scientific evidence extrapolated from studies classified as 2+

3. Results

3.1 Evidence Sources

The search yielded 1,752 articles. After scrutiny, 1,647 articles were excluded as duplicates or for failing to meet the inclusion criteria (shown in Figure 1), leaving 105 studies for inclusion in this review. Figure 1 illustrates the process involved in study selection.

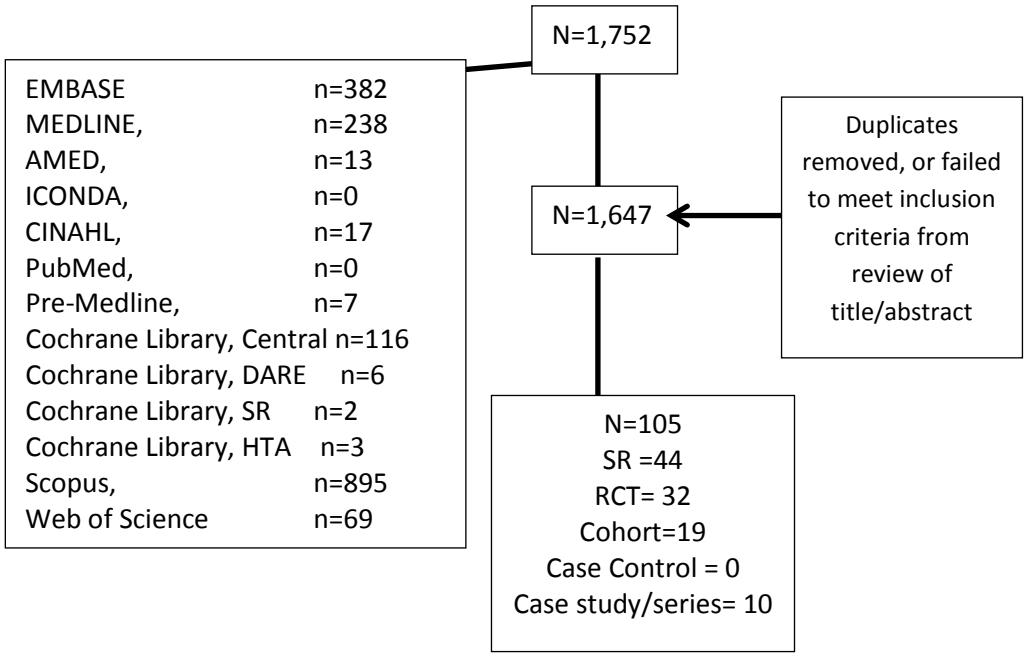

Figure 1: Flow chart of search results

3.2 Appraisal of the evidence

The literature selected for this review varied significantly in quality according to the SIGN critical appraisal checklists:

	N=	HQ(++)	AQ(+)	LQ(-)	R(0)
Systematic Reviews	44	16	18	8	2
Randomised Controlled Trials	32	15	13	4	0
Cohort studies	19	0	3	16	0

Critical appraisal scores for each study in this review are presented in Appendix 2. The main issues affecting the methodological quality of the studies included:

Systematic Reviews

A) Reviews did not address the potential for publication bias when reporting their findings.
B) Very few reviews addressed the potential for publication status to affect the studies included.
C) Conflicts of interest were not identified or reported.

D) Excluded studies were not listed.
E) Review findings were often reported as lumbar epidural steroid injections rather than by the individual approach used. It was difficult to isolate the potential effectiveness of individual approaches.
F) Reviews often failed to differentiate between primary and secondary outcomes when synthesising their findings. Most SRs used pain as a primary outcome and functional disability/surgery sparing etc. as secondary outcomes, but failed to differentiate between the two when synthesising the study findings in their reviews.

Randomised Controlled Trials

A) The studies often failed to ensure that the only difference between the two groups (Intervention vs control) was the treatment under investigation. With the small numbers reported in the RCTs it was difficult to ensure that the effect of confounders was dealt with. This was particularly important when considering the effect of secondary outcomes.
B) A number of studies failed to report the use of Intention to treat analysis when reporting the study's findings.
C) Subjects and investigators were rarely blinded to the intervention involved.
D) Most studies poorly defined the patient presentations in their inclusion criteria. Radiculopathy is a poor diagnostic category when considering a mechanical type intervention, however most studies into the effectiveness of LESI reported patient inclusion criteria of low back pain with radiculopathy. Some were more specific requiring MRI evidence of herniated nucleus pulposis as the cause of the radiculopathy. Likewise, with spinal stenosis many studies failed to report if this represented central spinal stenosis or lateral stenosis.

Cohort Studies

A) The baseline characteristics of the subjects were poorly described making it difficult to be confident that the groups were as similar as possible in all characteristics except for their exposure status, or the presence of specific prognostic factors or prognostic markers relevant to the study in question.
B) The sampling was rarely reported as consecutive, even with the retrospective cohort studies, making it difficult to be confident that all cases were reported on.
C) Outcomes were often poorly defined, with most studies reporting on self-reported complications or only reporting severe adverse events.

3.3 Findings

Lumbar epidural steroid injections (LESI) have presented a fertile ground for primary research and secondary evidence synthesis with an extensive number of systematic reviews (SRs) published on this topic.

The last significant secondary evidence review was presented by Shamliyan et al (2014). This review involved a review of evidence published up to January 10, 2014 and included 18 SRs, which reported on a total of 76 randomized controlled clinical trials (RCTs). Due to the comprehensive nature of Shamliyan et al's review, only RCTs that were published after this date and hence were not included in Shamliyan et al were included in this review on the effectiveness of LESI.

The extensive search strategy used in this review identified a further 26 SRs that were not included in Shamliyan et al's (2014) review. Seventeen (17) of these reviews were published within the search period of Shamliyan et al and nine (9) were published subsequently.

An extra 31 RCTs were identified that had been published since Shamliyan et al's review and were therefore not included in that review. This current review sought to take a comprehensive review of the efficacy of LESI, so included primary clinical trials where both the intervention and control group received LESIs if the data presented allowed a comparison within both groups to the baseline data.

3.4 Outcome Measures – Pain and Function

3.4.1 Systematic Reviews

Systematic Reviews

Shamliyan et al (2014)

Shamliyan et al (2014) (QS:AQ(+)) presented a SR investigating the short-term and long-term efficacy and safety of epidural steroid injections in the treatment of chronic lumbosacral pain in community dwelling adults and examining what patient characteristics may modify treatment benefits and harms. This review included guidelines, systematic reviews and randomized controlled clinical trials (RCTs) in English, plus large observational cohorts to assess treatment safety. Eighteen (18) SRs were identified that synthesized data from 65 RCTs, with a further 11 RCTs that were not included in these reviews also identified. The search strategy included all relevant articles published in English up to January 10, 2014.

This comprehensive review presented an overview of the SRs following the framework of the Cochrane collaboration. Although they did not undertake a meta-analysis, the authors calculated absolute risk difference, number needed to treat, and the number of attributable events per 1000 treated based on data from the published randomized trials, using Meta-Analyst© software and STATA© software. They also attempted to examine the role of patient characteristics, by undertaking subgroup analyses by patient demographics, pain type, prior treatment response, and comorbidities in systematic reviews and randomized trials, including significant interaction effects.

To assess the quality of evidence, the authors looked for a dose response association, the strength of association, and evidence of any reporting bias. The strength of the association was graded as large (when the relative risk (RR) was greater than 2), very large (when the RR was greater than 5.38), and small (when the RR was significant but less than 2). For standardized continuous measures of pain and function, the magnitude of the effect was defined based on standardized mean differences in standard deviation units, with small corresponding to standardized mean differences in standard deviation units of 0 to 0.5, moderate 0.5 to 0.8, and large greater than 0.8.

High quality of evidence was assigned to well-designed RCTs with consistent findings. The quality of evidence was downgraded to Moderate if at least 1 of 4 strength of evidence criteria was not met and to Low if 2 or more criteria were not met.

A low quality of evidence was assigned to nonrandomized studies, and upgraded for the rating if there was a strong or dose-response association. Evidence was defined as insufficient when no studies provided valid information about treatment effects. This approach was applied regardless of whether the results were statistically significant.

The authors identified that the SRs provided conflicting conclusions. A high-quality systematic review, which did not distinguish between interlaminar, caudal, or transforaminal epidural injection techniques for lumbosacral radicular syndrome, found no clinically important benefits with use of epidural steroids (Staal et al 2008). A number of other SRs, which included results from both RCTs and observational studies stratified by injection techniques and type of spinal disorders, reported good evidence of short-term and long-term pain reduction and improvement in function with epidural steroids (Lewis et al 2011, Roberts et al 2009, Rabinovitch et al 2009). Other SRs have concluded that there are short-term but not long-term benefits with epidural steroids in patients with sciatica (Pinto et al 2012, Pinto et al 2013, Choi et al 2013).

Shamliyan et al (2014) concluded that whilst the reviews have focused on statistically significant changes in outcomes, most reviews failed to address the rates of clinically significant improvements in pain and disability, number needed to treat, or attributable events for clinical decision making.

In terms of quality of evidence, Shamliyan et al (2014) reported:

High-quality evidence

- Epidural steroid injections provide short-term but not long-term leg-pain relief and improvement in function for patients with lumbosacral radicular syndrome when compared with placebo. The clinical importance of these small changes in pain and disability is questionable.
- Caudal corticosteroid injections are better than placebo in reducing leg pain at short-term but not long-term follow-up.
- High-quality evidence indicates that short-term post-procedural complications are uncommon, but that the risks of contamination and serious infections are very high.

Moderate-quality evidence

- Epidural steroids are not better than anesthetics in improving pain or disability or in reducing the need for surgery.

Low-quality evidence

- Caudal steroid injections result in short-term improvement in disability.
- There is similar effectiveness of different steroids on pain and disability.
- There is no dose-response association between steroid doses and improvement in outcomes.

Very low-quality evidence

- Transforaminal steroid injections are better than placebo in reducing leg pain at long-term follow-up, with no improvement in disability.
- There is insufficient evidence of any association between patient characteristics and steroid effects.

Shamliyan et al (2014) concluded that:

- When considering injection technique, no single specific injection technique improved lumbar pain.
- With regards to referred symptoms, one SR/MA (Pinto et al 2012) identified:
  - a statistically significant short-term reduction in leg pain with caudal injection, but not with interlaminar or transforaminal approaches.
  - a statistically significant reduction in long-term leg pain with transforaminal injection, but not with caudal or interlaminar approaches.
  - a statistically significant reduction in short-term disability with caudal injection, but not with interlaminar or transforaminal approaches.
- No evidence to suggest that a series of epidural injections was any more effective than a single injection,
- No evidence of improvement in benefits with increasing dose.
- No consistent evidence of superior efficacy of one steroid over the others. In fact, injection of anaesthetic alone resulted in reduction in pain and disability similar to that derived from a combination of steroids with anaesthetic
- Harms associated with LESI were rarely reported in individual RCTs and SRs. One SR (Parr et al 2012) reported a rate of dural puncture frequency between 2% and 5%, and rare cases of postdural puncture syndrome. One SR (Epstein et al 2013) concluded that the harms related to LESI outweighed any short-term benefits.
- Conclusions about cost-effectiveness of epidural steroid injections were inconsistent.

Appendix 5 presents the details extracted from the 18 SRs included in Shamliyan et al's (2014) study and the further 26 SRs found in this review, along with the level of evidence associated with their recommendations.

As described, this review identified a further 26 SRs which explored the efficacy of LESI, with or without anaesthetics.

Koes et al (1995)

Koes et al (1995) (QS:(AQ+)) was the first published SR that explored the efficacy of LESI for low-back pain and sciatica through reviewing randomized clinical trials in this area. They reported on 12 RCTs extending back to 1970 with a wide range of methodological qualities identified. They found that overall, 6 studies indicated that the epidural steroid injection was more effective than the reference treatment and 6 reported it to be no better or worse than the reference treatment. Of the six trials with a positive effect, steroid was compared with placebo injection (saline) (n = 4), lignocaine (n = 2) or with bupivacaine (n = 1). In the trials reporting no differences the epidural steroid Injection was compared to placebo injection (saline) (n = 2), procaine (n = 2), midazolam (n = 1), bupivacaine (n = 1), dry needling (n = 1), or lignocaine and morphine (n =1). There did not appear to be any consistent difference between the use of epidural steroids or anaesthetics in effectiveness. There appeared to be no relationship between the methodological quality of the trials and the reported outcomes. In conclusion, the authors identified significant flaws in the design of most studies (small sample sizes, lack of control of co-interventions, poor sampling, lack of blinding and limited long term follow-up). The studies reviewed showed inconsistent results for effectiveness of epidural steroid injections, with any benefits appearing to be of short duration only.

Study	QS	Conclusions	Level of Evidence
Koes et al (1995)	AQ(+)	• Significant flaws in most research • Inconsistent results for effectiveness of LESI, • Any benefits appearing to be of short duration only • No evidence of difference +/- anaesthetics	1+

Tonkovich-Quaranta and Winkler (2000)

Tonkovich-Quaranta and Winkler (2000) (QS:LQ(-)) presented a scoping review of the literature regarding the safety and efficacy of LESI in the treatment of low back pain (LBP) of various aetiologies. This review made no attempt to qualify the literature according to methodological quality, but reported all the literature related to clinical trials. The study also failed to report how many studies were found but discarded etc. but reported on 9 RCTs of which 6 were related to the use of epidural steroids for the management of sciatica and 4 for LBP of mixed aetiology. Whilst all of the studies identified in this review were included in Koes et al's (1995) review these authors divided the studies by patient clinical presentations. They identified that, based on the positive results in four of the six studies involving patients with sciatica, the use of epidural corticosteroids, either methylprednisolone 80 mg or triamcinolone 80 mg, may be effective in treating pain in these patients. The benefits were seen for as long as 12 weeks following administration and included not only subjective measures (i.e., VAS scores), but objective measures (i.e., degree of SLR) as well. The results in patients with LBP of mixed aetiology were less clear. The authors concluded that epidural steroids may be an effective treatment for LBP and that their use is warranted in

patients who have failed conservative therapy. Whilst this review failed to consider the quality of included studies, the classification of patients into different clinical presentations may improve the external validity of the review's findings.

Study	QS	Conclusions	Level of Evidence
Tonkovich-Quaranta and Winkler (2000)	LQ(-)	• LESI effective in treating pain (i.e., VAS scores), and objective measures (i.e., degree of SLR) associated with radiculopathy for up to 12 weeks.	1-
		• LESI effective in treating pain (i.e., VAS scores), associated with low back pain of mixed aetiology for up to 12 weeks	1-

Abdi et al (2005)

Abdi et al (2005) (QS:AQ(+)) undertook a SR into the role of epidural steroids in the management of chronic spinal pain (axial and radicular) in terms of both effectiveness and safety. This review included both cervical and lumbar injections and looked at each of the three approaches individually. The outcome measures included pain relief, functional improvement, psychological status and return to work. Short-term improvement was defined as less than 6 weeks, and long term improvement was defined as 6 weeks or longer. They included both RCTs and prospective cohort studies in their review. They identified 9 RCTs into lumbar interlaminar LESI, 5 RCTs and 4 prospective cohorts into transforaminal LESI and 12 RCTs into caudal LESI. They concluded that for lumbar radicular pain with interlaminar lumbar epidural steroid injections, the level of evidence was strong for short-term relief and limited for long-term relief. The evidence for lumbar transforaminal LESI for lumbar nerve root pain was strong for short-term and moderate for long term improvement. The evidence was limited for lumbar radicular pain in post lumbar laminectomy syndrome. The evidence for caudal LESI was strong for short-term relief and moderate for long-term relief. For managing chronic post lumbar laminectomy syndrome and spinal stenosis the evidence was limited for low back and radicular pain. The evidence was moderate for chronic low back pain.

Study	QS	Conclusions	Level of Evidence
Abdi et al (2005)	AQ(+)	• For interlaminar LESI, evidence for use in lumbar radicular pain was strong for short-term and limited for long-term improvement in pain and functional outcomes.	1+
		• For lumbar transforaminal LESI, the evidence for use in radicular pain was strong for short-term and moderate for long term improvement in pain and functional outcomes.	1+
		• For caudal epidural LESI, the evidence was strong for short-term and moderate for long-term improvement in pain and functional outcomes. For managing chronic post lumbar laminectomy syndrome and spinal stenosis the evidence was limited for low back and radicular pain. The evidence was moderate for chronic low back pain.	1+

Bhargava et al (2005)

Bhargava et al (2005) (QS:LQ(-)) undertook a limited SR of injection therapy for lumbar radiculopathy, limiting research evidence from 2003 to 2005. This review included both full text and abstracts of all research designs (both RCT and cohort studies). They concluded that all approaches to the interlaminar, caudal, and transforaminal epidural space provided long-term relief in 27—56% patients, and that whilst conclusive evidence was lacking, epidural space steroid instillation via the transforaminal approach for the treatment of lumbar radicular pain seemed effective. Whilst three common techniques are used to deliver medication into the epidural space, of these, a transforaminal approach seemed to be the best route for delivering medication to the ventral epidural space and/or the dorsal root ganglia.

Study	QS	Conclusions	Level of Evidence
Bhargava et al (2005)	LQ(-)	• All approaches to the interlaminar, caudal, and transforaminal epidural space provide long-term relief in 27—56% patients with radiculopathy.	1-
		• Epidural space steroid instillation via the transforaminal approach for the treatment of lumbar radicular pain seemed effective.	1-
		• The transforaminal approach seemed to be the best route for delivering medication to the ventral epidural space and/or the dorsal root ganglia.	1-

Luijsterburg et al (2007)

Luijsterburg et al (2007) (QS:AQ(+)) undertook a SR into the effectiveness of conservative treatments for lumbosacral radicular syndrome, which included corticosteroid injections. Unfortunately, in this review they failed to differentiate between epidural and extradural steroid injections and were therefore excluded from this review.

Armon et al (2007)

Armon et al (2007) (QS:AQ(+)) presented a review into the use of epidural steroid injections to treat radicular lumbosacral pain. This review considered both efficacy and safety of epidural steroid injections, however it did not differentiate between approaches. This review had stringent inclusions criteria leading to only 4 of the 37 studies they found on the topic being included. The inclusion criteria included

1) clear case definition;
2) clear measure of outcome (pain relief) using a standardized measure;
3) use of a control group (placebo or active);
4) randomization;
5) at least double-blind study design, so that neither patient nor assessor of measure or outcome would know the treatment arm; or triple blind, if the physician injecting the treatment also did not know what treatment was administered;
6) prospective study design;
7) adequate statistical analysis.

The review concluded that

1) Epidural steroid injections may result in some improvement in radicular lumbosacral pain when assessed between 2 and 6 weeks following the injection, compared to control treatments (Level C, Class I–III evidence). The average magnitude of effect is small and generalizability of the observation is limited by the small number of studies, highly selected patient populations, few techniques and doses, and variable comparison treatments;
2) In general, epidural steroid injection for radicular lumbosacral pain does not impact average impairment of function, need for surgery, or provide long-term pain relief beyond 3 months. Their routine use for these indications is not recommended (Level B, Class I–III evidence).

Study	QS	Conclusions	Level of Evidence
Armon et al 2007	AQ(+)	• LESI effective compared to control treatments in improving pain in patients with radicular lumbosacral pain when assessed between 2 and 6 weeks • LESI not effective compared to control treatments in average impairment of function, need for surgery, or provide long-term pain relief beyond 3 months.	1 1

Buenaventura et al (2009)

Buenaventura et al (2009) (QS:AQ(+)) undertook a SR of the effectiveness of transforaminal LESI for managing lumbar (low-back) and sciatica (leg) pain. Whilst they included both RCTs and prospective cohort studies in their search strategy, they identified only 4 RCTs of effectiveness of transforaminal LESI that met their inclusion criteria. Four prospective cohort studies were included in their review of complications. The outcome measures of interest included pain relief, functional assessment, psychological improvement, return to work, and change in opioid intake. They concluded that overall the evidence for transforaminal LESI was strong with Level II-1 for short-term relief and Level II-2 for long-term improvement in the management of lumbar nerve root and low back pain.

Study	QS	Conclusions	Level of Evidence
Buenaventura et al 2009	AQ(+)	Transforaminal LESI have significant effect in relieving chronic pain of lumbar disc herniation and radiculitis with indicated evidence levels of Level II-1 for short-term relief and Level II-2 for long-term relief	1

Parr et al (2009)

Parr et al (2009) (QS: (HQ++)) undertook a SR on the effectiveness of lumbar interlaminar epidural injections in managing various types of chronic low back pain with or without lower extremity pain. Conditions included disc herniation or radiculitis, post lumbar laminectomy syndrome, spinal stenosis, and chronic discogenic pain.

This review identified 6 RCTs that evaluated the effect of blind interlaminar epidural injections with or without steroids. Of the 5 randomized trials of blind lumbar Interlaminar epidurals for disc herniation and radiculitis, all included steroids, 2 were positive for short-term effects on pain, and 5 were negative for long-term relief of more than 6 months. Of the 2 RCTs investigating the effectiveness of blind lumbar Interlaminar epidural injections in spinal stenosis, both included steroids and neither were shown to be positive for short term or long-term relief. The authors concluded that blind lumbar Interlaminar epidural injections:

- Provided short term effect but no evidence of long term effect for pain related to disc herniation or radiculitis (Strong recommendation, based on low quality or very low-quality evidence, which may change when higher quality evidence becomes available)
- May provide long-term relief. However, the recommendation is weak based on moderate quality evidence, with best action differing depending on circumstances or patient or societal values.
- Provided no short or long term effect for spinal stenosis and discogenic pain (weak recommendation, based on low-quality or very low-quality evidence, and other alternatives may be equally reasonable).

As the authors concluded, caution must be exercised in the interpretation of these findings as all the studies included in this evaluation were blind Interlaminar epidural injections and did not represent contemporary interventional pain management practice.

Study	QS	Conclusions	Level of Evidence
Parr et al (2009)	HQ (++)	• Interlaminar LESI performed blind (without fluoroscopy) effective for short-term relief of pain (<3/12) of disc herniation or radiculitis	1
		• Interlaminar LESI performed blind (without fluoroscopy) not effective for long-term relief of pain of disc herniation or radiculitis	1
		• Interlaminar LESI performed blind (without fluoroscopy) effective for short term relief of pain of discogenic origin without radiculitis or disc herniation	1
		• Interlaminar LESI performed blind (without fluoroscopy) not effective for long term relief of pain of discogenic origin without radiculitis or disc herniation	1-

Colimon and Villalobos (2010)

Colimon and Villalobos (2010) (QS:R(0)) presented a review of the literature related to the three approaches to LESI. They classified the quality of the evidence according to the US Preventive Services Task Force (USPSTF) grading. Unfortunately, they failed to provide any details on the search strategy they undertook to find the evidence, nor much information on the number and characteristics of the studies that underpinned their findings.

Study	QS	Conclusions	Level of Evidence

Colimon and Villalobos 2010	R(0)	• Caudal LESI is indicated for patients with chronic LBP with or without radiating limb pain, who have not responded to conventional medical treatment
		• Level I evidence for short and long term pain control for chronic back pain and lower limb pain secondary to herniated disc and/or radiculitis and discogenic pain without herniated disk or radiculitis.
		• Level II-1 to II-2 evidence for the management of LBP due to post laminectomy syndrome and spinal stenosis.
		• Overall grade of recommendation for caudal LESI is 1A or 1B for lumbar pain with chronic herniated disk and radiculopathy or discogenic pain without herniated disk or radiculitis.
		• For patients with post laminectomy syndrome or spinal stenosis, the grade of recommendation is 1B/1C.
		• Interlaminar LESI is indicated in patients with herniated disk, radiculopathy, and lumbar channel stenosis.
		• Level II-2 evidence for short-term pain relief for chronic LBP and lower limb pain using blind lumbar interlaminar ESI, and for pain secondary to lumbar disc herniation and/or radiculitis.
		• Level III, for blind lumbar interlaminar ESI in LBP, secondary to spinal stenosis and chronic LBP of discogenic origin without herniated disc or radiculitis.
		• Overall grade of recommendation is:
		  • 1C for interlaminar lumbar epidural blind injection, herniated discs, and radiculitis; but the recommendation in the long term is 2B.
		  • 2C for blind lumbar interlaminar ESI, in spinal stenosis and discogenic pain without herniation and radiculitis.
			1-

Benny and Azari (2011)

Benny and Azari (2011) (QS:AQ(+)) completed a SR that focused on the efficacy of lumbosacral transforaminal LESI. They did not limit to RCTs only, but included observational cohort studies (retrospective and prospective). They reported on 8 randomized trials, 4 retrospective studies and 8 prospective studies. The majority of the studies they reviewed included radicular pain as a result of discogenic aetiologies, most commonly a herniated nucleus pulposis. There were a few studies which reported effectiveness of transforaminal LESI in patients with spinal stenosis, however these were lower level studies (i.e. prospective cohort studies, not RCTs). They reported that all 8 of the RCTs that were included showed a positive outcome in both the short term and long term in reducing pain.

All studies used either CT guidance or fluoroscopic guided transforaminal LESI, and in both cases the studies showed that transforaminal LESI were effective. There was no study which directly compared the two of these approaches

Benny and Azari (2011) also reported that the composition of the mixture used as an injectate varied from study to study. While some studies used a mixture of steroid and lidocaine others used only steroid depending on the preference of the physician performing the study, with no difference in effectiveness reported.

They concluded that the evidence was strong (i.e. *obtained from well designed controlled trials without randomization*) for use of transforaminal lumbar epidural injections of steroid for short term effect, and moderate (ie. *obtained from well-designed cohort or case control analytic studies, preferably from more than one center or research group*) for long term relief in managing radicular pain caused by nerve root irritation as a result of impingement, with an overall grading recommendation of strong, based on moderate quality evidence.

Study	QS	Conclusions	Level of Evidence
Benny and Azari 2011	AQ(+)	Transforaminal LESI effective in both short term and long term management of radiculopathy due to spinal stenosis or lumbar herniation.	1+

Fritzler and Sarafini (2011)

Fritzler and Sarafini (2011) (QS:LQ(-)) undertook a review that focused on the effectiveness of interventional pain management techniques (including epidural steroid injections (LESI)) in placebo controlled trials. This review used broad inclusion criteria but failed to report on the methodological quality of the included studies. They identified 4 placebo-controlled RCTs that studied the efficacy of LESI for lower extremity sciatica/radiculopathy and concluded that LESI appears superior to placebo in providing transient benefit with respect to patient disability scores up to 3 weeks and VAS pain scores up to 6 weeks. There appeared to be no evidence of benefit over placebo in terms of improved physical function, rates of return to work, or the need for future surgery. Transforaminal LESIs appeared superior to placebo in improving patient satisfaction and pain levels for a minimum of 2 weeks and potentially up to 16 months on average.

Study	QS	Conclusions	Level of Evidence
Fritzler and Sarafini 2011	LQ(-)	• LESI effective compared to placebo in reducing disability scores up to 3 weeks and VAS pain scores up to 6 weeks.	1-
		• LESI not effective compared to placebo in terms of improved physical function, rates of return to work, or the need for future surgery.	1-
		• Transforaminal LESIs appear superior to placebo in improving patient satisfaction and pain levels for a minimum of 2 weeks and potentially up to 16 months on average.	1-

Jacobs et al (2011)

Jacobs et al (2011) (QS:AQ(+)) completed a SR on the effects of surgery versus conservative therapy (including LESI) for patients with sciatica due to lumbar disc herniation. In total, five studies were identified, with only one study comparing surgery with epidural injections (Buttermann 2004). This trial (n = 100) had a high risk of bias and compared results following microdiscectomy with results after epidural steroid injection. Patients undergoing discectomy had the most rapid and greatest decrease in their symptoms at 3- and 6-month follow-up intervals, but not beyond 1 year. There were no significant differences between groups for back pain throughout the follow-up. Of the 50 patients, 27 who received a steroid injection had a subsequent microdiscectomy. Outcomes in this cross-over group were similar to those of the surgery group. Jacobs et al (2011) concluded that there was very low quality evidence (high risk of bias) that discectomy was beneficial over epidural steroid injections for the short term only.

Study	QS	Conclusions	Level of Evidence
Jacobs et al 2011	A(+)	• Discectomy was effective compared to LESI for the short term in patients with radiculopathy due to herniated lumbar disc	1

Ammendolia et al (2012)

Ammendolia et al (2012) (QS:HQ(++)) presented a SR of the literature related to non-operative treatment (including LESI) in patients with lumbar spinal stenosis with neurogenic claudication. A total of 21 RCTs were identified of which 3 reported on the effectiveness of LESI using different approaches. All 3 trials provided very low-quality evidence for all outcomes. One small trial (N = 29), evaluating intralaminar LESI plus epidural block compared with home exercise or inpatient physical therapy, demonstrated improvements in pain intensity, function, and quality of life at 2 weeks' follow-up. One trial evaluating caudal (N = 30) and another translaminar (N = 37) LESI showed no difference in global improvement compared with placebo injections. Ammendolia et al (2012) concluded that moderate- and high-grade evidence for non-operative treatment was lacking, prohibiting recommendations to guide clinical practice. As the authors warned, due to the expected rise in the prevalence of lumbar spinal stenosis with neurogenic claudication, large high-quality trials were urgently needed.

Study	QS	Conclusions	Level of Evidence
Ammendolia et al 2012	HQ (++)	LESI effective compared with home exercise or inpatient physical therapy in improving pain, function, and quality of life up to 2 weeks in patients with spinal stenosis	1

Bresnahan et al (2013)

Bresnahan et al (2013) (QS:AQ(+)) undertook a SR into the effectiveness of LESI for spinal stenosis and expanded the study to investigate the reimbursement amounts. They identified and reviewed 6 RCTs and 2 large observational studies. They concluded that both LESIs and anesthetic injections alone resulted in better short term improvement (<6

months) in walking distance compared with control injections, however there was little evidence of a long-term effect. Across the studies the authors could find no differences between LESIs and anesthetic injections in self-reported improvement in pain. One study indicated that transforaminal approaches had better improvement in pain scores (<4 months) compared with Interlaminar injections.

Study	QS	Conclusions	Level of Evidence
Bresnahan et al 2013	AQ (+)	• LESI (+/1 anesthetic) effective compared with control injections in improving walking distance in patients with spinal stenosis in short term	1
		• LESI (+/1 anesthetic) not effective compared with control injections in improving walking distance in patients with spinal stenosis in long term (>4 months)	1
		• LESI no more effective compared to anesthetic in self-reported improvement in patients with spinal stenosis.	1
		• Transforaminal approaches had better improvement in pain scores (4 months) compared with interlaminar injections.	1

Cohen et al (2013)

Cohen et al (2013) (QS:AQ(+)) undertook a comprehensive SR of the evidence for epidural steroids (including both lumbar and cervical). This review divided the evidence according to the three approaches to LESI and used levels of evidence based on US Preventive Services Task Force (USPSTF) criteria with comparative effectiveness described using USPSTF levels of certainty.

Lumbar Interlaminar Approach

Independent of the use of imaging during the procedure, SRs of interlaminar LESIs have yielded similar results. On balance, the authors felt that there was good evidence for the treatment of radicular pain due to disk herniation and somewhat weaker evidence for treatment of spinal stenosis, discogenic pain, and postsurgical pain. However, there was some diversity in the literature as was evidenced by some reviews that conclude there was good evidence for treating spinal stenosis (Botwin et al 2003) whereas others showed an unclear benefit for all conditions including radicular pain (Rozenberg et al 1999, Staal et al 2009).

Lumbar Transforaminal Approach

The authors concluded that SRs in this area were hampered by significant heterogeneity but generally found good evidence supporting short-term relief and mixed evidence in favour of long-term benefit for transforaminal LESIs in treating back pain with radicular symptoms due to disk herniation. One review found good evidence for the treatment of radicular pain secondary to disk herniation, but only fair or limited evidence for the

treatment of spinal stenosis, postsurgical pain, or axial pain in the absence of disk herniation. Reviews dedicated specifically to either spinal stenosis or postsurgical pain were lacking. Subgroup analyses in several clinical studies showed either comparable benefit in patients with herniated disk and spinal stenosis or only a small benefit in favour of herniated disk.

Caudal Approach

Meta-analyses provided conflicting results regarding the role of caudal LESIs in several pain conditions. Several SRs showed good (level I) evidence for both short- and long-term benefit in managing back and leg pain due to disk herniation, similar (level I) evidence for treating discogenic pain, and less compelling evidence for treating pain associated with spine surgery (level II-2) or spinal stenosis (level II-1). Overall, caudal LESIs are best supported in the treatment of radicular symptoms due to disk herniation and previous surgery and carry an extremely low risk of inadvertent dural puncture.

Cohen et al (2013) also explored the characteristics of the injectate, which they reported differed among studies and may have impacted on patient outcome. Both the dose and volume of steroid varied depending on the route of injection, with amounts of each typically increasing as transforaminal, interlaminar and caudal LESI are performed respectively. Owlia et al (2007) identified that an interlaminar LESI dose of 40 mg of methylprednisolone provided a similar reduction in pain with fewer adverse effects compared with 80 mg. Kang et al (2011) evaluating the effect of steroid dose during transforaminal LESI found no differences in efficacy between triamcinolone doses of 10, 20, and 40 mg, although 5 mg failed to provide a similar level of benefit. Rabinovitch et al (2009) concluded there was an independent, beneficial effect for volume, as the use of higher volumes may result in pain relief in and of itself. Revel et al (1996) found that steroid injected in a volume of 40 ml of saline provided superior pain relief than when the same dose of steroid was injected by itself at 18 months' follow-up.

Cohen et al (2013) also attempted to review the literature related to different types of steroid injections, but reported that the evidence was mostly limited to underpowered randomized or retrospective studies comparing particulate to nonparticulate steroids. Among 3 RCTs comparing different steroid preparations, 2 reported a nonsignificant benefit in favour of the depo-steroid group, with the study reporting a statistically significant difference for depo-steroids using the largest study cohort, suggesting a stronger powered finding. They concluded in summary that there was conflicting evidence, with a low degree of certainty that depo-steroids provided superior relief compared with non-depo-steroids.

When considering different pathologies, the efficacy of LESI varied. Lumbar herniated nucleus pulposus represented the most commonly studied condition, with the most comprehensive SRs demonstrating level I evidence supporting the role of LESI, particularly for short-term pain relief. For intermediate- and long-term benefit (>3 months), the benefit was significantly smaller and may well represent the effect of

disease evolution. The authors reported more limited evidence for the effectiveness of LESI for other pathologies, with the evidence for LESI in spinal stenosis less robust than for herniated disk, but more convincing than that for failed back surgery syndrome or axial back pain.

Study	QS	Conclusions	Level of Evidence
Cohen et al 2013	AQ(+)	• Transforaminal injections are more likely to yield positive results than interlaminar or caudal injections,	1+
		• LESI more effective for reducing pain in patients with lumbar herniated disk, compared with spinal stenosis or axial spinal pain.	1+

Dighe and Friedman (2013)

Dighe and Friedman (2013) (QS:(AQ+)) presented a SR on the use of caudal LESI in chronic back pain conditions. Their review attempted to evaluate the clinical effectiveness of (A) caudal LESI without local anaesthetics (LA), (B) caudal LESI plus LA and (C) caudal epidural injections of LA alone in: chronic back pain secondary to disc herniation or radiculopathy, disco-genic pain with predominantly low back pain, spinal stenosis and post-lumbar-surgery pain syndrome. They identified 11 RCTs, 6 of which focused on disc herniation or radiculopathy, 2 on discogenic pain, 2 on spinal stenosis and 1 on post-lumbar-surgery syndrome. Their findings were in agreement with Armon et al (2007) and Staal et al (2009) that the evidence for caudal epidural injections ranged from nil to possible, based on the cause of chronic back pain conditions. There was no convincing evidence for the efficacy of caudal epidural injections for long-term relief of back pain of any studied aetiology.

Study	QS	Conclusions	Level of Evidence
Dighe and Friedman 2013	AQ (+)	• Caudal LESI with or without steroid effective for pain relief in patients for disc herniation or radiculopathy in short term	1
		• Caudal LESI with or without steroid not effective for pain relief in patients for disc herniation or radiculopathy in long term	1+
		• Caudal LESI with or without steroid effective for pain relief in patients for with discogenic pain without herniation	1
		• Caudal LESI with or without steroid possibly effective for pain relief in patients with spinal stenosis	1-
		• Caudal LESI with or without steroid effective for pain relief in patients with post lumbar surgery syndrome in short and long term	1
		• Lumbar decompression surgery more effective compared to caudal LESI	1

		• Caudal LESI plus anesthetic more effective than anesthetic alone	1+

Dworkin et al (2013)

Dworkin et al (2013) (QS:LQ(-)) conducted a review of evidence, including SRs, clinical trials, and existing guidelines, for the interventional management of neuropathic pain. Dworkin et al's (2013) paper scored poorly on methodological quality as it lacked sufficient details of the studies included etc. The authors concluded that their assessment of the literature was consistent with the American Pain Society guidelines. For patients with prolapsed lumbar disc with radiculopathy there was moderate evidence of benefit supporting a weak recommendation for the use of LESI for short-term benefits, although there was insufficient evidence regarding pain relief beyond 12 weeks or for prevention of future spine surgery. This review could find no studies assessing the efficacy of LESI for treating patients with failed back surgery syndrome who have prominent radicular symptoms ("inconclusive" recommendation). However, on the basis of the evidence reviewed for the efficacy of LESI in the treatment of radiculopathy and their relative safety and ease of application, the authors believed LESI was a reasonable treatment option for clinicians and patients to consider when a patient has failed to respond to less invasive treatments and prior to considering more invasive treatments, such as spinal cord stimulation.

Study	QS	Conclusions	Level of Evidence
Dworkin et al 2013	LQ (-)	• LESI effective for pain relief in patients with radiculopathy in the short term	1
		• LESI not effective for pain relief or for prevention of future spine surgery in patients with radiculopathy in the long term (>12 weeks)	1-

Chien et al (2014)

Chien et al (2014) presented a SR comparing the effectiveness of transforaminal LESI (TF-LESI) with interlaminar LESI (IL-LESI) for lumbosacral radicular pain. This review only included controlled studies where the radicular pain was secondary to disc herniation or degeneration, the techniques were conducted using fluoroscopic guidance for needle placement and the study compared TF-LESI with IL-LESI.

They identified 8 studies, 5 of which were prospective (Gharibo et al 2011, Candido et al 2008, Rados et al 2011, Ackerman and Ahmad 2007, Kolsi et al 2000) and 3 that were retrospective (Smith et al 2010, Lee et al 2009, Schaufele et al 2006). The studies involved 249 patients with an average of 3.2 months' follow-up. In the short-term (up to 2 weeks), there was a 15% difference favouring TF-LESI vs. IL-LESI for pain relief. There was no difference at > 1 months. Combined pain improvements in all 5 prospective studies revealed < 20% difference between TF-LESI and IL-LESI (54.1% vs. 42.7%). There was slightly better functional improvement in IL-LESI groups (56.4%) vs. TF-LESI groups (49.4%) at 2 weeks. Combined data showed slight differences (TF-LESI 40.1% and IL-LESI 44.8%).

Study	QS	Conclusions	Level of Evidence
Chien et al 2014	HQ (++)	• Transforaminal fluoroscopy guided LESI more effective compared to fluoroscopy guided Interlaminar LESI in reducing pain in radiculopathy secondary to IV disc herniation/degeneration in the short term	1-
		• Transforaminal fluoroscopy guided LESI no more effective compared to Interlaminar fluoroscopy guided LESI in reducing pain in radiculopathy secondary to IV disc herniation/ degeneration in the long term	1-
		• Transforaminal fluoroscopy guided LESI no more effective compared to Interlaminar fluoroscopy guided LESI in functional improvement in patients with radiculopathy secondary to IV disc herniation/degeneration in the long or short term	1

Jamjoom and Jamjoom (2014)

Jamjoom and Jamjoom (2014) (QS:AQ(+)) undertook a SR investigating the effect of epidural injections performed intra-operatively during lumbar discectomy. They reported on 16 trials and concluded that there was relatively strong evidence that intraoperative epidural steroids were effective in reducing pain in the early stage and reducing consumption of analgesia. However, there was also relatively strong evidence that they were ineffective in reducing pain in the late stage and in reducing duration of hospital stay. As with many LESI studies, the heterogeneity between the trials made it difficult to make undisputed conclusions.

Study	QS	Conclusions	Level of Evidence
Jamjoom and Jamjoom 2014	AQ(+)	• Intraoperative LESI are effective in reducing pain and reducing consumption of analgesia in the early stage	1+
		• Intraoperative LESI are effective in reducing pain and reducing consumption of analgesia in the intermediate stage	1
		• Intraoperative LESI are not effective in reducing pain in the late stage	1+
		• Intraoperative LESI are not effective in reducing duration of hospital stay.	1

MacVicar et al 2013

MacVicar et al 2013 (QS:LQ(-)) completed a SR into the effectiveness of transforaminal LESI and included all study designs. They identified 39 primary research studies that reviewed the effect of transforaminal LESI on pain and concluded that for miscellaneous conditions, the available evidence was limited and was neither compelling nor conclusive. For disc herniation, the evidence was sufficiently abundant to show that transforaminal LESI, whilst not universally effective, nevertheless, benefited a substantial

proportion of patients and was not a placebo. The authors identified that success rates were higher in patients with contained herniations that cause only low-grade compression of the nerve.

Study	QS	Conclusions	Level of Evidence
MacVicar et al 2013	LQ(-)	Transforaminal LESI effective in reducing pain, restoring function, reducing the need for other health care, and avoiding surgery in patients with lumbar radicular pain caused by contained disc herniations	1

May and Comer (2013)

May and Comer (2013) (QS:AQ(+)) presented a SR on the effectiveness of surgery versus non-surgical treatments (including LESI) for spinal stenosis. They reported on 9 studies which looked at different methods of LESI with or without an anaesthetic. In 6 high quality trials LESI produced no statistically significant differences compared to physical therapy, saline, saline and anaesthetic or anaesthetic injection at long-term follow-up, with significant differences in short-term pain reported in one trial only. Bilateral transforaminal injections appeared to be more effective than interlaminar steroid injections for spinal stenosis. Percutaneous adhesiolysis and decompression surgery were more effective than LESI. The authors concluded that there was strong evidence (6 RCTS; n = 239) that LESI were no more effective than active controls, and that LESIs were no more effective than saline or anaesthetic in 5 out of 6 studies.

Study	QS	Conclusions	Level of Evidence
May and Comer 2013	AQ (+)	• LESI not effective compared to physical therapy, saline, saline and anaesthetic or anaesthetic injection at long-term follow-up in patients with spinal stenosis;	1+
		• Percutaneous adhesiolysis and decompression surgery were more effective than LESI in patients with spinal stenosis;	1
		• Bilateral transforaminal injection was more effective than an interlaminar steroid injection in patients with spinal stenosis;	1

Wang et al (2014)

Wang et al (2014) (QS:AQ(+)) undertook a SR/MA of RCTs assessing the value of tumour necrosis factor (TNF)-a inhibitors in the treatment of sciatica. Whilst not focused on LESI specifically, five of the RCTs used LESI as a control comparison group. Over the 5 RCTs identified, the authors calculated no benefit of tumour necrosis factor (TNF)-a inhibitors in the short term (WMD -0.82 95%CI -5.99, 4.36) or medium term (WMD 0.48 95%CI -2.75, 3.72) compared with LESI.

