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Nonoperative treatment for lumbar spinal stenosis with neurogenic claudication. An updated systematic review.

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ABSTRACT

Objectives: Neurogenic claudication due to lumbar spinal stenosis (LSS) is a growing public health problem that can significantly impact quality of life in older adults. We aimed to update our previous Cochrane review (2013) to determine the effectiveness of nonoperative treatment of LSS with neurogenic claudication.

Design: A systematic review was conducted. We updated our search in CENTRAL, MEDLINE, EMBASE, CINAHL, and ICL databases from February 2012 to September 2020 for randomized controlled trials where at least 1 arm provided data on nonoperative treatment.

Outcome measures: Outcomes included measures of pain, function, health related quality of life and adverse events.

Results: Of 13,817 citations screened, 156 were assessed and 23 new trials were identified and added to the original 21 trials. A total of 3,792 participants with neurogenic claudication randomized to 60 different comparison groups were assessed.

There is moderate quality evidence from 3 trials that: Manual therapy and exercise provides superior and clinically important short-term improvement in symptoms and function compared to medical care or community-based group exercise; Manual therapy, education and exercise delivered using a cognitive-behavioural approach, demonstrates superior and clinically important improvements in walking distance in the immediate to long-term compared to self-directed home exercises; Glucocorticoid plus lidocaine injection is more effective than lidocaine alone in improving statistical, but not clinically important, improvements in pain and function in the short-term.

The remaining 20 new trials demonstrated low or very low-quality evidence for all comparisons and outcomes, similar to the findings of our original review.

Conclusions: There is moderate quality evidence that a multimodal approach which includes manual therapy and exercise, with or without education is an effective treatment, and that epidural steroids are not effective for the management of LSS with neurogenic claudication. All other nonoperative interventions provided insufficient quality evidence to make conclusions on their effectiveness.

This systematic review was registered with PROSPERO registration number CRD42020191860.

ARTICLE SUMMARY

Strengths and limitations of this study

- This systematic review included a wide range of nonoperative interventions commonly used in clinical practice.
- This review used consistent inclusion and exclusion criteria for neurogenic claudication, which included the corroboration of a diagnosis of lumbar spinal stenosis with imaging.
- This review used rigorous methods recommended by the Cochrane Back and Neck Pain Review Group including the use of Grading of Recommendations, Assessment, Development and Evaluation (GRADE) to synthesize and summarize the quality of the evidence.
- Only English studies were included in this review.

- Most studies had small samples sizes with heterogeneity in interventions tested, limiting ability to pool data.

Key words: neurogenic claudication, lumbar spinal stenosis, systematic review, nonoperative treatment, elderly

INTRODUCTION

Lumbar spinal stenosis (LSS) causing neurogenic claudication is a highly prevalent and rapidly growing public health problem among older adults (1). It is characterized by bilateral or unilateral buttock pain and/or lower extremity discomfort, pain, weakness, or heaviness precipitated by walking and prolonged standing and relieved by stooping forward and sitting (2, 3). The underlying etiology is usually age-related osteoarthritic changes to lumbar intervertebral discs, facets joints and ligaments leading to narrowing of the central and/or lateral spinal canals and compression and/or ischemia of the spinal nerves (2, 4).

Limited walking ability is the dominant impairment in neurogenic claudication and the most common reason for seeking care (5). Limited walking ability due to LSS is associated with a significant decline in functional status, quality of life and independence in this population (2, 5).

Although lumbar spinal stenosis is the most common reason for spine surgery in older adults, most people with neurogenic claudication receive nonoperative care (6). A course of nonoperative care is also recommended prior to receiving surgical intervention (7). However, what constitutes effective nonoperative care remains unknown. In 2013 we published a Cochrane review evaluating

nonoperative treatment for LSS causing neurogenic claudication (8, 9). This review identified 21 randomized controlled trials assessing a variety of nonoperative treatments. However, the quality of the evidence was deemed low or very low and therefore no conclusions could be made on the effectiveness of nonoperative treatment for neurogenic claudication. The purpose of this study is to update this systematic review and the evidence for nonoperative treatments for neurogenic claudication. Our specific research question was: What nonoperative interventions are effective in improving outcomes in patients with neurogenic claudication due to lumbar spinal stenosis?

METHODS

This systematic review was registered with PROSPERO registration number CRD42020191860 and was conducted and reported according to the PRISMA guidelines (10).

Ethics Approval Statement

Ethics approval was not required for conducting this systematic review.

Patient and Public Involvement Statement

Patients or the public were not involved in the conduct of this systematic review.

Population, Interventions, Comparison and Outcomes (PICO Criteria)

The population of interest was individuals with imaging confirmed LSS (central or foraminal, with or without spondylolisthesis) and neurogenic claudication. Neurogenic claudication is a clinical diagnosis and was defined as buttock or leg pain and/or aching, numbness, tingling, weakness, or fatigue with or without back pain, precipitated by standing or walking. There were no age restrictions. The interventions of interest included all nonoperative treatments and the comparison was any treatment including surgery. Outcomes included at least one of the following measures: walking ability, pain intensity, physical function, quality of life, or global improvement.

Search and Study Selection

We replicated and updated our original electronic database search (from 1966 to January 2011) to September 2020. The search was performed by an experienced librarian in CENTRAL (Cochrane Library 2011 issue1), Medline, EMBASE, CINAHL and Index to Chiropractic Literature. The terms “spinal stenosis,” “lumbar spinal stenosis,” “neurogenic claudication,” “lumbar radicular pain,” "cauda equina," and “spondylosis” were combined with a highly sensitive search strategy to identify randomized controlled trials (RCTs).

Studies were included if they were RCTs published in peer reviewed English journals, at least one arm of the trial provided data on effectiveness of a nonoperative treatment and at least 80% of subjects had neurogenic claudication with imaging confirmed LSS. Studies evaluating subjects with radiculopathy caused by disc herniations without neurogenic claudication were excluded.

Studies with mixed populations were only included if separate data for subjects with neurogenic claudication due to lumbar spinal stenosis were provided.

Two pairs of reviewers independently screened all titles and abstracts identified by the search strategy. Full text of articles deemed to be potentially relevant were independently assessed by two reviewers who made the final decision for inclusion. A third reviewer was consulted if consensus was not reached.

Risk of Bias Assessment and Data Analysis

Two reviewers independently assessed methodological risk of bias and performed data extraction. Safety data (intervention side effects and/or complications) when available were also collected. Risk of bias was assessed using the 12-item criteria recommended by the Cochrane Back Review Group (11). Discrepancies in risk of bias scoring and data extraction were discussed during a consensus meeting. Reviewers who were authors of any of the included studies were recused from performing risk of bias assessment, data extraction, data analysis or synthesis of their own studies.

Low risk of bias was defined as fulfilling 6 or more of the 12 criteria including clearly described and appropriate randomization (Item A), and allocation concealment (Item B), and with no severe flaws. A severe flaw was defined *a priori* as a serious methodological deficiency not captured by the 12-item criteria that significantly increases the risk of bias such as very high dropout or cross-over rates and sample sizes less than 30 subjects per treatment arm.

For each comparison, outcomes were analyzed according to these follow-up time periods: immediate (up to one week following the intervention); short-term (between one week and three months); intermediate (between three months and one year) and; long-term (one year or longer). Outcome data were pooled, and meta-analyses were performed when trials were judged to be sufficiently homogeneous, both clinically and statistically.

Rehabilitation therapy was defined as treatment that utilized any combination of education, exercise instruction, manual therapy, heat and cold applications, electrotherapy, other physical therapy modalities, orthosis, and other assistive devices. Multimodal treatment included various combinations of rehabilitation therapy treatments, oral and other mediations, and spinal injections, but not surgery.

Data Synthesis

The quality of the evidence for each outcome and for each comparison was evaluated using GRADE (Grades of Recommendations, Assessment, Development and Evaluation (12, 13) Overall quality of the evidence was based on performance against five domains: 1)

risk of bias; 2) consistency of findings; 3) directness of comparisons; 4) precision of estimates; and 5) other considerations such as selective reporting.

The quality of the evidence starts at high when there are consistent findings among at least 75% of RCTs with low risk of bias and consistent, direct, and precise data and with no known or suspected publication bias. It downgrades a level for each domain not met. Treatment effects between comparators (more effective, less effective or no difference) were based on statistically significant and clinically important differences in outcomes.

High quality evidence - all five domains are met; further research is very unlikely to change the confidence in the estimate of effect.

Moderate quality evidence - one of the domains is not met; further research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate.

Low quality evidence - two domains are not met; further research is very likely to have an important impact on the confidence of the estimate of effect and is likely to change the estimate.

Very low-quality evidence - three or more domains are not met; there is great uncertainty about the estimate of effect.

Evidence provided by a single small trial was considered inconsistent and imprecise and thus provide “low” or “very low” quality evidence, depending on whether it was assessed as having a low or high risk of bias, respectively, and there were no other limitations.

Studies with both low risk of bias and inappropriate or unclear randomization and/or treatment allocation techniques were downgraded by two levels for the "risk of bias" domain.

The results below are reported based on statistically significant differences between comparators for each outcome. Differences considered clinically important will be specified when the quality of the evidence is moderate or higher. The MCIDs used are listed in Table 2. Adverse events for the new studies are detailed when reported by the author

RESULTS

Selection and Description of Included Trials

We screened 13,817 titles and abstracts and assessed 156 full-text articles. This resulted in 44 RCTs meeting the inclusion criteria, including 23 new trials. Figure 1 summarizes original and updated screening results. Supplemental Table 1 describes the characteristics of all included trials. In total, 3,792 participants (1,765 males, 1836 females and 191 participants of undisclosed gender (14, 15) were randomized to one of 60 comparison groups. Seventeen studies evaluated rehabilitation therapy or multimodal care (14, 16-31), 11 assessed epidural injections (32-42), 7 evaluated oral medications (15, 43-48), 6 assessed calcitonin (49-54), 2 evaluated acupuncture (55, 56) and 1 assessed spinal manipulation (57). Thirty-eight trials were conducted at tertiary care or university affiliated centres and 6 at medical/rehabilitation clinics (18, 24, 35-38). The mean age of participants was 63.3 years. The duration of symptoms

varied considerably amongst the studies with a mean ranging from 12 weeks to 15 years. Follow-up periods also varied significantly ranging from immediately following the intervention to 10-year post intervention.

Risk of Bias of Included Studies

The median and mean number of criteria met was 7 of 12 (range 2-11) (Table 1).

Table 1. Risk of bias assessment for studies on non-operative treatment for lumbar spinal stenosis with neurogenic claudication

Author	A	B	C	D	E	F	G	H	I	J	K	L	Total
Calcitonin													
Eskola 1992	?	?	+	+	+	?	+	-	?	?	?	+	5
Porter 1983	?	?	-	?	?	+	+	?	-	?	+	+	4
Porter 1988	?	?	+	?	?	-	+	+	?	?	?	+	4
Podichetty 2004	?	?	+	+	+	-	+	-	+	?	?	+	6
Tafazal 2007	?	?	+	+	+	+	+	+	-	?	?	+	7
Sahin 2009	?	?	-	-	+	-	?	+	+	?	?	+	4
Oral Medications													
Prostaglandin													
Matsudaria 2009	+	+	-	-	+	+	+	?	+	?	?	+	7*
Methylcabalin													
Waikakul 2000	-	?	-	-	+	+	+	?	+	?	?	+	5
Gabapentin													
Yaksi 2007	?	?	-	-	-	?	+	+	?	?	?	+	3
Pregabalin													
Markman 2015	+	+	+	+	+	+	+	+	?	+	-	+	10 ****
Gabapentin													
Park 2017	+	?	+	+	+	+	+	+	?	?	-	+	8 *****
Oxymorphone Hydrochloride													
Markman 2015 (2)	+	+	+	+	+	-	?	+	?	+	+	+	9 **** #

Oral Corticoid													
Rodrigues 2014	+	+	?	?	?	+	+	?	?	?	?	+	5
Rehabilitation Therapy or Multimodal													
Goren 2010	+	+	-	-	+	+	-	+	+	?	?	+	7 *
Koc 2009	?	?	-	-	+	+	+	-	+	?	?	+	5
Pua 2007	+	+	-	-	+	-	+	+	+	?	-	+	7 *
Whitman 2006	+	?	-	-	+	+	+	+	+	?	?	+	7
Minetama 2019	+	?	-	-	+	+	+	+	?	+	+	+	8 *****
Schneider 2019	+	+	-	-	+	-	+	+	+	?	+	+	8 *
Ammendolia 2018	+	+	-	-	+	+	+	+	+	+	+	+	10 *
Oğuz 2013	?	?	-	-	?	?	+	-	?	?	?	+	2
Homayouni 2015	+	+	-	-	+	+	+	-	-	+	?	+	7 ****
Marchand 2019	+	+	-	-	+	?	+	+	?	-	+	+	7 ****
Kim 2019	+	+	+	+	+	+	+	+	?	+	+	+	11 *
Spinal Manipulation													
Passmore 2017	-	+	-	-	+	+	+	-	+	+	+	+	8 ****
Acupuncture													
Kim 2016	+	+	-	-	-	-	+	+	-	+	+	+	7 ****
Qin 2020	+	+	+	-	+	+	+	+	+	-	+	+	10 *
Epidural Injections													
Cuckler 1985	?	?	+	+	+	+	+	+	+	?	+	+	9
Fukusaki 1988	?	?	?	?	+	+	+	+	+	?	+	+	7
Zahaar 1991	?	?	+	?	+	+	+	+	+	-	?	-	6
Brown 2012	+	-	+	-	?	+	+	-	?	?	-	+	5
Friedly 2014, 2017, Makris 2016	+	+	+	+	+	+	+	+	?	+	+	+	11 *
Song 2016	?	?	?	?	?	+	+	-	?	+	+	+	5
Milburn 2014	?	?	+	-	+	-	+	-	?	-	-	+	4
Hammerich 2019	+	+	-	-	+	-	+	?	?	-	+	+	6 ****
Sencan 2020	+	?	+	-	+	+	?	+	+	+	?	+	8 *****
Wei 2020	+	+	+	-	-	+	-	+	?	+	+	+	8 *

Percutaneous Epidural Adhesiolysis													
Karm 2018	+	?	+	-	+	-	+	+	?	-	-	+	6 *****
Surgery vs Physical Therapy													
Zucherman 2004, 2005, 2006	?	+	-	-	+	+		+	+	?	+	+	>6 **
Weinstein 2007, 2009, Abdu 2018	+	+	-	-	+	+	+	+	?	?	-	+	>6 *** ^
Amundsen 2000	+	?	-	-	-	+	+	+	-	?	-	?	4
Malmivaara 2007	+	+	-	-	+	+	+	+	+	?	?	+	8 *
Weinstein 2008, 2010, Lurie 2015	+	+	-	-	+	-	+	+	?	?	-	+	6 ^
Delitto 2015	+	+	-	-	+	?	+	-	+	-	+	+	7 ^

A Was the method of randomization adequate?, B Was the treatment allocation concealed?, C Was the patient blinded to the intervention?, D Was the care provider blinded to the intervention?, E Was the outcome assessor blinded to the intervention?, F Was the drop-out rate described and acceptable?, G Were all randomized participants analyzed in the group to which they were allocated?, H Are reports of the study free of suggestion of selective outcome reporting?, I Were the groups similar at baseline regarding the most important prognostic indicators?, J Were co-interventions avoided or similar?, K Was the compliance acceptable in all groups?, L Was the timing of the outcome assessment similar in all groups?, + Yes, - No, ? Unclear, * Low risk of bias if 6 or more items met, including valid randomization and treatment allocation techniques and no severe flaws, ** 2 year follow-up drop out rate 30%, 1 year < 20%; intention to treat inconsistent at 2 year f/u, *** Drop out rate <20% at 1 year, >20% at 4 years, **** < 30 participants per treatment arm, ***** Treatment allocation unclear, ^ Severe flaw due to high crossover rates, # Premature end of study

Although 31 studies met 6 or more criteria, only 9 were considered to have low risk of bias (19, 20, 24, 27, 28, 31, 37, 42, 43, 56). Among the remaining 22 studies that met 6 or more criteria, 13 failed to explicitly describe and/or use appropriate randomization procedures, allocation concealment, or both (16-18, 30, 32-34, 39, 41, 48, 52, 54, 57); three had severe flaws due to high crossover rates (21, 22, 25), which made the intention-to-treat analyses uninterpretable and 6 had other serious flaws including premature stopping of the trial (47), large number of participants lost to follow-up (40) and small sample size (less than 30 participants per arm) (26, 29, 46, 55).

Evidence of Effect of Interventions

Fifty-three of the 60 comparisons were examined in a single trial, most with small sample sizes. It was only possible to combine data from 2 trials (assessing surgery vs. multimodal treatment) for 1 outcome in a meta-analysis (19, 22). The 5 other studies (all assessing calcitonin) (49-52, 54) were combined qualitatively. The results of these pooled analyses were published in our previous reviews (8, 9). Heterogeneity in source population, intervention, and outcome instruments precluded pooling of data from other trials. Supplemental Table 2, a summary of GRADE assessment and outcomes, summarizes the quality of the evidence for outcomes for each comparison.

Calcitonin

There were no new studies assessing calcitonin. The conclusion from our previous review was that there is very low-quality evidence from 6 trials (49-54) (N= 231) that calcitonin is no better than placebo or paracetamol regardless of mode of administration or outcome assessed.

Oral Medication

We identified 4 new studies assessing 5 oral medications. There is low-quality evidence based on 1 small cross-over trial (46) (N=29), that pregabalin does not improve pain, distance walked, function or global health status immediately following the intervention compared to placebo. Adverse events were reported in 64% of the pregabalin group, the most common being dizziness, compared to 35% in the placebo group.

A small trial evaluating gabapentin plus conservative care (48) (N=45) provides very low-quality evidence demonstrating no significant improvement in back/leg pain, disability scores or global health in the short-term compared to conservative care plus botulinum toxin injection. Five patients (20.8%) reported mild to moderate pain at injection sites for a few days after botulinum toxin injections.

There is very low-quality evidence from 1 small trial (47) (N=24) that oxymorphone hydrochloride or propoxyphene and acetaminophen is no better than placebo in the immediate term for all outcomes assessed.

A single small trial provided very low-quality evidence (15) (N=61) that oral corticoids do not improve outcomes in the short-term compared to placebo.

The original review identified 3 studies assessing oral medications and concluded that there is low-quality evidence that prostaglandins improves walking distance and leg pain in the short-term compared with etodolac (a nonsteroidal anti-inflammatory drug) (43); very low-quality evidence that gabapentin improves walking distance and pain compared with placebo in the intermediate and long-term(45) and that methylcobalamin (vitamin B 12) plus conservative treatment improves walking distance in the intermediate and long-term compared with conservative treatment alone (44).

Rehabilitation Therapy and Multi-modal Treatment

We identified 8 new studies evaluating 13 rehabilitation therapy and/or multimodal treatment approaches, with one study being compared to surgery.