Study	QS	Conclusions	Level of Evidence
Wang et al 2014	AQ(+)	LESI no more effective compared to TNF-a inhibitors in terms of lower back and leg pain patient overall satisfaction (global perceived effect (satisfaction)) or return to work at the short term, medium-term and long-term follow-ups.	1+

Bicket et al (2015)

Bicket et al (2015) (QS:HQ(++)) undertook a SR/MA of the effectiveness of lumbar epidural steroid injections (LESI) in reducing the need for spinal surgery in patients with spinal pain. Surgical outcomes were divided by time intervals into short-term (<1 year) and long-term (>1 year) results. They identified 26 RCT studies representing 1707 LESI patients and 1616 control subjects. Bicket et al reported on 22 studies that compared LESI with non-LESI controls, with 5 studies comparing the outcomes on the short term (<1 year) need for surgery and 17 reporting on the outcomes of long term (<1 year) need for surgery. These studies were included in subsequent meta-analyses. They reported that LESI demonstrated a trend to reduction in the need for surgery for short-term (<1 year) outcomes (risk ratio, 0.68; 95% confidence interval, 0.41–1.13; p=.14), but not long-term (>1 year) outcomes (RR: 0.95, 0.77–1.19, p5.68).

The authors also undertook a secondary analysis, which sought to analyse the cross-over data presented in studies comparing surgical care with non-surgical care in which patients had LESI (n=4). Whilst the authors admitted this secondary analysis was not at the same level of evidence as the meta-analysis, they felt it provided useful information regarding the ability of LESI to prevent surgery in a clinical, rather than controlled, setting. This secondary analysis provided low-level evidence suggesting that between one-third and half of patients considering surgery who undergo LESI could avoid surgery.

Study	QS	Conclusions	Level of Evidence
Bicket et al 2015	HQ (++)	• LESI not effective in reducing need for surgery in short term	1+
		• LESI not effective in reducing need for surgery in long term	1+

Manchikanti et al (2015)

Manchikanti et al (2015) (QS:AQ(+)) also divided the LESI into the three approaches in their SR into the efficacy of epidural injections in the treatment of lumbar central spinal stenosis. They identified 7 RCTs that matched their inclusion criteria, which included both anaesthetics and steroid injectates. One RCT investigated caudal LESI, 5 investigated interlaminar LESI and 2 investigated transforaminal LESI. Due to lack of homogeneity and limited number of trials in each category no meta-analysis was performed. This SR, based on a high quality methodological quality assessment, concluded that caudal epidural

injections and lumbar Interlaminar epidural injections of local anesthetic with or without steroid provide effective and significant improvement in pain and function in central spinal stenosis.

There was Level II evidence for long-term results for caudal and interlaminar approaches. However, the evidence is Level III for short-term efficacy based on two moderate quality RCTs of transforaminal LESI. An interlaminar approach was reported to be superior to a caudal approach and a caudal approach superior to a transforaminal one.

The authors acknowledged that the findings of their SR did not correlate with other SRs (Kovacs et al 2011, Ammendolia et al 2012, and Bresnahan et al 2013). However, they felt this may have reflected the poor methodological quality of these three reviews, with issues such as lack of standardisation of intervention, inclusion of low quality studies and poor search strategies and evidence selection processes.

Study	QS	Conclusions	Level of Evidence
Manchikanti et al 2015	AQ(+)	• Transforaminal LESI effective for reducing pain in patients with spinal stenosis in short term	1
		• Caudal and lumbar interlaminar LESI effective for reducing pain in patients with spinal stenosis in long term	1
		• LESI with anaesthetic no more effective than LESI with anaesthetic and steroid in long or short term	1

Bhatia et al (2016)

Bhatia et al (2016) (QS:HQ(++)) undertook a SR/MA into the effectiveness of transforaminal LESI for the treatment of lumbosacral radicular pain from herniated intervertebral discs. They explored a wide range of outcomes including pain (up to 12 months), disability, psychological function and quality of life, as well as potential complications. They identified 8 RCTs which they incorporated into their meta-analysis. They concluded that on the basis of the quality of evidence and the strength of effect, it was recommended that, in outpatients with lumbosacral radicular pain secondary to herniated intervertebral disks, transforaminal LESI should be used to reduce pain up to 3 months after the intervention (strong recommendation; moderate-quality evidence). The modest analgesic benefit should be discussed with patients, and their preferences and values considered before proceeding with this intervention. This intervention should not be used to reduce physical disability at 1 to 3 months after the intervention (strong recommendation; high-quality evidence) or incidence of surgery at 12 months after the intervention (strong recommendation; moderate-quality evidence). They also noted that there was a lack of information about appropriate dosages and number of procedures. Whilst they concluded that dosage was unclear, the mean difference in pain scores in the RCTs (n=516) that used low doses of steroids (<40mg) (Mean Diff=-0.54 (-0.67 to -0.42)) was lower than those with higher doses (Mean Diff=-2.04 (-2.42 to –1.65)).

Study	QS	Conclusions	Level of Evidence
Bhatia et al 2016	HQ (++)	• Transforaminal LESI should be used to reduce pain up to 3 months in patients with radiculopathy from herniated lumbar disc	1++
		• Transforaminal LESI should not be used to reduce physical disability up to 3 months after the intervention or incidence of surgery at 12 months after the intervention in patients with radiculopathy from herniated lumbar disc	1++

Vorobeychik et al (2016)

Vorobeychik et al (2016) (QS:HQ(++)) undertook a SR of the evidence related to the effectiveness of non–Image-guided interlaminar LESI for lumbar radicular pain and spinal stenosis. They included all study designs and included outcomes such as pain relief, functional improvement, surgery rate, use of opioids, and complications. They identified 35 studies, including 9 RCTs, 11 pragmatic RCTs and 25 observational studies. They concluded that overall the evidence supporting the effectiveness of Interlaminar LESI for pain relief and functional improvement in patients with lumbar radicular pain due to disc herniation or neurogenic claudication secondary to lumbar spinal stenosis was limited. Despite this they concluded that in patients with lumbar radicular pain secondary to disc herniation or neurogenic claudication due to spinal stenosis, non–image-guided lumbar interlaminar epidural steroid injections appeared to have clinical effectiveness limited to short-term pain relief.

Study	QS	Conclusions	Level of Evidence
Vorobeychik et al 2016	AQ (++)	In patients with lumbar radicular pain secondary to disc herniation or neurogenic claudication due to spinal stenosis, non–image-guided lumbar interlaminar epidural steroid injections appear to have clinical effectiveness limited to short-term pain relief.	1+

Wei et al (2016)

Wei et al (2016) (QS:AQ(+)) presented a SR comparing the effectiveness of transforaminal and interlaminar approaches for pain and functional outcomes in patients with low back pain with lumbosacral radicular pain. They included both observational studies (n=4) and RCTs (n=9) in their review, representing 931 patients. They concluded that transforaminal LESI produced better pain relief compared with interlaminar LESI in RCTs ($p<0.01$), but not in the observational studies ($p=0.62$). However, there was no difference in functional improvements and Oswestry disability index (ODI) scores. There were also no differences between transforaminal and interlaminar LESI in regard to procedure frequency, surgery rate, and ventral epidural spread.

Study	QS	Conclusions	Level of Evidence
Wei et al 2016	AQ (+)	• Transforaminal LESI produced better pain relief compared with interlaminar LESI in RCTs, but not in observational studies.	1 / 2-
		• Transforaminal LESI produced no better functional improvement and Oswestry disability index (ODI) score than Interlaminar LESI	1
		• There were no differences between transforaminal and interlaminar LESI in regard to procedure frequency, surgery rate, and ventral epidural spread.	1

3.4.12 Randomised Controlled Trials

Randomised Controlled Trials

Appendix 6 presents the RCTs that were included in the systematic reviews reported above. Appendix 7 presents the data of these RCTs extracted from the SRs. The last date of searching in the SRs identified was July 2014 (Manchikanti et al (2015), however this review only focussed on the use of LESI for patients with spinal stenosis. The last relevant search dates for RCTs was to February 2013 (Cohen 2013, Bicket et al 2015). Therefore, a search of the relevant literature was undertaken from February 2013 to July 2016. A total of 32 relevant RCTs were identified in this review.

Candido et al (2013)

Candido et al (2013) (QS:HQ(++)) completed a randomized, blinded study comparing 2 different approaches, midline and lateral parasagittal, of lumbar Interlaminar epidural steroid injection (LESI) in patients with unilateral lumbosacral radiculopathic pain. They also examined the role of concordant pressure paresthesia occurring during LESI as a prognostic factor in determining the efficacy of LESI. 106 patients undergoing LESI for radicular low back pain, secondary to degenerative lumbar disc disease including protruding or bulging discs, desiccated discs, and herniated discs, were randomly assigned to one of 2 groups based on approach: midline interlaminar (MIL) and lateral parasagittal interlaminar (PIL) injection, with 2 ml of methylprednisolone acetate (120 mg) combined with 1 ml 1% lidocaine and 1 ml saline. Patients were asked to grade any pressure paresthesia as occurring ipsilaterally or contralaterally to their “usual and customary pain,” or in a distribution atypical of their daily pain. Outcome measures included the Oswestry Disability Index questionnaire, pain scores at rest and during movement, and use of pain medications on days 1, 7, 14, 21, 28, 60, 120, 180 and 365 after the injection. Both groups showed statistically and clinically significant pain relief in patients. Patients receiving LESI using the lateral parasagittal approach had longer pain relief then patients receiving LESI via a midline approach. They also had better quality of life scores and improvement in everyday functionality and used less pain medications than patients receiving LESI using a midline approach. Patients who had concordant pressure paresthesia and no discordant pressure paresthesia (i.e., “opposite side or atypical”) during interventional treatment had better and longer pain relief after LESI.

Study	QS	Conclusions
Candido et al (2013)	HQ (++)	• Patients receiving LESI using the lateral parasagittal interlaminar approach had longer pain relief then patients receiving LESI via a midline Interlaminar approach. • They also had better quality of life scores and improvement in everyday functionality and used less pain medications than patients receiving LESI using a midline approach. • Patients who had concordant pressure paresthesia and no discordant pressure paresthesia (i.e., "opposite side or atypical") during interventional treatment had better and longer pain relief after LESI.

Colhado et al (2013)

Colhado et al (2013) (QS:LQ(-)) conducted a double-blind, randomized experimental study into the evaluation of low back pain using different psychophysical methods. They randomly allocated the 60 patients with disc herniation into two groups receiving different injectates. One group received methylprednisolone 80 mg in 8 mL of 0.9% saline, whilst the second group received methylprednisolone 80 mg mixed with 5 mL of levobupivacaine and 3 mL of 0.9% saline. Pain measurement by means of psychophysical methods was performed immediately before, 30 minutes, 6 hours, 12 hours, and 24 hours after epidural blocking, and after 15 days. After 30 minutes of epidural block, the levobupivacaine group presented more significant reaction of reduction pain than the saline group. The magnitude and line-length scales were evaluated every period of time, showing no significant differences, except in 12 and 24 hours after the first block.

Study	QS	Conclusions
Colhado et al (2013)	LQ(-)	Lumbar epidural steroid with anaesthetic better than lumbar epidural with saline in reducing pain up to 24 hours

Ghai et al (2013)

Ghai et al (2013) (QS:HQ(++)) undertook a RCT to compare the therapeutic efficacy of the parasagittal interlaminar (PIL) approach and midline interlaminar (MIL) approach in 37 patients with unilateral radiculopathy. The injectates involved 2 ml methylprednisolone acetate (l ml = 40 mg) with 2 ml sterile normal saline under fluoroscopic guidance. Outcome measures included pain levels (VAS score) and disability and impairment using the modified Oswestry Disability Questionnaire (MODQ) over a 6-month period. The incidence of patients having effective pain relief was higher with the PIL approach (13/19 [68.4%]) vs MIL (3/18 [16.7%]) at the end of 6 months. A significantly higher relative success of effective pain relief was noted in the PIL group (relative risk, 4.10; 95% CI, 1.40–12.05; P = 0.001) at the end of the 6-month follow up with the requirement of fewer total injections (29 vs 41 in MIL, P = 0.043). Visual analog scale and modified Oswestry Disability Questionnaire scores were significantly lower in the PIL group compared with the MIL group at all time intervals after the procedure, suggesting the I-LESI administered with the parasagittal approach was significantly more effective for pain relief and improvement in disability than the midline approach for 6 months in the management of low back pain with lumbosacral radicular pain.

Study	QS	Conclusions
Ghai et al (2013)	HQ (++)	Interlaminar LESI administered with the parasagittal approach was significantly more effective for pain relief and improvement in disability than the midline approach for 6 months in the management of low back pain with lumbosacral radicular pain.

Habib et al (2013)

Habib et al (2013) (QS:AQ(+)) undertook a randomized, single-blinded prospective study comparing the effect of different dosages of an epidural corticosteroid injection on the hypothalamic-pituitary-adrenal axis. Whilst the main aim of the study was to explore the effect on the different dosages of steroid on the serum cortisol levels up to 4 weeks post injection, the study also presented data on the levels of back pain. 42 patients were randomly allocated to receive either 80 mg or 40 mg of methylprednisolone acetate diluted with 6 ml of normal saline but with no anaesthetic, however the authors did not report the approach to LESI they used. About 62%, 56%, and 39% of Group 1 patients (80mg of methylprednisolone acetate) had a favourable clinical response as opposed to 47% (P = 0362), 35% (P = 0.21), and 6% (P = 0.049) of Group 2 patients (40mg of methylprednisolone acetate) at weeks one, 3, and 4, respectively.

Study	QS	Conclusions
Habib et al (2013)	A (+)	• An LESI of 80 mg had higher rates of favorable clinical response than a 40 mg injection, but significantly more so at week 4 only. • This favorable response waned over a few weeks in both groups

Koh et al (2013)

Koh et al (2013) (QS:HQ(++)) undertook a double-blind, randomized, active-control trial comparing the effect of adding hypertonic saline to conventional transforaminal lumbar epidural steroid injections (TF LESI) to provide pain relief for chronic radiculopathy patients secondary to lateral canal spinal stenosis. They randomised 53 patients to receive TF LESI, involving either 2 mL of sodium chloride solution + triamcinolone acetonide or 2ml of triamcinolone acetonide. Outcome measures were taken at baseline, one, 2, 3, 4, and 6 months post procedure and included numerical rating scale (NRS) of pain, the Oswestry disability index (ODI), the proportion of substantial and moderate responders, and patient satisfaction. The results of this study suggested that the TF LESI was a useful modality in treating pain secondary to lateral canal spinal stenosis, and the short-term functional outcomes were also improved significantly, but that TF LESI showed limited long-term effects in treating patients with spinal stenosis. The addition of hypertonic saline demonstrated superior short-term pain relieving efficacy compared with conventional lumbar TFEI, but the overall mid- and long-term results showed no advantage.

Study	QS	Conclusions
Koh et al (2013)	HQ (++)	• Transforaminal LESI was a useful modality in treating pain secondary to lateral canal spinal stenosis, and the short-term functional outcomes were also improved significantly,

		• Transforaminal LESI showed limited long-term effects in treating patients with spinal stenosis. • The addition of hypertonic saline demonstrated superior short-term pain relieving efficacy compared with conventional transforaminal LESI, but the overall mid- and long-term results showed no advantage.

Manchikanti et al (2013b,2013c)

Manchikanti et al (2013b,2013c) (QS:AQ(+)) reported the same study conducted as a randomized, double-blind, active-controlled trial to assess the effectiveness of lumbar interlaminar epidural injections with local anaesthetic with or without steroids in managing chronic axial or discogenic low back pain. They randomly allocated 120 patients reporting lumbar axial or discogenic pain to two groups, one receiving 6 mL of lidocaine hydrochloride (0.5%), and the second receiving 5 mL of lidocaine mixed with 6 mg of nonparticulate betamethasone via an Interlaminar approach. Outcome measures included pain levels on a numerical rating scale (NRS), functional status (Oswestry Disability Index 2.0 (ODI)), employment status, and opioid intake at 3, 6, 12, 18, and 24 months. Both groups showed significant improvement over the 2 year period. Significant pain relief and functional status improvements were observed in 72% of patients receiving local anaesthetic alone and 67% of patients receiving local anaesthetic with steroids. Opioid intake was reduced from the baseline in each group for 2 years. The authors noted that these results were similar to the results of a trial for caudal epidural injections in axial or discogenic pain that had similar selection criteria (Manchikanti et al 2012). However, the interlaminar approach results may be somewhat superior compared to the caudal epidural injections at the end of 2 years where significant improvement was observed in 54% of the patients with local anaesthetic and 60% of the patients receiving local anaesthetic with steroids.

Study	QS	Conclusions
Manchikanti et al (2013b,2013c)	AQ (+)	• Significant pain relief and functional status improvement were observed in 72% of patients receiving local anaesthetic alone and 67% of patients receiving local anaesthetic with steroids via interlaminar LESI over 2 years. • Opioid intake was reduced from the baseline in each group for 2 years. • The interlaminar approach results may be somewhat superior compared to the caudal epidural injections at the end of 2 years where significant improvement was observed in 54% of the patients with local anaesthetic and 60% of the patients receiving local anaesthetic with steroids.

Park et al (2013)

Park et al (2013) (QS:AQ(+)) compared the short-term effects and advantages of ultrasound-guided caudal lumbar epidural steroid injections (UG-CLESI) with fluoroscopy guided lumbar epidural steroid injections (FG-CLESI) for unilateral radicular pain in the

lower lumbar spine. They randomly allocated 110 patients with lumbar radicular pain through confirmed herniated disk (n=42) or spinal stenosis (n=68), via lumbar computed tomography or magnetic resonance imaging. The injectate involved 20ml of the treatment drug, composed of 5 ml (Omnipaque 300) and 15 ml (13.0 ml of 0.5% lidocaine + 2 ml of dexamethasone 10 mg). The verbal numerical rating scale and the Oswestry Disability Index improved 2 and 12 wks after the injections in both groups, however there were no statistical differences in outcome measures or the effectiveness of the procedure between the groups. The authors completed multiple logistic regression analysis for possible outcome predictors for injection effectiveness at follow-up, looking at age, gender, symptom duration, number of injections, the cause (disc herniation vs spinal stenosis) and UG-CLESI vs FG-CLESI. No predictor was significantly related to effective outcome.

Study	QS	Conclusions
Park et al (2013)	AQ(+)	No differences in outcome measures or effectiveness of the procedure between ultrasound-guided caudal epidural steroid injections and fluoroscopy-guided epidural steroid injections

Rados et al (2013)

Rados et al (2013) (QS:LQ(-)) undertook a randomized, prospective study to compare the efficacy of interlaminar (IL) and transforaminal (TF) steroid injections over 6 months in patients with unilateral chronic lumbar radicular pain. 64 subjects with unilateral radicular pain were randomised into two groups, one received IL-LESI (involving 80 mg Depo-Medrol (methylprednisolone), mixed with 8 ml of 0.5% lidocaine), the other receiving TF-LESI (involving 40 mg Depo-Medrol in 3 ml of 0.5% lidocaine). The patients received a series of three IL or TF LESIs, at 2-week intervals. The outcome measure was the painDETECT questionnaire (PD-Q), which is designed to detect neuropathic pain components in back pain. The authors concluded that steroids were efficient in decreasing chronic radicular pain, both by way of IL and TF approach. Steroids were efficient not only in alleviating the overall pain, they also reduce the neuropathic component. There was no statistically significant difference in the efficiency of the two dosages and the two volumes of steroids with the IL and TF distribution of steroids (i.e. 40 mg steroids in 3 ml of 0.5% lidocaine with the TF approach is as efficient as a dose of 80 mg steroids in 8 ml of 0.5% lidocaine via IL approach).

Study	QS	Conclusions
Rados et al (2013)	LQ (-)	Steroids are efficient in reducing the overall pain, and the neuropathic component in chronic lumbar radicular pain, whether it is distributed by the interlaminar or transforaminal approach, and at either 3ml or 8ml dose.

Zhang et al (2013)

Zhang et al (2013) (QS:AQ(+)) undertook a RCT of the clinical effectiveness of oxygen-ozone therapy combined with steroid compared with injection of ozone alone in 172 adult patients with low back pain and radicular pain due to disc herniation. Injections

were performed in both the intradiscal and intraforaminal space with one group including 1ml of betamethasone. Visual analogue scale (VAS) and the Japanese Orthopedic Association's evaluation system for lower back pain syndrome (JOA score) were administered before treatment and at 3 weeks, 6 and 12-month follow-up period. Satisfactory clinical outcomes were obtained in both groups, with better effects in the epidural group at 3 weeks follow-up. However, there were no significant differences between two groups at 6 and 12 months with 79%-.80% improvement in the JOA and a 72% decrease in VAS score in both groups at the 12 months reassessment point.

Study	QS	Conclusions
Zhang et al (2013)	AQ(+)	• There was no significant statistical difference between treatment of epidural injection of oxygen ozone combined with steroid and ozone only in the 6 and 12 months follow-up. • LESI effective in reducing pain in patients with low back pain and radicular pain due to disc herniation over 12 months

Friedly et al (2014)

Friedly et al (2014) (QS:HQ(++)) conducted a multicentre double blind RCT into the effectiveness of LESI (both TF LESI and IL LESI) of glucocorticoids plus lidocaine (LES+AI) or lidocaine alone (LE-AI) in 400 patients with lumbar central spinal stenosis and moderate-to-severe leg pain and disability over a 6-week period. The injectates involved 1 to 3 ml of lidocaine followed by 1 to 3 ml of triamcinolone, betamethasone, dexamethasone or methylprednisolone. At 6 weeks, there were no significant between-group differences in the Roland Morris Disability Questionnaire (RMDQ) score (adjusted difference −1.0 points; 95% CI, −2.1 to 0.1; P = 0.07) or the intensity of leg pain (adjusted difference, −0.2 points; 95% CI, −0.8 to 0.4; P = 0.48). A prespecified secondary subgroup analysis with stratification according to type of injection (interlaminar vs. transforaminal) likewise showed no significant differences at 6 weeks. On reviewing the study data there were significant differences in the IL LESI group at the 3-week mark between the two treatment groups, with the IL LESI demonstrating statistically significant improvements in RMDQ and leg pain score with the combined LES+AI group compared to the LEAI group, whilst TF LESI failed to reach statistical significance at the 3-week mark between groups.

Study	QS	Conclusions
Friedly et al (2014)	HQ (++)	• Interlaminar LESI demonstrating statistically significant improvements in RMDQ and leg pain score with the combined LES+AI group compared to the LEAI group. • Transforaminal LESI failed to reach statistical significance at the 3-week mark between groups.

Ghai et al (2014)

Ghai et al (2014) (QS:HQ(++)) undertook a randomized, double-blind, active-control study, comparing the effectiveness of parasagittal interlaminar LESI with TF-LESI for managing low back pain with lumbosacral radicular pain in the same type of patients as Hashemi et al (2015). 62 patients were randomly located into either the parasagittal

interlaminar LESI or the TF-LESI group. Both groups received fluoroscopically guided epidural injections of methylprednisolone (80 mg) (via 2 mL of methylprednisolone acetate (l mL = 40mg) with 2 mL sterile normal saline). Outcome measures included pain levels (via VAS scores), disability (via ODI Scores) and patient satisfaction via a 7-point Patient Global Impression of Change (PGIC) at 2 weeks, 1, 2, 3, 6, 9, and 12 months post-intervention. Effective pain relief (≥ 50% pain relief from baseline on VAS) was observed in 76% (90% CI 60.6 – 88.5%) of patients in the TF group and 78% (90% CI 62.8 – 89.3%) of patients in the PIL (P = 1.00) group at 3 months. The pain relief survival period was comparable in both groups (P = 0.98). Significant reduction in VAS and improvement in MODQ were observed at all time points post-intervention compared to baseline (P < 0.001) in both groups. On average, patients in the PIL group received 1.84 and patients in the TF group received 1.92 procedures annually. The authors concluded that epidural injection delivered through the PIL approach is equivalent in achieving effective pain relief and functional improvement to the TF approach for the management of low back pain with lumbosacral radicular pain. The PIL approach can be considered a suitable alternative to the TF approach for its equivalent effectiveness, probable better safety profile, and technical ease.

Study	QS	Conclusions
Ghai et al (2014)	HQ (++)	• Parasagittal fluoroscopy guided interlaminar LESI effective in reducing pain in patients with low back pain with lumbosacral radicular pain at 12 months. • Parasagittal fluoroscopy guided Interlaminar LESI effective in improving disability (via ODI Scores) in patients with low back pain with lumbosacral radicular pain at 12 months.

Manchikanti et al (2014a)

Manchikanti et al (2014a) (QS:HQ(++)) presented a randomized, double-blind, active-controlled trial with 2-year follow-up of the effectiveness of Interlaminar lumbar epidural injections of local anaesthetic with or without steroids for managing chronic low back pain of disc herniation or radiculitis. They randomly allocated 120 patients to one group treated with Interlaminar lumbar epidural injections of local anaesthetic (LE-AI) (lidocaine 0.5%, 6 mL) and the second group treated with Interlaminar lumbar epidural injections of local anaesthetic with steroid (LES-AI) (0.5% lidocaine, 6 mL, mixed with 1 Ml non-particulate betamethasone). Outcome measures included numeric rating scale (NRS) of pain, functional status with Oswestry Disability Index (ODI), employment status and opioid intake over 2 years. The results showed significant improvement in 60% of patients in LES-AI and 70% of patients in LES+AI at the end of 2 years. Results were somewhat superior for pain relief at 6 months and functional status at 12 months in the steroid group, indicating that a patient's failure to respond to local anaesthetic alone may be treated with addition of steroids.

Study	QS	Conclusions
Manchikanti et al (2014a)	HQ (++)	• The results showed significant improvement in 60% of patients in Interlaminar LES-AI and 70% of patients in LE-A+SI at the end of 2 years. • Results were somewhat superior for pain relief at 6 months and functional status at 12 months in the steroid group, indicating that a patient's failure to respond to local anaesthetic alone may be treated with addition of steroids.

Manchikanti et al (2014b)

Manchikanti et al (2014b) (QS:AQ(+)) presented a randomized, double-blind, active-controlled trial with 2-year follow-up of the effectiveness of lumbar transforaminal epidural injections of local anaesthetic with or without steroids in managing chronic low back and lower extremity pain in patients with disc herniation and radiculitis. They randomly allocated 120 patients to one group treated with TF LESI+**A**I (lidocaine 1%, 1.5 mL + 0.5ml sodium chloride) and the second group treated with TF LESI+AI (lidocaine 1%, 1.5 mL + 0.5ml betamethasone). Outcome measures included numeric rating scale (NRS) of pain, functional status with Oswestry Disability Index (ODI), employment status and opioid intake over 2 years. At 2 years there was significant improvement in 65% of participants who received local anaesthetic alone and 57% of those who received local anaesthetic and steroid. This study suggested a lack of superiority of steroids compared with local anaesthetic at 2-year follow-up.

Study	QS	Conclusions
Manchikanti et al (2014b)	AQ (+)	• At 2 years there was significant improvement in 65% of participants who received local anaesthetic alone and 57% who received local anaesthetic and steroid, via lumbar transforaminal approach. • This study suggested a lack of superiority of steroids compared with local anaesthetic at 2-year follow-up.

Manchikanti et al (2014c)

Manchikanti et al (2014c) (QS:HQ(++)) reported again on two previously reported studies into the efficacy of epidural injections in managing lumbar central spinal stenosis pain. They reported on two randomized controlled trials of the caudal and lumbar interlaminar approaches that assessed 220 patients with lumbar central spinal stenosis. The analysis found that efficacy for both caudal and interlaminar approaches in managing chronic pain and disability was demonstrated. In the patients responsive to treatment, i.e. those with at least 3 weeks of improvement with the first 2 procedures, 51% reported significant improvement with caudal epidural injections, whereas it was 84% with local anaesthetic only with interlaminar epidurals, 57% with caudal and 83% with lumbar Interlaminar with local anaesthetic with steroid. The response rate was 38% with caudal and 72% with lumbar interlaminar with local anaesthetic only and 44% with caudal and 73% with lumbar interlaminar with local anaesthetic plus steroid when all patients were considered. In the interlaminar approach, results were superior for pain relief and functional status with fewer nonresponsive patients compared to the caudal approach.

Study	QS	Conclusions
Manchikanti et al (2014c)	HQ (++)	• The results showed significant improvement in patients suffering with chronic lumbar spinal stenosis with caudal and interlaminar epidural approaches with local anaesthetic only, or with steroids in a long-term follow-up of up to 2 years, in contemporary interventional pain management setting, with the interlaminar approach providing significantly better results.

Rahimzadeh et al (2014)

Rahimzadeh et al (2014) (QS:AQ(+)) undertook a prospective randomized trial of 25 subjects with low back pain due to failed back syndrome, who were randomly assigned to receive a transforaminal epidural injection of either Bupivacaine 5 mg (1 mL) + Triamcinolone 40 mg (1 mL) + Saline solution 10% (2 mL) + Hyaluronidase 1,500 IU reconstituted in 1 mL distilled water (HYL) or Bupivacaine 5 mg (1 mL) + Triamcinolone 40 mg (1mL) + Saline solution 10% (2 mL) + 1 mL distilled water (NSL) in a double blind fashion. Pain scores and total analgesic requirement were significantly lower in the HYL group at 2 and 4 weeks after blockade ($P < 0.01$). Patient satisfaction was higher in the HYL group. This study was hampered by its small subject size but the results were interesting over the short term

Study	QS	Conclusions
Rahimzadeh et al (2014)	AQ(+)	Adding hyaluronidase to the epidural injectate during transforaminal LESI was more effective in the management of chronic low back pain in patients with failed back surgery syndrome over a period of 4 weeks

Sinofsky et al (2014)

Sinofsky et al (2014) (QS:LQ(-)) reported a secondary analysis of a prospective randomized double-blind study of the short-term benefit of interlaminar and transforaminal epidural steroid injections. They specifically looked at the relationship between concordant versus discordant provocation during interlaminar epidural steroid injection and its effects on pain reduction at follow-up. 48 patients with radicular lumbosacral pain had Interlaminar epidural steroid injections (80 mg methylprednisolone and 2 mL of normal saline) under fluoroscopic guidance. Patients were asked to report if pain was provoked, and whether the pain was concordant or discordant with their baseline pain. Outcome measures included self-rated percentage of pain improvement, activity levels and analgesic consumption at 2-week follow-up. Provocation was observed in 37 out of 48 patients (77%), which was classified as concordant (22/37, 60%) or discordant (15/37, 40%) pain. The concordant group achieved a significant decrease in self-reported pain as compared to the discordant group at 2-week follow up (61%, $t = 2.45$, $P < 0.01$), however there was no significant differences between groups in regard to improvements in activity level and analgesic use. Concordant provocation during interlaminar epidural injection may therefore be a predictor of outcome.

Study	QS	Conclusions
Sinofsky et al (2014)	LQ (-)	With LESI via interlaminar or transforaminal approach, concordant provocation was related to decrease in self-reported pain as compared to the discordant group at 2-week follow up. However, there was no significant differences between groups in regard to improvements in activity level and analgesic use.

Spijker-Huiges et al (2014a)

Spijker-Huiges et al (2014a) (QS:AQ(+)) undertook a pragmatic, single-blinded, randomized controlled trial assessing the effectiveness of LESIs for pain and disability as an addition to usual care for acute lumbosacral radicular syndrome (LRS) in general practice. They randomly allocated 73 patients with LRS due to lumbar disc herniation into an intervention group, which received 80 milligrams of triamcinolone in 10 millilitres of normal saline, administered via a translaminar approach without additional imaging, one level above the presumed LRS; or a control group, who received usual care by their GP. 63 patients completed the longitudinal study, with 5 subjects dropping out of each group. Outcome measures included disability, as measured by the 24-point Roland-Morris Disability Questionnaire (RMDQ), pain and self-perceived impairment using a 0-10 numeric rating scale (NRS) at 2, 4, 6, 13, 26 and 52 weeks after the start of the treatment. The intervention group experienced significantly less symptoms than the control group for the RMDQ-score ($p = 0.0173$), the NRS back pain score ($p = 0.0115$) and the NRS score for self-perceived impairment ($p = 0.0361$). These differences between the groups remained constant during the whole follow-up period. There was a significant difference in mean patient satisfaction between the two groups. The intervention group rated their treatment 9.0 on a 0 to 10 scale, and the control group rated their treatment 7.2 on a 0 to 10 scale ($p = 0{,}006$). The differences, though statistically significant, were too small to be considered clinically relevant.

Study	QS	Conclusions
Spijker-Huiges et al (2014a)	AQ (+)	• Small, statistically significant, but not clinically relevant positive effect of LESIs (Interlaminar approach) on back pain, impairment and disability in acute lumbar radiculopathy at 1 year. • The authors do not recommend implementing LESIs as an additional regular treatment option in general practice.

Spijker-Huiges et al (2015)

Spijker-Huiges et al (2015) (QS:AQ(+)) reported on the same study cohort as Spijker-Huiges et al (2014a) and Spijker-Huiges et al (2014b), but only reported on 50 of the 63 subjects who completed the study. They fail to report why they selected these 50 subjects, suggesting a significant risk of allocation bias. In this study, they investigated the effect of adding LESI to usual care on quality of life and cost utility. Both groups experienced a significant increase in quality of life in (especially) the physical domains of the Medical Outcomes Study 36-Item Short-Form Health Survey. The intervention group scored significantly better than the control group at certain time points in the physical domain. The cost-utility analysis showed that with a negligible loss of utility (3d in perfect health), societal costs (193,354 euros per quality-adjusted life year lost) would be saved because of more productivity in the intervention group.

Study	QS	Conclusions
Spijker-Huiges et al (2014b)	AQ (+)	• The effect on pain and disability of LESI via interlaminar approaching lumbosacral radicular syndrome is small but significant, and at lower costs with no reported complications or adverse effects. • Segmental LESI could be considered by policy makers as an additional treatment option.

Chun and Park (2015)

Chun and Park (2015) (QS:HQ(++)) investigated the effect of different injectate volumes, using a combination of lidocaine and dexamethasone via a transforaminal approach, comparing a 3mg (low injectate volume) with an 8mg (high injectate volume) dose in 66 patients with radiculopathy secondary to either spinal stenosis or herniated nucleus pulposis (HNP). Unfortunately, they did not subclassify their patient group so it is impossible to identify if the effect was different between different patient groups. They classified benefit as meaningful pain relief i.e. ≥ 50% reduction from baseline VAS score at the 4-week mark. They also took secondary outcomes including the Roland-Morris Disability Questionnaire (RMDQ, range 0 – 24) score and adverse effects. Both groups demonstrated clinically and statistically significant improvement in radicular pain and it was revealed that the high volume group demonstrated significant pain relief compared to the low volume group (33.3 ± 25 vs. 46.3 ± 25, $P < 0.05$). Both groups demonstrated clinically and statistically significant improvement in functional status according to the RMDQ ($P < 0.05$), however there was no significant difference in functional status between the 2 groups (10.4 ± 4 vs. 11.5 ± 4, $P > 0.05$)

Study	QS	Conclusions
Chun and Park (2015)	HQ (++)	• Both groups (high and low volume) demonstrated clinically and statistically significant improvement in radicular pain • The high volume group demonstrated significant pain relief compared to the low volume group. • Both groups demonstrated clinically and statistically significant improvement in functional status according to the RMDQ ($P < 0.05$), however there was no significant difference in functional status between the 2 groups

Cohen et al (2015)

Cohen et al (2015) (QS:HQ(++)) investigated the use of LESI (both interlaminar (4ml) and transforaminal (3ml)) compared with gabapentin (orally) in 145 patients with radiculopathy secondary to either spinal stenosis or HNP. Unfortunately, they did not subclassify their patient group so it is impossible to identify if the effect was different between different patient groups. This was a unique study as they blinded patients and researchers by using sham epidurals and placebo pills. They reviewed outcomes over a three-month period. They reported no significant differences in pain scores at one month (adjusted difference 0.4, 95% confidence interval −0.3 to 1.2; P=0.25) and three months (adjusted difference 0.3, −0.5 to 1.2; P=0.43). One month after treatment LESI patients

had greater reductions in worst leg pain (−3.0, SD 2.8) than those treated with gabapentin (−2.0, SD 2.9; P=0.04) and were more likely to experience a positive successful outcome (66% v 46%; number needed to treat=5.0, 95% confidence interval 2.8 to 27.0; P=0.02). At three months, there were no significant differences between the two treatments.

Study	QS	Conclusions
Cohen et al (2015)	HQ (++)	• LESI (interlaminar and transforaminal) no better than oral gabapentin in pain scores at one month and three months. • One month after treatment LESI patients had greater reductions in worst leg pain than those treated with gabapentin and were more likely to experience a positive successful outcome. • At three months, there were no significant differences between the two treatments.

Denis et al (2015)

Denis et al (2015) (QS:HQ(++)) undertook a randomized double blind controlled trial comparing equivalent doses of a nonparticulate (dexamethasone) with a particulate (betamethasone) corticosteroid in lumbar transforaminal epidural steroid injections (TFESIs) in 56 patients with MRI evidence of either a herniated disc or foraminal stenosis. Outcome measures included pain (VAS), functional improvement (Oswestry Disability Index (ODI) at 3 months. Both groups showed statistically significant VAS decreases over time (P<0.009 for dexamethasone and P<0.033 for betamethasone). For ODI, the decrease over time was statistically significant only for the dexamethasone group (P<0.0002 vs P<0.079 for betamethasone). The improvement was modest at 1 month in the betamethasone group, but was estimated clinically significant at 3 and 6 months as well as at the three visits in the dexamethasone group. No differences on the VAS (p=0.209) and ODI (P=0.181) were found between the two groups at 3 months. At 6 months, improvement of ODI score was at the limit of statistical significance in favor of dexamethasone (P=0.050).

Study	QS	Conclusions
Denis et al (2015)	HQ (++)	• Pain relief and functional improvement are similar for both dexamethasone and betamethasone at 3 months. • Considering its safety profile, dexamethasone could be considered as first choice for transforaminal LESI

Evansa et al (2015)

Evansa et al (2015) (QS:HQ(++)) presented a RCT comparing ultrasound-assisted and fluoroscopy-controlled epidural steroid injections in patients with chronic lower back and extremity pain diagnosed with degenerative diseases of the spine (including disk degeneration and spinal stenosis). They randomly allocated 120 patients into two groups, one received interlaminar LESI under fluoroscopy, whilst the second group had IL-LESI under ultrasound guidance. Both groups had similar dosages of injectate (corticosteroid (methylprednisolone acetate 80 mg), along with 4 ml of 1% lidocaine, total volume 5 ml). Outcome measures included procedure time, visual analogue scale (VAS) for pain and the

Oswestry Low Back Pain Disability Index (ODI) over a three-month period. Both groups displayed significant improvement over the three-month period from baseline. There was no significant difference between the two groups in mean procedure time, number of needle insertion attempts or needle passes. The mean pain intensity and degree of disability scores before the procedure, and at 1 and 3 months post procedure, were similar in the two groups.

Study	QS	Conclusions
Evansa et al (2015)	HQ (++)	No difference between ultrasound-assisted and fluoroscopy-controlled interlaminar LESI over a three-month period, with both being effective.

Ghai et al (2015)

Ghai et al (2015) (QS:HQ(++)) conducted a randomized, double blind, active control study with a one year follow-up in which they randomly allocated 69 patients with chronic low back pain (LBP) with lumbosacral radicular syndrome (LRS) secondary to disc herniation to receive fluoroscopic guided LESI of either 8 mL of 0.5% lidocaine (group L, n = 34) or 6 mL of 0.5% lidocaine mixed with 80 mg (2 mL) of methylprednisolone acetate (group LS, n = 35) via a parasagittal Interlaminar approach. A significantly higher proportion of patients achieved effective pain relief (> 50% compared to baseline) at 3 months in group LS as compared to group L (P = 0.02). Similar results were obtained at 6, 9, and 12 months, respectively. The probability of achieving effective pain relief was significantly higher in group LS at various time-points during the one year follow-up as compared to group L (P = 0.01) A significant reduction in NRS and improvement in MODQ were observed at all time-points post-intervention compared to baseline (P < 0.001) in both groups. NRS and MODQ scores were significantly lower in group LS as compared to group L at all time intervals post baseline. On average patients in group L received 2.0 (0.85) and group LS received 1.7 (0.71) injections annually (P = 0.07). Using a parasagittal interlaminar approach and adding steroid to local anaesthetic may provide superior effectiveness in terms of extent and duration of pain relief for managing LBP with unilateral LRS, even though, local anaesthetic alone also was effective.

Study	QS	Conclusions
Ghai et al (2015)	HQ (++)	Using a parasagittal fluoroscopy guided Interlaminar approach and the addition of steroid to local anaesthetic may provide superior effectiveness in terms of extent and duration of pain relief for managing LBP with unilateral LRP over 12 months, even though, local anaesthetic alone also was effective.

Hashemi et al (2015)

Hashemi et al (2015) (QS:AQ(+)) conducted a randomized double-blind clinical trial to determine the distribution of a drug in the epidural space after parasagittal and midline Interlaminar FG-LESI in 56 patients with low back pain (LBP) and unilateral lumbosacral radicular pains. Whilst the study did not specifically identify disc herniation in their patient group, one of their inclusion criteria was MRI correlation to the symptomatology and disc level protrusion. The injectate was 2 ml of triamcinolone plus

bupivacaine (2 ml) and 6 ml sterile normal saline. Outcome measures included pain relief and disability (as measured by Oswestry Disability index) over a two-week period. The mean NRS was not significantly different at baseline, however, the mean NRS score was significantly lower in the parasagittal group compared to the midline group at 2 weeks (P = 0.0014). The mean ODI was significantly lower in the parasagital group compared to the midline group at 2 weeks (P = 0.0033).

Study	QS	Conclusions
Hashemi et al (2015)	AQ(+)	• Parasagittal fluoroscopy guided Interlaminar LESI more effective than midline Interlaminar for pain relief at 2 weeks. • Parasagittal fluoroscopy guided Interlaminar LESI more effective than midline Interlaminar for improving disability (measured by Oswestry Disability Index [ODI] at 2 weeks

Kennedy et al (2015)

Kennedy et al (2015) (QS:AQ(+)) investigated the difference in pain relief between particulate and non-particulate corticosteroids in 78 patients with radicular pain due to MRI diagnosed HNP. This study used a longer period of assessment, assessing patients at 2 weeks, 3 months and 6 months. Both groups received 1.5mls of injectate. At the 2-week follow-up, both groups showed clinically and statistically significant improvement in pain and functional measures, with a slightly (non-significant) higher level of pain relief with triamcinolone than dexamethasone (43.2 vs 31.7%). At the 33 and 6 months follow up there was no difference between the groups. ODI data also improved in each group without reaching a statistically significant difference between groups. Both groups moved from the "severe disability" range (score of 40–60) to the "minimal disability" range (score of 0–20) from baseline to 6 months follow-up. The average number of injections received for each group was 1.6 for dexamethasone and 1.4 for triamcinolone.

Study	QS	Conclusions
Kennedy et al (2015)	AQ(+)	• Transforaminal LESI are an effective treatment in reducing pain levels in patients with acute radicular pain due to disc herniation, over 6 months • Transforaminal LESI are an effective treatment in improving disability, reducing disability scores (as measured by Oswestry disability Index scores) in patients with acute radicular pain due to disc herniation over 6 months • Transforaminal LESI are an effective treatment in patients with acute radicular pain due to disc herniation, over 6 months and frequently only require 1 or 2 injections for symptomatic relief. • Dexamethasone appears to possess reasonably similar effectiveness when compared with triamcinolone. However, the dexamethasone group received slightly more injections than the triamcinolone group to achieve the same outcomes.

Koh et al (2015)

Koh et al (2015) (QS:HQ(++)) conducted a randomized, double-blinded, active-comparator controlled study into the effects of combining pulsed radiofrequency (PRF) treatment and transforaminal epidural injection (TF LESI) to treat patients with chronic radicular pain caused by lumbar spinal stenosis. They randomly allocated 62 patients to an intervention group (involving FG-TFLESI (2-3ml lidocaine with 20 mg of triamcinolone acetonide) + PRF) and a control group (involving just the FG-TFLESI). Outcome measures included radicular pain intensity, analgesic consumption, physical functioning, global improvement and satisfaction with treatment and adverse events over a 3-month period. Both groups demonstrated significant improvements in NRS pain score and functional capacity (ODI) during the 3-month follow-up period, however the Medication quantification scale did not change significantly from baseline. The number of patients with successful treatment results was higher in the PRF group at 2 months (P = 0.032) and 3 months (P = 0.018), however there were no significant differences observed in terms of the other outcome variables between the 2 groups.

Study	QS	Conclusions
Koh et al (2015)	HQ (++)	• Lumbar epidural steroid with anaesthetic via transforaminal approach combined with pulsed radiofrequency (PRF) treatment produced better results than lumbar epidural steroid with anaesthetic in reducing pain up to 3 months

Manchikanti et al (2015)

Manchikanti et al (2015) (QS:HQ(++)) undertook a randomized, double-blind, active controlled trial into the effectiveness of IL LESI with or without steroids in providing effective and long-lasting pain relief with improvement in functional status for the management of chronic low back and lower extremity pain related to lumbar central spinal stenosis. They randomised 120 patients into two groups, one receiving ILEAI (lidocaine 0.5%) 6 mL, whereas the other group received ILES-AI ((lidocaine 0.5%) 5 mL, mixed with 1 mL of steroids and 6 mg of betamethasone). Outcomes were assessed utilizing the numeric pain rating scale (NRS) and Oswestry Disability Index (ODI) at 3, 6, 12, 18, and 24 months post treatment. Significant relief and functional status improvement was seen in 72% (ILEAI) and 73% (ILES-AI) of patients at the end of 2 years (intention to treat analysis). Overall significant improvement was achieved for 65.7 ± 37.3 weeks (ILEAI) and 68.9 ± 37.7 weeks (ILES-AI) at the end of 2 years. The average number of procedures per patient was 5 to 6 in both groups. Lumbar Interlaminar epidural injections of local anaesthetic with or without steroids provided relief in a significant proportion of patients with lumbar central spinal stenosis.

Study	QS	Conclusions
Manchikanti et al (2015)	HQ (++)	• Lumbar interlaminar epidural injections of local anaesthetic with or without steroids provided relief in a significant proportion of patients with lumbar central spinal stenosis.

Pirbudak et al (2015)

Pirbudak et al (2015) (QS:LQ(-)) investigated the effect of tramadol-only treatment and tramadol + gabapentin treatment in 40 patients who had received a transforaminal LESI with anaesthetic (4 ml, triamcinolone acetonide and 0.25% bupivacaine mixture) for radiculopathy secondary to confirmed NHP of at least 3 months' duration. Whilst there was no control group for the transforaminal LESI, both groups demonstrated significant improvement at the 2-week reassessment mark with no between-group differences. Within the groups the VAS scores improved significantly (from 7.05+/-1.7 and 7.1 +/- 1.2, to 1.95 +/-1.27 and 1.15 +/-1.08 respectively), SLR increased (from 43.25^0 (30-60) and 44.50^0 (35–60), to 63.50^0 (30–75) and 60.25^0 (50–70)) and Oswestry disability index scores reduced (from 38.00 ± 9.78 and 35.25 ± 9.10 to 26.75 ± 9.63 and 25.00 ± 8.11)

Study	QS	Conclusions
Pirbudak et al (2015)	LQ(-)	• Transforaminal LESI effective for pain relief in patients with NHP of at least 3 months' duration, at 2 weeks • Transforaminal LESI effective for reducing disability scores (as measured by Oswestry disability Index scores) in patients with NHP of at least 3 months' duration, at 2 weeks • Transforaminal LESI effective for improving impairment, as measured by straight leg raise, in patients with NHP of at least 3 months' duration, at 2 weeks

Turan et al (2015)

Turan et al (2015) (QS:AQ(+)) undertook a study into the effectiveness of adding N_2O to LESI in reducing pain. Patients with recurrent low back pain scheduled for epidural steroid blocks were randomly assigned to receive either oxygen (O_2, n = 39) or the combination of 50% O_2 and 50% N_2O during and after each block (N_2O, n = 39). Before each injection and at a 3-month follow-up visit, patients completed questionnaires: Oswestry survey, 12-Item Short Form Health Survey questionnaire, Leeds Assessment of Neuropathic Symptoms and Signs pain scale, and Visual Analog Scale. Total opioid use per 24 hours was recorded. Epidural steroid injections were completed under fluoroscopy. Steroids and local anaesthetics were injected at the discretion of the blinded physician performing the block. There was no information presented by the authors on the volume of injectate or the approach used. Among the 68 patients who completed follow-up assessments, the estimated mean change in VAS pain score from baseline to 3 months after the final LESI was −1.4 (SD, 2.8). No difference was found in the change in VAS between patients given N_2O (mean [SD]: −1.6 [3.0] cm) and O_2 alone (−1.2 [2.6] cm), after the same covariable adjustment (difference: −1.03 [95% CI: −2.34, 0.28], N_2O −O_2; P = 0.12. The authors concluded that independent of randomized allocation, VAS pain scores reduced by an average of 1.4 ± 2.8 cm from a starting VAS of 6 three months after the final epidural steroid injection suggested minimal efficacy, especially as that small reduction may well have occurred without treatment in these spinal stenosis patients.

Study	QS	Conclusions
Turan et al (2015)	AQ (+)	N_2O administration did not improve pain or psychological or physical aspects of health-related quality of life when added to the LESI.

3.5 Outcome Measures – Pain and Function - Recommendations

1. The evidence does not support the use of lumbar epidural steroid injections, as a broad intervention category, for the first line relief of pain or improving disability in patients with radicular symptoms or low back pain	
Level A	
FOR	**AGAINST**
Level 1++ • LESI not effective in global effect compared to inactive control at short-term (< 6 weeks) follow-up for management of sciatica (Lewis et al 2011; SR (HQ++)) • LESI not effective compared to usual care at medium-term follow-up (<6 weeks, to 6 months) for global effect, pain intensity or CSOMs of sciatica. (Lewis et al 2011; SR (HQ++)) • LESI provided significant treatment effect on radiculopathy pain at 6 months of follow-up (weighted mean difference [WMD], −0.41; 95% CI, −0.66 to −0.16), but was no longer statistically significant after adjusting for the baseline pain score (WMD, −0.19; 95% CI, −0.61 to 0.24) (Choi et al 2013; SR (HQ++)) • LESI provided no significant treatment effect on back-specific disability more than a placebo or other procedure for radiculopathy (Choi et al 2013; SR (HQ++)) • LESI did not significantly decrease the number of patients with radiculopathy who underwent subsequent surgery compared with a placebo or other treatments (relative risk, 1.02; 95% CI, 0.83 to 1.24) (Choi et al 2013; SR (HQ++)) • LESI not effective in reducing need for surgery in short or long term in patients with low back pain (Bicket et al 2015; SR/MA (A+))	
Level 1+ • LESI not effective compared to chemonucleolysis for the global effect at short-term or medium-term follow-up (Lewis et al 2011; SR (HQ++)).	

Level 1 • LESI not as effective as disc surgery at reducing pain intensity at medium-term follow-up, but not at long-term follow-up (Lewis et al 2011; SR (HQ++)) • LESI no more effective than acupuncture for pain intensity in short term (< 6 weeks) (Lewis et al 2011; SR (HQ++)) • LESI not effective compared to placebo injections for general improvement in the short term (Staal et al 2008; SR (HQ++)) • LESI not effective compared to placebo injections for pain relief in the short term (Staal et al 2008; SR (HQ++)) • LESI no more effective compared to placebo injections for work disability in the short term (Staal et al 2008; SR (HQ++)) • LESI no more effective compared to NSAIDs for pain relief in the short term in post-laminectomy patients (Staal et al 2008; SR (HQ++)) • LESI no more effective compared to benzodiazepine for pain relief and general improvement both in the short and intermediate term (Staal et al 2008; SR (HQ++)) • LESI no more effective compared to morphine eventually combined with corticosteroids for pain relief in the short and intermediate term in post-laminectomy patients (Staal et al 2008; SR (HQ++)) • LESI recommended as a secondary intervention for low back pain with substantial neurologic involvement (Dagenais et al 2010; SR (A+)) • LESI no more effective than benzodiazepine injection for pain relief over short to intermediate term (Henschke et al 2010; SR (HQ++)) • LESI less effective compared with standard discectomy at 1 to 3 months for leg pain or disability in people with lumbar disc herniation (Jordan et al 2011; SR (A+)) • LESI (Interlaminar and Transforaminal) no better than oral gabapentin in pain scores at one month and three months (Cohen et al 2015; RCT HQ++)) • Percutaneous adhesiolysis and decompression surgery were more effective than LESI in patients with spinal stenosis (May and Comer 2013; SR (A+)) • Discectomy was effective compared to LESI for the short term in patients with radiculopathy due to herniated lumbar disc (Jacobs et al 2011; SR (A+)) • LESI worse than chemonucleolysis in the number of adverse effects (Lewis et al 2011; SR (HQ++))	**Level 1** • LESI recommended as a secondary intervention for low back pain with substantial neurologic involvement (Dagenais et al 2010; SR(A+)) • LESI effective compared with passive PT for global effect (at medium- and long-term follow-up) and activity restriction for global effect (medium-term follow-up) (Lewis et al 2011; SR (HQ++)) • LESI effective compared with home exercise or inpatient physical therapy in improving pain, function, and quality of life up to 2 weeks in patients with spinal stenosis (Ammendolia et al 2012; SR (HQ++))
RCT • LESI (interlaminar and transforaminal) no better than oral gabapentin in pain scores at one month and three months. One month after treatment LESI patients had greater reductions in worst leg pain than those treated with gabapentin and were more likely to experience a positive successful outcome. At three months, there were no significant differences between the two treatments. (Cohen et al 2015; RCT (HQ++))	

2. The evidence suggests that the use of lumbar epidural steroid injections, as a broad intervention category, for relief of pain or improving disability in patients with low back pain or radicular symptoms is effective in the short term, i.e. up to 6 weeks

Level A

FOR	AGAINST
	Level 1++ • LESI not effective in reducing need for surgery in short or long term (Bicket et al 2015; SR (HQ(++)) • LESI not effective in global effect compared to inactive control at short-term follow-up (Lewis et al 2011; SR (HQ++))
Level 1+ • LESI effective in reducing pain and improving functional status compared to inactive control at short-term (< 6 weeks) follow-up in patients with sciatica (Lewis et al 2011; SR (HQ++)) • LESI effective compared to usual care for overall recovery and functional status at short-term (< 6 weeks) follow-up, but not for pain intensity in patients with sciatica (Lewis et al 2011; SR (HQ++)) • LESI effective compared to non-opioids for reducing pain and improving functional status at short-term (< 6 weeks) follow-up (Lewis et al 2011; SR (HQ++)) • LESI effectiveness inconsistent. If any effectiveness mainly in short term on patients with low back pain and radiculopathy (Koes et al 1995; SR (A+)) • LESI demonstrated effectiveness compared with placebo for leg pain in the short term (mean difference, -6.2 [95% CI, -9.4 to -3.0]) in patients with radiculopathy (Pinto et al 2012; SR (HQ++)) • LESI demonstrated effectiveness compared with placebo for disability in the short term (mean difference, -3.1 [CI, -5.0 to -1.2]). in patients with radiculopathy (Pinto et al 2012; SR (HQ++)) • LESI effective compared with no LESI at increasing subjective global improvement and patient satisfaction in the short term (2 weeks), (Jordan et al 2011; SR (A+)) • For interlaminar LESI evidence for use in lumbar radicular pain was strong for short-term improvement in pain and functional outcomes (Abdi et al 2005; SR (A+)) • For lumbar transforaminal LESI the evidence for use in radicular pain was strong for short-term in pain and functional outcomes. (Abdi et al 2005; SR (A+)) • For caudal epidural LESI the evidence was strong for short-term improvement in pain and functional outcomes. • Interlaminar LESI may provide short-term benefit in the first 3–6 weeks. (Vorobeychik et al 2016; SR (A(+))	**Level 1+** • All approaches to the interlaminar, caudal, and transforaminal epidural space provide long-term relief in 27—56% patients with radiculopathy (Bhargava et al 2005; SR (A+))
Level 1 • LESI effective compared to control treatments in improving	

pain in patients with radicular lumbosacral pain when assessed between 2 and 6 weeks (Armon et al 2007; SR (A+)) • LESI (+/1 anaesthetic) effective compared with control injections in improving walking distance in patients with spinal stenosis in short term (Bresnahan et al 2013; SR A(+)) • LESI effective for pain relief in patients with radiculopathy in the short term (Dworkin et al 2013; SR (LQ-)) • LESI effective compared with home exercise or inpatient physical therapy in improving pain, function, and quality of life up to 2 weeks in patients with spinal stenosis (Ammendolia et al 2012; SR (HQ++)) • LESI effective in the immediate-term in reducing pain with positive correlation between LESI volume and pain relief: r=0.8027 (p=0.0017). (Rabonovitch et al 2009; SR (A+)) • LESI effective compared with no LESI at increasing subjective global improvement and patient satisfaction in the short term (2 weeks) (Jordan et al 2011; SR (A+))	
RCT • Transforaminal LESI effective for pain relief in patients with NHP of at least 3 months' duration, at 2 weeks (Pirbudak et al 2015; RCT (LQ-)) • Transforaminal LESI effective for reducing disability scores (as measured by Oswestry disability Index scores) in patients with NHP of at least 3 months' duration, at 2 weeks (Pirbudak et al 2015; RCT (LQ-)) • Transforaminal LESI effective for improving impairment, as measured by straight leg raise, in patients with NHP of at least 3 months' duration, at 2 weeks (Pirbudak et al 2015; RCT (LQ-))	

3. The evidence suggests that the use of lumbar epidural steroid injections, as a broad intervention category, for relief of pain or improving disability in patients with low back pain or radicular symptoms is not effective in the long term i.e. greater than 6 weeks

Level A

FOR	AGAINST
Level 1++ • LESI not effective compared to usual care at medium-term follow-up for global effect, pain intensity or CSOMs. (Lewis et al 2011; SR (HQ++)) • LESI not effective in reducing need for surgery in short or long term (Bicket et al 2015; SR (HQ++)) • LESI provided significant treatment effect on pain at 6 months of follow-up (weighted mean difference [WMD], −0.41; 95% CI, −0.66 to −0.16), but was no longer statistically significant after adjusting for the baseline pain score (WMD, −0.19; 95% CI, −0.61 to 0.24) (Choi et al 2013; SR (HQ++))	

Level 1+ • LESI not effective compared to inactive control for global effect, pain intensity or CSOMs at medium-term (> 6 weeks to 6 months) follow-up in patients with sciatica (Lewis et al 2011; SR (HQ++)) • LESI not effective compared to inactive control for global effect, pain intensity or CSOMs at long-term (>6 months) follow-up in patients with acute sciatica. (Lewis et al 2011; SR (HQ++)) • LESI no more effective compared with no LESI in reducing limb pain after more than 2 weeks in people with disc herniation (Jordan et al 2011; SR (A+)) • LESI no more effective compared with LESI in the longer term at improving disability, or functional outcomes such as straight leg raising and lumbar flexion, in people with disc herniation. (Jordan et al 2011; SR (A+)) • LESI not effective compared to non-opioids for global effect or CSOMs at medium-term (> 6 weeks, to 6 months) follow-up or adverse effects. (Lewis et al 2011; SR (HQ++)) • LESI not effective compared to physical therapy, saline, saline and anaesthetic or anaesthetic injection at long-term follow-up in patients with spinal stenosis (May and Comer 2013; SR (A+)) • LESI did not demonstrate effectiveness compared with placebo for pain or disability over the long term in patients with radiculopathy (Pinto et al 2012; SR (HQ++)) • LESI not effective compared with no LESI at increasing subjective global improvement and patient satisfaction in the longer term (after 2 weeks) in people with disc herniation. (Jordan et al 2011; SR (A+)) • LESI plus conservative treatment no more effective than conservative treatment at 6 weeks and 6 months for pain scores in people with disc herniation. (Jordan et al 2011; SR (A+)) • LESI plus conservative treatment no more effective than conservative treatment at 6 weeks and 6 months for mobility scores and reducing need for surgery in people with disc herniation (Jordan et al 2011; SR (A+)) • For Interlaminar LESI evidence for use in lumbar radicular pain was limited for long-term improvement in pain and functional outcomes (Abdi et al 2005; SR (A+))	**Level 1+** • All approaches to the interlaminar, caudal, and transforaminal epidural space provide long-term relief in 27—56% patients with radiculopathy (Bhargava et al 2005; SR (A+)) • For lumbar Transforaminal LESI the evidence for use in radicular pain was moderate for long term improvement in pain and functional outcomes. (Abdi et al 2005; SR (A+)) • For caudal epidural LESI the evidence was moderate for long-term improvement in pain and functional outcomes. For managing chronic postlumbar laminectomy syndrome and spinal stenosis the evidence was limited. (Abdi et al 2005; SR (A+))
Level 1 • LESI not effective compared to control treatments in average impairment of function, need for surgery, or provide long-term pain relief beyond 3 months (Armon et al 2007; SR (A+)) • LESI (+/1 anaesthetic) not effective compared with control injections in improving walking distance in patients with spinal stenosis in long term (>4 months) (Bresnahan et al 2013; SR A(+)). **RCT** • Small, statistically significant, but not clinically relevant positive effect of LESIs (Interlaminar approach) on back pain, impairment and disability in acute lumbar radiculopathy at 1 year. Spijker-Huiges et al 2014a; RCT (A+))	**RCT** • LESI effective in reducing pain in patients with low back pain and radicular pain due to disc herniation over 12 months (Zhang et al 2013; RCT A(+))

4. The evidence suggests that any benefit from the use of lumbar epidural steroid injections, as a broad intervention category, for relief of pain or improving disability in patients with back pain with or without radicular symptoms is due to the volume of injectate or process of administration, not the steroid

Level A

FOR	AGAINST
Level 1++ • LESI no better than LEN-SI in the short term for; For pain, the benefit favouring epidural nonsteroid over nonepidural injections is actually greater (risk difference [95% CI], 0.27 [0.15–0.39]) than the difference between LESI and epidural nonsteroid, suggesting that, at least in the short term, most of the benefit of epidural injections may derive from the solution itself, rather than the steroid. (Bicket et al 2013; SR (HQ++))	
Level 1+ • Irrespective of the medications injected there was a statistically significant difference when comparing the mean effect size where the volume injected was the same between the two groups (mean, standard deviation [SD]: 0.07, -0.26) with those where the volumes were different between comparison groups (mean, SD: 0.81, -0.6) in patients with radicular leg pain and/or low back pain, (Rabinovotch et al 2009; SR (A+)) • LESI no more effective compared to TNF-a inhibitors in terms of lower back and leg pain patient overall satisfaction (global perceived effect (satisfaction)) or return to work at the short term, medium-term and long-term follow-ups. (Wang et al 2014; SR (A+))	**Level 1+** • Caudal LESI plus anaesthetic more effective than anaesthetic alone (Dighe and Friedman 2013; SR (A+))
Level 1 • LESI effective in the immediate-term in reducing pain with positive correlation between LESI volume and pain relief: r=0.8027 (p=0.0017). (Rabinovotch et al 2009; SR (A+)) • In the intermediate term, there was a statistically significant positive correlation between volume and pain relief: r=0.9470 (p=.014). (Rabinovotch et al 2009; SR (A+)) • Transforaminal LESI as effective as a single transforaminal injection of bupivacaine or saline. (Roberts et al 2009; SR (A+)) • LESI no more effective than benzodiazepine injection for pain relief over short to intermediate term. (Henschke et al 2010; SR (HQ++)) • LESI no more effective compared to anaesthetic in self-reported improvement in patients with spinal stenosis (Bresnahan et al 2013; SR A(+)). • LEI with anaesthetic no more effective than LEI with anaesthetic and steroid in long or short term (Manchikanti et al 2015; SR (A+)) • Caudal LEI with or without steroid effective for pain relief in patients for disc herniation or radiculopathy in short term (Dighe and Friedman 2013; SR (A+))	

RCT • There was no significant statistical difference between treatment of epidural injection of oxygen ozone combined with steroid and ozone only in the 6 and 12 months follow-up. (Zhang et al 2013; RCT A(+) • This study suggested a lack of superiority of steroids compared with local anaesthetic at 2- year follow-up. (Manchikanti et al 2014b; RCT (A+)) • Transforaminal LESI failed to reach statistical significance at the 3-week mark between groups improvements in RMDQ and leg pain score with the combined LES+AI group compared to the LEAI group. Friedly et al 2014; RCT (HQ++)) • The results showed significant improvement in patients suffering with chronic lumbar spinal stenosis with caudal and interlaminar epidural approaches with local anaesthetic only, or with steroids in a long-term follow-up of up to 2 years, Manchikanti et al 2014c; RCT (HQ++)) • Both high volume and low volume LESI groups demonstrated clinically and statistically significant improvement in functional status according to the RMDQ ($P < 0.05$). The high-volume group demonstrated significant pain relief compared to the low volume group however there was no significant difference in functional status between the 2 groups (Chun and Park 2015; RCT (HQ++)) • An LESI of 80 mg had higher rates of favorable clinical response than a 40mg injection, but significantly more so at week 4 only. Habib et al 2013; RCT (A+)) • Significant pain relief and functional status improvement were observed in 72% of patients receiving local anaesthetic alone and 67% of patients receiving local anaesthetic with steroids via interlaminar LESI over 2 years (Manchikanti et al 2014; RCT (A+))	**RCT** • Using a Parasagittal fluoroscopy guided Interlaminar approach and the addition of steroid to LA may provide superior effectiveness in terms of extent and duration of pain relief for managing CLBP with unilateral LRP over 12 months, even though, local anaesthetic alone also was effective (Ghai et al 2015; RCT (HQ++)) • Results were superior for pain relief at 6 months and functional status at 12 months in the steroid group, indicating that a patient's failure to respond to local anaesthetic alone, may be treated with addition of steroids. (Manchikanti et al 2014a; RCT (HQ++)) • Interlaminar LESI demonstrating statistically significant improvements in RMDQ and leg pain score with the combined LES+AI group compared to the LEAI group, (Friedly et al 2014; RCT (HQ++)) • Adding hyaluronidase to the epidural injectate during Transforaminal LESI was more effective in the management of chronic low back pain in patients with failed back surgery syndrome over a period of 4 weeks (Rahimzadeh et al 2014; RCT (A+)) • Lumbar epidural steroid with anaesthetic better than lumbar epidural with saline in reducing pain up to 24 hours (Colhado et al 2013; RCT (LQ-)) • Steroids are efficient in reducing the overall pain, and the neuropathic component in chronic lumbar radicular pain, whether it is distributed by the Interlaminar or Transforaminal approach, and at either 3ml or 8ml dose (Rados et al 2013; RCT (LQ-))

The evidence suggests that the efficacy of lumbar epidural steroid injections is related to the approach and condition treated.

5. The evidence suggests that the transforaminal approach is effective in reducing pain in patients with radiculopathy, particularly secondary to herniation of nucleus pulposus and particularly in the short term.

Level A	
FOR	**AGAINST**
Level 1++ • Transforaminal steroids provide modest analgesic benefit at 3 months in patients with lumbosacral radicular pain secondary to herniated intervertebral disks, but they have no impact on physical disability or incidence of surgery (Bhatia et al 2016; SR/MA (HQ++))	

	Level 1+ •Transforaminal LEI with local anaesthetic and steroids, effective for pain relief with lumbar disc herniation in short term (Manchikanti et al 2012; SR (HQ++)) •Transforaminal LESI effective in both short term and long term management of radiculopathy pain due to spinal stenosis or lumbar herniation (Benny and Azari 2011 SR (A(+)). •For lumbar transforaminal LESI the evidence for use in radicular pain was strong for short-term and moderate for long term improvement in pain and functional outcome (Abdi et al 2005; SR (A+)) •Transforaminal injections are more likely to yield positive results than interlaminar or caudal injections for patients with radiculopathy and low back pain (Cohen et al 2013; SR (A+)) •All approaches to the interlaminar, caudal, and transforaminal epidural space provide long-term relief in 27—56% patients with radiculopathy (Abdi et al 2005; SR (A+))	
	Level 1 •Transforaminal LESI more effective than placebo for treating radicular symptoms from HNP (Roberts et al 2009; SR (A+)) •Transforaminal LESI effective as a surgery sparing intervention for treating radicular symptoms (Roberts et al 2009; SR (A+)) •Transforaminal LESI produced better pain relief compared with Interlaminar LESI in RCTs in patients with low back pain with lumbosacral radicular pain (Wei et al 2016; SR (A+)) •Transforaminal LESI more effective than interlaminar LESIs (ILESIs) and caudal LESIs for radicular pain (Roberts et al 2009; SR (A+)) •Transforaminal LESI with anaesthetic, effective for pain relief with lumbar disc herniation in long term (Manchikanti et al 2012; SR (HQ++)) •Transforaminal LESI with anaesthetic, effective for preventing surgery with lumbar disc herniation (Manchikanti et al 2012; SR (HQ++)) •Transforaminal LESI with anaesthetic, effective for pain relief with spinal stenosis in short and long term (Manchikanti et al 2012; SR (HQ++)) •Transforaminal LESI effective in reducing pain, restoring function, reducing the need for other health care, and avoiding surgery in patients with lumbar radicular pain caused by contained disc herniations (MacVicar et al 2013; SR (LQ--)) •Transforaminal LESI more effective for reducing pain in patients with lumbar herniated disk, compared with spinal stenosis or axial spinal pain. (Cohen et al 2013; SR (A+)) •Transforaminal LEI effective for reducing pain in patients with spinal stenosis in short-term (Manchikanti et al 2015; SR (A+)) •Bilateral transforaminal injection was more effective than an interlaminar steroid injection in patients with spinal stenosis; (May and Comer 2013; SR (A+)) •Transforaminal approaches had better improvement in pain scores (4 months) compared with interlaminar injections. (Bresnahan et al 2013; SR (A+)). •Transforaminal LESI recommended for chronic low back pain (Dagenais et al 2010; SR(A+))	

•Transforaminal LESI recommended as a secondary intervention for low back pain with substantial neurologic involvement (Dagenais et al 2010; SR(A+)) •Transforaminal LESI have significant effect in relieving chronic pain of lumbar disc herniation and radiculitis with indicated evidence levels of Level II-1 for short-term relief and Level II-2 for long-term relief (Buenaventura et al 2009; SR (A+))	
RCT • Transforaminal LESI are an effective treatment in reducing pain levels in patients with acute radicular pain due to disc herniation, over 6 months (Kennedy et al 2015; RCT (A+)) • Transforaminal LESI are an effective treatment in patients with acute radicular pain due to disc herniation, over 6 months and frequently only require 1 or 2 injections for symptomatic relief. (Kennedy et al 2015; RCT (A+)) • Transforaminal LESI was a useful modality in treating pain secondary to lateral canal spinal stenosis, and the short-term functional outcomes were also improved significantly, (Koh et al 2013; RCT (HQ++)) • Transforaminal LESI showed limited long-term effects in treating patients with spinal stenosis. (Koh et al 2013; RCT (HQ++)) • Transforaminal LESI effective for pain relief in patients with NHP of at least 3 months' duration, at 2 weeks (Pirbudak et al 2015; RCT (LQ-)) • Transforaminal LESI effective for improving impairment, as measured by straight leg raise, in patients with NHP of at least 3 months' duration, at 2 weeks (Pirbudak et al 2015; RCT (LQ-))	

6. The evidence suggests that the transforaminal approach is not effective in reducing disability and improving functional outcomes in patients with radiculopathy, particularly secondary to herniation of nucleus pulposus	
Level B	
FOR	**AGAINST**
Level 1++ • Transforaminal steroids provide modest analgesic benefit at 3 months in patients with lumbosacral radicular pain secondary to herniated intervertebral disks, but they have no impact on physical disability or incidence of surgery (Bhatia et al 2016; SR/MA (HQ++))	
	Level 1+ • For lumbar Transforaminal LESI the evidence for use in radicular pain was strong for short-term and moderate for long term improvement in pain and functional outcome (Abdi et al 2005; SR (A+))

Level 1 • Transforaminal LESI not effective for improvement in disability (standardised mean difference in ODI 0). (Quraishi 2012; SR (LQ-)) • Transforaminal fluoroscopy guided LESI no more effective compared to Interlaminar fluoroscopy guided LESI in functional improvement in patients with radiculopathy secondary to IV disc herniation/degeneration in the long or short term (Chien et al 2014; SR (HQ++)) • Transforaminal LESI produced no better functional improvement and Oswestry disability index (ODI) score than Interlaminar LESI in patients with low back pain with lumbosacral radicular pain (Wei et al 2016; SR (A+))	**Level 1** • Transforaminal LESI effective in reducing pain, restoring function, reducing the need for other health care, and avoiding surgery in patients with lumbar radicular pain caused by contained disc herniations (MacVicar et al 2013; SR (LQ--))
	RCT • Transforaminal LESI are an effective treatment in improving disability, reducing disability scores (as measured by Oswestry disability Index scores) in patients with acute radicular pain due to disc herniation over 6 months (Kennedy et al 2015; RCT (A+)) • Transforaminal LESI effective for reducing disability scores (as measured by Oswestry disability Index scores) in patients with NHP of at least 3 months' duration, at 2 weeks (Pirbudak et al 2015; RCT (LQ-))

7. The evidence suggests that lumbar epidural steroid injection, using a caudal approach, is effective in reducing pain and improving disability in patients with radiculopathy, spinal stenosis or low back pain independent of steroid or imaging

Level A

FOR	AGAINST
Level 1+ • For caudal epidural LESI the evidence was strong for short-term and moderate for long-term improvement in pain and functional outcomes (Abdi et al 2005; SR (A+))	**Level 1+** Caudal LEI with or without steroid not effective for pain relief in patients for disc herniation or radiculopathy in long term (Dighe and Friedman 2013; SR (A+))

Level 1 • Caudal LESI, with local anaesthetic, effective for short- and long-term relief of chronic pain secondary to disc herniation or radiculitis (Parr et al 2012; SR (HQ++)) • Caudal LESI, with local anaesthetic, effective for discogenic or axial pain without disc herniation, radiculitis (Parr et al 2012; SR (HQ++)) • Caudal LEI with or without steroid effective for pain relief in patients for with discogenic pain without herniation in short term (Dighe and Friedman 2013; SR (A+)) • Caudal LEI, with local anaesthetic with or without steroids, effective for spinal stenosis pain (Parr et al 2012; SR (HQ++)) • Caudal LEI, with local anaesthetic with or without steroids, effective for post-surgery syndrome (Parr et al 2012; SR (HQ++)) • Caudal LEI with or without steroid effective for pain relief in patients with post lumbar surgery syndrome in short and long term (Dighe and Friedman 2013; SR (A+)) • Caudal and lumbar interlaminar LEI effective for reducing pain in patients with spinal stenosis in long term (Manchikanti et al 2015); SR (A+))	
RCT • No differences in outcome measures or effectiveness of the procedure between ultrasound-guided caudal epidural steroid injections and fluoroscopy guided epidural steroid injections in patients with herniated disk or spinal stenosis, with both demonstrating improvements (Park et al 2013; RCT (A+))	

8. The evidence suggests that lumbar epidural steroid injection with anaesthetic, using a caudal approach, is more effective in reducing pain and improving disability in patients with radiculopathy, spinal stenosis or low back pain than steroid alone	
Level A/Level B	
FOR	**AGAINST**
	Level 1+ • Caudal LESI plus anaesthetic more effective than anaesthetic alone in reducing pain (Dighe and Friedman 2013; SR (A+))

Level 1 • Caudal LESI, with local anaesthetic, effective for short- and long-term relief of chronic pain secondary to disc herniation or radiculitis (Parr et al 2012; SR (HQ++)) • Caudal LEI with or without steroid effective for pain relief in patients for disc herniation or radiculopathy in short term (Dighe and Friedman 2013; SR (A+)) • Caudal LESI, with local anaesthetic, effective for discogenic or axial pain without disc herniation, radiculitis (Parr et al 2012; SR (HQ++)) • Caudal LEI with or without steroid effective for pain relief in patients for with discogenic pain without herniation in short term (Dighe and Friedman 2013; SR (A+)) • Caudal LEI, with local anaesthetic with or without steroids, effective for spinal stenosis pain (Parr et al 2012; SR (HQ++)) • Caudal LEI, with local anaesthetic with or without steroids, effective for post-surgery syndrome (Parr et al 2012; SR (HQ++) • Caudal LEI with or without steroid effective for pain relief in patients with post lumbar surgery syndrome in short and long term (Dighe and Friedman 2013; SR (A+)) • Caudal LESI plus anaesthetic more effective than anaesthetic alone (Dighe and Friedman 2013; SR (A+))	**Level 1** • Caudal LEI with or without steroid not effective for pain relief in patients for disc herniation or radiculopathy in long term (Dighe and Friedman 2013; SR (A+))

9. The evidence suggests that lumbar epidural steroid injection, using an interlaminar approach, is effective in reducing pain and improving disability in patients with radiculopathy, spinal stenosis or discogenic low back pain in the short term.
- **The parasagittal approach is more effective than the midline approach**
- **Effectiveness is better in the short term**

Level A

FOR	AGAINST
Level 1+ • Interlaminar LESI may provide short-term benefit in the first 3–6 weeks (Vorobeychik et al 2016; SR A+)	
Level 1 • For Interlaminar LESI evidence for use in lumbar radicular pain was strong for short-term and limited for long-term improvement in pain and functional outcomes. (Abdi et al 2005; SR (A+)) • Interlaminar LESI performed blind (without fluoroscopy) effective for short term relief of pain of discogenic origin without radiculitis or disc herniation (Parr et al 2009; SR (HQ++)) • Interlaminar LESI with local anaesthetic under	**Level 1** • Interlaminar LESI performed blind (without fluoroscopy) not effective for long term relief of pain of discogenic origin without radiculitis or disc herniation (Parr et al 2009; SR (HQ++)) • Interlaminar LESIs not effective for radiculopathy for long-term pain relief (Benoist et al 2012; SR (LQ-))

fluoroscopy effective for radiculitis secondary to disc herniation in short and long term (Benyamin et al 2012; SR (HQ++)) • Interlaminar LESI performed blind (without fluoroscopy) effective for short-term relief of pain (<3/12) of disc herniation or radiculitis (Parr et al 2009; SR (HQ++)) • Interlaminar LESI with local anaesthetics under fluoroscopy effective for discogenic pain in short and long term (Benyamin et al 2012; SR (HQ++)) • Interlaminar LESI with local anaesthetic under fluoroscopy effective for spinal stenosis pain in short and long term (Benyamin et al 2012; SR (HQ++)) • Caudal and lumbar interlaminar LEI effective for reducing pain in patients with spinal stenosis in long term (Manchikanti et al 2015; SR (A+))	
RCT • Interlaminar LESI administered with the parasagittal approach was significantly more effective for pain relief and improvement in disability than the midline approach for 6 months in the management of low back pain with lumbosacral radicular pain (Ghai et al 2013; RCT (HQ++)) • Parasagittal fluoroscopy guided Interlaminar LESI more effective than midline Interlaminar for pain relief at 2 weeks. (Hashemi et al 2015; RCT (A+)) • Parasagittal fluoroscopy guided Interlaminar LESI more effective than midline Interlaminar for improving disability (measured by Oswestry Disability Index [ODI] at 2 weeks (Hashemi et al 2015; RCT (A+)) • Parasagittal fluoroscopy guided Interlaminar LESI effective in reducing pain in patients with low back pain with lumbosacral radicular pain at 12 months (Ghai et al 2014; RCT (HQ++)) • Parasagittal fluoroscopy guided Interlaminar LESI effective in improving disability (via ODI Scores) in patients with low back pain with lumbosacral radicular pain at 12 months (Ghai et al 2014; RCT (HQ++)) • Patients receiving LESI using the lateral parasagittal Interlaminar approach had longer pain relief then patients receiving LESI via a midline Interlaminar approach. (Candido et al 2013; RCT (HQ++)) • They also had better quality of life scores and improvement in everyday functionality and used less pain medications than patients receiving LESI using a midline approach. (Candido et al 2013; RCT (HQ++)) • The effect on pain and disability of LESI via Interlaminar approaching lumbosacral radicular syndrome is small but significant, and at lower costs with no reported complications or adverse effects. (Spijker-Huiges et al 2014b; RCT (A+)) • Lumbar interlaminar epidural injections of local anaesthetic with or without steroids provide relief in a significant proportion of patients with lumbar central spinal stenosis. (Manchikanti et al 2015;	**RCT** • Small, statistically significant, but not clinically relevant positive effect of LESIs (Interlaminar approach) on back pain, impairment and disability in acute lumbar radiculopathy at 1 year. (Spijker-Huiges et al 2014a; RCT (A+))

RCT (HQ++)) • The results showed significant improvement in patients suffering with chronic lumbar spinal stenosis with caudal and interlaminar epidural approaches with local anaesthetic only, or with steroids in a long-term follow-up of up to 2 years, with the interlaminar approach providing significantly better results. (Manchikanti et al 2014c; RCT (HQ++)) • No difference between ultrasound-assisted and fluoroscopy-controlled Interlaminar LESI over a three-month period, with both being effective. (Evansa et al 2015; RCT (HQ++)) • The Interlaminar approach results may be somewhat superior compared to the caudal epidural injections at the end of 2 years where significant improvement was observed in 54% of the patients with local anaesthetic and 60% of the patients receiving local anaesthetic and steroids. (Manchikanti et al 2013, 2014c; RCT (A+))	

10. The evidence suggests that lumbar epidural steroid injections are of benefit during surgery for post-operative outcomes of pain in the short term, but not long term	
Level A	
FOR	**AGAINST**
Level 1+ • Intraoperative LESI are effective in reducing pain and reducing consumption of analgesia in the early stage (Jamjoom and Jamjoom 2014; SR (A+)) • Intraoperative LESI are not effective in reducing pain in the late stage (Jamjoom and Jamjoom 2014; SR (A+))	
Level 1 ▪ Intraoperative LESI are effective in reducing pain and reducing consumption of analgesia in the intermediate stage (Jamjoom and Jamjoom 2014; SR (A+))	**Level 1** • Intraoperative LESI are not effective in reducing duration of hospital stay. (Jamjoom and Jamjoom 2014; SR (A+))
RCT • Epidural steroids after a PELD reduce back pain and leg pain while improving functional outcomes in the short-term postsurgery period (Shin et al 2015; RCT (A+))	

11. The evidence suggests that the transforaminal approach is more effective in reducing pain, but not improving functional outcomes, in patients with radiculopathy	
Level A	
FOR	**AGAINST**
Level 1+ • Transforaminal injections are more likely to yield positive results than interlaminar or caudal injections for radiculopathy. (Cohen et al 2013; SR (A+)) • LESI more effective for reducing pain in patients with lumbar herniated disk, compared with spinal stenosis or axial spinal pain. (Cohen et al 2013; SR (A+))	
Level 1 • Transforaminal LESI more effective than interlaminar LESIs (ILESIs) and caudal LESIs for radicular pain (Roberts et al 2009; SR (A+)) • Bilateral transforaminal injection was more effective than an interlaminar steroid injection in patients with spinal stenosis (May and Comer 2013; SR (A+)) • Transforaminal approaches had better improvement in pain scores (4 months) compared with interlaminar injections (Bresnahan et al 2013; SR (A+)) • Transforaminal LESI produced better pain relief compared with Interlaminar LESI (Wei et al 2016; SR (A+)). • Transforaminal fluoroscopy guided LESI no more effective compared to Interlaminar fluoroscopy guided LESI in functional improvement in patients with radiculopathy secondary to IV disc herniation/degeneration in the long or short term (Chien et al 2014; SR (HQ++)) • Transforaminal LESI produced no better functional improvement and Oswestry disability index (ODI) score than Interlaminar LESI (Wei et al 2016; SR (A+)). • There were no differences between transforaminal and Interlaminar LESI in regard to procedure frequency, surgery rate, and ventral epidural spread. (Wei et al 2016; SR (A+)).	

3.6 Outcome Measures – Pain and Function - By condition

Reflecting the use of lumbar epidural injections in the community, 26 of the 38 SRs and 25 of the 34 RCTs involved patients with radiculopathy. Across the 26 SRs involving radiculopathy a range of diagnostic descriptors were used. Table 6 presents the results of the SRs by diagnostic label

The range of diagnostic labels used reflects a potentially significant source of bias when interpreting the evidence related to the efficacy of lumbar epidural steroid injections. The effectiveness of an intervention such as LESI will depend on the appropriateness of the intervention to the clinical condition. Broad 'symptom-based' diagnostic criteria such as 'radiculopathy' or 'low back pain with radiculopathy' without consideration of the potential causes for the irritation/compression of the nerve make it difficult to consider the clinical applicability of the evidence. Due to the nature of the diagnostic categories presented it is difficult to identify which groups are mutually exclusive, and which patients would necessarily benefit from the intervention.