There is moderate quality evidence from 1 trial (31) (N=259) that manual therapy and exercise provides superior and clinically important short-term improvement in symptoms and function compared to medical care or community-based group exercise and that community-based group exercise improves physical activity in the short-term compared to medical care. There were no reported serious adverse events in any group. There was a significantly greater rate of transient joint soreness associated with the manual therapy and exercise group (49%) compared with the community-based group exercise (31%) and medical care (6%) groups.

Another trial provides moderate quality evidence (27) (N=104) that comprehensive care (manual therapy, education and exercise delivered using a cognitive-behavioural approach) demonstrates superior and clinically important improvements in walking distance in the immediate, short, intermediate, and long-term and compared to self-directed home exercise. This study also provides low-quality evidence that comprehensive care improves overall pain and function in the long-term compared to self-directed home exercises. At 12 months, none of the 43 participants in the comprehensive group and 2 of the 46 participants in the self-directed group experienced adverse events. These adverse events were mostly attributed to a temporary increase in low back and/or leg pain.

There is low-quality evidence from 1 trial (28) (N=34) that a form of manual therapy (Mokuri Chuna), acupuncture and physician care, with or without a herbal remedy (Gang-Chuk Tang), improves low back pain in the intermediate term compared to oral aceclofenac, epidural steroids and physical therapy (heat and TENS).

A single study assessing supervised physical therapy (manual therapy, exercise, and body weight-supported treadmill) (30) (N= 86) provides low-quality evidence for improved symptoms, function and walking distance in the short-term compared to home exercises.

There is very low-quality evidence from 1 study (14) (N=120) that heat, TENS and home exercise instruction is no better than isokinetic exercise in the immediate, short and intermediate term for all outcomes and less effective than unloaded exercises in the immediate and short-term. Unloaded exercise was also found to be superior to isokinetic exercise in the immediate and short-term.

One small single study (26) (N=47) provides very low-quality evidence that aquatic exercise is more effective than physical therapy (exercise, ultrasound, heat and TENS) in improving pain and walking distance in the immediate term.

Another small single trial (29) (N=40) provides very low-quality evidence that a pre-surgical exercise program improves post-surgical outcomes in the immediate, but not in the short or intermediate terms.

There is low-quality evidence from 1 study (25) (N=169) that a structured physical therapy program (education and exercises) provides similar outcomes to decompression surgery in the long-term (2 years follow-up). Nine out of 82 participants receiving physical therapy reported adverse events consisting of worsening of symptoms whereas 33 out 87 participants reported surgery related complications, mainly attributable to reoperation, delay in wound healing and surgical site infection.

Our original review identified 9 rehabilitation therapy/multi-modal trials of which 5 were compared to surgical interventions. A meta-analysis was conducted for 2 of the surgical trials. Two of the original surgical trials have since published 8-year follow-up results (see below). All studies provide either low or very low-quality evidence.

A meta-analysis (8, 9) that includes 2 trials (22) (19) shows that laminectomy improves outcomes only at the 2 year follow-up compared to conservative care. One of these studies shows no difference in outcomes after an 8-year follow-up (58).

An interspinous surgical implant (17, 59, 60) was found to be superior to multi-modal treatment (epidural injections, pain medication, education, exercise, back brace, heat/ice, and massage). Another trial (16) provided inconclusive evidence when comparing laminectomy with or without fusion to lumbar orthosis and education.

Among patients with degenerative spondylolisthesis, 1 study (21) shows no difference in outcomes with laminectomy when compared to conservative care including after an 8-year follow-up (61).

One study showed that exercise plus ultrasound is no better than exercise plus sham ultrasound but better than no treatment, and exercise plus sham ultrasound is better than no treatment (24). Other studies demonstrated that in-patient physical therapy (ultrasound, heat and TENS) is more effective than home exercise plus oral diclofenac (23), unweighted treadmill walking plus exercise is no better than cycling plus exercise (20), and manual therapy, exercise and unweighted treadmill is more effective than flexion exercises, walking and sham ultrasound (18).

Epidural Injections

We identified 6 new studies evaluating epidural injections. There is moderate quality evidence from 1 study (37, 62) (N=400) that glucocorticoid plus lidocaine injection is better than lidocaine alone in improving pain and function at 3 weeks (short-term) but not at 6-weeks (short-term), 12 weeks (intermediate-term) or 12 months (long-term). The improved outcomes at 3 weeks were statistically significant but not considered to be of clinical importance (63). A follow-up subgroup analysis (64) using patient-prioritized Roland-Morris Disability Questionnaire (RMDQ) items, did not change the results. A total 21.5% of patients in the glucocorticoid-lidocaine group and 15.5% in the lidocaine alone group reported one or more adverse events (p=0.08). Adverse events included headaches, fever, infection, dizziness, cardiovascular/lung problems, leg swelling and dural puncture.

A small study (36) (N=29) provided very low-quality evidence that an injection of lidocaine is no better than a saline injection for all outcomes in the short-term.

There is very low-quality evidence from 1 study (38) (N=57) that steroid injections at the level of maximal stenosis improve pain and function in the immediate and short-term compared to steroid injections at 2 levels cephalad to the maximum level of stenosis.

A small trial (40) (N=54) provided very low-quality evidence that steroid injections are no better than steroid injections combined with physical therapy (manual therapy and exercise) in improving pain or function in the short-term but are more effective in improving pain in the intermediate and long-term.

There is very low-quality evidence from 1 study (41) (N=67) that interlaminar steroid injection improves pain and walking distance in the intermediate but not in the short-term compared to transforaminal steroid injection.

A 3-arm trial (42) (N=30) provided low-quality evidence that TNF alpha inhibitor (Etanercept) injections improved pain and function in the immediate, short and intermediate term compared to steroid or lidocaine injections and that steroid injections were no better than lidocaine for all outcomes and follow-up periods.

There is very low-quality evidence from 1 small trial (35) (N=38) that minimally invasive lumbar decompression surgery (MILD) is no better than epidural steroid injections for all outcomes in the short-term.

One small trial (39) (N=44) provided very low-quality evidence that an epidural inflatable balloon catheter (ZiNeu) improves pain and function in the intermediate term but not the short-term compared to a balloon-less catheter (Racz). Minor and transient adverse events were reported equally in both groups (no data provided), mostly pain and paresthesia at the injection site.

Our original review identified 4 trials evaluating 7 epidural injection approaches, all with very low-quality evidence for all outcomes. Two trials demonstrated that translaminar (32) or caudal (33) steroid injections were no better than placebo. Two other trials showed that translaminar epidural steroid plus a block was better than placebo or an epidural block alone (34), that translaminar epidural block was better than placebo (34), and that interlaminar epidural steroid plus a block was better than home exercise plus diclofenac or in-patient physical therapy (ultrasound, heat and TENS) (23).

Acupuncture

We identified 2 new studies assessing acupuncture. There is low quality evidence from 1 trial (56) (N=80) that acupuncture improves back and leg pain, symptoms and function in the immediate, short, and intermediate term compared to sham acupuncture. Three out of 40 participants in the acupuncture group reported short-term pain at the insertion site (1 also had a hematoma) and 5 out of the 40

participants in the sham group reported non-serious back pain or fatigue. There is very low-quality evidence from a small trial (55) (N=50) that acupuncture plus usual care is no better than usual care alone in the short-term for all outcomes.

Spinal Manipulation

We identified 1 study assessing spinal manipulation. There is very low-quality evidence from a very small trial (57) (N=14) that spinal manipulation alone is no better than a wait list control in the immediate term for all outcomes

DISCUSSION

We updated our systematic review on nonoperative treatments for LSS causing neurogenic claudication and identified 23 new trials that were added to the previous 21 studies. The highest number of studies, 17/44, evaluated rehabilitation therapy/multimodal treatment, 11 assessed epidural interventions, 7 oral medications, 6 calcitonin, 2 evaluated acupuncture and 1 assessed spinal manipulation. Of the 60 comparisons that were evaluated, 5 comparisons from 3 trials (27, 31, 37) provided moderate quality evidence. The remaining comparisons provide either low or very low-quality evidence. In our original review, all comparisons for all the interventions assessed were of low or very low-quality evidence. This lack of moderate or high-quality evidence limited our ability to make conclusions on the effectiveness of most nonoperative treatments.

There is now moderate evidence that a multimodal structured 6-week program consisting of manual therapy and exercise with or without education is an effective treatment approach (27, 31) for neurogenic claudication and that epidural steroid injections do not provide clinically important improvements in short or long-term outcomes compared to epidural lidocaine injections. However, given that these respective findings came from single studies, this evidence lacks consistency and therefore there is a possibility that replicating these trials in the future might result in substantially different conclusions. However, a recent clinical practice guideline for the management of LSS leading to neurogenic claudication concurred with our findings and recommended, based on moderate quality evidence, multimodal care consisting of education with home exercises and manual therapy (65). These guidelines also recommended against the use of epidural steroid injections, based on high quality evidence. A recent systematic review and meta-analysis of RCTs evaluating conservative nonpharmacological therapies for degenerative LSS also concluded, based on low to moderate evidence, that manual therapy and supervised exercises significantly improves outcomes compared to self-directed or group exercises (66). A recent clinical update published in the British Medical Journal recommended supervised exercise and manual therapy as a first line treatment for LSS and recommended against the use of epidural steroid injections (67). More dated systematic reviews did not recommend a combination of education, exercise, manual therapy as an effective treatment for LSS (7, 68, 69). However, these reviews did not include the more recent higher quality trials (27, 31) evaluating this multimodal approach.

A multimodal approach to the treatment of LSS would appear to be a rational approach given the complexity of neurogenic claudication with underlying physical, functional, and psychosocial factors impacting recovery (70). There is also a plausible rationale

for the lack of effectiveness of epidural steroid injections for neurogenic claudication since the dominant underlying pathophysiological mechanism appears to be neuro-ischemia rather than neuro-inflammation (4).