Table 6: Summary of SR/RCT results by condition and approach

Low Back Pain								
	Pain				Functional disability			
	Short Term		Long Term		Short Term		Long Term	
Systematic Reviews								
Staal et al 2008	N				N			
Henschke et al 2010	N							
Parr et al 2012	Y(CS)		Y(CS)		Y(CS)		Y(CS)	
Benyamin et al 2012	Y(IL)		Y(IL)					
Bicket et al 2013	N		N					
Fritzler and Sarafini 2011	Y *(6 weeks)*		N		Y *(6 weeks)*		N	
Parr et al 2009	Y(IL) *(<3 months)*		N(IL) *(> 3 months)*		Y(IL) *(<3 months)*		N(IL) *(>3 months)*	
Colimon and Villalobos 2010	Y(CS)		Y(CS)					
Colimon and Villalobos 2010	Y(IL)		Y(IL)					
Colimon and Villalobos 2010	Y (TF)		Y (TF)					
Dighe and Friedman 2013	Y(CS)		N(CS)					
Summary (SRs)	**Y=8** *CS=3 IL=3 TF=1*	**N=3**	**Y=5** *CS=2 IL=2 TF=1*	**N=4** *CS=1 IL=1*	**Y=3** *CS=1 IL=1*	**N=1**	**Y=2** *CS=1*	**N=1** *IL=1*

RCTs								
Colhado et al 2015	N							
Evansa et al 2015	Y(IL) *(3 months)*				Y(IL) *(3 months)*			
Manchikanti et al 2013	Y(IL)		Y(IL)		Y(IL)		Y(IL)	
Summary RCTs	Y=2 *IL=2*	N=1	Y=1 *IL=1*	N=0	Y=2 *IL=2*	N=0	Y=1 *IL=1*	N=0

Radiculopathy								
	Pain				Functional disability			
	Short Term		Long Term		Short Term		Long Term	
Systematic Reviews								
Rabinovotch et al 2009	Y							
Dagenais et al 2010	Y (TF)							
Lewis et al 2011	Y		N		Y		N	
Benoist et al 2012*	Y(IL)		N(IL)		Y(IL)		N(IL)	
Benoist et al 2012 *	Y(CS)		Y(CS)		Y(CS)		N(CS)	
Benoist et al 2012 *	Y (TF)		Y (TF)		Y (TF)		Y (TF)	
Pinto et al 2012	Y		N		Y		N	
Quraishi 2012	Y (TF)		Y (TF)		N(TF)		N(TF)	
Manchikanti et al 2012*	Y (TF)		Y (TF)		Y (TF)		Y (TF)	
Choi et al 2013			N				N	
Koes et al 1995	Y		N		Y		N	
Tonkovich-Quaranta and Winkler 2000	Y *(12 weeks)*							
Abdi et al 2005	Y(IL)		N(IL)		Y(IL)		N(IL)	
Abdi et al 2005	Y (TF)		Y (TF)		Y (TF)		Y (TF)	
Abdi et al 2005	Y(CS)		Y(CS)		Y(CS)		Y(CS)	
Parr et al 2009	Y(IL) (<3 months)		N(IL) *(>3 months)*		Y(IL) *(<3 months)*		N(IL) *(>3 months)*	
Buenaventura et al 2009	Y (TF)		Y (TF)		Y (TF)		Y (TF)	
Colimon and Villalobos 2010	Y(CS)		Y(CS)					
Colimon and Villalobos 2010	Y(IL)		Y(IL)					
Colimon and Villalobos 2010	Y (TF)		Y (TF)					
MacVicar et al 2013	Y (TF)		Y (TF)					
Armon et al 2007	Y		N		Y		N	
Dworkin et al 2013	Y *(12 weeks)*		N					
Vorobeychik et al 2016	Y(IL)							
Summary (SRs)	**Y=23** CS=3 IL=5 TF=8	**N=0**	**Y=10** CS=3 IL=1 TF=7	**N=9** CS=0 IL=3 TF=0	**Y=12** CS=2 IL=3 TF=4	**N=1** CS=0 IL=0 TF=1	**Y=5** CS=1 IL=0 TF=4	**N=10** CS=1 IL=3 TF=1

RCT								
Candido et al 2013	Y(IL)		Y(IL)					
Chun & Park 2015	Y (TF)							
Cohen et al 2015	**Y(TF)** *(<3 months)*				**Y(TF)** (<3 months)			
Cohen et al 2015	Y(IL) *(<3 months)*				Y(IL) *(<3 months)*			
Dennis et al 2015	Y(TF)		Y(TF)		Y(TF)		Y(TF)	
Ghai et al 2014	Y(TF)		Y(TF)		Y(TF)		Y(TF)	
Ghai et al 2014	Y(IL)		Y(IL)		Y(IL)		Y(IL)	
Ghai et al 2015	Y(IL)		Y(IL)		Y(IL)		Y(IL)	
Ghai et al 2013	Y(IL)		Y(IL)		Y(IL)		Y(IL)	
Habib et al 2013	Y *4 weeks*				Y *4 weeks*			
Hashemi et al 2015	Y(IL) 2 weeks				Y(IL) *2 weeks*			
Koh et al 2015	Y(TF) (*3 months)*				Y(TF) *(3 months)*			
Park et al 2013	Y(CS) *12 weeks*				Y(CS) *12 weeks*			
Rados et al 2013	Y(IL)		Y(IL)					
Rados et al 2013	Y(TF)		Y(TF)					
Sinofsky et al 2014	Y(IL)		Y(IL)		Y(IL)		Y(IL)	
Spijker-Huiges et al 2014	N		N		N		N	
RCT Summary	**Y = 16** CS=1 IL=8 TF=6	**N=1**	**Y=9** CS=0 IL=6 TF=3	**N=1**	**Y=13** CS=1 IL=6 TF=4	**N=1**	**Y=7** CS=0 IL=4 TF=2	**N=1**

Radiculopathy secondary to Herniated Disc

	Pain		Functional disability	
	Short Term	**Long Term**	**Short Term**	**Long Term**
Systematic Reviews				
Wei et al 2016 (HNP)	Y		Y	
Roberts et al 2009 (HNP)	Y (TF)	Y (TF)	Y (TF)	Y (TF)
Bhatia et al 2016 (HNP)	Y(TF) (*3 months)*	N(TF)		
Benny and Azari 2011 (HNP)	Y (TF)	Y (TF)		
Dighe and Friedman 2013 (HNP)	Y(CS)	N(CS)		
Cohen et al 2013 (HNP)	Y	Y	Y	Y
Chien et al 2014 (HNP) *	Y	Y	Y	Y
Benyamin et al 2012 (HNP)	Y(IL)	N(IL)		

Jordan et al 2011 (HNP)	Y		N		Y		N	
Parr et al 2012 (HNP)	Y(CS)		Y(CS)					
Benoist et al 2012 (HNP)*	Y		N		Y		N	
Summary (SRs)	**Y=11** CS=2 IL=1 TF=3	**N=0**	**Y=5** CS=1 IL=0 TF=2	**N=5** CS=1 IL=1 TF=1	**Y=6** CS=0 IL=0 TF=1	N=0	Y=3 CS=0 IL=0 TF=1	N=2 CS=0 IL=0 TF=0
RCT								
Kennedy et al 2014	Y(TF)		Y(TF) (6 months)		Y(TF)		Y(TF) *(6 months)*	
Manchikanti et al 2014	Y(TF)		Y(TF)		Y(TF)		Y(TF)	
Manchikanti et al 2013/14	Y(IL)		Y(IL)		Y(IL)		Y(IL)	
Pirbudak et al 2015	Y(TF) *2 Weeks*				Y(TF) *2 Weeks*			
Summary (RCTs)	**Y=4** CS=0 IL=1 TF=3	**N=0**	**Y=3** CS=0 IL=1 TF=2	**N=0**	Y=4 CS=0 IL=1 TF=3	N=0	Y=3 CS=0 IL=1 TF=2	N=0

Herniated disc								
	Pain				**Functional disability**			
	Short Term		**Long Term**		**Short Term**		**Long Term**	
Systematic Reviews								
Jordan et al 2011	Y		N		Y		N	
Parr et al 2012*	Y(CS)		Y(CS)					
Manchikanti et al 2012*	Y (TF)		Y (TF)		Y (TF)		Y (TF)	
Parr et al 2009	Y(IL) (<3 months)		N(IL) (> 3 months)		Y(IL) (<3 months)		N(IL) (>3 months)	
Buenaventura et al 2009	Y (TF)		Y (TF)		Y (TF)		Y (TF)	
Colimon and Villalobos 2010	Y(CS)		Y(CS)					
Colimon and Villalobos 2010	Y(IL)		Y(IL)					
Colimon and Villalobos 2010	Y (TF)		Y (TF)					
Dighe and Friedman 2013 (HNP)	Y(CS)		N(CS)					
Summary SRs	**Y=9** CS=3 IL=2 TF=3	**N=0**	**Y=6** CS=2 IL=1 TF=3	**N=3** CS=1 IL=1 TF=0	**Y=4** CS=0 IL=1 TF=2	N=0	**Y=2** CS=0 IL=0 TF=2	**N=2** CS=0 IL=1 TF=0

Stenosis								
	Pain				Functional disability			
	Short Term		Long Term		Short Term		Long Term	
Systematic Reviews								
Benoist et al 2012	Y(CS)		Y(CS)		Y(CS)		Y(CS)	
Parr et al 2012	Y(CS)							
Ammendolia et al 2012	Y		N		Y		N	
Manchikanti et al 2012	Y (TF)		Y (TF)					
Benyamin et al 2012*	Y(IL)		Y(IL)		Y(IL)		Y(IL)	
Colimon and Villalobos 2010	Y(CS)		Y(CS)					
Colimon and Villalobos 2010	Y(IL)		Y(IL)					
May and Comer 2013*	N		N		N		N	
Bresnahan et al 2013	Y		N		Y		N	
Benny and Azari 2011	Y (TF)		Y (TF)					
Dighe and Friedman 2013 (HNP)	Y(CS)		N(CS)					
Vorobeychik et al 2016	Y(IL)							
Manchikanti et al 2015	Y(TF)							
Manchikanti et al 2015			Y(CS)					
Manchikanti et al 2015			Y(IL)					
Summary (SRs)	Y=12 CS=4 IL=3 TF=3	N=1 CS=0 IL=0 TF=0	Y=8 CS=3 IL=3 TF=2	N=4 CS=1 IL=0 TF=0	Y=4 CS=1 IL=1 TF=0	N=1 CS=0 IL=0 TF=0	Y=2 CS=1 IL=1 TF=0	N=3 CS=0 IL=0 TF=0

RCT								
Koh et al 2013	Y(TF)		Y(TF)		Y(TF)		Y(TF)	
Manchikanti et al 2015	Y(IL)		Y(IL)		Y(IL)		Y(IL)	
Manchikanti et al 2014	Y(IL)		Y(IL)		Y(IL)		Y(IL)	
Manchikanti et al 2014	Y(CS)		Y(CS)		Y(CS)		Y(CS)	
Summary (RCTs)	**Y=4** CS=1 IL=2 TF=1	**N=0**	**Y=4** CS=1 IL=2 TF=1	**N=0**	**Y=4** CS=1 IL=2 TF=1	N=0	**Y=4** CS=1 IL=2 TF=1	

Recommendations

When considering the evidence according to the diagnostic category

- For axial low back pain the evidence suggests that the optimal approaches for reducing pain and improving functional outcomes are the caudal sacral or the Interlaminar approaches in the short term (up to 3 months). (Level B)
- For axial low back pain the evidence suggests that neither approach is better at achieving long term improvements in pain or functional outcomes (> 3 months). (Level B)
- For radiculopathy of non-specific causes the evidence suggests that the optimal approaches for reducing pain and improving functional outcomes are the transforaminal or interlaminar approaches in the short or long term. (Level B)
- For radiculopathy secondary to herniated disc the evidence suggests that the optimal approach for reducing pain and improving functional outcomes is the transforaminal approach in the short or long term. (Level B)
- For pain due to a herniated disc the evidence suggests that all approaches are equally effective in the short term for reducing pain and improving functional outcomes, with possibly slightly better long term effects with the transforaminal approach. (Level B)
- For pain due to spinal stenosis the evidence suggests that the optimal approaches for reducing pain and improving functional outcomes are the caudal/sacral and interlaminar approaches in the short or long term. (Level B)

3.7 Outcome Measures – Safety and Risk

This review also sought to synthesise the literature on complications of LESI. A total of 16 cohort studies and 10 case studies were identified and included in this section of the review.

A number of the systematic reviews included in the section on effectiveness of LESI also focused on risks of adverse events and complications, and have therefore been included in this section of the review.

3.7.1 Complications - Systematic Reviews

Koes et al (1995) reported that in the 12 RCTs they reviewed, no major complications or side effects were reported. Transient minor complaints that were reported included:

- Headache (Serrao et al 1992: n=8/52 (15%), Beliveau 1971: n=10/45 (22%), Ridley et al 1988: n=1/47 (2%))
- Nausea (Serrao et al 1992: n=1/52 (2%), Rocco et al. 1989: n=1/49 (2%))
- Irregular periods (Bush and Hillier 1991: n=1/59)
- Pruritis (Rocco et al.1989: n=1/49)
- Increased sciatic pain (Snoek et al. 1977: n= a few/72)

Four RCTs reported no side effects and three RCTs failed to make mention of side effects.

Armon et al (2007) reported that the most common complication was a transient headache whether or not associated with identifiable dural puncture. More serious complications were several cases of aseptic meningitis, arachnoiditis, and conus medullaris syndrome, typically after multiple subarachnoid injections. Two cases of epidural abscess, one case of bacterial meningitis, and one case of aseptic meningitis were also listed. A retroperitoneal hematoma was reported in one patient on anticoagulant therapy who received a fluoroscopically guided transforaminal injection of steroids (Karppinen et al, 2001). Transient complications have been encountered also during fluoroscopically guided caudal epidural injections, including insomnia, transient non-positional headaches, increased back pain, facial flushing, vasovagal reactions, nausea, and increased leg pain. The role of practitioner experience and radiologic confirmation of needle placement could not be determined based on the reports. The results of the one high quality study with radiologic confirmed needle placement did not provide direct comparison of techniques. Therefore, the utility of, or need for, fluoroscopic confirmation of needle placement was unclear from the evidence reviewed by Armon et al (2007).

Henschke et al (2010) in their review of the efficacy of injection therapy for chronic low back pain found that in the majority of studies reviewed, no adverse events or side effects associated with treatments were reported. Epidural injections were associated with nausea and headache in some patients; however, most trials were small and not designed to evaluate adverse events, so no clear conclusion could be drawn regarding the risks of injection therapy.

Jordan et al (2011) in their review of interventions for herniated lumbar discs reviewed adverse events reported in the literature from use of epidural steroids. They reported that one systematic review of conservative treatment for low back pain (Vroomen et al 2000) reported no serious adverse effects, although 26 subjects of 332 (7.8%) complained of transient headache or transient increase in sciatic pain. One review (dePalma et al, 2005) reported a 1.9% incidence of headache with epidural injections and a retroperitoneal haematoma in one person having anticoagulation treatment in one RCT. One RCT included in the review noted that 2 of 43 subjects (5%) reported clinically important adverse effects with LESI, whilst 3 of 42 subjects (7%) reported clinically important adverse effects with placebo (with non-significant differences between the groups). The authors also noted that headache occurred in two people in each group (5%), and thoracic pain in one subject in the control group (2%).

Parr et al (2009) and Benyamin et al (2012) explored the complications related to lumbar interlaminar epidural injections. They reported that the common complications were of 2 types: those related to the needle placement, and those related to drug administration. multiple infectious complications including epidural abscess, meningitis, and osteomyelitis/discitis have been reported in the literature (Benyamin et al 2012)

Epidural hematomas were potentially the most serious of the epidural injection complications and could develop spontaneously even in patients with no evidence of any bleeding tendency, anticoagulation, or traumatic needle insertion.

Neurological injuries were an uncommon complication that can occur when performing lumbar epidural steroid injections. Other complications include increased pain, seizures, chemical meningitis, dural puncture, subdural air, pneumocephalus, transient blindness, retinal necrosis, chorioretinopathy, hiccups, flushing, and arterial gas embolism. Side effects related to the administration of steroids are generally attributed either to the chemistry or the pharmacology of the steroids.

Finally, radiation exposure was also a potential problem with damage to eyes, skin, and gonads.

Parr et al (2012) in a review of the effectiveness of caudal LESI for low back pain concluded that whilst complications related to caudal epidural injections were rare, occasional complications may become worrisome. These complications included infection, either local or epidural; abscesses; discitis; intravascular injection, either intervenors or intraarterial, with hematoma formation, spinal cord infarction; extra epidural placement with subcutaneous injection; subdural injection, dural puncture with post lumbar puncture headache; nerve damage; intracranial air injection or increased intracranial pressure; pulmonary embolism; and adverse effects of steroids.

Manchikanti et al (2012a) in their systematic review of evidence on the effectiveness of transforaminal LESI in managing lumbar spinal pain reported that the most common and

worrisome complications, though rare, were related to neural trauma, vascular trauma, intravascular injection, and infection. None of the studies included in their review showed any major complications. Manchikanti et al (2012a) concluded that most if not all complications could be avoided by careful technique with accurate needle placement, sterile precautions, and a thorough understanding of the relevant anatomy and contrast patterns on fluoroscopic imaging. However, a number of case studies have reported complications including spinal cord injury and infarction and paraplegia following transforaminal injections (Glaser and Falco 2005, Houten and Errico 2002).

Benoist et al (2012) concluded that concerning safety, LESIs were generally well tolerated and most complications were related to technical problems during the procedure. However, the safety of ESIs should be questioned after the report of several cases of paraplegia complicating the foraminal route, a technique gaining popularity owing to its evidence of efficacy. Although quite exceptional, the seriousness of this adverse event suggests a need for research on alternative approaches to the foramen and on means to detect an eventual arterial injury, as well as on the use of a steroid agent with the least tendency to coalesce.

Bui and Bogduk (2013) and MacVicar et al (2013) in their reviews of the effectiveness of CT-guided transforaminal LESI identified two practice audits of complications (Botwin et al 2000, Karaman et al 2011), and five case studies reporting eight cases of catastrophic complications (Houten and Errico 2002, Huntoon and Martin 2004, Somyaji et al 2005, Glaser and Falco 2005, Kennedy et al 2009). Both Bui and Bogduk (2013) and MacVicar et al 2013 concluded that "complications" such as headache, postprocedure pain, facial flushing, vasovagal reactions, rash, transient leg weakness, erectile dysfunction, dizziness, increased blood sugar, hypertensive episode, and nausea which have been reported (Botwin et al 2000, Karaman et al 2011) do not constitute complications of transforaminal LESI as they are all transient phenomena that might be encountered with any injection involving corticosteroids. Whilst case reports have reported technical problems that occur during transforaminal LESI such as dural puncture (Goodman et al 2007), or unintended injection into a vein (Furman et al 2000) or into a disc (Haspeslagh et al 2004, Cohen et al 2008, Finn and Case 2005), Bui and Bogduk (2013) and MacVicar et al 2013 concluded that they do not constitute complications if they do not cause any impairment.

Epstein et al (2013) reviewed the evidence related to complications arising from interlaminar and transforaminal LESI and identified a range of common risks including increased neurological deterioration/paralysis/quadriplegia, intravascular injections (7.9-11.6%), cerebrospinal fluid (CSF) fistulas (0.4-6%), persistent positional headaches (28%), arachnoiditis (6-16%), hydrocephalus, air embolism, urinary retention, allergic reactions, intravascular injections (7.9-11.6%), stroke, blindness, neurological deficits/paralysis, hematomas, seizures, and death.

Chien et al (2014) in their review of the transforaminal versus Interlaminar LESI approach reported that despite the advantages of the transforaminal approach, the technique

carried certain unique risks. The transforaminal approach has been more often implicated in severe, permanent complications compared to interlaminar LESI, including intravascular injection in up to 23% of lumbar epidural injection cases (Nahm et al 2010), which can lead to spinal cord infarction and paralysis. Intravascular injection with transforaminal LESI can occur even with the use of digital subtraction angiography or following a negative lidocaine anaesthetic test dose (Chang et al 2012). The transforaminal approach has been linked to a 12-fold increased risk of intradiscal injection, compared to the interlaminar approach (Candido et al 2010, Cohen et al 2008). Additionally, transforaminal LESI do not decrease the risk of known complications of interlaminar LESI, such as dural and subdural punctures, hematoma formation and cauda equina syndrome (Chien et al 2014). Chien et al (2014) concluded that in an individual with lumbosacral radicular pain, the increased risk of complications associated with transforaminal LESI must be weighed against the possibility for superior pain relief and functional outcomes that reduce the rate of spinal surgery, which is itself associated with significant complications.

3.7.2 Complications – Randomised Controlled Studies

Side effects related to LESI from the RCTs reviewed in this systematic review are presented in table 7.

Table 7: Side effects related to LESI from the RCTs

	Caudal		Interlaminar		Transforaminal	
	Study	**%**	**Study**	**%**	**Study**	**%**
Adverse events			Friedly et al 2014	10	Friedly et al 2014	33
Pain at injection site			Candido et al 2013	MIL:30 PIL:22	Denis et al 2015	9.4
			Evensa et al 2015	16		
			Manchikanti et al 2015	0.2		
Headache	Park et al 2013	2.5	Candido et al 2013	MIL:12 PIL:22		
Nausea			Candido et al 2013	MIL:14, PIL:6		
Increased lumbar pain	Park et al 2013	7.5			Denis et al 2015	7.6
Increased radicular pain			Manchikanti et al 2015	0.2	Denis et al 2015	7.6
					Manchikanti et al 2014	4.6
Flushing			Evensa et al 2015	16	Denis et al 2015	9.4
Anxiety					Denis et al 2015	5.7
Vasovagal reaction	Park et al 2013	4			Denis et al 2015	1.9
High blood pressure					Denis et al 2015	1.9
Hyperglycemia					Denis et al 2015	1.9
Menometrorrhagia					Denis et al 2015	11.3
Change of mood					Denis et al 2015	1.9

Agitation					Denis et al 2015	3.8
Insomnia					Denis et al 2015	3.8
Dizziness	Friedly et al 2014	2	Evensa et al 2015	16	Denis et al 2015	1.9
Nausea/vomiting					Denis et al 2015	1.9
Delayed menstrual cycle					Denis et al 2015	1.9
Lower extremity edema					Denis et al 2015	2%
Headache					Denis et al 2015	1.9
Postdural puncture headache					Denis et al 2015	1.9
Skin irritation	Friedly et al 2014	2				
Dural puncture	Friedly et al 2014	0.5	Manchikanti et al 2013	0.5	Manchikanti et al 2014	4.6
	Manchikanti et al 2013b	24	Manchikanti et al 2014	1.6		
Rate of complications	0.5-24%		0.2%-30%		1.9%-33%	

3.7.3 Complications - Cohort studies

Johnson et al (1999) completed a retrospective cohort study involving 5,334 procedures in which epidurography (i.e. the use of fluoroscopy and radiologic contrast material) was used immediately before and after epidural steroid injection, of which 4,780 were lumbar, 669 cervical and 40 thoracic epidurals. All injections were performed by one of three experienced procedural neuroradiologists during a 5½-year period. They identified four complications including a significant hypotensive episode, a small dorsal epidural hematoma at the injection site, a severe vasovagal response after injection, and a case of tachycardia. The authors do not provide any information about the site of injection or the approach used in their report.

Botwin et al (2000) in a retrospective review reported complications in 207 patients receiving 322 fluoroscopically guided transforaminal LESI, which included 10 transient non-positional headaches that resolved within 24 hours (3.1%), 8 increased back pain (2.4%), 2 increased leg pain (0.6%), 4 facial flushing (1.2%), 1 vasovagal reaction (0.3%), 1 increased blood sugar (258mg/dL) in an insulin-dependent diabetic (0.3%), and 1 intraoperative hypertension (0.3%). No dural punctures occurred. The incidence of minor complications was 9.6% per injection with no major complications.

Furman et al (2000) undertook a prospective cohort study evaluating the incidence of vascular penetration during fluoroscopically guided, contrast-enhanced, transforaminal LESI among 761 patients. The overall rate of intravascular injections was 11.2%. There was

a statistically significant higher rate of intravascular injections (21.3%) noted with transforaminal LESI performed at S1 (n = 178), compared with those at the lumbar levels (8.1%, n = 583). Using flash or positive blood aspirate to predict intravascular injections was 97.9% specific, but only 44.7% sensitive. The authors concluded that there was a high incidence of intravascular injections in transforaminal ESIs that was significantly increased at S1.

Botwin et al (2001a) reported complications of fluoroscopically guided caudal LESI in 139 patients, who received 257 injections. Complications per injection included 12 episodes of insomnia the night of the injection (4.7%), 9 transient nonpositional headaches that resolved within 24 hours (3.5%), 8 increased back pain (3.1%), 6 facial flushing (2.3%), 2 vasovagal reactions (0.8%), 2 episodes of nausea (0.8%), and 1 increased leg pain (0.4%). No dural punctures occurred. Overall there was a total of 40 complications, representing an overall incidence of minor complications of 15.6%.

Botwin et al (2001b) explored the risk related to radiation exposure for the physician during fluoroscopically guided caudal LESI in 100 consecutive fluoroscopically guided caudal LESI performed on patients with radiculitis from either herniated nucleus pulposus or lumbar spinal stenosis. This study showed that radiation exposure to the physician performing fluoroscopically guided caudal LESI was well within safety limits when the physician adhered to proper technique.

Fitzgibbon et al (2004) presented a review of the 5,475 claims in the American Society of Anesthesiologists' Closed Claims Project database between 1970 and 1999. This report provided insight into less common major complications associated with LESI. There were 114 claims related to ESIs making up 40% of all invasive pain management claims (Fitzgibbon et al 2004). The types of complications included nerve injury: (28/114; 25%) Infection: (24/114; 21%), death/brain damage: (9/114; 8%), headache: (20/114; 18%), increased pain, no relief: (10/114; 9%). Nerve injury occurred in 28 of the 114 claims (14 related to LESI). Six of these resulted in paraplegia, one in quadriplegia. Fitzgibbon et al's (2004) analysis demonstrated that injury to the cord was more common in upper lumbar epidural injections. Two cases of spinal cord injury resulting from epidural hematomas following ESI, with both patients having been receiving anticoagulants.

No major neurologic complications (spinal hematomas) were encountered in a series of 1,035 individuals who received 1,214 epidural steroid injections while on antiplatelet therapy (Horlocker et al 2002). Minor complications (blood during needle placement) were encountered in 63 (5.2%), and transient worsening of symptoms or emergence of new neurologic symptoms for more than 24 hours after the injection occurred in 42 (4%) patients with median duration of 3 days and range 1 to 20 days. NSAIDs did not increase the frequency of minor hemorrhagic complications. However, increased age, needle gauge, needle approach, needle insertion at multiple interspaces, number of needle passes, volume of injectant, and accidental dural puncture were all significant risk factors for minor hemorrhagic complications. Whilst the LESI approach that was used was not

reported in the paper, the authors reported that a midline approach was used in 1,124 (93%) and paramedian in 56 (5%) patients, suggesting an Interlaminar approach. Fluoroscopic guidance was used in 343 (28%) cases and contrast injection was performed in 294 (24%) of the treatments. The authors concluded that epidural steroid injection was safe in patients receiving aspirin-like antiplatelet medications. Minor worsening of neurologic function may occur after epidural steroid injection and must be differentiated from etiologies requiring intervention.

Stalcup et al (2006) presented a retrospective cohort study of 2,217 patients who had undergone selective lumbar nerve root blocks. The authors defined selective lumbar nerve blocks (SLNBs) as injections, performed either under fluoroscopic guidance or computed tomography, into or adjacent to the intervertebral foramen and delivering an anaesthetic and corticosteroid mixture into the immediate vicinity of the nerve root. Minor complications were encountered in 98 of the 1,777 total patient visits, for an overall complication rate of 5.5%. All complications were transient, and no patient suffered lasting harm. There were 1,232 procedures in which the patient received a single injection, and a minor complication was encountered in 62 of these visits. The complication rate approached 5% for all needle-tip positions, which was not statistically different from the overall complication rate. However, there was an increased likelihood of complications in patients undergoing a multiple injection procedure compared to those who had only one injection. The authors concluded that SLNBs performed with fluoroscopic guidance have a low incidence of complications, and the specific needle-tip position within or adjacent to the lumbar neural foramen did not appear to be associated with the incidence of complications.

Trentman et al (2009) undertook a retrospective study of 249 patients undergoing their first cervical epidural steroid injection and matched for comparison against a first translaminar LESI performed by the same staff physician for vasovagal reactions and other adverse events. The incidence of vasovagal reaction was 7% more common ($P < 0.001$) in the cervical group (8%) than in the lumbar group (1%), equating to an additional vasovagal reaction for every 14 patients who were treated with cervical injection in comparison with those treated with lumbar injection. The authors reported that the higher rate of cervical vasovagal reactions may result from a combination of anxiety, the prone position with neck flexed, head drapes, and stimulus from a neck procedure, suggesting increased vigilance for patients undergoing translaminar cervical epidural steroid injections was warranted.

Candido et al (2010) presented a retrospective review comparing rates of intradiscal injection in fluoroscopy-guided transforaminal and interlaminar LESI. A total of 4,723 interlaminar LESIs and 2,412 transforaminal LESIs were performed over a three-year period. The study identified 7 intradiscal injections of which 6 were associated with the transforaminal approach (for a rate of 1:402 injections) and 1 was associated with the Interlaminar approach (for a rate of 1:4723 injections). Three of the 6 patients had undergone previous lumbar spinal surgery. Four of the 7 injections were done at the L4-5

level, 2 at the L2-3 level, and 1 at the L5-S1 level. None of the patients in this retrospective review sustained an infection. The relative rate of intradiscal injection was approximately 12 times higher after fluoroscopy-guided transforaminal compared to fluoroscopy guided Interlaminar LESI.

Chang et al (2011) undertook a retrospective review of the safety of CT-guided steroid injections with air used to localize the epidural space. They reviewed 751 patients who underwent 1,000 procedures. Procedures were performed at the L5/S1 levels (75%), L4/5 (15.5%), L3/4 (4.9%), L2/3 (1.3%), L1/2 (0.8%), and T12/L1 (0.1%). Of the 1,000 LESI in this review, the authors reported that no immediate or delayed clinically significant complications were reported during a standard 24-hour and 1-week follow-up (99% of patients had 24-hour follow-up and 93% had 2-week follow-up via phone or office consultation). The authors were clear to point out that only clinically significant complications were reported, although they failed to identify what made a complication clinically significant compared to not clinically significant.

Karaman et al (2011) assessed the complications of transforaminal LESI prospectively over 1,305 injections in 562 patients over a 5-year period. All of the interventions were performed under fluoroscopic guidance by the same physician using a standardized method, with a follow-up once in the third week. The overall incidence of vascular penetration encountered was 7.4%. Although major complications were not seen, the total rate of all minor complications was 11.5%. Whereas all of the minor complications were transient, the most frequent minor complication was vasovagal reaction (8.7%).

In a retrospective cohort study over a 7-year period, McGrath et al (2011) reviewed the results of 4,265 injections on 1,857 patients, involving 161 cervical interlaminar injections, 123 lumbar interlaminar injections, 17 caudal injections, and 3,964 lumbar transforaminal injections. They identified a lack of major complications and reported 103 minor complications, for an overall complication per injection rate of 2.4%. The most common complications were increased pain (1.1%), pain at the injection site (0.33%), persistent numbness (0.14%), and ‘‘other’’ (0.80%). When comparing complications between interlaminar and transforaminal approaches they reported less common complications with transforaminal injections (0.021%) than with interlaminar injections (0.06%).

Table 8: Rate of complications from 4,265 epidural injections
(from McGrath et al 2011)

Complication	Interlaminar	Transforaminal
Increased pain	0.021%	0.011%
Numbness	0%	0.0015%
Pain at injection site	0.018%	0.0023%
Other	0.021%	0.0068%
Total	0.06%	0.021%

Manchikanti et al (2012) presented a prospective evaluation of complications of 10,000 fluoroscopically directed epidural injections of which 39% were caudal epidurals, 23% cervical interlaminar epidurals, 14% lumbar Interlaminar epidurals, 13% lumbar transforaminal epidurals, 8% percutaneous adhesiolysis, and 3% thoracic interlaminar epidural procedures. They reported intravenous placement of the needle in 22% of the transforaminal procedures, with other complications including pain during the injection with back pain in 43% of the patients and leg pain in 22% of the patients. Postoperative complications were reported in 34% of the patients, including soreness at the injection site (18%), increased pain (5%), muscle spasms (4%), swelling (4%), headache (3%), minor bleeding (2%), dizziness (1%), nausea and vomiting (1%), fever (1%), numbness (1%), and voiding difficulty (1%). With fluoroscopically guided caudal LESI, intravascular placement occurred in 14% of patients. They also reported minor complications in 7% of patients, including soreness at the injection site (6%), increased pain (1%), muscle spasms (1%), headache (1%), and nausea and vomiting (1%) (See table 9).

Table 9: Rate of complications from 10,000 fluoroscopically directed epidural injections
(from Manchikanti et al 2012)

Complications	Interlaminar	Transforaminal	Caudal/Sacral
	N=1,450	N=1,310	N=3,985
Intravascular injection	0.5%	7.9%	3.1%
Return of blood	0.5%	3.7%	0.7%
Profuse bleeding	0.8%	0.2%	0.3%
Local haematoma	0.28%	0.2%	0.1%
Bruising	0%	0.4%	0.2%
Epidural haematoma	0%	0%	0%
Vasovagal reaction	0%	0.08%	0%
Nerve irritation	0.28%	4.6%	0%
Nerve damage	0%	0%	0%
Spinal Cord Infarct	0%	0%	0%
Disc entry	0%	0.08%	0%
Dural Puncture	0.8%	0%	0%
Headache	0.07%	0%	0%
Infection	0%	0%	0%
Abscess	0%	0%	0%
Facial flushing	0.13%	0.15%	0%
Rate of complications	0.13%-0.8%	0.08%-7.9%	0.1%-3.1%

Qureshi et al (2013) undertook a prospective observational study to assess the complication rate across 386 blind interlaminar epidural steroid injections, involving 361 lumbar, 20 cervical and 5 performed via the caudal approach. All the interventions were performed as an outpatient procedure by one of the two pain physicians. The authors explored both immediate events and those occurring 4 hours after LESI. Rates of complications are presented in Table 10.

Table 10: Rate of complications from 386 blind interlaminar epidural steroid injections (from Qureshi et al 2013)

	Lumbar Interlaminar	Caudal
	N=361	N=5
Vasovagal Reaction	3.3%	0%
Intravascular Injection	0.83%	0%
Flushing	2.21%	0%
Headache	1.1%	0%
Nerve irritation	0.27%	0%
Dural puncture	0.83%	0%
Cardiac Arrest	0.27%	0%
Bruises	0.83%	0%
Post Dural puncture headache	0.55%	0%
Rate of complications	0.27%-3.3%	0%

Plastaras et al (2015) undertook a retrospective cohort study from a multiphysician clinic of patients who underwent a fluoroscopically guided transforaminal LESI for lumbosacral radicular pain between 2004 and 2007. Complications data was collected using a survey both immediately and at 24 to 72 hours after the injection in 1,295 consecutive patients undergoing 2,025 fluoroscopically guided transforaminal LESI. Immediate complications and delayed complications occurred after 182 (9.2%) and 305 (20.0%) injections respectively. The most common immediate complications were: vasovagal reaction (4.2%) and interrupted procedure from intravascular flow (1.7%). Common delayed complications included: pain exacerbation (5.0%), injection site soreness (3.9%), headache (3.9%), facial flushing/sweating (1.8%), and insomnia (1.6%). Significant associations were identified between AEs and gender, age, pre-procedure VAS, steroid type, and fluoroscopy time. Trainee involvement in the procedure did not impact the complication rate.

3.7.4 Complications - Case studies

Other much less common complications reported in case studies include transient blindness (Young 2002), retinal hemorrhage and necrosis (Browning 2003, Kushner and Olson 1995), serous chorioretinopathy (Pizzimenti and Daniel 2005, Iida et al 2001), persistent recurrent intractable hiccups (McAllister et al 2005), flushing (Everett et al 2004, Kim et al 2010), chemical meningitis (Gutknecht 1987), arachnoiditis (Nelson and Landau 2001), discitis (Yue and Tan 2003) and epidural abscess (Hooten et al 2004).

When reviewing complications related to LESI, they can be divided into 6 major categories:

3.7.5 Complications - Neurologic Injury

Spinal cord damage can occur from needle entry into the cord. Traumatic spinal cord injury has been reported to be more common in patients who received sedation or general anaesthesia, especially in those who were unresponsive during the procedure.

In Fitzgibbon et al's (2004) retrospective review of the American Society of Anesthesiologists' Closed Claims, nerve injury occurred in 28 of the 114 claims (14 related to LESI). Six of these resulted in paraplegia, one in quadriplegia. Fitzgibbon et al's (2004) analysis demonstrated that injury to the cord was more common in upper lumbar epidural injections.

3.7.6 Complications - Vascular Insult

Infarction of the lower spinal cord resulting in paraplegia has also been described following thoracic and lumbar transforaminal injections in a number of case study reports (Kennedy et al 2009, Glaser and Falco 2005). Injection into the spinal medullary arteries can result in spinal cord infarction, typically in the distribution of the anterior spinal artery; the magnitude and location of the resultant neurologic injury appear to relate to the anatomic location of injection. Spinal cord infarction associated with the transforaminal approach is less common than direct spinal cord trauma, according to Fitzgibbon et al 2004.

Intravascular injection is also possible, but can be prevented by using fluoroscopy (Cannon and Aprill 2000). Previous studies using fluoroscopic confirmation with contrast have shown a rate of 6.4% to 9.2% for the caudal route (White et al 1980, Renfrew et al 1991). One multicenter study included 1,219 fluoroscopically guided lumbar spinal injection procedures and found the following rates of intravascular injections: caudal 10.9%, transforaminal 10.8%, and translaminar 1.9 (Sullivan et al 2000). This study also found that 74% of these vascular injections were not detected by aspiration prior to contrast injection. Another study including 577 transforaminal injections found intravascular injection rates of 8.8% for lumbar levels and 25.2% for the S1 level, with an overall rate of 12.7%. (Furman et al 2000).

All of the corticosteroid suspensions commercially available contain particles large enough to occlude capillaries and arterioles Animal studies have shown that direct injection of particulate steroid into the vertebral artery can result in irreversible posterior circulation strokes similar to those reported in case reports following transforaminal injection of steroid. (Okubadejo et al 2008). Depot preparations of methylprednisolone, triamcinolone and betamethasone form particles or aggregates that are larger than red blood cells and could form emboli in terminal vessels in the spinal cord (Bui and Bogduk 2013). Injection of the nonparticulate steroid solution, dexamethasone resulted in no apparent injury in the same animal model, suggesting preliminary evidence for the safety of this agent.

Embolization has most often been related to the transforaminal approach and has not been implicated as a mechanism for injury following caudal or interlaminar ESIs (Cohen et al 2013). Although transforaminal injections performed in the lumbar spine carry a much lower risk than in the thoracic or cervical regions, previous surgery has been associated with an increased risk of spinal cord infarct (Houten and Enrico 2002).

Wybier et al (2009) reported a case series of 12 cases of sudden paraplegia immediately following LESIs since 2002. The clinical pattern was similar in all cases: within a few

minutes after the procedures, acute abdominal and leg pain are followed by a complete sensorimotor deficit of the lower limbs. MRI performed a few hours after the procedure was usually normal. In contrast, MRI obtained 24–96 hours later disclose a central high-intensity zone of the spinal cord consistent with an acute ischemia. Of the 12 patients reported by Wybier et al (2009), 8 had previous surgery and in 10 patients the injection route was foraminal; this route was the only one used in the 4 nonoperated patients. The most probable mechanism of this complication is the violation of a radiculomedullary artery with embolization of macroaggregates of steroid, and subsequent deprivation of the arterial supply of the cord. The radiculomedullary artery, also known as the Adamkiewicz artery, usually arises from the left between T9 and L2. In a minority of individuals, it may arise at a lower level of the lumbar spine. At the level concerned, the nerve root runs in the foramen parallel to the artery, which can be damaged by the needle in the foraminal approach. The high prevalence of this complication in operated patients may be related to the abundant vasculature and neoangiogenesis of the scar tissue, enhancing the risk of vascular damage.

Karaman et al (2011) in their retrospective review of 1,305 injections via the transforaminal approach reported an overall incidence of vascular penetration of 7.4%.

The epidemiological evidence shows that CT guidance is not immune to vascular complications (Bui and Bogduk 2013). Of the eight reported cases of spinal cord infarction following lumbar transforaminal injection, five followed CT-guided procedures (Houten and Errico 2002, Huntoon and Martin 2004, Somyaji et al 2005, Kennedy et al 2009).

Bui and Bogduk (2013) and MacVicar et al (2013) recommended that, to reduce the risk of this complication, operators must perform an injection of an adequate volume of contrast medium under continuous, anteroposterior, fluoroscopic imaging, sufficient to ensure that no intraspinal vascular uptake is present. The fluoroscopic field of view should include the spinal canal proximal to the level of injection such that intraspinal arterial uptake may be detected. Other measures recommended include: digital subtraction imaging, the use of low-volume extension tubing to minimize needle movement between the injection of contrast medium and the injection of steroids, and administering a test injection of local anaesthetic before injecting any steroid.

In most cases, there is probably little that can be done to minimize the extent of neurologic dysfunction after a traumatic or embolic event has occurred. High-dose intravenous steroids administered in the hours immediately following traumatic spinal cord injury have been shown to result in a significant reduction in neuronal injury (Hall and Springer 2004).

Intraspinal bleeding is a potentially devastating complication from LESI that can result in paraplegia or quadriplegia. Both epidural and subdural hematomas have been reported following ESIs in patients without coagulopathy or concurrent use of anticoagulants.

The most important risk factor for bleeding is coagulopathy, either primary or pharmacological. Anticoagulants and antiplatelet drugs are contraindications to epidural injections of any sort. On the other hand, NSAIDs, do not appear to appreciably increase the risk of epidural bleeding. Horlocker et al (2002) reported no major haemorrhagic complications among 1,035 patients, one-third of whom had been taking NSAIDs (134 on aspirin, 249 on other NSAIDs, and 34 on multiple drugs) who underwent 1,214 ESIs, of which 80% were lumbar.

In an online survey conducted in 325 respondents (of 2,300 surveyed) who perform interventional pain management procedures, nearly 3 times as many thromboembolic complications (n = 162) were reported as were serious bleeding complications (n = 55) (Manchikanti et al 2012b). Among the thromboembolic events, 153 occurred following discontinuation of anticoagulation therapy, whereas 9 transpired despite antiplatelet therapy being continued. For the bleeding complications, 29 occurred after warfarin or antiplatelet therapy was discontinued, with 26 occurring in the context of continued anticoagulation treatment. These findings suggest that the decision to discontinue anticoagulation therapy for neuraxial injections must be made after careful consideration of the risks and benefits. Because of its location at the distal end of the spinal column, its shallow depth (which enables compression), and the fact that it can easily be accessed with a small gauge needle, the caudal approach might be considered when a LESI is strongly indicated and the risk of discontinuing warfarin or antiplatelet therapy is high.

3.7.7 Complications - Pharmacologic Effect of Corticosteroids - Hypercorticism and Adrenal Suppression

Theoretical pharmacological complications of steroid administration include suppression of pituitary adrenal axis, hypercorticism, Cushing's syndrome, osteoporosis, avascular necrosis of the bone, steroid myopathy, epidural lipomatosis, weight gain, fluid retention, and hyperglycemia (Parr et al 2009 and Benyamin et al 2012).

Tonkovich-Quaranta and Winkler (2000) in their scoping review reported on a range of adverse effects associated with the use of epidural steroids including:

- systemic absorption of the corticosteroid,
- a decrease in plasma cortisol concentrations, and
- suppression of the hypothalamic–pituitary–adrenal axis.

They cited a study by Knight and Burnell (1980) who reported on a series of four patients (out of 181 patients (2.2%)) who experienced adverse effects attributed to epidural steroid injections. The patients had received a total of 240–600 mg of methylprednisolone acetate via epidural catheter over two to three days. At the one-month follow-up all patients reported adverse effects associated with corticosteroid use. These included facial fattening/swelling, a hump between the shoulder blades, and the appearance of small, raised, scaly lesions on the back. The authors noted that the injections were given on consecutive days and in higher dosages than those used in clinical trials (Knight and Burnell 1980)

The systemic effects resulting from oral or intravenous administration of steroids are rarely observed after epidural injections. However, side effects can result in an identical clinical pattern as Cushing's syndrome as the active corticosteroid and other depot steroid preparations are slowly released over a period of days to weeks. Case studies have reported post-LESI effects such as fluid retention and weight gain, facial swelling, buffalo hump, skin bruising, scaly skin lesions, increased blood pressure and congestive heart failure (Stambough et al 1984, Tuel et al 1990).

Allergies to any of the medications used can occur, and serious reactions can usually be prevented by questioning patients before the procedure. Side effects induced by corticosteroids are not uncommon. When they occur, the patient typically experiences transient symptoms, including insomnia, facial flushing, a sense of "feeling hot" ("steroid fever"), palpitations, nausea, nonpositional headaches and a sense of agitation or anxiety. In most instances, these side effects are dose related and transient, usually resolving in the week after the procedure.

Manchikanti (2002) reviewed potential adverse events including complications related to the endocrine system: hyperglycemia or worsening of diabetes, adrenal suppression biologically detected following a series of ESIs performed with short intervals, hypertension with fluid retention and gain of weight.

Burn and Langdon (1974) measured plasma cortisol concentrations before and after epidural injection in a series of 72 outpatients. Patients were given an epidural injection consisting of 10 mL of lidocaine 1.5%, 7 mL of NaCl 0.9%, 1 mL of hydrocortisone acetate (25 mg), and 2 or 4 mL of methylprednisolone (80 or 160 mg). The authors found a statistically significant depression in plasma cortisol concentrations for both methylprednisolone dosages at one week after injection and for the 160mg dose at two weeks after injection. Kay et al. (1994) measured plasma cortisol and adrenocorticotropic hormone (ACTH) concentrations in 14 patients receiving a LESI of triamcinolone acetate 80 mg in 7 mL of lidocaine 1%. Patients received the injections weekly for three weeks. In addition, half the patients were randomized to receive intravenous midazolam 0.07 mg/kg prior to the epidural injection. They found that within 45 minutes of the first epidural injection, the plasma cortisol and ACTH concentrations dropped significantly ($p < 0.05$), and premedication with midazolam accentuated the depression. Plasma concentrations returned to normal within one month of the last injection for the group that did not receive midazolam. For the group that was premedicated with midazolam, plasma ACTH and cortisol still showed a statistically significant depression 30 days after the last epidural injection.

Another symptom of hypercorticism is steroid-induced myopathy, which is characterized by progressive proximal muscle weakness, increased serum creatinine kinase levels, and a myopathic electromyography and muscle biopsy specimen following a single epidural dose of triamcinolone in a case study by Boonen et al (1995).

Because severe cases of Cushing's syndrome and adrenal suppression have been described after a single, relatively small steroid dose, it is unlikely that this complication can be avoided in susceptible patients (Cohen et al 2013). Cohen et al (2013) reported that the most prudent guiding principle was to use repeated steroid injections only in those who experience significant benefit and to space the injections at long-enough intervals to allow complete recovery of adrenal function. Patients undergoing surgery within a few weeks of receiving deposteroids should be evaluated for adrenal suppression or should receive stress steroid coverage during the perioperative period. The most commonly used steroids, methylprednisolone acetate, triamcinolone acetamide, and betamethasone acetate and phosphide mixture, have all been shown to be safe at epidural therapeutic doses in both clinical and experimental studies (Cohen et al 2013)

Based on these studies, Tonkovich-Quaranta and Winkler (2000) recommended that injections of corticosteroids through an epidural catheter should not be given on consecutive days. Waiting one or two weeks between injections does not appear to allow enough time for plasma cortisol and ACTH concentrations to return to normal, and it may be more appropriate to wait one month between doses of epidural corticosteroids.

A decrease in bone marrow density in postmenopausal women was reported in a retrospective study performed in patients who had received a cumulative ESI dose of greater than 120 mg methylprednisolone compared with a control group treated with NSAIDs and muscle relaxants (Kang et al 2012). In a follow-up study by the same group performed in 352 postmenopausal women who had been treated with ESI, the authors found no association between the incidence of pathological fractures and either the number or total dose of glucocorticoids. (Yi et al 2012).

3.7.8 Complications - Altered Glucose Tolerance

Glucocorticoid administration reduces the hypoglycaemic effect of insulin and interferes with blood glucose control in diabetic patients. A prospective cohort study of 30 diabetic patients demonstrated significant changes in blood glucose levels that normalized within 2 days after LESI (Even et al 2012). The mean blood glucose level before LESI was 160, which increased to 286 immediately after injection. Long-term indices of disease were followed in 9 diabetic patients after a single LESI of 80 mg depo-MPA and were determined to have no effect on glycemic control.

Patients with diabetes receiving ESI should be counselled that blood glucose may increase after intervention, but that the effects should dissipate within 2 days. Glucose levels in diabetic patients should be monitored closely during the first 2 days following any type of steroid injection. Patients need to be informed that adjustment of their insulin dose may be required (Cohen et al 2013).

3.7.9 Complications - Dural Puncture

Accidental dural puncture during attempted epidural injection is associated with a headache incidence of greater than 50% (Charsley and Abram 2001). The headache

incidence among patients undergoing attempted ESI appears to be much lower, perhaps due to the older patient population, the smaller-gauge needles used, and/or the widespread use of fluoroscopic guidance. In a retrospective cohort study that included 284 interlaminar epidural injections, only 1 postdural puncture headache was reported, for an overall incidence of 0.004%. (McGrath et al 2011). Dural puncture may happen with a varying frequency between 2 and 5% (Chazerain 1998, Chou et al 2009), leading to symptoms of post-dural puncture syndrome including headache, nausea and vertigo. There is a risk of subdural injection of the steroid, its buffers and preservatives, carrying a potential neurotoxic effect and a risk of brain thrombophlebitis (Ergan et al 1997).

Conservative management of postdural puncture headache includes bed rest, hydration, caffeine, and mild analgesics. Following known dural puncture, an epidural blood patch can quickly and effectively reduce or eliminate the ensuing spinal headache (Cohen et al 2013).

Direct neurotoxicity caused by the unintentional intrathecal injection of corticosteroid suspensions has been hypothesized to result in arachnoiditis and aseptic meningitis in some individuals. However, the link between intrathecal corticosteroid administration and these neurotoxic syndromes is not at all clear. It is not clear whether a single intrathecal injection is likely to cause serious harm. The reported cases of arachnoiditis were associated with multiple intrathecal injections, and in most cases there was pre-existing neurologic disease. Arachnoiditis and aseptic meningitis are complications of intrathecal, not epidural, steroid injections. The use of a local anesthetic test dose and/or fluoroscopy and radiographic contrast are reliable means to prevent unintentional intrathecal administration.

Patients should be instructed to promptly report neurologic changes, new or increasing pain, headache, and fever. A system of night and weekend coverage should be available, and patients should know how to contact the on-call physician. There is a real possibility that if the patient later develops arachnoiditis as a result of ongoing disease or surgery, it may be attributed to the injection. At this time, there is no evidence that epidural injection of steroids, without dural puncture, will produce either aseptic meningitis or arachnoiditis.

Local anesthetic injection into the subarachnoid, subdural/extra-arachnoid, or extradural spaces may also result in sympathetic block and hypotension. Vasovagal reactions associated with the deep somatic pain of injection is another complication associated with these injections. When predictable, it can be effectively addressed by premedication with atropine. This reaction should be readily recognized with appropriate monitoring and is usually easily managed.

3.7.10 Complications - Infectious Complications

Any technique that penetrates the skin carries with it the risk of infection. Infectious complications following epidural are rare, but can occur. It has been proposed that patients have been exposed to at least a 1-2% risk of infection (probably many go

unreported/under-reported), with more serious infections observed in 0.1% of patients, 50% of which involve Staphylococcus aureus, resulting in discitis, osteomyelitis and epidural abscess, as well as meningitis according to a literature review by Goodman et al (2008).

An outbreak of fungal infections of the central nervous system occurred in the United States in late 2012 among patients who received LESI. Kainer, et al (2012) evaluated the outbreak of fungal infections that followed epidural or paraspinal injections of preservative-free MPA from one compounding pharmacy in New England. The median age of the 66 case-patients was 69 years (range, 23-91 years), with the median time from the last epidural injection to the development of symptoms being 18 days (range, 0-56 days). The presenting symptoms included meningitis alone (73%), cauda equina syndrome or focal infection (15%), and posterior circulation stroke, with or without meningitis (12%). At the time of admission, signs and symptoms were headache (in 73% of patients), new-onset or worsening back pain (in 50%), neurologic symptoms such as vertigo (in 48%), nausea (in 39%), and stiff neck (in 29%). A total of 21 patients had laboratory confirmation of Exserohilum rostratum infection, with 1 person developing an Aspergillus fumigatus infection. The risk of infection increased with exposure to a single lot of the compounded drug, older vials, higher administered doses, multiple procedures, female sex, age older than 60 years, and using an interlaminar approach to epidural entry, which is associated with a higher risk of dural puncture. More than 650 cases of fungal infection and 39 deaths were reported, Kainer, et al (2012).

Practitioners involved in the care of these patients were utilizing a compounding pharmacy that fell outside the direct regulatory oversight of the US Food and Drug Administration. This compounding pharmacy was preparing large batches of single-use, preservative-free vials of a depot formulation of MPA and marketing and distributing them widely across the United States.

Epidural abscess is a condition that can occur spontaneously, in the absence of injection or instrumentation of the spinal canal. Hooten et al (2004) in a retrospective review examining the cases of epidural abscess following LESI, reported 14 cases, 2 of which also presented with meningitis. Eight of the cases (67%) exhibited positive blood, CSF, or epidural pus cultures documenting Staphylococcus aureus, suggesting that appropriate antibiotic prophylaxis for these procedures is warranted.

Fitzgibbon et al (2004) reported infection as a cause for litigation in 24/114 cases involving ESI. There were 12 cases of meningitis, 3 cases of osteomyelitis, and 7 reports of epidural abscess; 2 cases involved multiple infection sites. Among the 7 cases of epidural abscess, 6 required surgical decompression, and 1 resulted in permanent lower-extremity motor dysfunction. In 1 claim, there was both meningitis and epidural abscess and, in another, a combination of meningitis, abscess, and osteomyelitis.

Meticulous sterile technique with attention to skin preparation should prevent the large majority of infectious complications. Steroid injections should be avoided if there is any

active infection. The incidence of infection following ESI is too low to justify routine prophylactic antibiotic use, and there are no data to support the benefit of prophylaxis in immunocompromised patients. The recommendation is that patients undergoing these procedures should receive appropriate pre-procedure prophylactic antibiotics.

3.7.11 Complications – Recommendations

- Minor complications associated with LESI are not uncommon but rarely require significant medical attention (Level B)
- Major complications associated with LESI are rare (Level B)
- Transforaminal LESI are associated with a higher incidence of major complications (Level B)

3.8 Outcome Measures – Economic

Across the literature reviewed there have been few cost analyses performed on LESI. Where cost has been included as an outcome measure, it is usually as a secondary measure not the primary measure of most research studies. This has serious consequences in terms of sufficient powering of the studies for a definitive finding.

In the current era characterized by the need to alter the trajectory of rapidly ascending health care costs, the cost-effectiveness of any intervention has assumed an increasingly important role.

Because of the high costs of surgery, health care utilization, disability, and lost productivity, any cost-benefit analysis for LESI is to a large extent contingent on reducing alternative health care utilization (e.g., surgery and health care provider visits) and expediting or enhancing return to work. A number of ways have been suggested to identify cost-benefit from use of LESIs. One is to evaluate whether they facilitate return to work, as lost productivity accounts for over half of the economic costs of low back pain, whether they prevent expensive treatments like surgery (Bicket et al 2015), or calculating the actual costs of the intervention.

In individuals unemployed secondary to low back pain, the likelihood of returning to work declines exponentially with the length of disability. Those remaining out of work for more than 3 months are unlikely to return to work regardless of the intervention. Consequently, core domain outcome measures for chronic pain used in studies often do not even include return to work as a potentially achievable outcome. Cohen et al (2013) identified a number of studies that have looked at return to work as a secondary outcome. The majority of these clinical trials have failed to report a significant difference between return-to-work rates or missed work days when LESI and control groups are compared. Yet, some RCTs indicate that in well-selected patients, LESI may improve work status. More patients returned to work in the LESI group than in the control group in several RCTs (63% vs 25% in Breivik et al (1976), 54% vs 40% in Kraemer et al (1997) and 53% vs 33% in Rogers et al (1992), although all are limited by the small number of participants. In a large-scale (n = 228), double-blind, placebo-controlled cost-effectiveness health care assessment on the efficacy of LESI for sciatica, Price et al (2005) found no statistically significant difference in the proportion of subjects unable to return to work 1 year after treatment with LESI (24.1% in the treatment group vs 22.2% in the control group), although the mean number of days the treatment group missed work because of radiculopathy declined more than the number of days in the control group (65 vs 33).

3.8.1 Surgery Sparing

Using surgical intervention as a primary outcome measure of the cost effectiveness of ESI is challenging. However, the ability to prevent surgery is an important outcome measure for LESI, as it is objective (whereas pain is always subjective), reflects sustained and long-term treatment failure, and can dramatically alter cost-utility analyses. The evidence related to surgery sparing is unclear. Bicket et al 2015 in a systematic review on the effectiveness of LESI in reducing the need for surgery reported that there was a small surgery-sparing effect in the short term compared with control injections and a reduction

in the need for surgery in some patients who would otherwise proceed to surgery. In long term studies, the surgery-sparing effect of LESI failed to reach statistical significance. As the authors reported, the long-term effectiveness of LESI is limited because of either disease progression of the spine or of the duration of action of the steroid. Also in most controlled studies, LESI were not routinely repeated on an ''as-needed'' basis, as is often done in clinical practice. RCTs that allowed for multiple injections were more likely to report positive outcomes than studies that limited the number of injections to one (Roberts et al. 2009).

Cohen et al (2013) concluded that the evidence for a surgery sparing effect from LESI was conflicting. They reported an RCT from Riew et al (2000) that compared the operative rate in patients with herniated disc or spinal stenosis who were randomized to receive a series of either lumbar transforaminal LESI or epidural bupivacaine (anaesthetic). At follow-up periods ranging between 13 and 28 months, 29% of patients in the treatment group underwent surgery, which favourably compared with a 67% operative rate in the control group. In their subsequent paper, when following up the cohort 5 years later most patients who had avoided surgery for the initial year continued to avoid surgery (Riew et al 2006). Radcliff et al (2012) analysed data from the multicentre, randomized SPORT study comparing surgery to nonsurgical treatment for herniated disc, and found that fewer patients who received ESI within 3 months of enrolment expressed a preference for surgery (19% vs 56%), and a higher percentage crossed over from surgical to nonsurgical management (41% vs 12%), than those who did not receive ESI. In contrast, the large majority of RCTs that have included surgery sparing as secondary outcome measures have failed to find a difference in operative rates between ESI and placebo treatments (Cohen et al 2013). As identified by Cohen et al (2013) nearly all of these studies are underpowered to detect a difference and incorporate some degree of bias through patient selection.

With regards to spinal stenosis, the literature reports modest long-term results with surgery for spinal stenosis; quality-adjusted life year (QALY) cost is $77,600 with 62%, or $48,112 of the total cost, as direct medical costs. In contrast, caudal epidural injections have shown to have a cost utility of $2,155 per QALY with direct medical costs (Manchikanti et al 2015). While surgery may be essential in severe symptomatic stenosis, for all other conditions conservative management with epidural injections in conjunction with physical therapy modalities and exercise programs is a cost-effective modality to manage mild to moderate symptomatic central spinal stenosis as well as those patients who have contraindications or are unwilling to undergo surgery. (Manchikanti et al 2015).

3.8.2 Health care utilisation

Studies evaluating the ability of ESI to reduce health care utilization as a secondary outcome measure have yielded conflicting results (Cohen et al 2013). Karppinen et al (2001) found no overall difference in healthcare costs between treatment and control groups, although the LESI group had lower medication and therapy costs at 4-week follow-up. Price et al (2005) in a large review concluded that LESIs do not provide good economic

value in terms of the cost per quality-adjusted life year (QALY) for the treatment from the perspective of both the provider and purchaser. Based on the NICE threshold of £30,000 per QALY they concluded that LESIs failed the NICE QALY threshold, However, as the authors warned, the private benefits of short-term pain relief and improved function from LESI may be highly valued by the individual, affecting the ability to transpose these findings to private clinical practice.

Quraishi et al (2012) reported on an RCT from Karpinnen et al (2001), looking at cost effectiveness related to transforaminal LESI for patients with radiculopathy, that found that at the 4-week follow-up period the patients who had received steroid/local anaesthetic injection had utilized fewer therapy visits and fewer drugs resulting in significantly lower costs. However, at all other times there was no significant cost difference in the groups.

Bresnahan et al (2013) undertook a study to investigate the reimbursement amounts related to LESI from their institution and from the literature. They identified two observational studies that looked at reimbursement from LESI in the USA. Friedly et al (2007) conducted an observational study that described use trends and cost outcomes of LESI in a Medicare population. They reported rates of lumbar ESI increased 271%, from 1994 to 2001, with a mean number of lumbar injections of 2.5 per patient and a mean number of days between injections of 110. Over this time reimbursed costs per injection nearly doubled, from $115 to $227, with the total cost of physician professional fees paid by Medicare increasing from $24 million to $175 million. Manchikanti et al (2010) used observational data to compare use and charges for ESI in the Medicare population in 1997, 2002, and 2006. All ESI procedures increased 119%, from 1997 to 2006, with the rate of LESI 49% higher in 2006 versus 2002. From 1997 to 2006 the total estimated charges to Medicare during this period grew by 87%, going from $397 million to $744 million. Bresnahan et al (2013) undertook a study of their own institution and identified 279 individual Medicare beneficiaries who received a total of 404 ESIs over 1 year. A total of 186 patients received a single injection, whereas 63 received 2 injections, 28 received 3 injections, and 2 had 4 injections, with a mean number of days between injections ranging from 43 to 105.2 days. Other frequent service item categories used in relation to an ESI procedure included fluoroscopy (98.76%), iodine low osmolar contrast material (96.04%), anesthetics (19.55%), and sedatives (16.83%). The mean total payment for technical fees was $505 per episode and $132 for mean total professional fee payments. Stratifying by visit, patients who received 1, 2, 3, or 4 LESI episodes had cumulative, mean total reimbursement amounts (technical and professional fees) of $652, $1,260, $1,855, and $2,403, respectively. They estimated that typical pre-LESI events (i.e. specialist visits and lumbar MRI without contrast) add approximately $645 in payments, in addition to payments for health care use subsequent to the ESI event.

Spijker-Huiges et al (2014b) reported on the same study as Spijker-Huiges et al (2014a), this time assessing the costs and cost-effectiveness of adding LESI to usual care but only on the 63 patients who completed the study. Sixty-three patients were included in the analysis. Mean total costs were €4,414 or $5,985 in the intervention group and €5,121 or

$6,943 in the control group. This difference was mostly due to loss of productivity. The point estimate for the incremental cost-effectiveness ratio was − €730 or − $990 (1-point diminishment on the numerical rating scale back pain score in 1 patient in the course of 1 year would save €730 or $990). Bootstrapping showed a 95% confidence interval of − €4,476 to €951 or − $6,068 to $1,289. The cost-effectiveness acceptability curve showed that without additional investment the probability that epidural steroids are cost effective was more than 80%.

3.8.3 Specific Approaches

MacVicar et al (2013) in their systematic review identified that patients who had transforaminal LESI tended to have fewer sick days, fewer resorted to surgery, and twice as many had at least 75% reduction in pain (44% +/- 20% compared with 21% +/- 16%), but statistical significance did not emerge, possibly because of the small sample sizes involved. However, MacVicar et al (2013) concluded that for those patients with contained herniations, transforaminal LESI was significantly cost-effective at 12 months, achieving a cost-reduction of $12,666 per responder.

This finding was supported by Manchikanti et al 2012, which concluded that, considering the low risk and less expensive nature of the procedure compared to surgical interventions, transforaminal epidural injections with or without steroids appeared to be cost effective. (Manchikanti et al 2012)

Manchikanti et al (1999) reviewed the cost-effectiveness of caudal epidural injections with lidocaine and steroids, and concluded that the results of caudal LESI are equivalent to transforaminal LESI. (Parr et al 2012).

3.8.4 Recommendations

- The evidence suggests that LESI may present a cost-effective intervention in the short term through reducing other health expenditure, reducing the need for expensive surgery and reducing sick days. Any significant cost effectiveness associated with LESI is dependent on repeat injections on an as needed basis (Level C Recommendation).

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5. Appendices

Appendix 1 - Copies of the SIGN Checklists

SIGN Critical Appraisal Tool for Systematic Reviews and Meta-analyses

SIGN

Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C,. et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, **7**:10 doi:10.1186/1471-2288-7-10. Available from http://www.biomedcentral.com/1471-2288/7/10 [cited 10 Sep 2012]*

Study identification (*Include author, title, year of publication, journal title, pages*)

Guideline topic:	Key Question No:

Before completing this checklist, consider:

Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by:

Section 1: Internal validity

	In a well conducted systematic review:	***Does this study do it?***
1.1	The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	Yes □ No □ **If no reject**
1.2	A comprehensive literature search is carried out.	Yes □ No □ Not applicable □ **If no reject**
1.3	At least two people should have selected studies.	Yes □ No □ Can't say □
1.4	At least two people should have extracted data.	Yes □ No □ Can't say □
1.5	The status of publication was not used as an inclusion criterion.	Yes □ No □
1.6	The excluded studies are listed.	Yes □ No □
1.7	The relevant characteristics of the included studies are provided.	Yes □ No □
1.8	The scientific quality of the included studies was assessed and reported.	Yes □ No □
1.9	Was the scientific quality of the included studies used appropriately?	Yes □ No □
1.10	Appropriate methods are used to combine the individual study findings.	Yes □ No □ Can't say □ Not applicable □

1.11	The likelihood of publication bias was assessed appropriately.	Yes □ No □ Not applicable □
1.12	Conflicts of interest are declared.	Yes □ No □
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review?	High quality (++) □ Acceptable (+) □ Low quality (-)□ Unacceptable – reject 0 □
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes □ No □
2.3	**Notes:**	

SIGN Critical Appraisal Tool for Controlled trials

Methodology Checklist 2: Controlled Trials

Study identification (*Include author, title, year of publication, journal title, pages*)		
Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper a **randomised controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: 1. Paper not relevant to key question ☐ 2. Other reason ☐ (please specify):

SECTION 1: INTERNAL VALIDITY

In a well conducted RCT study…		***Does this study do it?***
1.1	The study addresses an appropriate and clearly focused question.	Yes ☐ No ☐ Can't say ☐
1.2	The assignment of subjects to treatment groups is randomised.	Yes ☐ No ☐ Can't say ☐
1.3	An adequate concealment method is used.	Yes ☐ No ☐ Can't say ☐
1.4	The design keeps subjects and investigators 'blind' about treatment allocation.	Yes ☐ No ☐ Can't say ☐
1.5	The treatment and control groups are similar at the start of the trial.	Yes ☐ No ☐ Can't say ☐
1.6	The only difference between groups is the treatment under investigation.	Yes ☐ No ☐ Can't say ☐
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	Yes ☐ No ☐ Can't say ☐
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	Yes ☐ No ☐ Can't say ☐ Does not apply ☐
1.10	Where the study is carried out at more than one site, results are comparable for all sites.	Yes ☐ No ☐ Can't say ☐ Does not apply ☐

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	How well was the study done to minimise bias?	High quality (++)☐

	Code as follows:	Acceptable (+)☐ Low quality (-)☐ Unacceptable – reject 0 ☐
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	
2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.	

SIGN Critical Appraisal Tool for Cohort studies

SIGN

Methodology Checklist 3: Cohort studies

Study identification (*Include author, title, year of publication, journal title, pages*)		
Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper really a cohort study? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist..

Reason for rejection: 1. Paper not relevant to key question ☐ 2. Other reason ☐ (please specify):

Please note that a retrospective study (ie a database or chart study) cannot be rated higher than +.

Section 1: Internal validity

	In a well conducted cohort study:	Does this study do it?	
1.1	The study addresses an appropriate and clearly focused question.[i]	Yes □ Can't say □	No □
	SELECTION OF SUBJECTS		
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.[ii]	Yes □ Can't say □	No □ Does not apply □
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.[iii]	Yes □	No □ Does not apply □
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.[iv]	Yes □ Can't say □	No □ Does not apply □
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed.[v]		
1.6	Comparison is made between full participants and those lost to follow up, by exposure status.[vi]	Yes □ Can't say □	No □ Does not apply □

ASSESSMENT			
1.7	The outcomes are clearly defined.[vii]	Yes □ Can't say □	No □
1.8	The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable.[viii]	Yes □ Can't say □	No □ Does not apply □
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.[ix]	Yes □ Can't say □	No □ □
1.10	The method of assessment of exposure is reliable.[x]	Yes □ Can't say □	No □
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.[xi]	Yes □ Can't say □	No □ Does not apply□
1.12	Exposure level or prognostic factor is assessed more than once.[xii]	Yes □ Can't say □	No □ Does not apply □
CONFOUNDING			
1.13	The main potential confounders are identified and taken into account in the design and analysis.[xiii]	Yes □ Can't say □	No □
STATISTICAL ANALYSIS			
1.14	Have confidence intervals been provided?[xiv]	Yes □	No □
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How well was the study done to minimise the risk of bias or confounding?[xv]	High quality (++) □ Acceptable (+) □ Unacceptable – reject 0	
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes ☐ Can't say ☐	No ☐
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes □	No □
2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.		

Appendix 2: Summary of Studies and quality scores for articles included in this review

Author and year	SIGN Score	Approach	Studies (Patient No)	Outcome	Conclusions	Evidence				Grade
						1	2	3	4	
Novak and Nemeth 2008 *Lumbosacral radiculopathy,*	AQ(+)	All approaches	11 RCT, 1CCT, 2 Prospective cohort (n=NS)	Pain, function	• There is no evidence to suggest guidelines for frequency and timing of ESIs or to help to define what constitutes the appropriate partial response to trigger a repeat injection.	0	1	1	0	1
Staal et al 2008 *(SR/MA)* *Subacute and chronic low-back pain (**Radiculopathy excluded)*	HQ (++)	All approaches	7 RCTs (n=101)	Pain, function	• LESI not effective compared to placebo injections for general improvement in the short term	0	1	0	1	1
					• LESI not effective compared to placebo injections for pain relief in the short term	0	1	0	1	1
					• LESI no more effective compared to placebo injections for work disability in the short term	0	1	0	1	1
					• LESI no more effective compared to NSAIDs for pain relief in the short term in post-laminectomy patients	0	1	0	1	1
					• LESI no more effective compared to benzodiazepine for pain relief and general improvement both in the short and intermediate term	0	1	0	1	1
					• LESI no more effective compared to morphine eventually combined with corticosteroids for pain relief in the short and intermediate term in post-laminectomy patients	0	1	0	1	1
Roberts et al 2009 (SR) *Lumbar Radiculopathy*	AQ (+)	*Fluoroscopically guided transforaminal epidural*	9 RCTs (n=617)	Pain, function	• Transforaminal LESI more effective than placebo for treating radicular symptoms from HNP	0	1	0	1	1
					• Transforaminal LESI effective as a surgery sparing intervention for treating radicular symptoms	0	1	0	1	1
					• Transforaminal LESI more effective than interlaminar LESIs (ILESIs) and caudal LESIs for radicular pain	0	1	0	1	1
					• Transforaminal LESI as effective as a single transforaminal injection of bupivacaine or saline.	0	1	0	1	1

Author and year	Quality	Approach	Studies (patient No)	Outcomes	Conclusions	Grade				Evidence
						1	2	3	4	
Rabinovotch et al 2009 (SR) *Radicular leg pain and/or low back pain*	AQ (+)	*All approaches*	15 RCTs, 1 CCT (n=886)	Pain (short term to long term)	• LESI effective in the immediate-term in reducing pain with positive correlation between LESI volume and pain relief: r=0.8027 (p=0.0017).	0	1	1	0	1
					• In the short term there was a non-statistically significant positive correlation between LESI volume and pain relief: r=0.5019 (p=.168).	0	1	1	0	1
					• In the intermediate term there was a statistically significant positive correlation between volume and pain relief: r=0.9470 (p=.014).	0	1	1	0	1
					• There was insufficient data to calculate the correlation coefficient in the long-term category.	0	1	0	1	1
					• Irrespective of the medications injected there was a statistically significant difference when comparing the mean effect size where the volume injected was the same between the two groups (mean, standard deviation [SD]: 0.07, -0.26) with those where the volumes were different between comparison groups (mean, SD: 0.81, -0.6),	1	1	1	0	1+
Dagenais et al 2010 (SR) Acute/chronic LBP +/- radicular referral	AQ (+)	*Not specified*	10 CG (n=NS)	Neurological improvement	• Transforaminal LESI recommended for chronic low back pain	0	1	1	0	1
					• LESI recommended as a secondary intervention for low back pain with substantial neurologic involvement	0	1	1	0	1
					• Transforaminal LESI recommended as a secondary intervention for low back pain with substantial neurologic involvement	0	1	1	0	1

Author and year	SIGN Score	Approach	Studies (patient No)	Outcome	Conclusions	Grade				Evidence
Henschke et al 2010 (SR) *LBP*	HQ (++)	*All approaches*	2 RCTs (n=88)	Pain	• LESI no more effective than benzodiazepine injection for pain relief over short to intermediate term.	0	1	0	1	1
					• LESI no more effective than targeted epidural placement for pain relief over the short to intermediate term.	0	1	0	1	1
Jordan et al 2010 (SR) Herniated disc	AQ (+)	*All approaches*	5 SRs and 5 RCTs (n=NS)	Pain, disability	• LESI effective compared with no LESI at improving limb pain at 2 weeks.	0	1	0	0	1 -
					• LESI no more effective compared with no LESI in reducing limb pain after more than 2 weeks in people with disc herniation	0	1	1	1	1+
					• LESI no more effective compared with LESI in the longer term at improving disability, or functional outcomes such as straight leg raising and lumbar flexion, in people with disc herniation.	0	1	1	1	1+
					• LESI effective compared with no LESI at increasing subjective global improvement and patient satisfaction in the short term (2 weeks),	0	1	0	1	1
					• LESI not effective compared with no LESI at increasing subjective global improvement and patient satisfaction in the longer term (after 2 weeks) in people with disc herniation.	0	1	0	1	1
					• LESI plus conservative treatment no more effective than conservative treatment at 6 weeks and 6 months for pain scores in people with disc herniation.	0	1	0	1	1
					• LESI plus conservative treatment no more effective than conservative treatment at 6 weeks and 6 months for mobility scores and reducing need for surgery in people with disc herniation	0	1	0	1	1
					• LESI less effective compared with standard discectomy at 1 to 3 months for leg pain or disability in people with lumbar disc herniation	0	1	0	1	1

Author and year	SIGN Score	Approach	Studies (patient No)	Outcome	Conclusions	Grade				Evidence
						1	2	3	4	
Lewis et al 2011 (SR) Sciatica	HQ (++)	*All approaches*	12 RCTs (n= NS)	Pain and function	• LESI effective in reducing pain and improving functional status compared to inactive control at short-term follow-up (< 6 weeks)	1	1	1	0	1+
					• LESI not effective in global effect compared to inactive control at short-term follow-up	1	1	1	1	1++
					• LESI not effective compared to inactive control for global effect, pain intensity or CSOMs at medium-term follow-up	1	1	1	0	1+
					• LESI not effective compared to inactive control for global effect, pain intensity or CSOMs at long-term follow-up.	1	1	0	1	1+
					• LESI effective compared to usual care for overall recovery and functional status at short-term follow-up, but not for pain intensity.	1	1	1	0	1+
					• LESI not effective compared to usual care at medium-term follow-up for global effect, pain intensity or CSOMs. However, usual care was associated with significantly fewer adverse effects than LESI	1	1	1	1	1++
					• LESI effective compared to non-opioids for reducing pain and improving functional status at short-term follow-up	1	1	0	1	1+
					• LESI not effective compared to non-opioids for global effect or CSOMs at medium-term follow-up or adverse effects.	1	1	0	1	1+
					• LESI not effective compared to chemonucleolysis for the global effect at short-term or medium-term follow-up.	1	1	0	1	1+
					• LESI worse than chemonucleolysis in the number of adverse effects	1	1	0	1	1+
					• LESI effective compared with passive PT for global effect (at medium- and long-term follow-up) and activity restriction for global effect (medium-term follow-up)	1	1	0	1	1+
					• LESI no more effective than acupuncture for pain intensity	1	1	0	1	1+
					• LESI not as effective as disc surgery at reducing pain intensity at medium-term follow-up, but not at long-term follow-up	1	1	0	1	1+

Author and year	SIGN Score	Approach	Studies (patient No)	Outcome	Conclusions	Grade				Evidence
Benoist et al 2012 (SR) *Low-back pain with radiculopathy*	LQ (-)	*All approaches*	21 SRs (n=NS)	Pain, function complicati on	• LESI have a moderate short-term pain relief effect in patients with radiculopathy related to discal herniation	0	0	1	0	1-
					• Interlaminar LESIs effective for radiculopathy for short term pain relief, but limited for long-term pain relief.	0	0	1	0	1-
					• Interlaminar LESIs not effective for radiculopathy for long-term pain relief.	0	0	1	1	1
					• Limited evidence for effectiveness of interlaminar LESIs for spinal stenosis	0	0	0	1	2-
					• Effectiveness of Caudal approach for discal pathology was strong for short-term and moderate for long-term pain relief.	0	0	0	1	1-
					• Effectiveness of Transforaminal approach was strong for short-term (<6 weeks) and moderate for long term results (>6 weeks).	0	0	0	1	1-
					• The results were equivalent whether using steroids with local anaesthetic or local anaesthetic alone	0	0	0	1	1-
					• Concerning safety, ESIs are generally well tolerated and most complications are related to technical problems during the procedure.					
Pinto et al 2012 *Sciatica*	HQ (++)	*All approaches*	22 RCTs (n=2184)	Pain, disability and functional limitations	• LESI demonstrated effectiveness compared with placebo for leg pain in the short term (mean difference, -6.2 [95% CI, -9.4 to -3.0])	1	1	1	0	1+
					• LESI demonstrated effectiveness compared with placebo for disability in the short term (mean difference, -3.1 [CI,-5.0 to -1.2]).	1	1	1	0	1+
					• LESI did not demonstrate effectiveness compared with placebo for pain or disability over the long term	1	1	1	0	1+

Author and year	SIGN Score	Approach	Studies (patient No)	Outcome	Conclusions	Grade				
						1	2	3	4	
Quraishi 2012 (SR/MA) *Lumbar radiculopathy*	LQ (-)	*Transforaminal*	5 RCTs (n=368)	Pain, disability	Transforaminal LESI effective for improvement in pain (standardised mean difference in VAS 0.2 in favour of steroid injection),	1	0	0	0	1-
					Transforaminal LESI not effective for improvement In disability (standardised mean difference in ODI 0).	1	0	0	1	1
					Transforaminal LESI not more effective compared to transforaminal anaesthetic or saline for improvement In pain or disability at 3 months and 12 months	0	0	0	1	1-
Parr et al 2012 (SR) *Chronic low back pain with or without lower extremity pain*	HQ (++)	*Caudal Epidural Injections*	11 RCTs and 5 NonRCTs (n=1,252)	Pain, functional/ psychological status, return to work, complication	Caudal LESI, with local anaesthetic and steroids, effective for short- and long-term relief of chronic pain secondary to disc herniation or radiculitis	0	1	0	1	1
					Caudal LESI, with local anaesthetic and steroids, effective for discogenic or axial pain without disc herniation, radiculitis, facet joint pain, or SIJ pain	0	1	0	1	1
					Caudal LEI, with local anaesthetic with or without steroids, effective for spinal stenosis pain	0	1	0	1	1
					Caudal LEI, with local anaesthetic with or without steroids, effective for post-surgery syndrome	0	1	0	1	1
Manchikanti et al 2012 (SR) *Chronic low back and lower extremity pain of at least 3 months duration*	HQ (++)	*Transforaminal Injections*	13RCTs and 10 Non-RCTs (n=2363)	Pain, functional/ psychological status, return to work, complications	Transforaminal LEI with local anesthetic and steroids, effective for pain relief with lumbar disc herniation in long term	0	1	1	0	1
					Transforaminal LEI with local anesthetic and steroids, effective for pain relief with lumbar disc herniation in short term	0	1	1	1	1+
					Transforaminal LEI with local anesthetic only effective for pain relief with lumbar disc herniation in short and long term	0	1	1	0	1
					Transforaminal LEI with local anesthetic and steroids, effective for preventing surgery with lumbar disc herniation	0	1	1	0	1
					Transforaminal LEI with local anesthetic and steroids, effective for pain relief with spinal stenosis in short term	0	1	1	0	1
					Transforaminal LEI with local anesthetic and steroids, effective for pain relief with spinal stenosis in long term	0	1	1	0	1
					The evidence for axial low back pain and post lumbar surgery syndrome is poor, inadequate, limited, or unavailable.					

Author and year	SIGN Score	Approach	Studies (patient No)	Outcome	Conclusions	Grade				
						1	2	3	4	
Benyamin et al 2012 (SR) *Chronic Low Back and Lower Extremity Pain*	HQ (++)	*Interlaminar*	15RCTs and 11 NonRCTs (n=3001)	Pain, functional/ psychological status, return to work, complications	• Interlaminar LESI with local anesthetic and steroids under fluoroscopy effective for radiculitis secondary to disc herniation in short and long term	0	1	1	0	1
					• Interlaminar LESI with local anesthetic and steroids not under fluoroscopy not effective for radiculitis secondary to disc herniation in long term	0	1	0	0	1-
					• Interlaminar LESI with local anesthetics and steroids under fluoroscopy effective for discogenic pain in short and long term	0	1	0	1	1
					• Interlaminar LESI with local anesthetic and steroids under fluoroscopy effective for spinal stenosis pain in short and long term	0	1	0	1	1
Choi et al 2013 (SR/MA) *LBP plus radiculopathy*	HQ (++)	*All approaches*	29 RCTs (n=843)	Pain, functional Improvement in 6-12 months, Need for surgery	• LESI provided significant treatment effect on pain at 6 months of follow-up (weighted mean difference [WMD], −0.41; 95% CI, −0.66 to −0.16), but was no longer statistically significant after adjusting for the baseline pain score (WMD, −0.19; 95% CI, −0.61 to 0.24)	1	1	1	1	1++
					• LESI provided no significant treatment effect on back-specific disability more than a placebo or other procedure	1	1	1	1	1++
					• LESI did not significantly decrease the number of patients who underwent subsequent surgery compared with a placebo or other treatments (relative risk, 1.02; 95% CI, 0.83 to 1.24).	1	1	1	1	1++
Bui and Bogduk 2013 (SR) Radicular pain	LQ (-)	*CT guided Transforaminal*	19 Non-RCT (observational studies) (n=NS)	Pain, complications	• CT Guided Transforaminal LESI is no more effective than fluoroscopy-guided injections and is not demonstrably safer.	0	0	0	1	2-

Author and year	Quality Score	Approach	Studies (patient No)	Outcomes	Conclusions	Grade				Evidence
						1	2	3	4	
Bicket et al 2013 (SR/MA) *Back pain with or without radiculopathy;*	HQ (++)	*All approaches*	43 RCT (n=3641)	Pain after 12 weeks	• Lumbar epidural nonsteroid injections (LEN-SI) were more effective than nonepidural injections to achieve positive outcomes (risk ratio, 2.17; 95% CI, 1.87–2.53) and provide greater pain score reduction (mean difference, −0.15; 95% CI, −0.55 to 0.25).	1	1	1	0	1+
					• LESI no better than LEN-SI in the short term *For pain, the benefit favoring epidural nonsteroid over nonepidural injections is actually greater (risk difference [95% CI], 0.27 [0.15–0.39]) than the difference between LESI and epidural nonsteroid, suggesting that, at least in the short term, most of the benefit of epidural injections may derive from the solution itself, rather than the steroid.*	1	1	1	1	1++
Epstein 2013 (SR) Not specified	R(0)	*Transforaminal*	43 Observational studies (n=NS)	Adverse Events	Although the benefits for epidural steroid injections may include transient pain relief for those with/ without surgical disease, the multitude of risks attributed to these injections outweighs the benefits.	0	0	0	1	2-

Author and year	SIGN Score	Approach	Studies (patient No)	Outcomes	Conclusions	Grade				Evidence
						1	2	3	4	
Koes et al 1995 (SR) *Low-back pain and sciatica*	AQ(+)	*All approaches*	12 RCTs (n=262)	Pain, function	• LESI effectiveness inconsistent. If any effectiveness mainly in short term	0	1	1	1	1+
Tonkovich-Quaranta and Winkler 2000 (SR) *Sciatica, or LBP of mixed etiologies*	LQ (-)	Not reported	9 RCTs (n=448)	Pain	• LESI effective in treating pain (i.e., VAS scores), and objective measures (i.e., degree of SLR) associated with radiculopathy for up to 12 weeks.	0	0	1	0	1-
					• LESI effective in treating pain (i.e., VAS scores), associated with low back pain of mixed etiology for up to 12 weeks	0	0	1	0	1-
Parr et al 2009 (SR) *Chronic Low Back and Lower Extremity Pain*	HQ (++)	*Interlaminar*	5 RCTs and 2 Observational studies	Pain relief (short-term relief = up to 6 months and long-term > 6 months), functional status, psychological status, return to work, and reduction in opioid intake	• Interlaminar LESI performed blind (without fluoroscopy) effective for short-term relief of pain (<3/12) of disc herniation or radiculitis	0	1	1	0	1
					• Interlaminar LESI performed blind (without fluoroscopy) not effective for long-term relief of pain of disc herniation or radiculitis	0	1	1	1	1+
					• Interlaminar LESI performed blind (without fluoroscopy) effective for short term relief of pain of discogenic origin without radiculitis • or disc herniation	0	1	0	1	1
					• Interlaminar LESI performed blind (without fluoroscopy) not effective for long term relief of pain of discogenic origin without radiculitis or disc herniation	0	1	0	1	1
Benny and Azari 2011 (SR) *Radicular back pain*	AQ(+)	*Transforaminal*	9 RCTs, 4 retrospective and 8 prospective cohort studies (n=1559	Pain and avoiding surgery	Transforaminal LESI effective in both short term and long term management of radiculopathy due to spinal stenosis or lumbar herniation.	0	1	1	1	1+

Author and year		Approach	Studies (patient No)	Outcome	Conclusions	Grade				Evidence
						1	2	3	4	
Fritzler and Sarafini 2011 (SR) Back pain	LQ (-)	*NR*	4 RCTs (n=594)	Pain, disability, physical function, rates of return to work, need for future surgery	• LESI effective compared to placebo in reducing disability scores up to 3 weeks and VAS pain scores up to 6 weeks.	0	0	0	1	1-
					• LESI not effective compared to placebo in terms of improved physical function, rates of return to work, or the need for future surgery.	0	0	0	1	1-
					• Transforaminal ESIs appear superior to placebo in improving patient satisfaction and pain levels for a minimum of 2 weeks and potentially up to 16 months on average.	0	0	0	1	1-
Jacobs et al 2011 (SR) *Sciatica due to herniated disc*	AQ(+)	*Not reported*	1 RCT (n=50)	Pain	• Discectomy was effective compared to LESI for the short term in patients with radiculopathy due to herniated lumbar disc	0	1	0	1	1
Ammendolia et al 2012 (SR) *Lumbar Spinal Stenosis With Neurogenic Claudication*	HQ (++)	*Not reported*	4 RCT (n=149)	Walking ability, pain, function, quality of life, and global improvement.	• LESI effective compared with home exercise or inpatient physical therapy in improving pain, function, and quality of life up to 2 weeks in patients with spinal stenosis	0	1	0	1	1
MacVicar et al 2013 (SR) *Radicular pain*	LQ(-)	*Transforaminal injections*	22 outcome studies, 11 pragmatic trials, and 6 explanatory trials.	Pain	• Transforaminal LESI effective in reducing pain, restoring function, reducing the need for other health care, and avoiding surgery in patients with lumbar radicular pain caused by contained disc herniations,	0	0	1	0	1
May and Comer 2013 (SR) *Spinal Stenosis*	AQ(+)	*All approaches*	9 RCTs	Pain and Disability	• LESI not effective compared to physical therapy, saline, saline and anaesthetic or anaesthetic injection at long-term follow-up in patients with spinal stenosis;	0	1	1	1	1+
					• Percutaneous adhesiolysis and decompression surgery were more effective than LESI in patients with spinal stenosis;	0	1	0	1	1
					• Bilateral transforaminal injection was more effective than an interlaminar steroid injection in patients with spinal stenosis;	0	1	0	1	1