Although we cannot make firm conclusions about the effectiveness of nonoperative treatments for neurogenic claudication, this review is important because it provides important information regarding the state of current evidence regarding nonoperative treatments. This can be used to inform clinical practice guidelines and aid clinicians and patients in making clinical decisions regarding treatment options. This is particularly important with respect to interventions that have higher risks and costs such as epidural injections and surgery. About 25% of all epidural injections are performed for LSS (71, 72) yet the evidence from our current review and those of others (73-75) do not support their use. The number and associated costs of surgical procedures for degenerative LSS is growing, especially decompression surgery with complex fusion (76, 77). LSS continues to be the most common reason for spine surgery in older adults (6, 76). High quality evidence for the effectiveness of surgery is also lacking based on our current review and the findings of other systematic reviews (78, 79). Clinical trials evaluating surgery for LSS are difficult to conduct due to challenges in recruitment and blinding (patient and practitioner) and high costs (80). One ongoing clinical trial is comparing decompression surgery with sham surgery which should help to evaluate the potential role of the placebo effect of surgery for LSS (81).

Oral medication is often the first line treatment in primary care management of LSS (5). Pregabalin and gabapentin are commonly prescribed medications for LSS despite the growing evidence that these medications are not effective for back-related leg symptoms and may cause more harm than good (82-84).

New to this updated review are clinical trials on acupuncture and spinal manipulation, however, the quality of the evidence was insufficient to make conclusions on their effectiveness. A systematic review and meta-analysis of RCTs and controlled clinical trials published in Chinese, found no conclusive evidence for the effectiveness and safety of acupuncture for LSS (85). Passive unimodal treatments such as acupuncture and spinal manipulation are unlikely to provide long-term benefit but more likely to provide benefit when combined with a comprehensive approach to managing LSS (27), not unlike recommendations for managing chronic low back pain (86).

This review is also important because it provides a comprehensive assessment and identification of significant knowledge gaps in this area to guide future research. This includes the need for higher quality studies that assess commonly used non-operative treatments particularly in primary care settings, that are adequately powered and have low risk of bias and long-term follow-up. Future RCTs should follow the CONSORT guideline (87) when planning trials and reporting study findings in an attempt to improve transparency and reduce bias.

The strengths of this review include the evaluation of a wide range of nonoperative interventions and the use of consistent inclusion and exclusion criteria for neurogenic claudication, which included the corroboration of a diagnosis of LSS with imaging. The use of these criteria to define the study population increases the likelihood that participants in the included studies had the diagnosis of neurogenic claudication due to narrowing of the central canal or lateral foraminae (88-90). Other strengths of this review include the use of rigorous methods recommended by The Cochrane Collaboration, the World Health Organization, and the Cochrane Back and Neck Pain Review Group.(13) This included the use of the GRADE method to synthesize and summarize the quality of the evidence. Limitations of this review include the potential for language bias because only English articles were accepted. We also included studies with small samples sizes which are more prone to high risk of bias (91). Over half of the included studies had less than 30 subjects per arm at baseline, and none of these studies could be pooled because of high heterogeneity across studies. However, the exclusion of studies with small samples sizes in this review would not have changed our conclusions. The definition of a severe flaw and the criteria used to assess risk of bias (low vs. high) were arbitrary, therefore alternative definitions and criteria could have impacted the findings and conclusions of this review. The validity of MCIDs used in this review is unknown. Although most were derived from studies with neurogenic claudication (63, 92, 93) others were based on an arbitrary improvement of at least 30% (94). There are no agreed upon MCIDs in LSS and therefore different MCIDs thresholds could have potentially altered our conclusions. The location and severity of the stenosis on imaging was not deemed important in this review. Imaging findings often do not correlate with patient symptoms or severity and therefore imaging by itself is a not reliable diagnostic tool in this population (67, 95, 96). Neurogenic claudication is the clinical entity of interest in this review and, although usually caused by LSS, the diagnosis is made

clinically without imaging (97). Neurogenic claudication symptoms, by definitions improve with flexion, due to the increased volume around the involved nerve roots irrespective of where the stenosis is located (e.g., centrally or at the lateral recess). However, it is uncertain whether the effectiveness of some interventions, such as epidural steroid injections is dependent on location of the spinal stenosis. This is a different research question requiring future research.

CONCLUSIONS

There is moderate quality evidence that a multimodal approach that includes manual therapy and exercise, with or without education is a safe and effective treatment, and that epidural steroids are not effective for the management of LSS causing neurogenic claudication. All other studies evaluating nonoperative interventions provided insufficient quality evidence, limiting the ability to make conclusions about their effectiveness. With the growing prevalence and significant personal, social, and economic burden of LSS, more high-quality evidence for nonoperative interventions is urgently needed to guide clinical practice.

CONTRIBUTORSHIP STATEMENT

CA was involved in the conception and design of the study, screening of articles, risk of bias assessment, Grade analysis, writing the first draft of the manuscript, revision of the manuscript and administrative support. AB, MS, AF, CC, JO were involved in screening

of articles, risk of bias assessment, Grade analysis and critical revision of the manuscript. CH, JP, AA, KS, JJY, AA participated in screening of articles, risk of bias assessment, data extraction and critical revision of the manuscript.

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The remaining authors CH, JP, AB, MS, AF, KS, AA, AA2 and JO declare no funding disclosures.

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Figure Legend

Figure 1. Study Flow Diagram

Table Legend

Table 1. Risk of Bias Assessment

Supplemental Tables

Supplemental Table 1. Characteristics of Included Studies

Supplementals Table 2. Summary of Grade Assessment and Outcomes

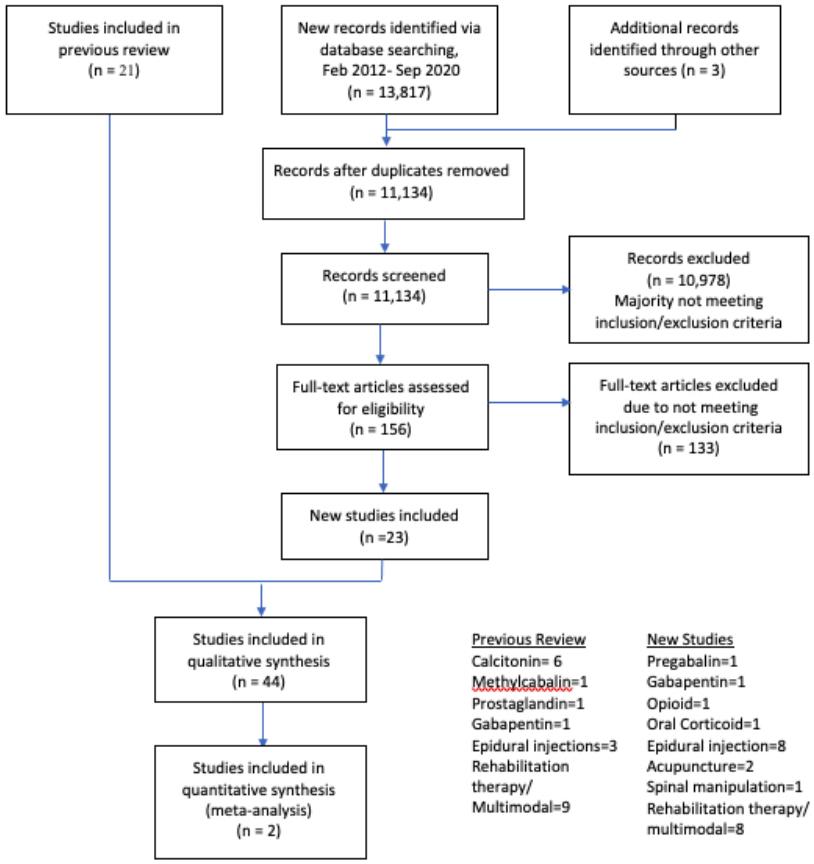

Figure 1. Study Flow Diagram

Figure 1. Study Flow Diagram

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Supplemental Table 1. Characteristics of included studies

Study	Participants and Settings	Interventions	Outcomes/Follow-up	Results (Group 1 is reference group)
Calcitonin				
Eskola 1992	39 subjects with an average of 6 years of pain, average age of 56.6 years of age, 20 males and 19 females. **Setting:** Orthopaedic hospital in Finland.	1) 100IU Calcitonin injection every other day for 4 weeks (n=20) 2) Placebo treatment (Miacalcic Sandoz 100IU) every other day for 4 weeks (n=19)	1) VAS 2) Treadmill test 3) Coping with ADLs 4) Digitest Ergojump 5) Blood tests **Follow-up:** 1, 3, 4, 6 and 12 months	**Between group WMD and 95% CI** **Pain (VAS) (mm):** -0.050 (-0.053 to -0.047) **Walking distance (meters):** -18.5 (-240.37 to 203.37) **Adverse events:** The calcitonin injection group reported minor nausea and rash in 8% of the subjects.
Podichetty 2004	55 subjects with an average age of 68.5 years and an average of 36.2 weeks of the condition in the intervention group and 29.8 weeks in the placebo group, 33 males and 22 females. **Setting:** Spinal center in the United States	1) 400 IU intranasal calcitonin daily for 6 weeks followed by open label 6-week extension (n=36) 2) Placebo nasal spray daily for 6 weeks, followed by open label 6-week extension, during which all patients received 400IU calcitonin (n=19)	1) VAS 2) Walking capacity 3) ODI 4) Stenosis specific questionnaire 5) Satisfaction with pain levels, functional status, and treatment received 6) SF-36 7) Symptom diary **Follow-up:** 12 weeks	**Between group MD, 95% CI, p values** **12 weeks:** **Pain VAS (mm):** 0.5 (-0.85 to 1.93): p=0.44, **Walking time (seconds)**: 42.2 (-86.9 to 170.4): p=0.5 **Walking distance (feet)**: 163.3 (-311.16 to637.84); p=0. 0.49 **SF-36 MCS:** -4.22 (-10.41 to1.97) ; p=0.18 **SF-36 PCS:** 0.43 (-3.73 to 4.59); p= 0.84
Porter	41 subjects with	1) 100 IU salmon calcitonin injection	1) Walking chart	Insufficient data provided to calculate mean difference in