Author and year		Approach	Studies (patient No)	Outcomes	Conclusions	Grade				Evidence
						1	2	3	4	
Armon et al 2007 (SR) *Radicular lumbosacral pain*	AQ(+)	All approaches	6 RCTs (n=425)	Pain	• LESI effective compared to control treatments in improving pain in patients with radicular lumbosacral pain when assessed between 2 and 6 weeks	0	1	1	0	1
					• LESI not effective compared to control treatments in average impairment of function, need for surgery, or provide long-term pain relief beyond 3 months.	0	1	1	0	1
Bresnahan et al 2013 (SR) *Lumbar Spinal Stenosis*	AQ(+)	*All approaches*	6 RCTs (n=290) and 2 observational studies (n=279)	Effectiveness evidence (clinical and economic)	• LESI (+/1 anesthetic) effective compared with control injections in improving walking distance in patients with spinal stenosis in short term	0	1	1	0	1
					• LESI (+/1 anesthetic) not effective compared with control injections in improving walking distance in patients with spinal stenosis in long term (>4 months)	0	1	0	1	1
					• LESI no more effective compared to anesthetic in self-reported improvement in patients with spinal stenosis.	0	1	0	1	1
					• Transforaminal approaches had better improvement in pain scores (4 months) compared with interlaminar injections.	0	1	0	1	1
Dworkin et al 2013 (SR) *Neuropathic pain*	LQ (-)	All approaches	7 SRs	Pain, need for surgery	• LESI effective for pain relief in patients with radiculopathy in the short term	0	0	1	1	1
					• LESI not effective for pain relief or for prevention of future spine surgery in patients with radiculopathy in the long term (>12 weeks)	0	0	0	1	1-
Cohen et al 2013 (SR) *Radiculopathy, radicular pain, sciatica, low back pain,*	AQ(+)	*All approaches*	11 SRs, 8 RCTs (n=691) and 5 Retrospective cohort (n=629)	Effectiveness	• Transforaminal injections are more likely to yield positive results than interlaminar or caudal injections,	0	1	1	1	1+
					• LESI more effective for reducing pain in patients with lumbar herniated disk, compared with spinal stenosis or axial spinal pain.	0	1	1	1	1+

Author and year		Approach	Studies (patient No)	Outcomes	Conclusions	Grade				Evidence
						1	2	3	4	
Chien et al 2014 (SR) *Lumbosacral radicular pain secondary to IV disc herniation/degeneration*	HQ (++)	Transforaminal vs Interlaminar)	5 RCTs and 3 Retrospective cohort studies (n= 506)	Pain relief, functional status	• Transforaminal fluoroscopy guided LESI more effective compared to fluoroscopy guided Interlaminar LESI in reducing pain in radiculopathy secondary to IV disc herniation/degeneration in the short term	0	1	0	0	1-
					• Transforaminal fluoroscopy guided LESI no more effective compared to Interlaminar fluoroscopy guided LESI in reducing pain in radiculopathy secondary to IV disc herniation/degeneration in the long term	0	1	0	0	1-
					• Transforaminal fluoroscopy guided LESI no more effective compared to Interlaminar fluoroscopy guided LESI in functional improvement in patients with radiculopathy secondary to IV disc herniation/degeneration in the long or short term	0	1	0	1	1
Jamjoom and Jamjoom 2014 (SR) Intraoperative epidural steroids in lumbar discectomy)	AQ(+)	Intraoperative	16 RCTs (n= 1310)	Postoperative Pain, postoperative consumption of analgesia, duration of hospital stay and complication rates	• Intraoperative LESI are effective in reducing pain and reducing consumption of analgesia in the early stage	0	1	1	1	1+
					• Intraoperative LESI are effective in reducing pain and reducing consumption of analgesia in the intermediate stage	0	1	1	0	1
					• Intraoperative LESI are not effective in reducing pain in the late stage	0	1	1	1	1+
					• Intraoperative LESI are not effective in reducing duration of hospital stay.	0	1	1	0	1
Wang et al 2014 (SR/MA) *(Tumor Necrosis Factor- Inhibitors vs epidural steroids)* Sciatica	AQ(+)	All approaches	5 RCTs	Pain, satisfaction, return to work	• LESI no more effective compared to TNF-a inhibitors in terms of lower back and leg pain patient overall satisfaction (global perceived effect (satisfaction)) or return to work at the short term, medium-term and long-term follow-ups.	0	1	1	1	1+

Author and year		Approach	Studies (patient No)	Outcomes	Conclusions	Grade				Evidence
						1	2	3	4	
Dighe and Friedman 2013 (SR) (Lumbar intervertebral disc, disco-genic pain, spinal stenosis, post-lumbar-surgery syndrome, chronic back pain, sciatica)	AQ(+)	Caudal Epidural Injections	11 RCTs 6RCTs – disc herniation 2RCTs – discogenic pain 2RCTs – Spinal Stenosis 1RCt – Post lumbar surgery syndrome	Pain	Caudal LEI with or without steroid effective for pain relief in patients for disc herniation or radiculopathy in short term	0	1	1	0	1
					Caudal LEI with or without steroid not effective for pain relief in patients for disc herniation or radiculopathy in long term	0	1	1	1	1+
					Caudal LEI with or without steroid effective for pain relief in patients for with discogenic pain without herniation	0	1	0	1	1
					Caudal LEI with or without steroid possibly effective for pain relief in patients with spinal stenosis	0	1	0	0	1-
					Caudal LEI with or without steroid effective for pain relief in patients with post lumbar surgery syndrome in short and long term	0	1	0	1	1
					Lumbar decompression surgery more effective compared to Caudal LESI	0	1	0	1	1
					Caudal LESI plus anesthetic more effective than anesthetic alone	0	1	1	1	1+
Bicket et al 2015 (SR/MA) *All LBP patients who need surgery*	HQ (++)	All approaches	26 RCTs in SR, 21 RCTs in M/A (n=3271)	Need for surgery	LESI not effective in reducing need for surgery in short term	1	1	1	1	1++
					LESI not effective in reducing need for surgery in long term	1	1	1	1	1++
Manchikanti et al 2015 (SR) *Lumbar Central Spinal Stenosis*	AQ(+)	All approaches	7 RCTs(n=460)	Pain, functional status	Transforaminal LEI effective for reducing pain in patients with spinal stenosis in short-term	0	1	0	1	1
					Caudal and lumbar interlaminar LEI effective for reducing pain in patients with spinal stenosis in long term	0	1	0	1	1
					LEI with anaesthetic no more effective than LEI with anaesthetic and steroid in long or short term	0	1	1	1	1
Vorobeychik et al 2016 *Lumbar radicular pain, spinal stenosis*	AQ(+)	Non–Image-Guided Interlaminar	39 studies 9 RCTs, 11 Prag RCTs, 25 observational,	Pain, functional status	In patients with lumbar radicular pain secondary to disc herniation or neurogenic claudication due to spinal stenosis, non–image-guided lumbar interlaminar epidural steroid injections appear to have clinical effectiveness limited to short-term pain relief.	0	1	1	1	1+

Appendix 3: Critical Appraisals of Systematic Reviews

Reference (author, year)		Quest												
Study	Year	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9	1.10	1.11	1.12	2.1	2.2
Ammendolia et al	2012	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	N	HQ (++)	Y
Andreisek et al	2013	Y	Y	Y	Y	N	N	N	N	N	Y	N	Y	A(+)	Y
Armon et al	2009	Y	N	N	N	N	Y	Y	Y	Y	Y	N	Y	A(+)	Y
Benny & Azori	2011	Y	N	N	N	N	Y	Y	Y	Y	Y	N	N	A(+)	Y
Benoist et al	2012	Y	N	N	N	N	N	Y	Y	N	Y	N	N	LQ(-)	Y
Benyamin et al	2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	HQ (++)	Y
Bicket et al	2013	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	N	HQ (++)	Y
Bicket et al	2015	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	N	HQ (++)	Y
Bresnahan et al	2013	Y	Y	Y	Y	-	N	Y	Y	Y	CS	N	N	A(+)	Y
Bui & Bogduk	2013	N	N	Y	Y	N	N	N	N	N	N	N	N	LQ(-)	Y
Chien et al	2014	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y	HQ (++)	Y
Cohen et al	2013	Y	Y	N	N	N	N	Y	Y	Y	Y	N	N	A(+)	Y
Dagenais et al	2010	Y	Y	Y	Y	N	N	Y	Y	Y	Y	N	N	A(+)	Y
Dighe & Friedman	2013	Y	Y	N	N	N	Y	Y	Y	N	Y	N	N	A(+)	Y
Dworkin et al	2013	N	Y	N	N	N	N	Y	Y	Y	Y	N	N	LQ(-)	Y
Epstein	2013	N	N	N	N	N	N	N	N	N	N	N	N	R(0)	Y
Fritzler et al	2011	Y	N	N	N	N	N	Y	N	N	N	N	N	LQ(-)	Y
Henschke et al	2010	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	HQ (++)	Y
Jacobs et al	2011	Y	Y	Y	Y	N	N	Y	Y	Y	Y	N	Y	A(+)	Y
Jamjoom et al	2014	Y	Y	Y	Y	N	Y	N	Y	Y	Y	N	Y	A(+)	Y
Jordan et al	2010	Y	Y	N	N	N	N	Y	Y	Y	Y	N	Y	A(+)	Y

Reference (author, year)		Quest													
Study	**Year**	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**1.11**	**1.12**	**2.1**	**2.2**
Koes et al	**1995**	Y	N	Y	N	N	N	Y	Y	Y	Y	N	N	A (+)	Y
Lewis et al	**2011**	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N	HQ (++)	Y
Luijsterburg et al	**2007**	Y	Y	Y	N	N	N	Y	Y	Y	Y	N	N	A (+)	Y
Macvicar et al	**2013**	Y	Y	N	Y	N	Y	N	N	N	Y	N	N	LQ(-)	Y
Manchikanti et al	**2012**	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	HQ (++)	Y
Manchikanti et al	**2015**	Y	Y	Y	N	N	Y	Y	Y	Y	Y	N	N	A (+)	Y
May & Comer	**2013**	Y	Y	Y	Y	N	N	N	Y	Y	Y	N	Y	A (+)	Y
Parr et al	**2009**	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	N	HQ (++)	Y
Parr et al	**2012**	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	HQ (++)	Y
Pinto et al	**2012**	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	HQ (++)	Y
Quraishi	**2012**	Y	Y	N	N	Y	N	Y	N	N	N	N	N	LQ(-)	Y
Rabinovitch et al	**2009**	Y	Y	N	Y	N	Y	Y	Y	N	Y	N	N	A (+)	Y
Roberts et al	**2009**	Y	Y	N	N	N	N	Y	Y	Y	Y	N	N	A (+)	Y
Shamliyan	**2014**	Y	Y	CS	CS	Y	N	Y	Y	Y	NA	N	Y	A(+)	Y
Staal et al	**2011**	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	HQ (++)	Y
Tonkovich-Quaranta	**2011**	Y	Y	N	N	N	N	Y	N	N	Y	N	N	LQ(-)	Y
Vorobeychik et al	**2016**	Y	N	Y	Y	N	Y	N	Y	Y	N	N	Y	AQ(+)	
Wang et al	**2014**	Y	Y	N	Y	Y	Y	Y	Y	N	Y	N	N	A (+)	Y

Vorobeychik et al 2016 Y N Y Y N Y N Y Y N N Y

Appendix 4: Critical Appraisals of Randomised Controlled Trials

Reference (author, year)		Quest												
Study	**Year**	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**2.1**	**2.2**	**2.3**
Candido et al	2015	Y	Y	Y	N	Y	Y	Y	5.7%	CS	NA	++	Y	Y
2.4	This study showed that the lateral parasagittal interlaminar approach was more effective than the midline interlaminar approach in targeting low back pain with unilateral radicular pain secondary to degenerative lumbar disc disease. It also showed that pressure paresthesia occurring ipsilaterally during an LESI correlates with pain relief and may therefore be used as a prognostic factor													
Chun et al	2015	Y	Y	Y	Y	Y	Y	Y	6.0%	CS	NA	++	Y	Y
2.4	Injectate at a volume of 8 mL was more effective than injectate at a volume of 3mL for radicular pain in a lumbar transforaminal steroid injection, although both of the injectates contained the same dose of dexamethasone.													
Cohen et al	2015	Y	Y	Y	Y	Y	Y	Y	49.6%	Y	N	++	Y	Y
2.4	Although epidural steroid injection might provide greater benefit than gabapentin for some outcome measures, the differences are modest and are transient for most people.													
Colhado et al	2015	Y	Y	N	CA	N	N	Y	0.0%	N	NA	-	Y	Y
2.4	This research tries to bring to health care an original method for measuring low back pain. It is noteworthy that in the future, more research is needed to apply this method in clinical and scientific fields.													
Dennis et al	2015	Y	Y	Y	Y	Y	Y	Y	17.8%	N	N	++	Y	Y
2.4	According to this study, pain relief and functional improvement are similar for both dexamethasone and betamethasone at 3 months. Considering its safety profile, dexamethasone could be considered as first choice for TFESI. However, given that the study was underpowered, more research is needed to support a recommendation of systematically using dexamethasone in TFESI.													
Evansa et al	2015	Y	Y	Y	N	Y	Y	Y	6.6%	CS	NA	++	Y	Y
2.4	We have demonstrated the feasibility of ultrasound-assisted epidural steroid injections													
Friedly et al	2014	Y	Y	Y	Y	Y	N	Y	3.5%	Y	N	+	Y	Y
2.4	In the treatment of lumbar spinal stenosis, epidural injection of glucocorticoids plus lidocaine offered minimal or no short-term benefit as compared with epidural injection of lidocaine alone.													
Ghai et al	2013	Y	Y	Y	Y	Y	Y	Y	0.0%	CS	NA	++	Y	Y
2.4	Epidural steroid injection administered with the PIL approach was significantly more effective for pain relief and improvement in disability than the MIL approach for 6 months in the management of low back pain with lumbosacral radicular pain.													
Ghai et al	2014	Y	Y	Y	Y	Y	Y	Y	0.0%	N?	NA	++	Y	Y
2.4	Epidural injection delivered through the PIL approach is equivalent in achieving effective pain relief and functional improvement to the TF approach for the management of low back pain with lumbosacral radicular pain. The PIL approach can be considered a suitable alternative to the TF approach for its equivalent effectiveness, probable better safety profile, and technical ease.													
Ghai et al	2015	Y	Y	Y	Y	Y	Y	Y	18.8%	Y	NA	++	Y	Y
2.4	Using a PIL approach and the addition of steroid to LA for EI may provide superior effectiveness in terms of extent and duration of pain relief for managing CLBP with unilateral LRP, even though, local anesthetic alone also was effective													

Reference (author, year)		Quest												
Study	**Year**	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**2.1**	**2.2**	**2.3**
Habib et al	2013	Y	Y	Y	N	Y	N	Y	16.6%	N	NA	+	Y	Y
2.4	Epidural corticosteroid injection of methylprednisolone acetate in both groups was associated with very high rates of secondary adrenal insufficiency, but significantly more so in Group 1 at week one. This suppression was transient, with recovery of the gland in most patients noted over the ensuing weeks. An epidural corticosteroid injection of 80 mg had higher rates of favorable clinical response than a 40 mg injection, but significantly more so at week 4 only. This favorable response waned over a few weeks in both groups													
Hashemi et al	2015	Y	Y	Y	Y	Y	N	Y	0.0%	NA	NA	+	Y	Y
2.4	Parasagital epidural injection showed higher infiltration of the drug to the ventral epidural space compared to the midline approach. The higher infiltration of the ventral epidural space provides better improvement of clinical disability and pain in the parasagittal group.													
Hong et al	2015	Y	Y	Y	N	Y	Y	Y	0.0%	NA	NA	+	Y	Y
2.4	The Whitacre needle had the benefit of reducing the incidence of intravascular injection with minimal differences in technical difficulties and the amount of radiation exposure during lumbar TFESI.													
Kennedy et al	2014	Y	Y	Y	Y	Y	N	Y	0.0%	N	N	+	Y	Y
2.4	Transforaminal epidural corticosteroid injections are an effective treatment for acute radicular pain due to disc herniation, and frequently only require 1 or 2 injections for symptomatic relief. Dexamethasone appears to possess reasonably similar effectiveness when compared with triamcinolone. However, the dexamethasone group received slightly more injections than the triamcinolone group to achieve the same outcomes.													
Kim et al	2013	Y	Y	Y	Y	Y	N	Y	8.2%	NA	NA	+	Y	Y
2.4	Epidural steroid injections were associated with statistically significant elevations in PBG in patients with diabetes for up to 4 days after the procedure. The higher dose of triamcinolone increased FBG and PBG greater than a lower dose did without affecting pain control, employment status, or clinical outcome. Thus, with respect to glucose and pain control, 20 mg of triamcinolone appears to be recommended rather than 40 mg in patients with diabetes.													
Koh et al	2013	Y	Y	Y	Y	Y	Y?	Y	22.0%	Y	NA	+	Y	Y
2.4	Superior short-term pain relieving efficacy, but limited long-term effects of hypertonic saline, when added to TFEIs.													
Koh et al	2015	Y	Y	Y	Y	Y	Y	Y	20.9%	Y	NA	++	Y	Y
2.4	The TFEI provided significant short-term pain relief and PRF can be applied in conjunction with TFEI to achieve higher treatment efficacy compared with TFEI alone.													
Manchikanti et al	2013	Y	Y	Y	Y	N?	N	Y	21.6%	Y	NA	+	Y	Y
2.4	Lumbar interlaminar epidural injections of local anesthetic with or without steroids are effective in patients with chronic axial low back pain of discogenic origin without facet joint pain, disc herniation, and/or radiculitis													
Manchikanti et al	2014	Y	Y	Y	Y	Y	Y	Y	15.0%	Y	NA	++	Y	Y
2.4	Lumbar interlaminar epidural injections of local anesthetic with or without steroids is an effective modality, in patients with chronic function limiting low back and lower extremity pain secondary to disc herniation after failure of conservative modalities													
Manchikanti, Cash et al	2013	Y	Y	Y	Y	N	Y	Y	9.1%	Y	NA	+	Y	Y
2.4	Lumbar interlaminar epidural injections of local anesthetic with or without steroids might be effective in patients with disc herniation or radiculitis, with potential superiority of steroids compared with local anesthetic alone at 1 year follow-up.													

Reference (author, year)		Quest												
Study	**Year**	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**2.1**	**2.2**	**2.3**
Manchikanti, Cash et al	2014	Y	Y	Y	Y	N	Y	Y	26.6%	Y	NA	+	Y	Y
2.4	Transforaminal epidural injections of local anesthetic with or without steroids might be an effective therapy for patients with disc herniation or radiculitis. The present evidence illustrates the lack of superiority of steroids compared with local anesthetic at 2-year follow-up.													
Manchikanti, Cash et al	2015	Y	Y	Y	Y	Y	Y	Y	11.6%	Y	NA	++	Y	Y
2.4	Lumbar interlaminar epidural injections of local anesthetic with or without steroids provide relief in a significant proportion of patients with lumbar central spinal stenosis.													
Manchikanti, Falco et al	2014	Y	Y	Y	Y	Y	N	Y	20.0%	Y	NA	+	Y	Y
2.4	The results of this assessment showed significant improvement in patients suffering with chronic lumbar spinal stenosis with caudal and interlaminar epidural approaches with local anesthetic only, or with steroids in a long-term follow-up of up to 2 years, in contemporary interventional pain management setting, with the interlaminar approach providing significantly better results.													
Manchikanti, Singh et al	2013	Y	N	N	N	NA	Y	Y	10.0%	Y	NA	0	Y	Y
2.4	Significant relief and functional status improvement as seen in 71% of the 70 patients with percutaneous adhesiolysis utilizing local anesthetic steroids and hypertonic sodium chloride solution may be an effective management strategy in patients with chronic function limiting low back and lower extremity pain with central spinal stenosis after failure of conservatie management and fluoroscopically directed epidural injections.													
Park et al	2013	Y	Y	Y	N	Y	Y	Y	8.3%	N	NA?	+	Y	Y
2.4	The ultrasound approach with colour Doppler mode may avoid intravascular injection induced complications. The results showed similar improvements in short-term pain relief, function, and patient satisfaction with both ultrasound and fluoroscopic guidance.													
Pirbudak et al	2015	Y	Y	Y	N	Y	N	Y	0.0%?	N	NA	-	Y	Y
2.4	Similar improvements in VAS, ODI, and SLET values were observed in both groups in the second week. The inflammation markers were not different after treatment, neither within the groups nor between the groups. This study revealed that tramadol + gabapentin treatment was not superior to tramadol treatment													
Radcliff et al	2013	Y	N	N	N	Y	N	Y	0.0%	N	N	0	Y	Y
2.4	Despite equivalent baseline status, ESIs were associated with significantly less improvement at 4 years among all patients with spinal stenosis in SPORT. Furthermore, ESIs were associated with longer duration of surgery and longer hospital stay. There was no improvement in outcome with ESI whether patients were treated surgically or non-surgically.													
Rados et al	2013	Y	Y	N	N	CS	N	Y	8.5%	N	NA?	-	Y	Y
2.4	Steroids are efficient; besides alleviating the overall pain, they also reduce the neuropathic component in chronic lumbar radicular pain, whether it is distributed epidurally by the IL or TF approach.													
Rahimzadeh et al	2014	Y	Y	Y	Y	Y	N	Y	0.0%?	N	NA	+	Y	Y
2.4	We conclude that adding hyaluronidase to the epidural injectate was effective in the management of chronic low back pain in patients with failed back surgery syndrome demonstrated over a period of 4 weeks.													
Shin et al	2014	Y	Y	Y	N	Y	N	CS?	13.5%	Y	NA	-	Y	Y
2.4	To reduce the risk of intravascular injection, the use of Whitacre needles without intrasacral bone contact may be a safer and more effective approach.													
Shin et al	2014	Y	Y	Y	Y	Y	N	Y	3.0%	N	NA	+	Y	Y
2.4	Epidural steroids after a PELD reduce back pain and leg pain while improving functional outcomes in the short-term post-surgery period.													

Reference (author, year)		Quest												
Study	**Year**	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**2.1**	**2.2**	**2.3**
Sinofsky et al	2014	Y	N	N	N	N	CS	Y	7.7%	N	NA	0	Y	Y
2.4	The concordant group demonstrated significantly higher pain reduction as compared to the discordant group. There were no significant differences between the 2 groups in terms of improved function or reduced analgesic requirements. Concordant provocation during interlaminar epidural injection may be a predictor of outcome													
Spijker-Huiges et al	2014	Y	Y	Y	N	Y	N	Y	13.7%	Y	NA	+	Y	Y
2.4	The effect on pain and disability of epidural steroids in lumbosacral radicular syndrome is small but significant, and at lower costs with no reported complications or adverse effects. Segmental epidural steroid injections could be considered by policy makers as an additional treatment option													
Spijker-Huiges et al	2014	Y	Y	Y	N	Y	N	Y	13.7%	Y	NA	+	Y	Y
2.4	We found a small, statistically significant, but not clinically relevant positive effect of SESIs on back pain, impairment and disability in acute LRS. We do not recommend implementing SESIs as an additional regular treatment option in general practice.													
Spijker-Huiges et al	2015	Y	Y	Y	Y	Y	N	Y	31.5%	Y	NA	+	Y	Y
2.4	Although the beneficial effects of SESIs are small and the natural course of LRS is predominantly favorable, we think decision makers can consider implementing SESIs in daily practice with the purpose of saving resources. Caution must be taken, and further research should be directed at identifying patient subgroups who might benefit from SESIs, with additional focus on (costs of) complications and adverse effects.													
Turan et al	2015	Y	Y	Y	N	Y	N	Y	12.8%	Y	NA?	+	Y	Y
2.4	N_2O administration did not improve pain or psychological or physical aspects of health-related quality of life. N_2O does not appear to be an effective treatment for chronic neuropathic back pain.													
Zhang et al	2013	Y	Y	Y	N	Y	N	Y	0.0%?	N	NA	+	Y	Y
2.4	In our study, oxygen-ozone nucleolysis provides excellent pain relief in most herniated disc patients who failed to respond to conservative therapy. And there was no significant statistical difference between treatment of injection of oxygenozone combined with steroid and ozone only in the 6 and 12 months follow-up. Therefore, O2–O3 seems to play a role in pain relief, and we suggest the administration of the O2–O3 mixture as a first-choice treatment before recourse to surgery or when surgery is not possible and the addition of epidural steroid infiltration is not required.													

Appendix 5: Critical appraisals of cohort studies examining adverse events

Reference (author, year)		SIGN Item (**Y** = yes, **N** = no, **DNA** = does not apply, **CS** = cannot say, **-** = not reported)																
Study	**Year**	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**1.11**	**1.12**	**1.13**	**1.14**	**2.1**	**2.2**	**2.3**
Plastaras et al	2015	Y	DNA	N	N	-	N	Y	Y	Y	Y	CS	DNA	N	N	LQ(-)	Y	Y
2.4	Fluoroscopically guided lumbosacral TFESI is associated with a similar rate of minor AEs both immediately and 24 to 72 hours after procedure that are typical of other axial corticosteroid injections. Permanent AEs were not found in this sample																	
Schneider et al	2014	Y	DNA	N	N	-	N	Y	N	N	Y	CS	DNA	N	N	LQ(-)	Y	Y
2.4	Vasovagal reactions have an overall occurrence rate of 3.5% in TFESIs. Although there is a potential for bias, this study does appear to demonstrate that when a trainee is involved in a TFESI, there is nearly twice the rate of vasovagal reaction																	
Qureshi et al	2013	Y	CS	N	N	-	N	CS	CS	Y	Y	CS	Y	Y	N	LQ(-)	CS	Y
2.4	Blind interlaminar epidural steroid injections are safe when performed with proper technique, monitoring and under recommended sterile precautions. The minor complications are common with this procedure but major complications are rare																	
Kainer et al	2012	Y	CS	N	N	-	DNA	Y	DNA	Y	Y	Y	N	N	Y	LQ(-)	N	N
2.4	Epidural glucocorticoid injections can lead to localized infection, and fungal pathogens can invade the dura, leading to meningitis and, in some patients, invasion of the posterior circulation vasculature leading to stroke, haemorrhage, or both																	
Kang et al	2012	Y	Y	N	CS	-	DNA	Y	CS	Y	Y	Y	DNA	Y	N	+	CS	Y
2.4	ESI treatments using less than a total of 200mg triamcinolone had no significant effect on BMD. However, the decrease in BMD of postmenopausal women who received more than 200mg of triamcinolone in one year indicates that ESI involving doses > 200mg/year should be avoided																	
Manchikanti et al	2012	Y	N	N	N	-	N	CS	CS	N	Y	N	N	N	N	LQ(-)	Y	Y
2.4	Major complications are rare and minor side effects are common																	
Chang et al	2011	Y	DNA	N	N	-	DNA	CS	N	N	N	N	N	N	N	LQ(-)	N	Y
2.4	The use of air to localize the epidural space in CT-guided ESIs has a high success rate and a very low rate of complications																	
Karaman et al	2011	Y	DNA	N	N	-	DNA	Y	Y	Y	Y	CS	DNA	N	N	LQ(-)	Y	Y
2.4	The frequency of major complications is pretty rare in transforaminal lumbar epidural steroid injections in expert hands and in the conditions in which safety precautions are taken																	
Candido et al	2010	Y	Y	N	N	-	DNA	CS	DNA	Y	Y	CS	DNA	N	N	LQ(-)	N	Y

Reference (author, year)		SIGN Item (**Y** = yes, **N** = no, **DNA** = does not apply, **CS** = cannot say, **-** = not reported)																
Study	**Year**	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**1.11**	**1.12**	**1.13**	**1.14**	**2.1**	**2.2**	**2.3**
2.4	Our data demonstrate that intradiscal injection is a rare complication during LESI, but occurs more frequently with TFESI than with LESI																	
Trentman et al	2009	Y	N	N	N	-	DNA	CS	CS	N	CS	DNA	DNA	N	Y	LQ(-)		Y
2.4	The risk of vasovagal reaction is significantly higher for cervical translaminar epidural steroid injections than for lumbar injections																	
McGrath et al	2007	Y	N	N	N	-	DNA	CS	N	Y	Y	CS	DNA	Y	Y	LQ(-)	Y	Y
2.4	These results suggest that ESIs are a safe and well-tolerated intervention for cervical or lumbar pain and radiculopathy																	
Stalcup et al	2006	Y	N	Y	N	-	DNA	CS	N	Y	Y	CS	N	N	Y	LQ(-)	CS	Y
2.4	SLNBs performed with fluoroscopic guidance have a low incidence of complications, all of which were minor. The specific needle-tip position within or adjacent to the lumbar neural foramen does not appear to be associated with the incidence of complications																	
Fitzgibbon et al	2004	Y	N	N	N	-	N	CS	DNA	N	CS	N	DNA	N	N	LQ(-)	N	N
2.4	Brain damage and death were associated with epidural steroid injection only when opioids or local anaesthetics were included																	
Horlocker et al	2002	Y	N	N	N	-	N	CS	N	Y	Y	CS	N	CS	N	LQ(-)	N	Y
2.4	ESIs are safe in patients receiving aspirin-like antiplatelet medications. However, pain clinic personnel should be aware that minor worsening of neurologic function may occur after ESI and must be differentiated from aetiologies requiring intervention																	
Botwin et al	2001	Y	Y	Y	N	7.3 %	N	Y	N	Y	Y	CS	N	Y	N	+	Y	Y
2.4	No major complications occurred. The incidence of minor complications was 15.6% per injection. All reactions resolved without morbidity and no patient required hospitalization																	
Botwin et al	2001b	Y	N	N	CS	-	DNA	Y	CS	Y	Y	DNA	Y	N	N	LQ(-)	Y	Y
2.4	Average radiation exposure for technicians during these procedures was below the limit of detectability																	
Botwin et al	2000	Y	Y	DNA	CS	-	DNA	Y	Y	Y	Y	CS	N	CS	N	+	Y	Y
2.4	There were no major complications. The incidence of minor complications was 9.6% per injection. All reactions resolved without morbidity, and no patient required hospitalization																	
Furman et al	2000	Y	N	N	DNA	-	DNA	CS	DNA	Y	Y	N	N	N	N	LQ(-)	N	Y

Reference (author, year)		SIGN Item (**Y** = yes, **N** = no, **DNA** = does not apply, **CS** = cannot say, **-** = not reported)																
Study	**Year**	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**1.11**	**1.12**	**1.13**	**1.14**	**2.1**	**2.2**	**2.3**
2.4	There is a high incidence of intravascular injections in transforaminal ESIs. Fluoroscopically guided procedures without contrast confirmation are instilling medications intravascularly and therefore not into the desired epidural location. This finding confirms the need for not only fluoroscopic guidance but also contrast injection instillation in lumbosacral transforaminal ESIs																	
Johnson et al	1999	Y	N	N	N	-	N	N	N	CS	Y	N	N	CS	N	LQ(-)	N	Y
2.4	Epidurography followed by therapeutic epidural steroid injection (with or without a local anesthetic) is a safe radiologic procedure that is easily performed by skilled proceduralists on an outpatient basis without intravenous sedation and cardiac monitoring																	

Appendix 6: List of Randomised Controlled Trials within Systematic Reviews

	Year	Benyamin et al	Bicket et al (a)	Choi et al	Henschke et al	Jordan et al	Lewis et al	Manchikanti et al (a)	Novak & Nemeth	Parr et al (a)	Pinto et al	Quraishi	Rabinovitch et al	Roberts et al	Staal et al	Andreisek et al	Armon et al	Benny & Azori	Ammendolia et al	Bicket et al 2 (b)	Bresnahan et al	Chien et al	Cohen et al	Dighe & Friedman	Dworkin et al	Fritzler et al	Jacob et al	Koes et al	Luijsterburg et al	Macvicar et al	Manchikanti et al (b)	May & Comer	Parr et al (b)	Tonkovich-Quaranta	Wang et al	Epstein	Benoist et al	Bui et al	Dagenais et al	Jamjoom et al	Total References
Takada et al	2005												1		1																										2
Wilson-Macdonald	2005		1	1					1				1			1				1			1	1						1		1									10
Dreyfuss et al	2006																						1																		1
Riew et al	2006			1														1		1			1							1											5
Schaufele et al	2006																	1																							1
Ackerman & Ahmad	2007	1						1		1				1		1		1				1	1		1					1											10
Anderberg et al	2007		1																				1																		2
Becker et al	2007		1																				1											1							3
Dincer et al	2007															1																								1
Gallucci et al	2007															1																								1
Jeong et al	2007							1								1		1					1							1											5
Kapural et al	2007	1																																						1
Owlia et al	2007															1							1																	2
Candido et al	2008	1						1						1								1	1																		5
Cohen et al	2008																								1																1
Manchikanti et al (a)	2008			1						1																					1										3
Manchikanti et al (b)	2008									1																															1
Manchikanti et al (c)	2008		1	1						1													1																		4
Manchikanti et al (d)	2008		1							1													1																		3
Rasmussen et al	2008																						1																		1
Cohen et al	2009		1																															1						2
Fish et al	2009																						1																		1
Gelalis et al	2009															1																									1
Hegihara et al	2009																			1																					1
Koc et al	2009	1		1												1					1		1								1	1									7
Laiq et al	2009			1																1			1																		3
Lee et al	2009	1						1								1		1			1		1								1	1									8
Manchikanti et al	2009																														1										1
Murata et al	2009			1																																					1
Sayegh et al	2009		1	1												1				1			1																		5
Tafazel et al	2009		1	1		1		1			1	1								1			1							1		1									10
Teske et al	2009			1												1																									2
Gerszten et al	2010			1				1															1																		3
Ghahreman et al	2010		1	1				1			1					1				1			1	1						1											9
Lee et al	2010	1																																							1
Makki et al	2010									1																															1
Manchikanti et al (a)	2010																						1																		1
Manchikanti et al (b)	2010	1		1																																					2
Manchikanti et al (c)	2010									1														1																		2
Manchikanti et al (d)	2010	1		1							1												1	1																		5
Park et al	2010							1								1							1							1											4
Yousef et al	2010									1																															1
Amr	2011	1																																							1
Aref et al	2011															1																									1
Burgher et al	2011			1				1								1																									3
Gharibo et al	2011							1	1																															2
Iversen et al	2011		1	1						1	1					1							1	1	1																8
Kang et al	2011															1							1																		2

	Year	Benyamin et al	Bicket et al (a)	Choi et al	Henschke et al	Jordan et al	Lewis et al	Manchikanti et al (a)	Novak & Nemeth	Parr et al (a)	Pinto et al	Quraishi	Rabinovitch et al	Roberts et al	Staal et al	Andreisek et al	Armon et al	Benny & Azori	Ammendolia et al	Bicket et al 2 (b)	Bresnahan et al	Chien et al	Cohen et al	Dighe & Friedman	Dworkin et al	Fritzler et al	Jacob et al	Koes et al	Luijsterburg et al	Macvicar et al	Manchikanti et al (b)	May & Comer	Parr et al (b)	Tonkovich-Quaranta	Wang et al	Epstein	Benoist et al	Bui et al	Dagenais et al	Jamjoom et al	Total References
Kim et al	**2011**	1														1							1																		3
Manchikanti et al (a)	**2011**		1	1						1						1								1																		5
Manchikanti et al (b)	**2011**		1	1						1	1																														4
McCahon et al	**2011**									1																															1
Nam et al	**2011**		1																			1								1											3
Park et al	**2011**															1																									1
Rados et al	**2011**	1						1								1						1	1		1				1												7
Brown	**2012**																				1		1	1																	3
Cohen et al	**2012**		1								1									1			1											1							5
Manchikanti et al (a)	**2012**																						1																		1
Manchikanti et al (b)	**2012**	1	1																					1																	3
Manchikanti et al (c)	**2012**	1	1																				1																		3
Manchikanti et al (d)	**2012**		1																											1										2
Manchikanti et al (e)	**2012**		1																				1																		2
Manchikanti et al (f)	**2012**			1						1																															2
Manchikanti et al (g)	**2012**		1																				1																		2
Manchikanti et al (h)	**2012**		1																				1																		2
Manchikanti et al (i)	**2012**		1																																					1
Manchikanti et al (j)	**2012**		1																																					1
Ohtori et al	**2012**																																	1						1
Manchikanti et al	**2014**																													1										1
Milburn et al	**2014**																													1										1
Total References		15	44	31	3	4	12	14	13	15	23	6	15	9	8	57	7	9	2	21	6	4	62	11	5	7	1	11	14	12	8	8	6	8	4	1	0	0	0	0	**476**

Appendix 7: Data Extraction of Randomised Controlled Trials within Systematic Reviews

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient	Pathology
Ackerman and Ahmad	2007		Randomized, evaluator blinded	TF, IL and Caudal groups	triamicinolone		Pain relief: 2, 12, 24 wk	Pain improvement at 2 wks: TF 72.1% vs IL 35.2%. Pain score reduced in all 3 groups at 2 wk, but significantly reduced in the TF group. TF group had significantly more patients with complete and partial relief at 12 and 24 weeks. There were more reports of complete pain relief with ventral contrast spread.	TF > IL or caudal at 24 wks. Functional improvement at 2 wks: TF 53.3% vs IL 60.6%	DISABILITY: ODI QoL: Oswestry Beck depression score		Fluoroscopy and contract dye used for injections	L5-S1 disc herniation on imaging	S1 radiculopathy from HNP
Anderberg et al	2007		Prospective RCT	Transforaminal	methylprednisolone	Mepivicane	VAS, unvalidated qu developed by authors: 3 wk		Mod improvement in both groups but no diff btwn groups			MRI confirmed pathology		Cx radiculopathy
Arden et al, Price et al	2005		Double blind, prospective RCT	Interlaminar	Conflict in the lit: triamcinolone acetonide vs depomethylprednisolone	Conflict in the lit: none vs bupivacaine	Analgesic use, missed work, VAS: 3, 6, 12 and 52 wk		Within group VAS, ODI improvements in Rx group noted at 3 wk (p=0.016) and thru-out study. No within group diff for control at 3 wk but some afterward. Btwn group diffs in VAS and ODI only at 3 wk. No diff in other outcomes. Pts needing surgery/total patients: Rx group 17/113 vs control 13/95	ROM: physical function DISABILITY: surgery, ODI: 3, 6, 12 and 52 wk RTW: Work status QoL: SF-36			Ortho, rheum and pain clinic pts, mixed (>4 wk to <18 mo) duration of Sx	Unilateral Lx radiculopathy
Barre et al	2004		Retrospective	Caudal	triamcinolone	lignocaine		pain relief and function 35% at 12 mo				Fluoroscopy used		Spinal stenosis
Becker et al	2007		Double blind, prospective RCT	Interlaminar (oblique)	triamcinolone	unspecified LA	VAS: 6, 10, 22 wk		Within group VAS, ODI improvements in all groups. Trend toward superiority in control group at all time points. Btwn group diff in VAS only at 22wk with autologous serum group >5mg triamcinolone. No btwn group diff in ODI	DISABILITY: ODI: 6, 10, 22 wk				Unilateral Lx radiculopathy
Beliveau	1971		RCT	Caudal	Methylprednisolone	procaine	Pain scale: followed up to 3 mo		Within group differences thru-out 3 mo in both groups. No btwn group diff.	ROM: Physical exam			unknown duration of Sx	Unilateral LxSx Radiculopathy
Breivik et al	1976		Double blind, prospective RCT	Caudal	methylprednisolone	bupivacaine	Pain, work status: followed up to 3-20 mo	% of pts with considerable pain relief: Rx group 56% vs control group 26%, before crossover	Within groups, both improved from baseline at follow up. % of pts with considerable pain relief: Rx group 56% vs control group 26%, before crossover	ROM: Physical exam, spinal reflexes, Lasegues's test, sphincter disorders			Pain unresponsive to conserv Rx for several months to several years	Chronic Lx radiculopathy
Buchner et al	2000		Single blind, prospective RCT		methylprednisolone	bupivacaine	VAS: 2 and 6 wk, 6 mo		No diff btwn groups at 6 wks and 6 mo but trend towards better results in Rx ghoup for pain relief and mobility (not stat signif). Greater improvement in SLRT at 2 wks in Rx group (p=0.03)	ROM: SLRT DISABILITY: Hannover Functional ability Qu: 2 and 6 wk, 6 mo		Pt with concordant MRI imaging of abnomality or disc herniation, SLR <60 degrees	Pts ,50 yo, no previous surgery	radicular Lxsciatic pain

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient	Pathology
Burgher et al	2011		Double blind RCT	transforaminal	triamcinolone	lignocaine	NRS: 1 mo		Addition of clonidine to LA yielded better results than triamcinolone	DISABILITY: RMDQ, ODI: 1 mo QoL: Centre for Epidemiologic Studies Depression scale				Acute LxSx radiculopathy due to disc herniation
Bush and Hilliier	1991		Double blind, placebo control, prospective RCT	Caudal	triamcinolone acetonide	procaine hydrochloride	VAS: 4 and 52 wks		Within groups at 4 wks, no improvement in control but improvement in Rx group (S/E measures p = 0.02, SLRT p = 0.01). But at 1 year, signif within group improvement in both groups with min diff btwn groups. Rx group SLR signif better but no data presented. Pts needing surgery/total patients: Rx group 1/13 vs control 2/15	ROM: Physical exam/angle of SLR QoL: Grogono and Woodgate Symptomatology Qu			Rheumatology clinic pts, acute (>1 mo - 12 mo) duration of Sx	Lumbosacral radiculopathy
Butterman	2004		Prospective RCT	Interlaminar	betamethasone		Medication use: 1-2 yrs, VAS: 4-6 mo	Greater reduction in leg pain at 3 and 6 mo for microdiscectomy. No diff in leg pain at 1, 2 and 3 yrs.	Among the 50 pts in the Rx groupd, 27 (46%) did not have surgery. Though ESI was not as effective as discectomy, there was signif effectiveness of up to 3 yrs in nearly 50% of pts who had not had improvement with 6 or more wks or non-invasive care.	ROM: Neuro status: 1-3 mo DISABILITY: Crossover to undergo surgical Rx: followed 2-3 yr, ODI: 7-12 mo QoL: Self perceived recovery and satisfaction with Rx: 2-3 yrs		MRI or CT confirmation of >25% of the CSA of spinal canal. Sx at least for 6 wks	Sx >3 yr	Lx disc herniation or radiculitis
Butterman	2004		non RCT	Interlaminar or transforaminal	Betamethasone		Use of pain medication, VAS: 2 yrs		ESI were effective at improving pain and function at short term follow up. However at 2 yrs, less than 1/3 had not had additional invasive Rx	DISABILITY: ODI: 2yrs QoL: Opinion of Rx success		fluoroscopy used to guide injections		Degenerative disc disease
Candido et al	2008		Prospective RCT, single blind	Transforaminal and Interlaminar	methylprednisolone	lignocaine	VAS: 6 mo	Pain improvement at 1 mo: TF 16.5% vs IL 23.1% Pain improvement at 6 mo: TF 25.5% vs 39.2%	No diff btwn groups up to 6 mo (but study underpowered)	DISABILITY: ODI: 6MO		Fluoroscopy and contract dye used		Unilat radiculopathy from HNP and degen disc disease, spinal stenosis
Carette et al	1997		Double blind, prospective RCT	Interlaminar	methylprednisolone acetate	none	Consumption of analgesia, McGill Pain Qu, VAS: 3 and 6 wk, 3 mo		Both groups improved from baseline btwn 3 and 12 wks. No sig diff btwn groups except Rx pts had greater finger to floor movt (p=0.006) and less sensory deficits (p=0.03) at 3 wks. At 6 wks, less leg pain on VAS (p = 0.03) in Rx group, reduced need for analgesics btwn 3-6 wks (p = 0.01) in Rx group. Pts needing surgery/total patients: Rx group 20/78 vs control 20/80	ROM: physical exam and functional capacity DISABILITY: ODI or RMQ (conflicting data) 3 and 6 wk, 3 mo		Pts needed to have CT evidence of a herniated disc at a level corresponding to Sx and score > 20 on ODI	Uni hosp pts, mixed (>4wk to <1y) duration of Sx	LxSx radiculopathy due to herniated nucleus propulsus
Cohen et al	2009		Double blind, prospective RCT	Transforaminal	Etanercept (not a steroid)	none	VAS, medication use: followed up to 6 mo		Within group improvement at baseline throughout study. Etanercept > control	ROM: Functional capacity DISABILITY: surgery rate QoL: satisfaction			Duration of Sx < 9 mo	LxSx radiculopathy
Cohen et al	2012		Double blind, prospective RCT	Transforaminal	methylprednisolone or etanercept	bupivacaine	Medication use, VAS/NRS (conflicting data): 1, 3, 6 mo		Within group diff throughout 6 mo in all groups. Non stat sig diff favouring steroids at 1 mo but not at 3 or 6 mo. Pts needing surgery/total patients: Rx group 12/54 vs control 5/30	ROM: Functional capacity DISABILITY: surgery rate, ODI: 1 mo QoL: satisfaction			Pts from 6 military and civlian hospitals, mixed (>4 wk to < 6 mo) duration of Sx	LxSx radiculopathy secondary to disc pathology