1983	10 in a double blind RCT crossover, 37 males and 4 females with mean age of 55.4 years. **Setting:** Infirmary in England	four times per week, sometimes with Maxalon for nausea (n=5) 2) Matching placebo (n=5) Only responders randomized	and ability to walk more than 1 mile 2) ODI **Follow-up:** 10 weeks	walking distance or ODI among the 10 patients enrolled in RCT. **Adverse events:** The calcitonin injection group reported minor nausea and rash in 4% of the subjects.
Porter 1988	42 subjects, 35 male, 7 female, average age of 53.6 years in 20 subjects and 56.7 years in 22 subjects, median duration of back pain reported was 11 years for 19 subjects, and 14 years for 22 subjects. Median duration of claudication was 1.25 years for 20 subjects and 4.5 years for 22 subjects. **Setting:** Infirmary in England	1) 100 IU of salmon calcitonin injected subcutaneously 4 times per week for 8 weeks (n=20) 2) 1 ml of saline injected 4 times per week for 8 weeks (n=22)	1) VAS 2) Claudication threshold 3) 3 level mobility assessment 4) Analgesic requirements 5) 3 level sleep disturbance 6) Treatment success defined as 100% improvement in walking distance and able to walk 800 m. **Follow-up**: 4 and 8 weeks	**Difference in median score from baseline between groups** **Pain score (VAS) (mm):** 4 weeks: -9 8 weeks: -5.5 **Walking distance until symptoms onset (meters):** 4 weeks: -14 8 weeks: 42 **Walking distance until pain prevents walking (meters):** 4 weeks: -41 8 weeks: -99 No significant between group differences. No p values or 95% CI provided.
Sahin 2009	45 subjects 31 males and 14 females, average	1) 200 IU intranasal calcitonin daily for 8 weeks (n=23)	1) VAS 2) Walking capacity	**Percent change between groups:** **8 weeks:** **VAS at rest:** 4.7%, p>0.05

	ages of 57.65 years in calcitonin group and 54.45 years in paracetamol group. **Setting:** Physical and Rehabilitation Medicine Department in Turkey	2) Up to 1500mg of paracetamol daily for 8 weeks (n=22) Both groups took part in a physical therapy and exercise program 5 times per week for 15 sessions.	3) RMDI 4) Ranges of motion **Follow-up:** 8 weeks	**VAS with motion:** -7.9%, p>0.05 **Roland Morris**: 8.2%, p>0.05 **Walking distance**: -15.4%, p>0.05
Tafazal 2007	40 subjects, 30 males, 10 females, average of 67 years in the intervention group and 70.2 years in the placebo group, average of 38.7 months with symptoms in the calcitonin group and 30.9 months in the placebo group. **Setting:** University hospital in England	1) Placebo nasal spray NaCl for 4 weeks (n=20) 2) 200 IU nasal salmon calcitonin for 4 weeks (n=20)	1) VAS 2) Shuttle walking test 3) 4-point subjective outcome of overall assessment (excellent, good, fair, poor) 4) ODI 5) Modified Somatic Perception Questionnaire 6) Modified Zung Depression Score **Follow-up:** Baseline, 4, 10, 16 weeks	**4 weeks: Between group MD 95% CI** **ODI:** -0.7 (1.7 to -3.5) **LBOS**: -3.0 (-0.6 to -4.7) **VAS leg (mm):** -10 (-4.0 to -13) **VAS back (mm)**: -6.0 (-6 to -12) **Shuttle walk distance (m)**: -13 (-7 to -35) **16 weeks: between group MD, p values** **ODI**: 0.1, p=0.44; **LBOS**: 0.7, p=0.93; **VAS leg (mm):** -4, p=0.66; **VAS back (mm):** 16, p=0.03; **Shuttle walking distance (m):** -11, p=0.39

Oral Medication				
Matsudaira 2009	79 subjects, 24 males and 24 females, with an average age of 69.6 years in the Limaprost group and 72.2 in the Etodolac group. **Setting:** Orthopaedic surgery in a medical faculty in Japan	1) Oral prostaglandin E1 derivative (15 g Limaprost) 3 times daily for 8 weeks (n=39) 2) 400 mg of etodolac (NSAID) twice daily for 8 weeks (n=40)	1) SF-36 2) Verbal pain rating scales 3) Walking distance 4) LBP severity 5) Leg pain severity 6) Leg numbness severity 7) Treatment satisfaction **Follow-up:** 8 weeks	**SF-36 subscales MD, p values** 8 weeks: **physical function:** 9.4, p=0.01, **role physical:** 13.7, p=0.03, **bodily pain**: 15.5, p<0.01: **General health**: 6.6, p=0.08; **vitality**: 11.3, p=0.02; **social functioning**: 8.0, p=0.17; **role emotional:** 10.2, p=0.07; **mental health:** 12.2, p<0.01. **Secondary outcomes** not provided in a way that MD can be extracted: 8 weeks: **low back pain:** p=0.77; leg pain p=0.08; **Leg numbness:** p<0.01; **walking distance** p<0.01; **patient subjective improvement** p<0.01; **patient satisfaction** p<0.01 all in favor of limaprost **Adverse events:** 5% of subjects in both groups reported gastrointestinal upset.
Waikakul 2000	152 subjects, 68 males and 84 females with an average age of 66.8 years. 44 of the subjects had symptoms for less than one month, 98 had symptoms for more than one month. **Setting:** Hospital in Thailand	1) Conservative treatment consisting of education, activity modification, exercise and physical therapy. NSAIDs, muscle relaxants, and analgesics as necessary. Vitamin B1, B6, and B12 3 times per day (n=82) 2) Conservative treatment plus Methlcobalin ESAI, 1.5mg per day in 3 divided doses after meals for 6 months (n=70)	1) Presence of pain on spinal motion 2) Claudication distance 3) Medication intake (NSAIDs, muscle relaxants, and steroids) **Follow-up:** every month for two years	**Walking distance** **Percent able to walk > 1000 meters** 6 mo: 71.3% vs. 88.6%, p<0.05 12 mo: 81.3% vs. 97.1%, p< 0.05 18mo: 83.8% vs. 97.1% p <0.05 **Adverse events:** There were no reported adverse effects in subjects in methylocabalin group
Yaksi 2007	55 subjects, 22 males, 33 females, average age of 50.8 years. **Setting:** Hospital	1) 900 mg of gabapentin per day increased weekly by 300 mg to a maximum of 2400 mg (n=28) 2) Placebo (n=27)	1) VAS – low back and leg pain during movement 2) Walking distance	**Between group difference, p values** **Pain (VAS) (mm) no raw data** 3rd mo 3.4 vs. 1.9, p =0.039 4th mo 4.1 vs.2.0, p =0.006 **Walking Ability, no raw data**

	department of physical medicine and rehabilitation in Turkey	Both groups received physical therapy exercises, a lumbosacral corset with steel bracing and NSAID treatments	3) Presence or absence of motor and/or sensory deficits **Follow-up:** 15 days, 1, 2, 3, 4 months	Grp 1: longer walking distance at end of 2nd mo ($p < 0.05$), 3rd mo ($p < 0.05$) and 4th mo ($p < 0.005$) **Adverse events:** some subjects randomized to the gabapentin group (no data specified) experienced mild to moderate drowsiness and/or dizziness.
Markman 2015	29 participants, 20 males, 9 females, Eligible subjects were older than 50 years (mean 70 .1 years) with at least one level of radiographically confirmed lumbar spinal stenosis and symptoms of neurogenic claudication for at least 3 months. **Setting:** Hospital in Rochester, New York	1) Pregabalin group (n=14) 2) Active placebo (Diphenhydramine) (n=15) Cross over study after 7 day wash out period. Pregabalin was started at 75 mg PO twice daily or diphenhydramine, 6.25 mg) and increased on day 4 to 150 mg PO twice daily (12.5 mg diphenhydramine) for 7 days. Pregabalin was decreased to 75 mg PO twice daily (6.25 mg diphenhydramine) on day 11 for 3 days of tapering.	1) NRS - time to first moderate pain symptom during a 15-minute treadmill test (Tfirst) (NRS - greater than 4) **Follow-up:** day 10 of intervention period	**Between group MD, 95% CI, p values** **Treadmill testing pain at rest (NRS)** 0.29 (0.41 to 0.98): p=0.40 **Treadmill testing final pain (NRS)** 0.25 (-0.44 to 0.94): p=0.46 **Treadmill testing distance walked (m)** -24.06 (-75.63 to 27.52): p=0.35 **Treadmill testing recovery time (min)** -0.79 (-1.86 to 0.28): p=0.1 **Treadmill testing patient global assessment of pain** -0.08 (-0.45 to 0.29): p=0.6 **Treadmill testing RMDQ** 1.50 (0.38 to 2.62): p=0.01 **Adverse events:** Complications were reported in 64% of subjects in group 1, the most common being dizziness, compared to 35% in group 2.
Park 2017	45 subjects, 21 in GPN Group (17 female, 4 males, mean age 66.1± 10.5), and 24 in BTX group (15 female and 9 males, mean age	1) Conservative treatments plus gabapentin (group GPN): Gabapentin 300 to 1200mg/d - titrated to patient characteristics, comorbidities, and reported side effects (n=21) 2) Conservative treatments plus BTX	3) NRS - back/leg pain intensity 4) Cramp frequency (no./wk) 5) Cramp severity (0-4	No statistically significant difference between groups and lack of reporting of quantitative data **Adverse events:** Five patients (20.8%) in group 2 reported mild to moderate pain at injection sites for a few days.

	66.2±8.2) **Setting:** Outpatient department for interventional pain management in Korea	injection (group BTX): The BTX (botulinum toxin type A [Nabota]) dose was 100U in 5mL of 0.9% saline injected into the gastrocnemius medialis and lateralis. (n=24) Conservative treatments: education, exercise, analgesic medication, injection therapy including epidural injections, and physical therapy	criteria) 6) Insomnia severity – (ISI 0-28) 7) ODI 8) Patient global impression of change **Follow-up:** 2 weeks, 1 and 3 months.	
Markman 2015 - 2	24 participants, 12 males and 12 females, (mean age 72 years) LSS by imaging with symptoms of neurogenic claudication **Setting:** Translational Pain Research Center at a University in Rochester, New York	1) Oxymorphone hydrochloride (Opana IR, 5 mg) (n=8) 2) Propoxyphene/acetaminophen (Darvocet, 100 mg/650 mg) (n=8) 3) Placebo: 3 separate visits (random order with at least 3 day washout periods) (n=8)	1) NRS (at rest) 2) NRS (final pain rating) 3) AUC 4) 4) Distance walked (m) 5) Recovery time (min) 6) ZCQ 7) Patient global assessment of pain 8) RMDQ 9) ODI **Follow-up:** Study was prematurely terminated	**Between group MD, 95% CI, p values** **Treadmill testing pain at rest (NRS)** Grp 1 vs Grp 3: -0.04 (-0.72 to 0.65): p-0.89 Grp 2 vs Grp 3: -0.27 (-0.95 to 0.41): p=0.32 Grp 1 vs Grp 2: 0.23 (-0.45 to 0.92): p=0.40 **Treadmill testing final pain (NRS)** Grp 1 vs Grp 3: 0.2 (-0.74 to 1.14): p=0.60 Grp 2 vs Grp 3: 0.53 (-0.40 to 1.46): p=0.16 Grp 1 vs Grp 2: -0.33 (-1.26 to 0.61): p=0.39 **Treadmill testing distance walked (m)** Grp 1 vs Grp 3: -12.41 (-63.01 to 38.20): p=0.54 Grp 2 vs Grp 3: -23.41 (-73.60 to 26.79): p=0.25 Grp 1 vs Grp 2: 11 (-39.53 to 61.54): p=0.59 **SSSQ symptom severity score** Grp 1 vs Grp 3: -0.03 (-0.19 to 0.13): p=0.61 Grp 2 vs Grp 3: 0.01 (-0.15 to 0.17): p=0.85 Grp 1 vs Grp 2: -0.04 (-0.20 to 0.11): p=0.49 **SSSQ physical function score** Grp 1 vs Grp 3: 0.04 (-0.16 to 0.09): p=0.47 Grp 2 vs Grp 3: 0.11 (-0.01 to 0.23): p=0.03 Grp 1 vs Grp 2: -0.15 (-0.27 to -0.02): p=0.01 **Patient global assessment of pain** Grp 1 vs Grp 3: -0.03 (-0.52 to 0.47): p=0.90 Grp 2 vs Grp 3: 0.13 (-0.36 to 0.61): p=0.52

				Grp 1 vs Grp 2: -0.15 (-0.64 to 0.34): p=0.44 **The study was prematurely terminated because of the removal of propoxyphene acetaminophen from the US market.**
Rodrigues 2014	61 patients with lumbar canal stenosis (50–75 years; canal area < 100 mm^2 at L3/L4, L4/L5, and/or L5/S1on MRI; and claudication within 100 m). 31 in the corticoid group (mean age 58.23 (6.38), and 30 in the placebo group (mean age 58.33 (6.19)) **Setting:** Hospital in São Paulo, Brazil	1) Oral corticoid group received 1 mg/kg of oral corticoids daily, with a dose reduction of one-third per week for 3 weeks (n=31) 2) Control group was administered placebo for the same period (n=30)	1) SF-36 2) RMDQ 3) 6-min walk test 4) VAS 5) Likert scale **Follow-up:** 3, 6 and 12 weeks	**Between group comparison** **VAS (6 weeks)** Corticoid vs Placebo: 1.53 to -0.02 (in favour of placebo)
Rehabilitation Therapy and Multimodal Care				
Goren 2010	45 subjects, 13 males, 32 females, average ages in groups of 57.4, 49.13, and 53.06. 7 subjects with pain duration of 3-6 months, 7 with pain duration of 6-12 months, and	1) Stretching and strengthening exercises for lumbar, abdominal, leg muscles as well as low intensity cycling exercises were given as therapeutic exercises. Ultrasound was applied with 1mHz, 1.5W/cm2 intensity, in continuous mode on the back muscle for 10 minutes (n=17) 2) Same as group 1 with Ultrasound on off- mode (n=17)	1) VAS (out of 10) 2) Treadmill test at 3 km/h for maximum of 15 minutes or 750m. 3) ODI 4) Analgesic consumption 5) Physiatrist	**Pain (VAS) (mm) within group MD** 3 weeks: Grp 1: -2.2 for **back pain;** -1.47 for **leg pain** Grp 2: -1.94 for **back pain;** -2.47 for **leg pain** Grp 3: 0.40 for **back pain;** -0.54 for **leg pain** Between groups differences: Leg pain: Grp 1> Grp 3 (p<0.01), Grp 2> Grp 3 (p<0.01) **Walking Ability (within group MD)** 3 weeks: Grp 1: 94.30 seconds

	31 with pain duration of greater than 12 months. **Setting:** Rehabilitation center in Turkey	3) No exercise-no treatment (n=16)	assessment **Follow-up:** End of 3-week treatment period only	Grp 2: 114.94 seconds Grp 3: -66.10 seconds No significant change between groups **Disability (ODI) (within group MD)** 3 weeks: Grp 1: -3.94 Grp 2: -7.8 Grp 3: -3.6 ODI between groups differences Grp 1> Grp 3 ($p<0.05$), Grp 2> Grp 3 ($p<0.05$)
Koc 2009	29 subjects, 21 male, 8 female, average ages of 62.6, 61.1, and 53.1 years in the three groups, average pain duration of 5.7 years, 5.0 years, and 5.7 years in the three groups. **Setting**: Medical school department of physical medicine and rehabilitation in Turkey	1) Conservative inpatient physical therapy program 5 days a week for 2 weeks. PT included applications of ultrasound 1.5 W/cm2 for 10min, hot pack for 20min, and TENS for 20min to the lumbar region (n=13) 2) Lumbar epidural steroid injections, 10 ml of solution containing 60mg of triamcinolon acetonide (1.5 mL), 15 mg of 0.5% bupivacain hydrochloride (3 mL), and 5.5 mL of physiologic saline (0.9%NaCl) was injected in 3.5minutes. (n=10) 3) Control group (n=10) All patients included were trained to pursue a home-based therapeutic exercise program performed twice daily for a period of 6 months, and oral diclofenac sodium 75mg was administered to all patients twice daily for 2 weeks	1) VAS 2) Treadmill walk test 3) Nottingham Health Profile 4) RMDI 5) Functional testing including finger to floor distance, sit-to-stand, and a weight carrying test **Follow-up:** 2 weeks, 1, 3 and 6 months	No raw data provided. No significant between group differences for all outcomes and follow-ups except: **Pain (VAS)** 2 weeks: Grp 2 less pain than Grp 3 p= 0.008 **Disability (RMDI)** 2 weeks: Grp 2 less disability than Grp 3 p= 0.007 **Quality of Life (Nottingham Health Profile) (no data provided)** Grp 2 had significantly higher improvement than Grp 3 at 2 weeks in mobility subgroup scores. **Adverse events:** 1 subject reported angina pectoralis and 1 reported gastric complaints (group not specified).
Pua 2007	68 subjects, 35 males, 33	1) Unweighted treadmill training: Weeks 1 and 2, participants walked	1) VAS for pain over past	**Pain (VAS) (mm) MD and 95% CI** 6 weeks: 2 (-5 to 10)