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient	Pathology
Cuckler et al	1985		double blind, prospective RCT	Interlaminar	methylprednisolone	procaine	>75% pain relief, proportion of improved pts: 24 h, every 3 mo for 13-60mo		After 24 h, signif improvements in both groups. No diff btwn groups. At mean 21 mo followup, 24% of Rx group improved cf 15% control (p value not signif). Pts needing surgery/total patients: Rx group 16/42 vs control 7/31	QoL: S/E improvement		All pts had radiologic findings consistent with their Sx or findings and had failed to improve after 2 wk of conservative Rx	private practice pts, mixed (mean Group A 17.3/Group B 13.1 wk) duration of Sx	Acute Lx hermiated disc or spinal stenosis
Dashfield et al	2005		RCT	Caudal	triamcinolone	lignocaine	Pain relief, short form McGill Pain Qu: 6 wks, 3 and 6 mo		No signif diff btwn groups for any of the measures at any time. Both caudal injection and endoscopic injection benefitted pts with signif improvement at 3 and 6 mo	QoL: Hosp Anxiety and Depression Scale: 6 wks, 3 and 6 mo				
Devulder et al	1999		non blinded RCT	transforaminal	methylprednisolone	bupivacaine	verbal pain scale rating: 6 mo	No stat signif diffs btwn groups. Overall pain relief was most prominent after 1mo but decreased at 3 and 6 mo	Differences found among the three groups but results diminished at 3 and 6 mo follow up.			EMG confirming chronic nerve pathology and imaging confirming nerve fibrosis		Failed back surgery syndrome
Dilke et al	1973		Double blind, placebo control, prospective RCT	Interlaminar	methylprednisolone	none	Consumption of pain relief, proportion of improved pts: 3 months	Stat highly signif diffs in respect to relief of pain, in favour of the Rx group	Signif diff in no of pts not returned to work (3 in Rx group and 14 in control group). No diff in no of days bed rest or days in hosp. Pts needing surgery/total pats: Rx group 7/52 vs control 10/48	ROM: Physical Exam DISABILITY: Rate of surgery RTW: Work status			hospital pts, mixed duration (1wk to 2 y) of Sx	Unilateral LxSx radiculopathy
Dreyfus et al	2006		RCT	transforaminal	Dexamethasone OR triamcinolone	lignocaine			Non signif trend favouring particulate steroid					Unilateral Cx radiculopathy
Finckh et al	2006		RCT		Methylprednisolone		VAS						Acute pts (<6 wk)	Sciatica
Friedman et al	2008		RCT				VAS						pt with 1 wk duration	Sciatica
Fukusaki et al	1998		RCT	translaminar	Methylprednisolone	Mepivicane			Showed improved walking distance only immediately after injection (1 wk) then no signif diffs btwn groups and effect dissipated in all pts to less than 10% effectiveness level.	ROM: Walking distance, excellent>100m good 20-100m				Spinal stenosis
Gharibo et al	2011		Prospective RCT	Transforaminal and Interlaminar	triamcinolone	bupivacaine		pain improvement TF 73.4% vs IL 44.3%	TF> IL at 2 wk follow up. According to another paper, Functional improvement TF 43.6% vs IL 49.3%			Fluoroscopy and contract dye used	Sx < 1 yr	Unilateral radiculopathy from disc disease

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient	Pathology
Gerszten et al	2010		Prospective RCT	Transforaminal			VAS: 2 yr		Among 40 pts in Rx group, 50% did not receive surgery. At one yr follow up, nucleoplasty pts fared better than TF pts	DISABILITY: Crossover to undergo surgical Rx: followed 2 yr QoL: SF-36 2 YR				HNP
Ghahreman et al	2010		Double blind, prospective RCT	Transforaminal	triamcinolone, IM steroids	bupivacaine	Proportion of pts with >50% pain relief lasting >1 mo, use of rescue meds, VAS: 1, 3, 6, 12 mo.	54% steroid +LA, 7% LA, 19% saline, 21% IM steroid and 13% IM saline achieved pain relief but relife of pain diminished over time in all groups.	Within group diff at 1 mo for TF steroids, TF saline and IM steroids. Btwn group: TF steroids > TF saline = IM steroids > IM saline and TF LA. No diff in surgery rates btwn groups. Pts needing surgery/total patients: Rx group 10/28 vs control 31/122	ROM: Pt Specified Functional Outcomes Scale DISABILITY: surgery rate QoL: SF-36, Roland Morris instrument, Psychological improvement		Disc herniation confirmed by CT or MRI. Fluoroscopic guided injection	hospital pts, mixed duration of Sx	LxSx radiculopathy secondary to herniated disc
Genevay et al	2004		non RCT		Methylprednisolone		Leg and back VAS, proportion of pts with gd result: 6 wks			DISABILITY: number of discectomies, ODI: 6 wks QoL: Roland Morris: 6 wk				Acute severe sciatica
Haimovic et al	1986		RCT		Dexamethasone								Duration of Sx NR	Sciatica
Hedeboe et al	1982		RCT		Dexamethasone								Duration of Sx <8 wk	Sciatica
Hegihara et al	2009		Prospective RCT		betamethasone	lignocaine	pain relief: 1 week		Pts needing surgery/total patients: Rx group 3/34 vs control 7/35	DISABILITY: Rate of surgery, 1 wk				Lx radiculopathy
Helliwell et al	1985		RCT	Interlaminar	methylprednisolone	none	VAS: 1 and 3 mo						unspecified source of pts, subacute and chronic duration (3 wk-12mo) of Sx	Sciatica

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient	Pathology
Hesla and Breivik	1979		Double blind, prospective, crossover RCT	Caudal	Methylprednisolone	bupivacaine			Within group improvement in both groups. Rx > control	RTW: followed up to 1 y			Mean duration of Sx 3.2 wks	Chronic Lx radiculopathy
Hofferberth et al	1982		RCT		Dexamethasone								36 month range of Sx duration	Sciatica
Holve et al	2008		RCT		prednisolone		VAS						Acute pts (1 wk)	Sciatica
Iversen et al	2011		Double blind, prospective RCT	Caudal	Triamcinolone acetonide	none	VAS: 6, 12 and 52 wk	Negative for short term (<6 wks) or long term pain relief	Within group diff for all groups. No signif diff btwn Rx and control groups. Pts needing surgery/total patients: Rx group 1/37 vs control 14/79	DISABILITY: ODI: 6, 12 and 52 wk QoL: European QoL measure: 6, 12 and 52 wk			Hospital pts, chronic (>12 wk) duration of Sx	Lx radiculopathy
Jeong et al	2007		Randomized, single blind	Transforaminal	Triamcinolone	bupivacaine	VAS: 6 -12 mo		Non signif trend favouring preganglionic > ganglionic at 1 mo, but no diff at 6 mo follow up			Nerve root compression documented by CT or MRI. Fluoroscopic guided injections		LxSx radiculopathy from HNP or spinal stenosis, for scheduled one level TF from L1 to S1
Kang et al	2011		Double blind RCT	Transforaminal	triamcinolone			Signif pain reduction in all groups except 5 mg after first injection. Non signif trend of better pain reduction with increaseing dose, after second injection						Lx radiculopathy from HNP
Karppinen et al	2001		Triple blind, prospective RCT	Transforaminal	methylprednisolone	bupivacaine	VAS: 2 and 4 wk, 3, 6 and 12 mo	For leg pain, immed (p=0.02) effect and 2 wk (p=0.02) effect favour steroids, at 4 wks, 3 and 12 mon, no diff and at 6 mo steriod arm worse (p=0.003). For back pain, steroid group worse at 3 (p=0.02) and 6 mo (p=0.03), no diff at other times	Within groups, both improved for leg and back pain at all time points. At 2 wk, Rx (45%) > control group (24%) for reduction of leg pain p<0.01. No diff at 1 yr, although at 6 mo the control group > Rx group. Pts needing surgery/total patients: Rx group 18/80 vs control 15/80	ROM: Physical exam, SLRT, Lx flexion DISABILITY: ODI: 2 and 4 wk, 3, 6 and 12 mo RTW: Economic analysis QoL: Nottingham health Profile		Injected under fluoroscopy with contrast injection to confirm localization	GP-referred pts in catchment area of Uni Hosp, mixed (>3 to <28 wk) duration of Sx	Unilateral LxSx Radiculopathy, from back to below knee
Kim and Brown	2011		Randomized, single blind	Interlaminar	Methylprednisolone OR dexamethasone	bupivacaine	pain medication usage, VAS: 2-3 mo		Non signif trend favouring particulate steroid			fluoroscopy used to guide injections	Sx greater than or equal to 6 mo	Lx radiculopathy

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Klenerman et al	1984		Double blind, placebo control, prospective RCT	Interlaminar	methylprednisolone	bupivacaine to control	VAS: 2wk, 2 mo		Within groups, improvement in all groups. Btwn groups, no diff at 10 wk. Pts needing surgery/total patients: Rx group0/19 vs control 2/44	ROM: Physical exam DISABILITY: rate of surgery			Day Care Unit pts, mixed duration (<6 mo)	Unilateral sciatica
Koc et al	2009		RCT	interlaminar	triamcinolone	bupivacaine			Signif improvements in pain and functional parameters within all groups. Pain and functional Ax scores were signif more improved in ESI cf controls at 2nd wk.	ROM: Finger to floor distance, sit to stand test, treadmill walk test, weight carrying test: 6 mo DISABILITY: Roland Morris Disability Index QoL: Knottingham Health profile		fluoroscopy used to guide injections		Spinal stenosis
Kolsi et al	2000		Double blind, prospective RCT	Transforaminal and Interlaminar	Cortivazol	lignocaine	Leg/back pain VAS, % improvement, analgesic use: to 28 d	Pain improvement at 28 days: TF 62.8% vs IL 63.5%	No diff btwn groups up to 4 wk. Functional improvement at 4 wks: TF 34.8% vs IL 50.9%	ROM: Schobers finger floor test, and EIFEL score		imaging of HNP, Fluoroscopy and contract dye used		Sciatic or femoral neuralgia
Kraemer et al (1)	1997		Prospective RCT	Interlaminar and transforaminal	triamcinilone	unspecified LA	Leg/back pain ratings, ability to do sports, proportion of improved pts: 3 mo		Within group diff in all groups. TF epidural steroid > IL epidural steroid > control group. Pts needing surgery/total patients: Rx group 11/87 vs control 6/46	ROM: Physical exam RTQ: work status		CT guidance for some injections	Unspecified source of pts, unspecified duration of Sx	Unilateral LxSx radiculopathy secondary to single nerve root compression
Kraemer et al (2)	1997		Double blind, prospective RCT	Transforaminal		none	Leg/back pain ratings, ability to do sports, proportion of improved pts: 3 mo		For within group analysis, >75% of pts in both groups had fair or good results. Rx group > control group	ROM: Physical exam RTW: work status		CT guidance for some injections	Unspecified source of pts, unspecified duration of Sx	Unilateral LxSx radiculopathy secondary to single nerve root compression
Laiq et al	2009		Prospective RCT	Interlaminar	methylprednisolone	lignocaine	VAS: up to 6 mo		Pts needing surgery/total patients: Rx group 4/26 vs control 6/26	DISABILITY: Rate of surgery QoL: PT satisfaction			Sx duration >2 wk	Lx radiculopathy
Lee et al	2006		Retrospective	Transforaminal	triamcinolone	bupivacaine			Preganglionic TF trends towards but is not signif better than conventional approach at 2 wk follow up					Lx radisculopathy receiving on level TF from L1 to S1
Lee et al (1)	2009		Randomized, evaluator blinded	Transforaminal and Interlaminar	triamcinolone	lignocaine	NRS, Roland 5 point pain score	Signif pain reduction from 2 wks to 4 mo after Rx in both groups. In Spinal stenosis pts, a more signif reduction in Roland 5 point was seen with TF cf IL	TF> IL up to 4 mo	QoL: PT satisfaction index		Fluoroscopy used for injections		Axial LBP due to HNP or spinal stenosis
Lee et al (2)	2009		Retrospective	TF, IL and Caudal groups	triamcinolone	lignocaine	Pain scores: 2 mo	TF and IL > Caudal at 2 mo. Pain improvement at 1 mo: TF 78% vs IL 64.5%. Pain improvement at 2 mo: TF 68.2% vs 51.6%	satisfaction and pain scores: TF and IL> caudal up to 2 mo. Function: TF>IL> caudal	ROM: Functional Capacity: 2 mo QoL: PT satisfaction index 2 mo		Fluoroscopy and contrast dye used		LxSx radiculopathy from Spinal stenosis or HNP

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Lee et al (3)	2009		Retrospective	Transforaminal	Dexamethasone OR triamcinolone				Non signif trend favouring particulate steroid					Cx radiculopathy who failed IL ESI or had prev surgery
Lee et al	2010		Retrospective	Caudal		LA		Pain relief and function 86% at 3 mo, 69% at 6 mo and 46% at 12 mo				Fluoroscopy used		Degen Lx spinal stenosis
Manchikanti et al	1999		Retrospective case-control	TF, IL and Caudal groups	betamethasone OR methylprednisolone	lignocaine	> 50% pain relief: 12 mo		TF and Caudal > IL at 1-3 mo but no diff btwn groups at 3-6 or 6-12 mo follow ups. ESI under fluoroscopy by caudal or TF route is a valuable, safe and cost effective technique.	RTW: Economic analysis		blind interlaminar vs fluoroscopic guided caudal/transforaminal injections		LBP and leg pain
Manchikanti et al	**2008 Part 2**		Double blind, prospective RCT	Caudal	betamethasone OR methylprednisolone	lignocaine	Opioid uptake, NRS: followed up to 1 yr		Within group pain improvement in both groups. No diffs in any outcome measures for btwn group differences.	DISABILITY: ODI: followed up to 1 yr RTW: employment			Sx at least 6 mo duration	Lx disc herniation or radiculitis
Manchikanti et al	**2008 Part 3**		Double blind, active control, prospective RCT	Caudal	betamethasone	lignocaine	Opioid uptake, NRS: followed up to 1 yr	Pain relief 60% vs 69% at 3 mo, 60% vs 66% at 6 mo and 56% vs 61% at 12 mo	Within group pain improvement in both groups. Parr 2012 states function control 56% vs Rx group 57% at 3 mo, 56% vs 63% at 6 mo and 54% vs 61% at 12 mo. No diffs in any outcome measures for btwn group differences.	DISABILITY: ODI: followed up to 1 yr RTW: employment			Sx at least 6 mo duration	Failed back surgery pts with leg pain
Manchikanti et al	**2008 Part 4**		Double blind RCT	Caudal		lignocaine		Pain relief and function 66% vs 62% at 3 mo, 58% vs 56% at 6 mno, 48% vs 46% at 12 mo (From Parr 2012, no idea which group is which)				Fluoroscopy used		Spinal stenosis
Manchikanti et al	**2010**		Double blind RCT	Interlaminar	betamethasone	xylocaine	Opioid use, NRS: 3, 6 and 12 mo	Pain relieved for longer duration in both groups (74% control and 86% Rx group)	Overall, 67% of patients in Group I without steroids and 85% in Group II with steroids with Lx disc herniation or radiculitis showed signif improvement. The results were superior and patients were classified with successful response to initial 2 epidural injections (80% vs. 86%).	DISABILITY: ODI: 3, 6 and 12 mo RTW: employment		fluoroscopy used to guide injections	Specialty referral centre pts, chronic (>6 mo) duration of Sx	Discogenic LBP
Manchikanti et al	**2010**		Blinded, active control RCT	Caudal	betamethasone	lignocaine	Opioid use, NRS: 3, 6 and 12 mo	Pain relief 60% vs 69% at 3 mo, 60% vs 66% at 6 mo and 56% vs 61% at 12 mo	Improvement in pain and disability reduction for longer duration Rx group 59% vs 53% in controls - Conflict in data re numbers: Parr 2012 states function control 56% vs Rx group 57% at 3 mo, 56% vs 63% at 6 mo and 54% vs 61% at 12 mo. No signif diffs after 1 yr.	DISABILITY: ODI: 3, 6 and 12 mo RTW: employment				Post Lx surgery syndrome

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Manchikanti et al	2010		Double blind, prospective RCT	Interlaminar	betamethasone	xylocaine	Opioid use, improvement of pain >50%, NRS: up to 1 yr		Signif improvement in 77% of patients in Group I and 67% in Group II. In the successful group, signif improvement reported in 84% in Group I and 71% in Group II. This is an active control practical trial which fits contemporary interventional pain management practices.	DISABILITY: ODI: followed up to 1 yr RTW: employment		fluoroscopy used to guide injections		Lx discogenic pain without herniation or radiculitis
Manchikanti et al	2011		Double blind, prospective RCT	Caudal	betamethasone OR methylprednisolone	lignocaine	Opioid uptake, NRS: 3, 6 and 12 mo	Signif pain relief and functional status improvement in 68% of Rx group and 55% of controls	Within group pain improvement in both groups. No diffs in any outcome measures for btwn group differences.	DISABILITY: ODI: 3, 6 and 12 mo RTW:: employment			unspecified source of pts, chronic (>6 mo) duration of Sx	Lx discogenic pain without herniation or radiculitis
Manchikanti et al	2011		Double blinded active control RCT	Caudal	betamethasone OR methylprednisolone	lignocaine	Opioid uptake, NRS: 3, 6, 12 mo		Signif pain relief and/or functional status improvement in 55% of the pts in LA and 68% of the steroid/LA group with better results in successful group in > 80% pain relief and over 62% functional status improvement.	ROM: Functional capacity, 3, 6, 12 mo DISABILITY: ODI: 3, 6 and 12 mo RTW:: employment			chronic pain	LBP of discogenic origin without Facet jnt pain, disc herniation, radiculitits and/or SIJ pain
Manchikanti et al	2012		RCT	Interlaminar	betamethasone	xylocaine	Opioid use, improvement of pain >50%, NRS: up to 1 yr		Signif improvement in 77% of patients in Group I and 67% in Group II. In the successful group, signif improvement reported in 84% in Group I and 71% in Group II. This is an active control practical trial which fits contemporary interventional pain management practices.	DISABILITY: ODI: followed up to 1 yr RTW: employment		fluoroscopy used to guide injections		chronic Lx axial or discogenic pain
Manchikanti et al	2012		Double blind, prospective RCT	Interlaminar	betamethasone	lignocaine	Opioid uptake, NRS: followed up to 1 yr		Within group pain improvement in both groups. No diffs in any outcome measures for btwn group differences.	DISABILITY: NDI RTW: employment			Sx at least 6 mo duration	Cx post surgery syndrome
Manchikanti et al	2012		Double blind, prospective RCT	Caudal	betamethasone OR methylprednisolone	lignocaine	Opioid uptake, NRS: followed up to 1 yr		Within group pain improvement in both groups. No diffs in any outcome measures for btwn group differences.	DISABILITY: ODI: followed up to 1 yr RTW: employment			Sx at least 6 mo duration	Lx disc herniation or radiculitis
Manchikanti et al	2012		Double blind, prospective RCT	Caudal	betamethasone	lignocaine	Opioid uptake, NRS: followed up to 1 yr		Within group pain improvement in both groups. No diffs in any outcome measures for btwn group differences. Signif pain relief and improvement in ODI scores were seen in both groups at 12 mo with 70% in the LA group and 60% in the steroid group in total pts; whereas, it was 80% in the LA group and 72% in the steroid group. In this group which successfully responded to the first 2 epidural injections.	DISABILITY: ODI: followed up to 1 yr RTW: employment		fluoroscopy used to guide injections	Sx at least 6 mo duration	Lx spinal stenosis with radiculopathy
Manchikanti et al	2012		Double blind, prospective RCT	Interlaminar	betamethasone	lignocaine	Opioid uptake, NRS: 3, 6, 12 mo	pain relieved for longer duration in both groups (70% control and 63% Rx group)	Within group pain improvement in both groups. No diffs in any outcome measures for btwn group differences.	DISABILITY: ODI: followed up to 1 yr RTW: employment			Sx at least 6 mo duration	Lx spinal stenosis

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Manchikanti et al	2012		Double blind, prospective RCT	Interlaminar	betamethasone	lignocaine	Opioid uptake, NRS: followed up to 1 yr		Within group pain improvement in both groups. No diffs in any outcome measures for btwn group differences.	DISABILITY: ODI: followed up to 1 yr RTW: employment			Sx at least 6 mo duration	Cx spinal stenosis
Manchikanti et al	2012		Double blind, prospective RCT	Interlaminar	betamethasone	lignocaine	Opioid uptake, NRS: followed up to 1 yr		Within group pain improvement in both groups. No diffs in any outcome measures for btwn group differences.	DISABILITY: ODI: followed up to 1 yr RTW: employment			Sx at least 6 mo duration	chronic Lx axial or discogenic pain
Manchikanti et al	2012		Double blind, prospective RCT	Interlaminar	betamethasone	lignocaine	Opioid uptake, NRS: followed up to 1 yr		Within group pain improvement in both groups. No diffs in any outcome measures for btwn group differences.	DISABILITY: ODI: followed up to 1 yr RTW: employment			Sx at least 6 mo duration	Cx disc herniation or radiculitis
Manchikanti et al	2012		Double blind, prospective RCT	Caudal	betamethasone	lignocaine	Opioid uptake, NRS: followed up to 1 yr		Within group pain improvement in both groups. No diffs in any outcome measures for btwn group differences.	DISABILITY: ODI: followed up to 1 yr RTW: employment			Sx at least 6 mo duration	Post Lx surgery syndrome
Manchikanti et al	2012		Double blind RCT	Caudal		lignocaine		Pain relief and function 66% vs 62% at 3 mo, 58% vs 56% at 6 mno, 48% vs 46% at 12 mo (From Parr 2012, no idea which group is which)				Fluoroscopy used		Spinal stenosis
Manchikanti et al	2012		Double blind RCT	Interlaminar	betamethasone	xylocaine	Opioid use, NRS: 3, 6 and 12 mo	Pain relieved for longer duration in both groups (74% control and 86% Rx group)	Overall, 67% of patients in Group I without steroids and 85% in Group II with steroids with Lx disc herniation or radiculitis showed signif improvement. The results were superior and patients were classified with successful response to initial 2 epidural injections (80% vs. 86%).	DISABILITY: ODI: 3, 6 and 12 mo RTW:: employment		fluoroscopy used to guide injections		Chronic Lx pain from disc herniation or radiculitis
Matthews et al	1987		Double blind, prospective RCT	Caudal	methylprednisolone	bupivacaine OR lignocaine	treatment usage, proportion of improved pts: 1,3 and 12 mo		Within group improvement in both groups at 1 mo, 67% Rx group pts recovered vs 56% of controls, not stat signif. At 3 mo, Rx group significantly more pain free than control. Pts needing surgery/total patients: Rx group 1/23 vs control 0/34	DISABILITY: Rate of surgery			unspecified source of pts, acute and subacute duration (8 d to 3 mo) of Sx	Uniradicular Lx pain with neuro deficit
McCahon et al	2011		RCT		methylprednisolone	bupivacaine	VAS: 12 wks		There was signif diff in pts receiving the low dose methylprednisolone (40mg) ie active control group	DISABILITY: ODI 12 wks QoL: Hosp Anxiety and Depression Scale: 12 wks				Low back and lower extremity pain from any cause
McGregor et al	2001		RCT	Caudal and Interlaminar	hydrocortisone	bupivacaine	VAS: 6 mo		No stat signif changes in either group in the ODI	DISABILITY: ODI 6 mo QoL: SF36, Euro QoL: 6mo				

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Meadeab et al	2001		Double blind, prospective RCT	Caudal	prednisolone	none	VAS: followed up to 4 mo		Within groups, non signif trend of improvement in steroid + saline and saline only groups, but not steroid only group. Non signif trend of steroid only group > steroid and saline, saline only group up to 30 d. After 30 d, strong trend toward superiority of saline only vs other two groups.	ROM: Physical exam, functional improvement: followed up to 4 mo QoL: Psychological improvement: followed up to 4 mo				Post surgical LxSx radiculopathy, not caused by nerve compression
Mendoza-Lattes et al	2009		Retrospective case-control	Caudal and Transforaminal	methylprednisolone OR betemethasone	Bupivacaine in TF group only	VAS: 2 yr	VAS 7.4 to 4.4 caudal group, TF 7.9% to 5.7% at 3 mo	C=TF throughout 2 yr followup. Approx 60% of pts improved. Surgery avoided in caudal group -59% vs TF -55.6%	DISABILITY: ODI 2 yrs QoL: SF36, 2 yrs		Fluoroscopy used		Lower Lx radiculopathy
Nam and Park	2011		Prospective RCT	Transforaminal	triamcinolone	lignocaine	VAS: followed up to 12 wk		Within group diffs for both groups to 12 wk. Steroid > control for function and pain scores	DISABILITY: ODI: followed up to 12 wk		clinical and radiological measures included in outcome measures		Lx scoliosis and stenosis
Ng et al	2005		Double blind RCT	Transforaminal	methylprednisolone	bupivacaine	VAS: 6 and 12 wk	Improvement in both groups for leg pain. But not stat signif btwn two groups. Baseline C: VAS 76.9 (60–82.5); ODI 48.4 (36–58) T: VAS 73 (60–80); ODI 47.8 (36–56) 6 weeks C: VAS 55.9 (±4); ODI 35.5 (±3) T: VAS 51 (±4.2); ODI 40 (±2.8) VAS p = 0.85 ODI p = 0.21 3 months C: VAS 54.7 (±5.2); ODI 36.1 ± 3.2) T: VAS 50 (±5); ODI 37.8 (±3.4)	Corticosteroids did not provide additional benefit. Improvements in both groups for ODI and walking distance, but not stat signif btwn groups.	DISABILITY: ODI: 6 and 12 wk QoL: PT Satisfaction			Spine Specialist clinic pts, subacute and chronic (>6 wk) duration of Sx	Sciatica from disc herniation or foraminal spinal stenosis
Noe and Haynsworth	2003		Retrospective	Interlaminar	betamethasone OR methylprednisolone				particulate > non particulate steroid for pain reductionl, improvement in disability	DISABILITY: ODI: 1 mo				LBP
Ohtori et al	2012		Prospective RCT		Dexamethasone		leg and back pain VAS: 1 mo						Duration of Sx 1-12 mo	Sciatica due to Lx spinal stenosis
Owalia et al	2007		Randomized, case matched for age/sex	Interlaminar	methylprednisolone	lignocaine			No difference between groups for pain improvement. Fewer complications in low dose group					Lx radiculopathy from HNP
Park et al	2010		RCT	transforaminal	Dexamethasone OR triamcinolone	lignocaine	VAS: 4 wk		Particulate > non particulate steroid for pain reduction (71% triamcinolone vs 40% dexamethasone)	DISABILITY: ODI: 1 mo QoL: Modified somatic perception qu: 4 wk			MRI showed nerve root compression	Lx radiculopathy

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Price et al	2005		Double blind, prospective RCT	"epidural"	triamcinolone	bupivacaine	Analgesis consumption and leg/back VAS: followed up to 1 yr		Within group improvements across all time points for both groups. Btwn groups, Rx group > control for pain and function better at 3 wk but not after. Pts needing surgery/total patients: Rx group 15/120 vs control 14/108	ROM: Physical exam: followed up to 1 yr DISABILITY: ODI: followed up to 1 yr RTW: work status: followed up to 1 yr QoL: QoL & psych status: followed up to 1 yr			Sx < 18 mo in duration	Unilateral LxSx radiculopathy
Porsman et al	1979		RCT		Dexamethasone								Duration of Sx <6 wk	Sciatica
Radcliff et al	2012		retrospective subgroup analyses of prospective RCT and observational study comparing surgery with conserv care in pts with herniated disc	TF, IL or caudal					Pts who crossed over surgery to no surgery within 3 mo of enrolment ESI 24/59 (41%) vs non ESI 37/304 (12%). Proportion of pts expressing preference for non surgical Rx ESI 139/453 (31%) vs non ESI 86/154 (56%)	ROM: Cross over to undergo non surgical or surgical Rx: 4 yrs			Sx >6 wks in duration	Radicular pain due to herniated disc
Radcliff et al	2013		retrospective subgroup analyses of prospective RCT and observational study comparing surgery with conserv care in pts with spinal stenosis	TF, IL or caudal					Pts who crossed over surgery to no surgery within 3 mo of enrolment ESI 7/21 (33%) vs non ESI 13/122 (11%). Pts who crossed over from non surgical to surgical group within 3 mo of enrolment ESI 28/48 (58%) vs non ESI 27/85 (32%). Proportion of pts expressing preference for non surgical Rx ESI 43/69 (62%) vs non ESI 68/207 (33%).	ROM: Cross over to undergo non surgical or surgical Rx: 4 yrs			Duration of Sx >6 wks	Lx spinal stenosis
Rados et al	2011		Prospective RCT	Transforaminal and Interlaminar	Methylprednisolone	lignocaine	VAS: 6 mo	Pain improvement TF 45.6% vs IL 43.5%	No diff in groups through 6 mo. Functional improvement TF 28.3% vs IL 25%	DISABILITY: ODI 6 MO		Fluoroscopy and contract dye used		Chronic unilateral Lx radiculopathy
Revel et al	1996		Active control, blind RCT	Caudal	prednisolone		Use of analgesics, pain relief: 6 mo	Pain relief and function at 6 mo 19% vs 45%	High injection volume > low injection volume for pain reduction at 18 mo. Proportion of pts who were relieved of their sciatica was signif higher in the forceful injection group (45%) than the control (19%)	ROM: Waddell's and Main's Functional score, Schober's test, Finger Floor distance, SLR QoL: satisfaction index				LxSx pain from failed back surgery syndrome and with epidural fibrosis
Ridley et al	1988		Double blind, placebo control, prospective cross over RCT	Interlaminar	methylprednisolone	none	Rest/walking VAS, proportion of improved pts: 1, 2 and 4 wks, 3 and 6 mo	Short term signif better in relief of pain for Rx group.	Within group improvement only in the Rx group. Rx > control group. % of pts reporting improvement after 2 d 90% Rx group and 19% control. Short term signif better in relief of pain for Rx group. However at 6 mo the benefit disappeared in 35% of pts, even though 65% of successfully treated subjects sustained improvement up to this time.	ROM: Physical exam: followed up to 6 mo			Rheumatology clinic pts, mixed duration (mean 24.4, SD 26.8 months) of Sx	Sciatic nerve compression

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Riew et al	2000 and 2006		Double blind, prospective RCT	Transforaminal	betamethasone	bupivacaine			26/55 pts chose to have surgery, with most being in control group (p< 0.004). A trend towards a decrease in neuro Sx from baseline to final follow up in non surgery opting pts, subgroup analyses provided without numbers of pts or magnitudes of effects. Pts needing surgery/total patients: Rx group 8/28 vs control 18/27. At the 13-28 mo followup, need for surgery was signif less in the Rx (29%) than control (67%). At 5 yr, diff became non signif due to lost follow ups (8 pts in Rx group).	ROM: Physical exam: 13-28 mo DISABILITY: Rx failure if pt opted to have surgery QoL: North American Spinal Society Qu: at least 1 yr post injection		Radiological confirmation of disc herniation or central/formai nal stenosis. Injections given under fluoroscopic guidance with contract injeciton for verificaiton of localization	Pt over 21 yrs of age, referred to 4 spinal surgeons, refractory to at least 6 wk of non operative Rx, prev operated pts included	Radicular Lx pain due to NR compression at two levels or less
Rocco et al	1989		Double blind, prospective RCT		triamcinolone	lignocaine, morphine	Pain relief, daily ordinal scale of pain, VAS, W-HYMPI: followed up to mo		Within group diff in VAS for 1-3 d in all groups. Btwn groups no signif diff in short or long term pain relief. Trend to improved long term pain relief in triamcinolone only group.		Study terminated early due to complications in the triamcinolone + morphine group		unknown duration of Sx	Post laminectomy
Rogers et al	1992		Double blind, prospective RCT	Interlaminar	methylprednisolone acetate	lignocaine	Analgesic consumption, verbal rating scale of pain (5 categories): 1 month		Within group diffs in both groups in all outcomes except analgesic consumption. Rx group > control. Rx group produced signif better results than control group.	ROM: Physical exam: followed up to 1 mo RTW: work status: followed up to 1 mo			unspecified source of pts, mixed (>1 to <240 mo) duration of Sx	Sciatica and limited SLR
Sayegh et al	2009		Double blind, prospective RCT	Caudal	Betamethasone	lignocaine			Within group diffs for both groups. Rx group > control. Pts needing surgery/total patients: Rx group 13/93 vs control 19/90	ROM: Physical exam: followed up to 1 yr DISABILITY: ODI: followed up to 1 yr			Sx > 1 mo in duration	LBP +/- radiculopathy
Schaufele et al	2006		Retrospective case-control	Transforaminal and Interlaminar	methylprednisolone			Pain improvement at 2-3 wks: TF 45.8% vs IL 19.2%	TF > IL, variable follow up period averaging 3 wks			Fluoroscopy and contrast dye used		LxSx radiculopathy from single level HNP
Serrao et al	1992		RCT		methylprednisolone		McGill pain qu, PLCQ, VAS, Verbal pain diary		No signif diff for pain and activity scores. Significantly less self administered medication in control.				1 wk - 6 mo duration of Sx	LBP +/- radiculopathy
Shakir et al	2013		Retrospective	Transforaminal	Dexamethasone OR triamcinolone	lignocaine			No diff in pain score reduction btwn groups					Cx radiculopathy
Smith et al	2010		Retrospective case-control	Transforaminal and Interlaminar	methylprednisolone	lignocaine		Pain improvement TF 30.5% vs IL 39.5%				Fluoroscopy and contract dye used		LxSx radiculopathy from spinal stenosis

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient	Pathology
Snoek et al	1977		Double blind, placebo control, prospective RCT	Interlaminar	methylprednisolone acetate	none	Analgesic consumption, VAS, proportion of improved pts: Conflict in Lit regarding follow up times: 8-20 mo vs 12-10 h and 48-24 h		Within group diffs for both groups. % of patients improved after 2 days with regard to: LBP 33% Rx group, 25% control; radiating pain 26% vs 13%; sciatic nerve stretch tolerance 36% vs 25% of controls; s/e improvement 67% vs 42% . No stat signif diff btwn groups. Pts needing surgery/total patients: Rx group 14/27 vs control 14/24	ROM: Physical exam and PT Ax DISABILITY: Rate of surgery			hosp neuro dept pts, mixed duration (12d to 36 wk) of Sx	Unilateral LxSx radiculopathy from herniated disc
Southern et al	2003		Retrospective	caudal	betamethasone	lignocaine		23% pain relief and function at 12 mo				Fluoroscopy used		
Stav et al	1993		Prospective RCT		methylprednisolone	lignocaine	Medication consumption, VAS: followed up to 1 yr		Within group diffs for both groups. Rx group > control. Small % improvement in control group (11%)	ROM: physical exam: followed up to 1 yr RTW: work status: followed up to 1 yr			Sx > 6 mo	Chronic Cxbrachialgia +/- radiculopathy
Swerdlow and Sayle-Creer	1970		RCT	Caudal or interlaminar	methylprednisolone	lignocaine	proportion of improved pts, unknown time point						hospital pts, mixed duration of Sx	Sciatica
Tafazal et al	2009		Double blind, prospective RCT	Transforaminal		bupivacaine	Leg/back VAS: 1 yr	Baseline C: VAS 76.4 (70–90); ODI 46.6 (34–58) T: VAS 72.7 (60–80); ODI 43.4 (32–54) 6 weeks (n = 141) C: VAS 57.8 (±3.4); ODI 38.1 (±2.1) T: VAS 46.6 (±3.3); ODI 34.6 (±2.1) VAS p = 0.12 ODI p = 0.93 3 months (n = 124) C (n = 59): VAS 53.8 ± 4.1; ODI 35.9 (±2.6) T (n = 65): VAS 48.2 (3.6); ODI 34.1 (2.3) VAS p = 0.74 ODI p = 0.69 1 year subsequent surgery/injection (n = 129)	Within group diffs for both groups. No btwn group diffs. Trend for Rx group to have better pain relief of leg pain only at 6 wk. Greater improvement in pts with herniated disc than stenosis at 3 mo. Pts needing surgery/total patients: Rx group 9/55 vs control 14/51	DISABILITY: ODI: 1 yr QoL: Lower back outcome scale, Modified somatic perception questionnaire and s/e improvement: 1 yr			Specialist Spinal clinic pts, chronic (>6 mo) duration of Sx	Unilat LxSx radiculopathy from herniated disc or spinal stenosis
Thomas et al	2003		Double blind RCT	Transforaminal and Interlaminar	Dexamethasone		Dallas pain qu, VAS: 6 mo		TF > IL up to 6 mo, TF group was superior to control on Schober, finger-to-floor, Dallas questionnaire at day 6. TF was superior to control on VAS at day 30. TF was superior to control on VAS, Roland Morris, and ¾ Dallas questionnaire subsections at 6 mo. Surgical rate was similar.	ROM: Schober, finger to floor distance, SLR, neuro evaluation: 6 mo QoL: Roland Morris questionnaire:6 mo		HNP on imaging	Sx < 3 mo	LxSx radiculopathy from HNP
Vad et al	2002		Prospective RCT	Transforaminal	betamethasone	lignocaine	NRS: conflict in lit re follow up: 12 mo vs 16 mo	Baseline C (n = 23): VAS 9.4 ± 1.3 T (n = 25): VAS 8.8 ± 1.2 Average f/u [16 months (12–21)] C: VAS 3.6 (±1.1) T: VAS 1.6 ± 0.8 p <0.05 favouring Rx group	Within group diffs for both groups. Rx group (84%) > control (48%) achieved a 'successful outcome', with max improvement reached at 6 wks (steroid) and 12 wks (control). Diffs were stat signif with p<0.05	ROM: Finger to floor distancephysical exam: conflict in lit: 12 mo vs 16 mo DISABILITY: RMQ: 12 mo QoL: Roland Morris LBP questionnaire		MRI with HNP with <50% intervertebral foraminal narrowing	Private practice affiliated with hosp, subacute and chronic (>6 wk to >6 mo) duration of Sx	LxSx radiculopathy due to HNP
Valat et al	2003		Double blind, prospective RCT		methylprednisolone acetate	none	VAS: days 5, 20 and 35		Within group improvements in both groups. Nonsignif trend to larger improvement in Rx group cf control at 20 d but not 35 d. Pts needing surgery/total patients: Rx group 1/42 vs control 2/42	ROM: rate of surgery, physical exam and functional capacity: followed up to 35 d DISABILITY: RMQ: days 5, 20 and 35			Pts from 5 Rheumatology Dept in Uni Hospitals, mixed (>15 d to <6 mo) duration of Sx	LxSx radiculopathy due to HNP

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient	Pathology
Wilson-MacDonald et al	2005		Double blind, prospective RCT	Interlaminar	Methylprednisolone	bupivacaine	Oxford Pain Scale		Improvement in pain within Rx group and btwn Rx and control up to 35 d (p< 0.0004). Within group diffs not noted for control group. No long term diffs btwn groups or decrease in rate of operation. Pts needing surgery/total patients: Rx group 18/44 vs control 15/48	ROM: % needing surgery: up to 2 yr DISABILITY: ODI: follwed up to 2 yr			conflict in lit re duration of Sx: 6 mo or more of Sx vs > 6 wks	LxSx Radiculopathy, including spinal stenosis pts
Yates	1978		RCT		triamcinolone	lignocaine	% improvement,		The 2 Rx groups showed better improvement in SLR than the two control groups. No data on pt level presented. Stat signif improvement in SLR with steroid Rx	ROM: SLR, Lx spine ROM				LBP and sciatica
Yousef et al	2010		Double blind, active control, prospective RCT	Caudal	steroid	LA	Opioid intake, VAS: 6 wks, 3, 6 and 12 mo	Signif improvement in short term p relief noted in both groups but signif long term p relief achieve only in group 2 pts	Pain relief and function 85% vs 80% at 3 no, 25% vs 75% at 6 mo, 5% vs 45% at 12 mo.	ROM: Lx spine ROM		fluoroscopy used		
Zahaar	1991			Caudal					No difference in global improvement cf placebo					Lx neurogenic syndromes