	females, average age of 58 years, 12 week median pain duration **Setting:** Hospital in Singapore	with a relatively pain-free gait which translated to 30–40% of body weight. In weeks 3 to 6, participants were encouraged to walk at a moderate intensity. The duration of each treadmill session was limited by participant tolerance or to a maximum of 30 minutes. 2x per week for 6 weeks = 12 sessions (n=33) 2) Cycling on upright bicycle: During weeks 1 and 2, participants cycled at their comfortable pace at 50 to 60 rpm. Participants were instructed to assume a flexed posture. In weeks 3 to 6, participants were encouraged to exercise at a moderate intensity and the duration of each cycling session was limited by participant tolerance or to a maximum of 30 minutes. 2x per week for 6 weeks for 12 sessions (n=35)	week 2) Patient perceived benefit on a 6-point scale 3) ODI 4) RMDI 5) Walking ability **Follow-up:** 3 and 6 weeks	**Disability (ODI), OR, 95% CI** 6 weeks: OR 1.10 (0.41 to 2.98) **Patient perceived benefit, OR, 95% CI** 6 weeks: OR 0.50 (0.17 to 1.48) **Walking ability** (≥800 m), **OR, 95% CI** 6 weeks: OR 1.14 (0.44 to 2.94) **Adverse events:** 1 subject in treadmill group reported increase in pain.
Whitman 2006	58 subjects, 31 males, 27 female, 29 (group 1) with an average age of 70 years, 29 (group 2) with an average age of 68.9, median low back pain duration of 108 months in Group 1's 29 subjects and 60 months in Group 2's 29	1) Flexion Exercise and Walking Group: 45-60 minutes twice per week for 6 weeks. Lumbar flexion exercises along with self-pace treadmill walking program, and sub-therapeutic ultrasound. The duration of each treadmill session was based on that patient's tolerance on that specific day and could extend up to 45 minutes. (n=29) 2) Manual Therapy, Exercise and Walking Group: 45-60 minutes twice per week for 6 weeks - Manual	1) Global Rating of Change (15-point scale) 2) NPRS for lower limb 3) Walking Tolerance test 4) ODI 5) Medication consumption 6) Satisfaction subscale of the Spinal	**Patient Global Assessment (somewhat better or greater)** 6 weeks: 41% vs. 79% p<0.001 1 year: 21% vs. 38% p>0.05 **Number needed to treat for benefit for perceived recovery and 95% CI** 6 weeks: 2.6 (1.8 to 7.8) 1 year: 4.8 (-2.3 to 21.3) long term: 4.4 (- 2.1 to 22.7) **Pain (NPRS lower extremity)** **Within group MD, 95% CI** 6 weeks: 1.1 (0.2 to 2.0) vs. 1.5 (0.5 to 2.5) 1 year: 1.2 (0.4 to 1.9 vs. 1.0 (-0.2 to 2.2);

	subjects, lower extremity median pain duration of 48 months in Group 1's 29 subjects and 24 months in Group 2's 29 subjects. **Setting:** University in the United States	physical therapy (thrust and non thrust) to the thoracic and lumbar spine, pelvis, and lower extremities and specific exercises at discretion based on the underlying impairments. Patients received specific exercises to address impairments in mobility, strength, and/or coordination. Exercises were performed in the clinic and as part of a home exercise program. Patients also underwent a bodyweight supported treadmill ambulation program using a cable and trunk harness system to unload a specific amount of weight from the patient while the patient walks as comfortably as possible on a treadmill (n=29).	Stenosis Scale 7) Additional use of health care resources **Follow-up:** 6 weeks, 1 year, long term mail survey (averaging 29 months)	Long term: 1.8 (0.6 to 3.0) vs. 2.0 (0.7 to 3.4) Between group MD not statistically significant at any follow-up period **Walking Ability (improvement in meters) within group MD, 95% CI** 6 weeks: 176.5 (-9.5 to 362.4) vs. 339.7 (218.4 to 461) 1 year: 130.4 (-55.3 to 316.2) vs. 209.8 (67.5 to 352.1) Between group improvement not statistically significant at any follow-up **Disability (ODI) within group MD** 6 weeks: 6.55 (1.87 to 11.23) vs. 10.48 (6.5 to 14.4) 1 year: 5.03 (1.71 to 8.35) vs. 7.14 (1.5 to 12.8) Between group differences not statistically significant at any follow-up
Minetama 2019	86 patients, 39 men and 47 women, average age 72.7 years 43 patients (20 men and 23 women, average age 72.3 years to the PT group 43 patients (19 men and 24 women, average age 73.2 years) to the HE group. Duration symptoms 20 months	1) Physical therapy + home exercise program (n=43) 2) Home exercise (HE) program alone (n=43) Supervised physical therapy twice a week for 6 weeks, including manual therapy, individually tailored stretching and strengthening exercises, cycling, and body weight-supported treadmill walking. The manual therapy included manipulation, stretching, and massaging of the thoracic and lumbar spine, pelvis, and lower extremities. The individually tailored muscle exercises included those for the trunk (eg, abdominal planks, side bridge, and/or back extension) and lower	1) ZCQ 2) Satisfaction 3) SPWT (m) 4) NRS 5) JOABPEQ-acquired points 6) SF-36 7) HADS 8) PCS 9) PASS-20 10) TSK-11 11) Daily steps **Follow-up:** 6 weeks	**Between group MD, 95% CI** **ZCQ - Symptom severity** −0.4 (−0.6 to −0.2): statistically significant **ZCQ - Physical function** −0.4 (−0.6 to −0.2): statistically significant **SPWT (m)** 455.9 (308.5 to 603.2): statistically significant **NRS - Leg pain** −1.4 (−2.5 to −0.3): statistically significant **SF-36 - Physical functioning** 9.2 (2.1 to 16.3): statistically significant **SF-36 - Bodily pain** 10.4 (3.3 to 17.5): statistically significant **Daily steps** 723.4 (199.1 to 1,283.5): statistically significant

	Setting: Spine care center at a university hospital in Japan	extremities (eg, unloading hip and/or knee exercise with ankle weight and/or standing squats). The typical dosage for strengthening exercises was a total of 2 to 3 sets with 10 repetitions, each of 6-second contraction. The typical duration of stretching was three repetitions of 30 seconds. All patients in both groups were asked to take a daily walk that did not exacerbate their lower extremity symptoms using a pedometer and walking diary and to perform a HE program consisting of lumbar flexion exercises including three 30-second bouts of both single and double knee-to-chest exercises, ten 6-second bouts of trunk raises and bridging in the supine position, and a 4-point kneeling exercise at least twice daily.		
Schneider 2019	259 subjects, 122 males and 137 women with an average age of 72.4, 68 patients had symptoms for less than 6 months, 191 had symptoms for greater than 6 months **Setting:** Outpatient research clinic in Pittsburgh	1) Medical care (MC) (n=88) 2) Group exercise (GE) (n=84) 3) Manual therapy + exercise (MTE) (n=87) **Medical Care:** 3 visits to a physical medicine physician over 6 weeks. Primarily prescription of oral medications in any combination of nonnarcotic analgesics, anticonvulsants, antidepressants. Optional referral for epidural steroid injections if inadequate pain relief by oral medication, severe neurogenic claudication, and/or patient preference.	1) SSS 2) SPWT 3) Physical Activity **Follow-up:** 2 and 6 months	**Between group MD, 95% CI** **SSS (2 months)** GE vs MC: 0.4 (-1.3 to 2.1) MTE vs MC: -2.0 (-3.6 to -0.4) MTE vs GE: -2.4 (-4.1 to -0.8) **SPWT (2 months)** GE vs MC: 79.9 (-74.5 to 234.5) MTE vs MC: 122.9 (-25.7 to 271.6) MTE vs GE: 43.0 (-111.8 to 197.9) **Physical activity (2 months)** GE vs MC: 28.7 (2.7 to 54.8) MTE vs MC: 20.4 (-4.5 to 45.3) MTE vs GE: -8.3 (-34.5 to 17.6) **SSS (6 months)** GE vs MC: -0.5 (-2.3 to 1.3) MTE vs MC: -1.1 (-2.8 to 0.6) MTE vs GE: -0.6 (-2.4 to 1.2)

		Physician rendered general guide and on gentle stretching and advice to stay active. **Group Exercise:** Supervised exercise classes at 2 local senior community centers. 2x 45-min classes/week, 6 weeks. Taught by senior fitness instructors. Participants self-select level of exercise based on fitness level (easy to medium) **Manual Therapy + Exercise:** 2x 45minute sessions per week, 6 weeks by either 2 chiropractors or 2 physiotherapists. Sessions included 3 interventions: 1. Warm-up procedure on stationary bicycle 2. Manual therapy procedures (lumbar distraction, hip, lumbar/sacroiliac joint and neural mobilizations 3. Individualized instruction in spinal stabilization exercises and home stretching Practitioner determined what muscles required stretch/strengthening and appropriate exercises added to program.		**SPWT (6 months)** GE vs MC: 86.5 (-75.7 to 248.8) MTE vs MC: 73.8 (-84.1 to 231.7) MTE vs GE: -12.7 (-175.6 to 150.1) **Physical activity (6 months)** GE vs MC: 21.3 (-6.9 to 49.4) MTE vs MC: -2.9 (-30.1 to 24.3) MTE vs GE: -24.2 (-52.5 to 4.0) **Adverse events:** There were no reported serious adverse events in any group. There was a significantly greater rate of transient joint soreness associated with group 3 (49%) compared with group 2 (31%) and group 1 (6%).
Ammendolia 2018	104 patients, 45 males and 59 females, 48 in comprehensive group and 51 in self-directed group, with an average age of 69.4	1) Comprehensive (n=48) 2) Self-directed (n=51) **Comprehensive:** Chiropractor providing 2x/week of 15-20-minute treatment sessions over a 6-week period followed by a single (booster) session, 4 weeks later.	1) SPWT Distance 2) Clinical Significance - 30% improvement in SPWT no. (%) 3) Clinical	**Between group MD, 95% CI, p values** **SPWT** 8 wks: 345.4 (150.0 to 540.7): p=0.00 3 mo: 304.1 (77.9 to 530.3): p=0.01 6 mo: 421.0 (181.4 to 660.6): p=0.00 12 mo: 473.2 (203.9 to 742.4): p=0.00 **30% improvement in SPWT** 8 wks: 24 (6-40): p=0.01 3 mo: 21 (4-38): p=0.02