Appendix 8: Data extraction table for Randomised Controlled Trials

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient and Pathology
Candido et al	2013	USA	Prospective, Blinded RCT	Interlaminar (Midline and lateral parasagittal)	methylprednisolone acetate + lidocaine	+	11-point pain NRS; @ rest and during movement. 20 minutes before the procedure, day 1, 7, 14, 21, 28, 60, 120, 180, and 365.	Results of this study showed statistically and clinically significant pain relief in patients undergoing LESI by both the MIL and PIL approaches. Patients receiving LESI using the lateral parasagittal approach had statistically and clinically longer pain relief then patients receiving LESI via a midline approach	Lateral parasagittal interlaminar more effective than the midline interlaminar approach in targeting low back pain with unilateral radicular pain secondary to degenerative lumbar disc disease.	DISABILITY: ODI; 20 minutes before the procedure, day 1, 7, 14, 21, 28, 60, 120, 180, and 365.		Intermittent fluoroscopic	106 patients undergoing LESI for radicular low back pain
Chun & Park	2015	South Korea	Prospective, Active Control RCT	Transforaminal	Dexamethasone	-	VAS @ 4 weeks	The VAS of the high-volume injectate group (DL8) was significantly lower than that of the low-volume injectate group (DL3) (33.3 ± 25 vs. 46.3 ± 25 (p = 0.036)	8 mL was more effective 3mL for radicular pain TFESI; same does of dexamethasone.	DISABILITY: RMDQ @ 4 weeks			66 patients experiencing lumbar radicular pain with a pain intensity of ≥ 40/100 who had been diagnosed with a herniated nucleuspulposus or spinal stenosis after a series of physical, neurologic, and radiologic examinations.
Cohen et al	2015	USA	Multicentre RCT	Interlaminar & Transforaminal	depomethylprednisolone bupivacaine; gabapentin pills	-	Average leg pain score on a 0-10 NRS @ 1 & 3 months; reduction in analgesic drugs (>20%)	No sig dif @ 1 month: M=3.3(SD = 2.6), change from baseline M=−2.2 (SD 2.4) ESI vs. M=3.7 (SD 2.6) and M= −1.7 (SD 2.6) gabapentin (adjusted difference 0.4 points, 95% CI −0.3 to 1.2; =0.25. No sig dif @ 3 months: M=3.4 (SD 2.7) + M=−2.0 (SD 2.6) ESI vs M= 3.7 (SD 2.8) and M=−1.6 (SD 2.7) gabapentin (adjusted difference 0.3, 95% CI −0.5 to 1.2; P=0.43)	Although epidural steroid injection might provide greater benefit than gabapentin for some outcome measures, the differences are modest and are transient for most people	ROM: Worst leg pain over past week; average & worst back pain DISABILITY: ODI QoL: global perceived effect (measured as no non-rescue interventions + affirmative to following select statements)	The proportion of patients reporting one or more adverse events from the injection was 8% (n=6) in the epidural steroid injection group and 10% (n=7) in the gabapentin group (P=0.75)	MRI	145 people with lumbosacral radicular pain secondary to herniated disc or spinal stenosis for less than four years in duration and in whom leg pain is as severe or more severe than back pain
Colhado et al	2015	Brazil	Double Blind RCT	NR	methylprednisolone + levobupivacaine without epinephrine	-	Tourniquet test on upper limb; Magnitude estimate + line length pain scales; 10 cm VAS + 101-point NRS of least to most pain; verbal scale of 5 points; before, 30 min, 6, 12, 24 hours, & 15 days after		Pain evaluation was carried out before the block and 30 minutes, 6, 12, and 24 hours after it. After 30 minutes of epidural block, the levobupivacaine group presented more significant reaction of reduction pain than the saline group. The magnitude and line-length scales were evaluated every period of time, showing no significant differences, except in 12 and 24 hours after the first block. The exponential function to every evaluation ranged from 0.87 to 1.00.				60 patients with low back pain
Dennis et al	2015	Canada	Double Blind RCT	Transforaminal	Dexamethasone OR betamethasone	+	VAS @ baseline, 1, 3, 6 months	No dif on VAS (as con: (P=0.209) or cat: (>50% (P=0.058) or >75% (P=0.865)) or ODI (P=0.181) @ 3 months. @ 6 months ODI improvement @ sig. limit in favour for dexamethasone (P=0.050).	According to this study, pain relief and functional improvement are similar for both dexamethasone and betamethasone at 3 months. Considering its safety profile, dexamethasone could be considered as first choice for TFESI. However, given that the study was underpowered more research is needed to support a recommendation of systematically using dexamethasone in TFESI.	DISABILITY: ODI @ baseline, 1, 3, 6 months; complications	No serious complications were observed in either group	Fluoroscopy	56 Patients with debilitating radicular pain
Evansa et al	2015	Switzerland	RCT	Interlaminar (median or paramedian)	methylprednisolone acetate + lidocaine	+	VAS @ baseline, 1 + 3 months	VAS @ 1 month similar for Fluoroscopy (M=3.5, SD=2.0) vs. ultrasound (M=3.4, SD=1.9) (p=<0.05). VAS @ 3 month similar for Fluoroscopy (M=4.0, SD=2.3) vs. ultrasound (M=4.1, SD=2.0) (p=<0.05).	There was no significant difference between the two groups in mean procedure time, number of needle insertion attempts or needle passes. The mean pain intensity and degree of disability scores before the procedure, and at 1 and 3 months post-procedure, were similar in the two groups.	DISABILITY: ODI @ baseline, 1 + 3 months	No serious complications were observed in either group	Fluoroscopic OR ultrasound-assisted	112 adult patients with axial chronic lower back and extremity pain diagnosed with degenerative diseases of the spine

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient and Pathology
Friedly et al	2014	USA	Double Blind Multisite RCT	Interlaminar & Transforaminal	Lidocaine+/- triamcinolone, betamethasone, dexamethasone, or methylprednisolone	-	10 point NRS for intensity of leg pain	No sig dif between-groups for RMDQ score: (adjusted dif for glucocorticoid-lidocaine group and lidocaine-alone group, −1.0 points; 95% confidence interval [CI], −2.1 to 0.1; P = 0.07) or intensity of leg pain (adjusted difference, −0.2 points; 95% CI, −0.8 to 0.4; P = 0.48) @ 6 weeks	In the treatment of lumbar spinal stenosis, epidural injection of glucocorticoids plus lidocaine offered minimal or no short-term benefit as compared with epidural injection of lidocaine alone.	DISABILITY: RMDQ @ 6 weeks		Fluoroscopic	400 patients who had lumbar central spinal stenosis and moderate-to severe leg pain and disability
Ghai et al	2014	India	Double Blind, Active Control RCT	Parasagittal interlaminar OR Transforaminal	Methylprednisolone	-	VAS @ baseline 2 weeks, 1, 2, 3, 6, 9, and 12 months	Effective pain relief (≥ 50% pain relief from baseline on VAS) was observed in 76% (90% CI 60.6 – 88.5%) of patients in the TF group and 78% (90% CI 62.8 – 89.3%) of patients in the PIL (P=1.00) group at 3 months	Epidural injection delivered through the PIL approach is equivalent in achieving effective pain relief and functional improvement to the TF approach for the management of low back pain with lumbosacral radicular pain. The PIL approach can be considered a suitable alternative to the TF approach for its equivalent effectiveness, probable better safety profile, and technical ease.	DISABILITY: MODI @ baseline 2 weeks, 1, 2, 3, 6, 9, and 12 months	No serious complications were observed in either group	C-arm fluoroscopic	62 patients with a diagnosis of CLBP and unilateral lumbosacral radicular pain
Ghai et al	2015	India	Double Blind, Active Control RCT	Parasagittal interlaminar	Lidocaine OR lidocaine + methylprednisolone acetate	+	NRS @ baseline 2 weeks, 1, 2, 3, 6, 9, and 12 months	A sig. pain relief @ 3 months with mixed group [30 (86%, 90% CI 73% – 93%)] vs. anaesthetic alone [17 (50%, 90% CI 36% – 64%)] (p=0.02). Similar @ 6, 9, and 12 months.	Using a PIL approach and the addition of steroid to LA for EI may provide superior effectiveness in terms of extent and duration of pain relief for managing CLBP with unilateral LRP, even though, local anesthetic alone also was effective.	DISABILITY: MODI @ baseline 2 weeks, 1, 2, 3, 6, 9, and 12 months	No major complications were encountered in either group; however, intravascular spread of contrast was noted during 2 injections (one in each group) requiring relocation.	Fluoroscopic	69 patients with a diagnosis of CLBP
Ghai et al	2013	India	Double Blind RCT	Interlaminar (Midline or parasagittal)	Methylprednisolone	+	VAS @ baseline 15 days, 1, 2, 3, and 6 months	Pain relief higher with PIL (13/19 [68.4%]) vs MIL (3/18 [16.7%]) @ 6 months (relative risk, 4.10; 95% confidence interval, 1.40–12.05; P = 0.001) with the requirement of fewer total injections (29 vs 41 in MIL, P = 0.043).	Epidural steroid injection administered with the PIL approach was significantly more effective for pain relief and improvement in disability than the MIL approach for 6 months in the management of low back pain with lumbosacral radicular pain.	DISABILITY: MODI @ baseline 15 days, 1, 2, 3, and 6 months	No serious complications were observed in either group	Fluoroscopic	37 patients with low back pain associated with unilateral lumbosacral radicular pain
Habib et al	2013	Israel	Single Blind, prospective, RCT	NR	Methylprednisolone acetate @ 40mg or 80mg	-	VAS @ baseline, weeks 1,3, & 4	The rate of secondary adrenal insufficiency in Group 1 was 86%, 22%, and 17% of patients versus 53% (P = 0.024), 15% (P = 0.874), and 12% (P = 0.715) of Group 2 patients at weeks one, 3, and 4, respectively. About 62%, 56%, and 39% of Group 1 patients better clinical response (VAS) as opposed to 47% (P = 0362), 35% (P = 0.21), and 6% (P = 0.049) of Group 2 patients at weeks one, 3, and 4, respectively.	Epidural corticosteroid injection of methylprednisolone acetate in both groups was associated with very high rates of secondary adrenal insufficiency, but significantly more so in Group 1 at week one. This suppression was transient, with recovery of the gland in most patients noted over the ensuing weeks. An epidural corticosteroid injection of 80 mg had higher rates of favorable clinical response than a 40 mg injection, but significantly more so at week 4 only. This favorable response waned over a few weeks in both groups.	OTHER: Stimulation test of one µg of adrenocorticotropin hormone @ baseline, weeks 1,3, & 4		Computed tomographic	42 patients with low back pain due to radiculopathy
Hashemi et al	2015	Iran	Double Blind RCT	Interlaminar (Midline or parasagittal)	Triamcinolone + bupivacain	NR	NRS @ 2 weeks	EPR in 76.5% of patients in the PIL and 24.5% of patients in the MIL (p=0.001) @ 2 weeks. ODI sig. higher in the PIL (78%) compared to the MIL (26%) @ 2 week (p=0.002). Infiltration of the drug into the ventral epidural space was successfully achieved in 75% of cases in PIL but in only 25% of the cases in MIL	Parasagital epidural injection showed higher infiltration of the drug to the ventral epidural space compared to the midline approach. The higher infiltration of the ventral epidural space provides better improvement of clinical disability and pain in the parasagittal group.	DISABILITY: ODI @ 2 weeks		Fluoroscopy	56 patients with a diagnosis of low back pain (LBP) and unilateral lumbosacral radicular pains

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient and Pathology
Kennedy et al	2014	USA	Multicentre, Double Blind, Prospective, RCT	Transforaminal	Dexamethasone or triamcinolone	+	NRS @ baseline, 2 weeks, 3, & 6 months	A greater percentage of subjects receiving triamcinolone achieved ≥50% pain relief at 2 weeks than those receiving dexamethasone (43.2 vs 31.7%); however, this did not reach statistical significance and the 95% CIs were overlapping. This trend disappeared by 3 and 6-month follow-up, with greater than 70% of both groups achieving at least 50% pain reduction with no differences between groups.	Transforaminal epidural corticosteroid injections are an effective treatment for acute radicular pain due to disc herniation, and frequently only require 1 or 2 injections for symptomatic relief. Dexamethasone appears to possess reasonably similar effectiveness when compared with triamcinolone. However, the dexamethasone group received slightly more injections than the triamcinolone group to achieve the same outcomes.	DISABILITY: ODI @ baseline, 2 weeks, 3, & 6 months		Fluoroscopy	78 consecutive subjects with acute uni-level disc herniation resulting in unilateral radicular pain.
Koh et al	2015	South Korea	Double Blind, Active Control RCT	Transforaminal	Pulsed radiofrequency + triamcinolone acetonide	+	NRS @ baseline, 1, 2, and 3 months	The number of patients with successful treatment results was higher in the PRF group at 2 months (P = 0.032) and 3 months (P = 0.018). No significant differences were observed in terms of the secondary outcome variables between the 2 groups.	The TFEI provided significant short-term pain relief and PRF can be applied in conjunction with TFEI to achieve higher treatment efficacy compared with TFEI alone	DISABILITY: 10-item ODI @ baseline, 1, 2, and 3 month QoL: MQS + 7-point Likert scale GPE @ baseline, 1, 2, and 3 month	No serious adverse events were noted in either groups	Fluoroscopy	62 patients with Lumbosacral radicular pain lasting ≥12 weeks
Koh et al	2013	South Korea	Double Blind, Active Control RCT	Transforaminal	Triamcinolone + hypertonic saline or nomal saline	+	NRS @ baseline, 1, 2, 3, 4, and 6 months	In the hypertonic group, there was a statistically significant improvement in the mean pain score compared with the baseline pain score throughout the whole study period (P < 0.001, P = 0.004 at 6 months); in the control group, statistical significance was observed at one (P < 0.001), 2 (P < 0.001), 3 (P < 0.001), and 4 months (P < 0.001). Statistically significant difference between the 2 group at the 2- (P = 0.024) and 3-month (P = 0.012) follow-up.	Superior short-term pain relieving efficacy, but limited long-term effects of hypertonic saline, when added to TFEIs.	DISABILITY: ODI @ baseline, 1, 2, 3, 4, and 6 months	No reports of serious complications during injection, except one patient in the hypertonic group experienced burning pain during injection and declined to participate further in the study	Fluoroscopy	53 patients with chronic lumbosacral radiculopathy secondary to spinal stenosis lasting ≥ 12 weeks
Manchikanti et al	2015	USA	Double Blind, Active Control RCT	Interlaminar	Lidocaine OR Lidocaine, steroids, and betamethasone.	+	NRS @ baseline, 3, 6, 12, 18, and 24 months	Overall significant improvement was seen in 72% of patients in Group I (M=3.8 ± SD=1.8) and 73% of patients in Group II (M=3.6 ± SD=1.7) at the end of 24 months for NPR.	Lumbar interlaminar epidural injections of local anesthetic with or without steroids provide relief in a significant proportion of patients with lumbar central spinal stenosis	DISABILITY: ODI @ baseline, 3, 6, 12, 18, and 24 months RTW: Employment Status		Fluoroscopy	120 patients with central spinal stenosis with radicular pain of at least 6 months duration
Manchikanti et al (b)	2013	USA	Double Blind, Active Control RCT	Interlaminar	Lidocaine alone OR Lidocaine+ non-particulate betamethasone.	+	NRS + Opioid intake @ baseline, 3, 6, 12, 18, and 24 months	Overall significant improvement was seen in 73% of patients in Group I (M=3.9 ± SD=1.3) and 72% of patients in Group II (M=3.6 ± SD=1.4) at the end of 24 months for NPR.	Lumbar interlaminar epidural injections of local anesthetic with or without steroids are effective in patients with chronic axial low back pain of discogenic origin without facet joint pain, disc herniation, and/or radiculitis.	DISABILITY: ODI @ baseline, 3, 6, 12, 18, and 24 months RTW: Employment Status QoL: Weight changes @ baseline, 3, 6, 12, 18, and 24 months		Fluoroscopy	120 patients with lumbar axial or discogenic pain

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient and Pathology
Manchikanti et al (a)	2014	USA	Double Blind, Active Control RCT	Transforaminal	Lidocaine + sodium chloride OR Lidocaine + betamethasone	+	NRS + Opioid intake @ baseline, 3, 6, 12, 18, and 24 months	At 2 years there was significant improvement in all participants in 65% who received local anaesthetic alone (M= 4.0 ± SD=1.6) and 57% who received local anaesthetic and steroid (M= 4.2 ± SD=1.6)	Transforaminal epidural injections of local anesthetic with or without steroids might be an effective therapy for patients with disc herniation or radiculitis. The present evidence illustrates the lack of superiority of steroids compared with local anesthetic at 2-year follow-up.	DISABILITY: ODI @ baseline, 3, 6, 12, 18, and 24 months RTW: Employment Status QoL: Weight changes @ baseline, 3, 6, 12, 18, and 24 months		Fluoroscopy	120 patients with disc herniation and radiculitis.
Manchikanti et al (b)	2014	USA	RCT	Caudal and interlaminar	Non-particulate preservative-free betamethasone, & preservative free lidocaine.	+	NRS + Opioid intake @ baseline, 3, 6, 12, 18, and 24 months	The analysis found efficacy for both caudal and interlaminar approaches in managing chronic pain and disability from central spinal stenosis was demonstrated. In the patients responsive to treatment, those with at least 3 weeks of improvement with the first 2 procedures, 51% reported significant improvement with caudal epidural injections, whereas it was 84% with local anaesthetic only with interlaminar epidurals, 57% with caudal and 83% with lumbar interlaminar with local anaesthetic with steroid. The response rate was 38% with caudal and 72% with lumbar interlaminar with local anaesthetic only and 44% with caudal and 73% with lumbar interlaminar with local anaesthetic with steroid when all patients were considered. In the interlaminar approach, results were superior for pain relief and functional status with fewer nonresponsive patients compared to the caudal approach.	The results of this assessment showed significant improvement in patients suffering with chronic lumbar spinal stenosis with caudal and interlaminar epidural approaches with local anesthetic only, or with steroids in a long-term follow-up of up to 2 years, in contemporary interventional pain management setting, with the interlaminar approach providing significantly better results.	DISABILITY: ODI @ baseline, 3, 6, 12, 18, and 24 months RTW: Employment Status QoL: Weight changes @ baseline, 3, 6, 12, 18, and 24 months		Fluoroscopy	220 patients with lumbar central spinal stenosis
Manchikanti et al [c]	2013	USA	Double Blind, Active Control RCT	Interlaminar	Lidocaine alone OR Lidocaine+ non-particulate betamethasone.	+	NRS + Opioid intake @ baseline, 3, 6, 12 months	The proportion of patients with significant reduction in NRS (>50% reduction from baseline) with 67% in Group I (M=4.0 ± SD=1.6) and 85% in Group II (M=3.4 ± SD=1.2).	Lumbar interlaminar epidural injections of local anesthetic with or without steroids might be effective in patients with disc herniation or radiculitis, with potential superiority of steroids compared with local anesthetic alone at 1 year follow-up.	DISABILITY: ODI @ baseline, 3, 6, 12 months RTW: Employment Status QoLWeight changes @ baseline, 3, 6, 12 months		Fluoroscopy	120 patients with disc herniation and radiculitis.
Manchikanti et al [c]	2014	USA	Double Blind, Active Control RCT	Interlaminar	Lidocaine alone OR Lidocaine+ non-particulate betamethasone.	+	NRS + Opioid intake @ baseline, 3, 6, 12, 18, and 24 months	At 2 years there was significant improvement in all participants in 63% who received local anaesthetic alone (M= 4.1 ± SD=1.7) and 70% who received local anaesthetic and steroid (M= 3.7 ± SD=1.4)	Lumbar interlaminar epidural injections of local anesthetic with or without steroids is an effective modality, in patients with chronic function limiting low back and lower extremity pain secondary to disc herniation after failure of conservative modalities.	DISABILITY: ODI @ baseline, 3, 6, 12, 18, and 24 months RTW: Employment Status QoL: Weight changes @ baseline, 3, 6, 12, 18, and 24 months		Fluoroscopy	120 patients with disc herniation and radiculitis.

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient and Pathology
Park et al	2013	South Korea	Prospective, Single Blind, RCT	Caudal	Omnipaque + lidocaine + dexamethasone	+	Verbal NRS @ baseline, 2 weeks, & 12 weeks	No Sat Diff. in VNRS between fluoroscopic (M=2.64 ± SD= 0.49) and ultrasound (M=2.53 ± SD= 0.42)	The ultrasound approach with colour Doppler mode may avoid intravascular injection-induced complications. The results showed similar improvements in short-term pain relief, function, and patient satisfaction with both ultrasound and fluoroscopic guidance.	DISABILITY: ODI @ baseline, 2 weeks, & 12 weeks QoL: Patient Satisfaction 5-point scale		Fluoroscopic OR ultrasound-assisted	120 patients with unilateral radicular pain
Pirbudak et al	2015	Turkey	Prospective, Single Blind, RCT	Transforaminal	Triamcinolone acetonide +bupivacaine	NR	VAS @ baseline and 2 week follow up	VAS @ week 2; no stat. sig. diff. between group T (M=1.95 ± SD=1.27) and group TG (M=1.15 ± SD=1.08) (P > 0.05)	This study revealed that tramadol + gabapentin treatment was not superior to tramadol treatment	ROM: SLET @ baseline and 2 week follow up DISABILITY: ODI @ baseline and 2 week follow up		Fluoroscopy	40 patients with herniated disc-derived acute lumbar radicular pain
Rados et al	2013	Croatia	Prospective RCT	Interlaminar and Transforaminal	Methylprednisolone + lidocaine	+	PD-Q @ baseline, 2, 4, 6, 12, & 24 weeks.	The trend equation (y = –1.1393x + 25.269) for the TFESI shows a faster recovery than the ILESI (y = –0.8089x + 26.654). The statistically significant difference in the two groups is proved between the first and the sixth visit (ILESI, p = 0.014; TFESI, p = 0.001).	Steroids are efficient; besides alleviating the overall pain, they also reduce the neuropathic component in chronic lumbar radicular pain, whether it is distributed epidurally by the IL or TF approach.			Fluoroscopy	64 patients with unilateral chronic lumbar radicular pain.
Rahimzadeh et al	2014	Iran	Prospective RCT	Transforaminal	Hyaluronidase OR bupivacaine and triamcinolone		VAS @ baseline, 1, 2, 3, 4 weeks; Opioid intake @ baseline, 1, 2, 3, 4 weeks	Pain scores and total analgesic requirement were significantly lower in the HYL group at 2 and 4 weeks after blockade (p < 0.01).	We conclude that adding hyaluronidase to the epidural injectate was effective in the management of chronic low back pain in patients with failed back surgery syndrome demonstrated over a period of 4 weeks	ROM: NRS on movement or static @ baseline, 1, 2, 3, 4 weeks		Fluoroscopy	33 patients with FBSS
Shin et al	2015	South Korea	RCT	Transforaminal	Triamcinolone + Saline OR just Saline		VAS (for back, leg, & back + leg) @ 1, 4, & 26 weeks + mean hospital stay	A significant decrease in visual analogue scale (VAS) scores (back, leg) and Oswestry Disability Index at all examinations (P < 0.01).	Epidural steroids after a PELD reduce back pain and leg pain while improving functional outcomes in the short-term postsurgery period.	DISABILITY: ODI (for back, leg, & back + leg) @ 1, 4, & 26 weeks RTW: Mean return to work	No complications or adverse effects of the intervention were reported		100 patients who had undergone a PELD because of a herniated lumbar disc
Sinofsky et al	2014	USA	Prospective, Double Blind RCT	Interlaminar	Methylprednisolone	-	Self-rated percentage of pain + daily analgesic consumption.	The concordant group achieved a significant decrease in self-reported pain as compared to the discordant group at 2-week follow-up (61%, t = 2.45, P < 0.01). There were also significantly more patients in the concordant group who reported 75% pain reduction as compared to the discordant group (X = 6.44, df(1), P < 0.05).	The concordant group demonstrated significantly higher pain reduction as compared to the discordant group. There were no significant differences between the 2 groups in terms of improved function or reduced analgesic requirements. Concordant provocation during interlaminar epidural injection may be a predictor of outcome.	ROM: Self-rated changes in functional activity		Fluoroscopy	48 patients with radicular lumbosacral pain.

Author	Year	Country	Study design	Approach	Steroid	+/- Local Anaesthetic	Outcome Measure	Results	Findings	FUNCTIONAL OUTCOMES: Range of Movement (ROM), Disability, Return To Work (RTW), Quality of Life (QoL), OR other	Safety and Risk	Imaging	Patient and Pathology
Spijker-Huiges et al (a)	2014	The Netherlands	Pragmatic RCT	Segmental epidural steroid injection	Triamcinolone	NR	NRS @ 2, 4, 6, 13, 26, and 52 weeks	Mean NRS total pain (SD) for intervention (M=7.7, SD=1.2) vs control (M=6.9, SD=1.7). There was no significant interaction between the groups in the follow-up period.	The effect on pain and disability of epidural steroids in lumbosacral radicular syndrome is small but significant, and at lower costs with no reported complications or adverse effects. Segmental epidural steroid injections could be considered by policy makers as an additional treatment option.	DISABILITY: RMDQ @ 2, 4, 6, 13, 26, and 52 weeks QoL: Health related QOL and cost questionnaire	No complications or adverse effects of the intervention were reported		73 patients with acute radiculopathy
Spijker-Huiges et al	2015	The Netherlands	Pragmatic RCT	Segmental epidural steroid injection	Triamcinolone	NR	NRS @ 4, 13, 26, and 52 weeks; Medical Outcomes Study 36- Item Short-Form Health Survey pain section	Both groups experienced a significant increase in quality of life in (especially) the physical domains of the Medical Outcomes Study 36-Item Short-Form Health Survey. Within the Medical Outcomes Study with Pain sections, SESI at 52 weeks corrected mean SF-36 scores (95% CI) 49.7 (45.8-53.6) vs. UC corrected mean SF-36 scores (95% CI) 51.2 (47.2-55.2) with a difference of 1.5 (-4.1 to 7.1).	Although the beneficial effects of SESIs are small and the natural course of LRS is predominantly favorable, we think decision makers can consider implementing SESIs in daily practice with the purpose of saving resources. Caution must be taken, and further research should be directed at identifying patient subgroups who might benefit from SESIs, with additional focus on (costs of) complications and adverse effects.	DISABILITY: RMDQ @ 4, 13, 26, and 52 weeks QoL: Medical Outcomes Study 36- Item Short-Form Health Survey	Focus on (costs of) complications		50 patients in the acute phase of lumbosacral radicular syndrome
Spijker-Huiges et al (b)	2014	The Netherlands	Pragmatic RCT	Segmental epidural steroid injection - Translaminar	Triamcinolone	-	NRS @ 2, 4, 6, 13, 26, and 52 weeks	At initial measurement the intervention group (M=7.7, SD =1.2), experienced significantly less symptoms than the control group (M=6.9, SD=1.7) for the NRS back pain score (p = 0.0115) and this remained consistent throughout follow-up.	We found a small, statistically significant, but not clinically relevant positive effect of SESIs on back pain, impairment and disability in acute LRS. We do not recommend implementing SESIs as an additional regular treatment option in general practice.	RMDQ @ 2, 4, 6, 13, 26, and 52 weeks QoL: NRS of self-perceived impairment @ 2, 4, 6, 13, 26, and 52 weeks	No complications or adverse effects of the intervention were reported.		63 patients in the acute phase of lumbosacral radicular syndrome
Turan et al	2015	USA	RCT	NR	NR	+	LANSS pain scale + VAS	The change in Verbal Analogue Scale score did not differ in patients given N2O (mean [SD], −1.6 [3.0] cm) and O2 (−1.2 [2.6] cm), with difference −0.13 (95% confidence interval: -1.43, 1.17), N2O - O2 P=0.84.	N_2O administration did not improve pain or psychological or physical aspects of health-related quality of life. N_2O does not appear to be an effective treatment for chronic neuropathic back pain.	DISABILITY: MODI QoL: 12-Item Short Form Health Survey (SF-12) questionnaire for functional health and well-being		Fluoroscopy	78 patients with recurrent low back pain scheduled for epidural steroid blocks
Zhang et al	2013	China	Prospective RCT	Intradiscal and intraforaminal	Oxygen-ozone + Betamethasone	+	JOA Score + VAS @ baseline, 3 weeks, 6 & 12 months.	Satisfactory clinical outcomes were obtained in both groups. The reduction of VAS score from baseline to the end of the study was 7.68 to 2.17 and 7.49 to 2.23 in group A and group B respectively and there were remarkable improvements of mean JOA score and recovery rate in every follow-up time in both groups. Furthermore, in 3 weeks follow-up the JOA recovery rate of group B is higher than that of group A, which there was significant different, but there were no significant differences between two groups in 6 and 12 months.	In our study, oxygen-ozone nucleolysis provides excellent pain relief inmost herniated disc patients who failed to respond to conservative therapy. And there was no significant statistical difference between treatment of injection of oxygen-ozone combined with steroid and ozone only in the 6 and 12 months follow-up. Therefore, O2–O3 seems to play a role in pain relief, and we suggest the administration of the O2–O3 mixture as a first-choice treatment before recourse to surgery or when surgery is not possible and the addition of epidural steroid infiltration is not required.		There were no complications	Radiographic	172 consecutive adult patients with low back pain and radicular pain

Appendix 9 - Data extraction for cohort studies examining adverse events

Author	Year	Country	Population	# Injections	Injectate	Approach	Prevalence of Adverse Events	Imaging	Conclusions
Plastaras et al.	2015	United States	Persons (19-89yrs) attending a multiphysician academic Physical Medicine and Rehabilitation clinic between 2004 and 2007	1295	betamethasone or triamcinolone following 1% lidocaine anaesthetic test dose	Lumbosacral transforaminal ESI using the subpedicular transforaminal technique	9.2% experienced immediate (from time of procedure to discharge from clinic visit) adverse events and 20.0% experienced delayed adverse events (24 to 72 hours following procedure). Two immediate adverse events occurred in >1% of procedures: vasocagal episode (4.2%) and intravascular flow that interrupted the procedure (1.7%). Delayed events occuring in >1% of procedures included: pain exacerbations (5.0%), injection site soreness (3.9%), headache (3.9%), facial flushing/sweating (1.8%) and insomnia (1.6%). Five patients required emergency/hospitalisation for low back pain without leg symptoms (n=3), self-limited dizziness - with cardiac history (n=1) and gastroenteritis (n=1).	Fluroscopy	Fluoroscopically guided lumbosacral TFESI is associated with a similar rate of minor AEs both immediately and 24 to 72 hours after procedure that are typical of other axial corticosteroid injections. Permanent AEs were not found in this sample
Correa et al.	2015	Colombia	Persons with chronic radicular pain receiving treatment between July 2010 and December 2011	254	Methylprednisolone	Transforaminal lumbar (54.33%), interlaminar lumbar (17.72%), caudal (15.75%), and	One complication was reported for the lumbar transforaminal injection	Fluroscopy	Epidural methylprednisolone is a safe therapeutic option for the treatment of radicular pain

Author	Year	Country	Population	# Injections	Injectate	Approach	Prevalence of Adverse Events	Imaging	Conclusions
						Interlaminar cervical (12.20%)			
Schneider et al.	2014	United States	Persons undergoing TFESI at a single acadaemic medical centre between March 2004 and January 2009	4482	Not reported	Transforaminal epidural injection (with or without trainee)	Incidence of vasovagal reaction = 2.7% for physician only, 4.9% for trainees	Fluroscopy	Vasovagal reactions have an overall occurrence rate of 3.5% in TFESIs. Although there is a potential for bias, this study does appear to demonstrate that when a trainee is involved in a TFESI, there is nearly twice the rate of vasovagal reaction
Qureshi et al.	2013	Pakistan	Persons undergoing ESI at an interventional pain clinic from July 2009 to November 2012	386	Methylprednisolone acetate with 1% lidocaine	Lumbar (361), Cervical (20), and caudal (5) - using blind approach	For lumbar interlaminar ESI - immediate rections: vasovagal reaction (3.32%), intravascular entry (0.83%), flushing (2.21%), headache (1.1%), transient nerve irritation (0.27%), dural puncture (0.83%), cardiac arrest (0.27%) - delayed - PDPH (0.55% - abbreviation not expanded), bruises (0.83%)	Blind approach	Blind interlaminar epidural steroid injections are safe when performed with proper technique, monitoring and under recommended sterile precautions. The minor complications are common with this procedure but major complications are rare
Kainer et al.	2012	United States	All patients who had undergone epidural or paraspinal glucocorticoid injection procedures at a single	124	Methylprednisolone	Lumbar epidural (110), cervical epidural (12), sacroiliac-	RR of CNS fungal infection for translaminar ESI = 2.5 (95%CI: 1.3 to 4.8) and for use of contaminated methylprednisolone = 6.2 (95%CI: 2.6	Not reported	Epidural glucocorticoid injections can lead to localized infection, and fungal pathogens can invade the dura, leading to

Author	Year	Country	Population	# Injections	Injectate	Approach	Prevalence of Adverse Events	Imaging	Conclusions
			clinic since July 1, 2012, to assess for risk factors for infection. Outcomes included fungal meningitis or nonbacterial and nonviral meningitis of subacute onset, posterior circulation stroke when no cerebrospinal fluid was obtained, or spinal or paraspinal osteomyelitis or epidural abscess at the site of injection			joint (1), other (1)	to 14.5)		meningitis and, in some patients, invasion of the posterior circulation vasculature leading to stroke, haemorrhage, or both
Kang et al.	2012	South Korea	Post menopausal women with lower back pain receiving either medications without ESI or ESI > 4 times with a cumulative triamcinolone dose of >120mg	42 cases	Triamcinolone with 0.5% lidocaine	Lower lumbar	No significant difference in BMD between or within groups from baseline to one-year after treatment.	Not reported	ESI treatments using less than a total of 200mg triamcinolone had no significant effeect on BMD. However, the decrease in BMD of postmenopausal women who received more than 200mg of triamcinolone in one year indicates that ESI involving doses > 200mg/year should be avoided
Manchikanti et al.	2012	United States	Persons undergoing epidural procedures from May 2008 to	1450 lumbar interlaminar epidurals,	Not reported	Caudal epidurals (39%, cervival	**Lumbar interlaminar** = 0.5% Intravascular entry, 0.5% return of blood, 0.8% profuse bleeding, 0.1%	Fluroscopy	Major complications are rare and minor side effects

Author	Year	Country	Population	# Injections	Injectate	Approach	Prevalence of Adverse Events	Imaging	Conclusions
			December 2009 at a specialty referral centre private pain management practice	3985 caudal epidurals, and 1310 transforaminal epidurals		interlaminar epidurals (23%), lumbar interlaminar epidurals (14%), lumber transforaminal epidurals, percutaneous adhesiolysis (8%), thoracic interlaminar epidural	local haematoma, 0.28% transient nerve root irritation, 0.8% dural puncture, 0.07% postlumbar puncture headache, 0.13% facial flushing - **lumbar transforaminal** = 7.9% Intravascular entry, 3.7% return of blood, 0.2% profuse bleeding, 0.2% local haematoma, 0.4% bruising, 0.08% vasovagal reaction, 4.6% transient nerve root irritation, 0.61% jacet joint entry, 0.08% disc entry, 0.15% facial flushing - **caudal epidural** = 3.1% intravascular entry, 0.7% return of blood, 0.3% profuse bleeding, 0.1% local haematoma, 0.2% bruising		are common
Yi et al.	2012	South Korea	Post menopausal women with lower back pain treated with ESI at a single pain mangement centre between Januuary 2009 and December 2011, divided into groups of those with and without fractures	352 cases	Triamcinolone	Not reported	No significant correlation between number of ESIs and BMD or fracture	Not reported	ESIs were not associated with low BMD or fracture
Chang et al.	2011	United States	Persons undergoing epidural procedures from May 2008 to December 2009 at a specialty referral centre	751	Betamethasone acetate (91.5% of cases) and methyl prednisolone	Lumbar region	None	CT-imaging	The use of air to localize the epidural space in CT-guided ESIs has a high success rate and a very low

Author	Year	Country	Population	# Injections	Injectate	Approach	Prevalence of Adverse Events	Imaging	Conclusions
			private pain management practice		(4.7% of cases)				rate of complications
Karaman et al.	2011	Turkey	Persons with radiculopathy not responding to first line physiotherapy and medical care, referred to a single hospital-based pain clinic from November 2003 to December 2008	1305	Triamcinolone with 0.25% bupivacaine	Transforaminal lumbar	Vascular penetration 7.4%, no major complications, minor complications: vasovagal reaction 8.7% and flushing 0.9%	Fluroscopy	The frequency of major complications is pretty rare in transforaminal lumbar epidural steroid injections in expert hands and in the conditions in which safety precautions are taken
Candido et al.	2010	United States	Persons underoing LESI/TFESI at a single academic treatment centre between July 2004 and June 2007	2412 transforaminal and 4723 lumbar	Not reported	Transforaminal and interlaminar lumbar	6 for transforaminal ESI and 1 for lumbar ESI	Fluroscopy	Our data demonstrate that intradiscal injection is a rare complication during LESI, but occurs more frequently with TFESI than with LESI
Trentman et al.	2009	United States	Persons undergoing translaminar cervical ESI, matched with those undergoing lumbar ESI, performed between December 1996 and May 2005. Patients who had undergoine previous ESIs were excluded from the study	249	Not reported	Cervical or lumbar ESI	1% in lumbar compared with 8% in cervical ($p<0.001$, 95%CI: 0.04 to 0.12). Multiple logistic regression modeling indicated that the characteristics that were the most strongly associated with the type of procedure were foraminal stenosis, spinal stenosis, use of the sitting position, use of contrast, and use of local anesthesia. The adjusted odds of cervical injection were 14 times higher among patients with vasovagal reaction than among	Fluroscopy (85% for lumbar and 71% for cervical) and Contrast media (20% for lumbar and 39% for cervical)	The risk of vasovagal reaction is significantly higher for cervical translaminar epidural steroid injections than for lumbar injections

Author	Year	Country	Population	# Injections	Injectate	Approach	Prevalence of Adverse Events	Imaging	Conclusions
							patients without vasovagal reaction (P = 0.001, 95%CI: 2.7 to 68). Incidence of adverse effects for lumbar ESIs include blood (1% of procedures), dural puncture (1%), localised pain (10%), paresthesia (13%), and postoperative problems (2%)		
McGrath et al.	2007	United States	Persons attending a musculoskeletal physiatry practice between July 2002 and June 2009	4265	Not reported	Lumbar transforaminal (3964), lumbar interlaminar (123), cervical interlaminar (161), and caudal (17)	No major complications. Overall rate of minor complications for TL = 0.021% per injection (IL=0.06%). Minor complications included: increased pain (TF = 0.011% / IL = 0.021%), pain at injection site (TF = 0.0.0023% / IL = 0.018%), persistent numbness (TF = 0.0015% / IL = 0%), and 'other' (TF = 0.0068% / IL = 0.021%). Complications less common in transforaminal injections (2.1%) than in interlaminar (6.0%) (95%CI: 1.7% to 2.6%)	Fluroscopy and contrast media	These results suggest that ESIs are a safe and well-tolerated intervention for cervical or lumbar pain and radiculopathy
Stalcup et al.	2006	United States	Persons undergoing selective lumbar nerve blocks (divided into those receiving single or multiple ESIs) between April 1997 to May 2002, having failed to receive benefit from conventional	1777 (total), of which 1232 were cases receiving single injections	Betamethasone or depomedrol with 0.25% bupivacaine	Selective lumbar nerve blocks (not specified)	Of 1777 injections, 98 resulted in minor complications: Leg weakness / light-headed (N=54), pain increased (N=41,), other complications (N=3). Non-significant difference on complication incidence for needle tip position (p=0.48)	Fluroscopy	SLNBs performed with fluoroscopic guidance have a low incidence of complications, all of which were minor. The specific needle-tip position within or adjacent to the lumbar neural foramen does not appear to be associated with the incidence of

Author	Year	Country	Population	# Injections	Injectate	Approach	Prevalence of Adverse Events	Imaging	Conclusions
			treatments						complications
Fitzgibbon et al.	2004	United States	Claims (from the American Society of Anesthesiologists Closed Claims Project) related to chronic pain, recorded between 1970 and 1999	284 chronic pain management claims	Not reported	Epidural steroidal injection (not specified) + agents (anaesthetic and/or opioid)	ESIs accounted for 40% of all chronic pain management claims. For these claims resulting from ESI - 25% resulted in nerve injury, 21% in infections, 8% in death/brain damage, 18% in headache, 9% in increased pain/no relief, 4% for retained catheter, and 16% for 'other'	Not reported	Brain damage and death were associated with epidural steroid injection only when opioids or local anesthetics were included
Horlocker et al.	2002	United States	Persons receiving ESIs at ambulatory pain treatment centres - considered by NSAID status	1214	Various	ESIs - 80% in lumbar region	Blood noted during needle or catheter placement in 5.2% patients (minor haemorrhagic complication). No major complications reported. Increased age, needle gauge, needle approach, needle insertion at multiple interspaces, number of needle passes, volume of injectant, and accidental dural puncture were significant risk factors for minor hemorrhagic complications. 42 patients with new neurologic symptoms or worsening of preexisting complaints that persisted more than 24 h after injection. Twenty-seven patients reported a new (or exacerbated) sensory deficit, 12 patients reported weakness, and nine patients complained of new or	Fluroscopy - 28%, contrast media - 24%	ESIs are safe in patients receiving aspirin-like antiplatelet medications. However, pain clinic personnel should be aware that minor worsening of neurologic function may occur after ESI and must be differentiated from aetiologies requiring intervention

Author	Year	Country	Population	# Injections	Injectate	Approach	Prevalence of Adverse Events	Imaging	Conclusions
							worsened pain		
Botwin et al.	2001	United States	Persons presenting with radiculopathy and receiving caudal ESI at single treatment centre	257	Betamethasone acetate or triamcinolone acetonide with 0.5% lidocaine	Caudal	The incidence of minor complications was 15.6% per injection. Insomnia on night following injection (4.7%), transient non-positional headaches resolving within 24hrs (3.5%), facial flushing (2.3%), vasovagal reactions (0.8%), nausea (0.8%), increased leg pain (0.4%)	Fluroscopy	No major complications occurred. The incidence of minor complications was 15.6% per injection. All reactions resolved without morbidity and no patient required hospitalization
Botwin et al.	2001b	United States	Radiological technicians performing fluroscopically guided caudal ESIs	100	Betamethasone acetate with 0.5% lidocaine	Caudal	The average/cumulative exposure per procedure was 4.10/410 mREM at the “ring” badge, 2.47/247 mREM at the “glasses” badge, 3.98 /398 mREM at the “outside apron” badge and 0.15/15 mREM at the “inside” apron; no radiation was detectable at the “outside room” control badge	Fluroscopy	Average radiation exposure for technicians during these procedures was below the limit of detectability
Botwin et al.	2000	United States	Persons presenting to a multidisciplinary spine care practice with complaints of lower back and radicular pain dur to herniated nucleus pulposus (HNP) or lumbar spinal stenosis (LSS)	322	Betamethasone acetate or methylprednisolone plus 1% lidocaine	Transforaminal	No major complications noted. Incidence of minor complications = 9.6% per injection. Minor complications include: transient nonpositional headaches resolving within 24 hours (3.1%), increased back pain (2.4%), increased leg pain (0.6%), facial flushing (1.2%), vasovagal reaction (0.3%), increased BGL in person receiving insulin therapy for diabetes (0.3%) and	Fluroscopy and contrast media	There were no major complications. The incidence of minor complications was 9.6% per injection. All reactions resolved without morbidity, and no patient required hospitalization

Author	Year	Country	Population	# Injections	Injectate	Approach	Prevalence of Adverse Events	Imaging	Conclusions
							intraoperative hypertension (0.3%)		
Furman et al.	2000	United States	Persons with either lumbar disc pathology or spinal stenosis receiving treatment with TFESI from March 1998 to July 1999 at a single treatment clinic	761	Not reported	Lumbar (583) and S1 transforaminal (178)	Overall rate of intravascular injection = 11.2% (21.3% for TF and 8.1% for L - p<0.001)	Fluroscopy and contrast media	There is a high incidence of intravascular injections in transforaminal ESIs. Fluoroscopically guided procedures without contrast confirmation are instilling medications intravascularly and therefore not into the desired epidural location. This finding confirms the need for not only fluoroscopic guidance but also contrast injection instillation in lumbosacral transforaminal ESIs
Johnson et al.	1999	United States	Persons with back or neck pain with or without radiculopathy, attending a outpatient clinic over a 5.5yr period	5334	Not reported	lumbar (4780), cervical (669), or thoracic (40)	Hypotensive episode (N=1), dorsal epidural haematoma (N=1), vasovagal response (N=1), tachycardia (N=1)	Contrast media	Epidurography followed by therapeutic epidural steroid injection (with or without a local anesthetic) is a safe radiologic procedure that is easily performed by skilled proceduralists on an outpatient basis without intravenous sedation and cardiac monitoring