	(comprehensive) and 71.7 (self-directed) neurogenic claudication >3 months, imaging-confirmed canal narrowing, walk >20m and not surgical candidates in next 12 months **Setting:** Academic hospital outpatient clinic in Toronto	Education: Self-management strategies via cognitive behavioral approach. Body repositioning (pelvic tilt) when standing and walking. Exercises: Standardized set of exercises demonstrated gradually over 6 weeks and was a part of structured home exercise program. Cycling, muscle stretching, strengthening, conditioning for back and lower extremity fitness and to facilitate lumbar flexion Manual therapy: Spinal manipulation; joint, soft tissue and neural mobilization; lumbar flexion-distraction; and manual muscle stretching applied each visit. Participants received an instructional video and workbook and pedometer. **Self-directed:** Instructional Video, workbook, pedometer and a single 15-to 30-minute training session with an experienced independent licensed chiropractor, independent of the comprehensive program, Training session: Describe 6-week program, review workbook, explain pedometer use and recording of weekly walking steps. Video and workbook: Educational information and the same exercise instruction and self-management strategies received by the comprehensive group	Significance - 50% improvement in SPWT no. (%) 4) ZCQ-S 5) ZCQ-F 6) ZCQ-S + ZCQ-F 7) ODI 8) ODI walk 9) NRS Back 10) NRS Leg **Follow-up:** 8 weeks, 3, 6, and 12 months	6 mo: 19 (2-35): p=0.02 12 mo: 22 (4-39): p=0.02 **50% improvement in SPWT** 8 wks: 26 (8-42): p=0.01 3 mo: 19 (-1.0 to 36): p=0.06 6 mo: 17 (-2 to 35): p=0.09 12 mo: 24 (5-40): p=0.01 **ZCQS** 8 wks: -0.19 (-0.37 to -0.02): p=0.03 3 mo: -0.15 (-0.37 to 0.08): p=0.19 6 mo: -0.02 (-0.22 to 0.19): p=0.87 12 mo: -0.22 (-0.47 to 0.02): p=0.07 **ZCQF** 8 wks: -0.02 (-0.22 to 0.17): p=0.81 3 mo: -0.18 (-0.39 to 0.03): p=0.09 6 mo: -0.11 (-0.33 to 0.11): p=0.34 12 mo: -0.27 (-0.49 to 0.04): p=0.02 **ZCQS+ZCQF** 8 wks: -0.24 (-0.56 to 0.07): p=0.13 3 mo: -0.36 (-0.75 to 0.03): p=0.07 6 mo: -0.23 (-0.58 to 0.12): p=0.20 12 mo: -0.48 (-0.90 to -0.06): p=0.03 **ODI** 8 wks: -0.02 (-0.07 to 0.02): p=0.30 3 mo: -0.04 (-0.09 to 0.01): p=0.13 6 mo: -0.02 (-0.07 to 0.02): p=0.34 12 mo: -0.03 (-0.08 to 0.02): p=0.30 **ODI Walk** 8 wks: -0.2 (-0.6 to 0.1): p=0.14 3 mo: -0.4 (-0.9 to 0.03): p=0.07 6 mo: -0.9 (-1.3 to -0.4): p<0.001 12 mo: -0.2 (-0.7 to 0.2): p=0.32 **NRS Back** 8 wks: -1.4 (-2.2 to -0.5): p=0.002 3 mo:-0.6 (-1.4 to 0.3): p=0.03 6 mo: -0.7 (-1.7 to 0.3): p=0.16 12 mo: -0.4 (-1.3 to 0.4): p=0.32

				NRS Leg 8 wks: -0.7 (-1.5 to 0.1): p=0.09 3 mo: 0.05 (-0.85 to 0.96): p=0.91 6 mo: -0.9 (-1.9 to 0.003): p=0.58 12 mo: -0.5 (-1.6 to 0.6): p=0.37 **SF-36 Bodily Pain** 8 wks: 2.0 (-4.9 to 8.9: p=0.57 3 mo: -4.5 (-12.4 to 3.5): p=0.27 6 mo: -3.3 (-10.2 to 3.6): p=0.35 12 mo: 10 (2.1 to 17.9): p=0.013 **SF-36 Physical Function** 8 wks: 4.2 (-3.9 to 12.4): p=0.31 3 mo: 9.2 (1.1 to 17.3): p=0.027 6 mo: 5.8 (-2.1 to 13.6): p=0.15 12 mo: 8.2 (0.2 to 16.2): p=0.045 **Adverse events:** At 12 months, 0 participants out of 43 in group 1 and 2 out of 46 participants in group 2 experienced adverse events that were mostly attributed to a temporary increase in low back and/or leg pain.
Oğuz 2013	120 patients, 30 in group 1 with an average age of 57.1 years old, 30 in group 2 with an average age of 55.8 years old and group 3 with an average age of 57.4 years old, LSS symptoms, narrowing by MRI **Setting:** University	1) Standard exercise group (n=30) 2) Isokinetic exercise program (n=30) 3) Unloading exercise group (n=60) All groups physician-guided (5x/week for 3 weeks) then at-home (3x/week) **Standard Exercise:** 15 sessions of TENS, hot packs with home exercise instruction. **Isokinetic exercise:** 20 minutes/day, 5 sessions/week for a total of 15 sessions with a physician. Isokinetic exercises:	1) VAS 2) ODI 3) Beck Depression Inventory **Follow-up:** 4, 12 and 24 weeks	**Between group MD, p value** **VAS** After treatment: Grp 1 vs Grp 2:0.37, p>0.05 Grp 1 vs Grp 3: 1.36, p<0.05 Grp 2 vs Grp 3: 0.99, p<0.05 4th week: Grp 1 vs Grp 2: 1.43, p>0.05 Grp 1 vs Grp 3: 1.17, p<0.05 Grp 2 vs Grp 3: -0.26, p>0.05 12th week: Grp 1 vs Grp 2: 0.93, p>0.05 Grp 1 vs Grp 3: 0.71, p>0.05 Grp 2 vs Grp 3: -0.22, p>0.05 24th week: Grp 1 vs Grp 2: 1.08, p>0.05

	department of physical medicine and rehabilitation in Turkey	rates of 60°/sec, 120°/sec, 180°/sec with 70° of body movement (50° flexion to 20° extension) Each session had 3 sets, each set had 5 repetitions at described velocity, with 20s rest between each set. **Unloaded exercise:** 5 sessions of unloading exercise per week, for a total of 15 sessions with a physician. Walking with unloading exercise devise: session 1-5 = 45% body weight, session 6-15 = 30% body weight. Treadmill walking at 1.2 km/hr for 20 minutes, or until pain due to neurogenic claudication was felt. Subjects advised to follow exercise program s at home at least 3x/week after discharge.		Grp 1 vs Grp 3: 0.46, p>0.05 Grp 2 vs Grp 3: -0.62, p>0.05 **ODI** After treatment: Grp 1 vs Grp 2: -0.8, p>0.05 Grp 1 vs Grp 3: 1.8, p<0.05 Grp 2 vs Grp 3: 2.6, p<0.05 4th week: Grp 1 vs Grp 2: 1.5, p>0.05 Grp 1 vs Grp 3: 2.6, p>0.05 Grp 2 vs Grp 3: 1.1, p<0.05 12th week: Grp 1 vs Grp 2: 1, p>0.05 Grp 1 vs Grp 3: 1.3, p>0.05 Grp 2 vs Grp 3: 0.3, p>0.05 24th week: Grp 1 vs Grp 2: 0.4, p>0.05 Grp 1 vs Grp 3: 0.5, p>0.05 Grp 2 vs Grp 3: 0.1, p>0.05 **Total Gait Duration** After treatment: Grp 1 vs Grp 2: 64.6, p>0.05 Grp 1 vs Grp 3: -50.5, p>0.05 Grp 2 vs Grp 3: -115.1, P<0.05 4th week: Grp 1 vs Grp 2: 45.9, p>0.05 Grp 1 vs Grp 3: -18.4, p>0.05 Grp 2 vs Grp 3: -64.3, p<0.05 12th week: Grp 1 vs Grp 2: 52.23 p>0.05 Grp 1 vs Grp 3: -0.67 p>0.05 Grp 2 vs Grp 3: -52.9 p>0.05 24th week: Grp 1 vs Grp 2: 35.2, p>0.05 Grp 1 vs Grp 3: 1.9, p>0.05 Grp 2 vs Grp 3: -33.3, p>0.05

Homayouni 2015	47 subjects, 23 male, 24 female, 24 in group one, mean age 55.56, 12 male, 12 female, 23 in group two, mean age 55.68, 11 male, 12 female **Setting:** University-based pain clinics in Iran	1) Treatment in therapeutic pools with water temperature of 29–30 degrees Celsius. Every aquatic session started with warm up and ended with cool down, with duration of 10–15 min for each of them. Participants should have attended aquatic physical therapy sessions every other day for a total duration of 24 sessions. Each session included ambulation, side walking, chain walking, forward walking with kickboard, stretching of each muscle group including adductors, abductors, flexors and extensors of the hip, knee flexors and ankle plantar flexors and dorsiflexors. Other interventions were mini-squat, pelvic curl, pelvic tilt, and knee to chest, double knee lift, and deep-water exercise. (n=25) 2) Passive modalities by physical therapists including continuous mode ultrasound (US) 1.5W/ cm2 for 10 min and hot pack and trans-electrical nerve stimulation (TENS) for 20 min to the lumbar region. Also, the therapists instructed the patients in this group to perform trunk muscle endurance, William's and stretching exercises. The patients were treated using these passive modalities and were given exercises under supervision of physiotherapists for 10 sessions. They were instructed to perform the learned exercises 30 min	1) VAS 2) Walking ability **Follow-up:** Immediately after therapy, 3 months	**All between group comparisons** **Walking ability** Grp 1 > Grp 2: p=0.02 **VAS** Grp 1 > Grp 2 p=0.001

		a day at home in the following weeks until the end of the eighth week. (n=25)		
Marchand 2019	40 participants, 17 females and 23 males, 20 in the intervention group with an average age of 66.7 years old and 20 in the control group with an average age of 71.5 years old, with history and diagnostic imaging of LSS **Setting:** Regional hospital in Quebec	1) Exercise 3x week / 6 weeks prior to surgery (n=20) 2) Regular hospital preoperative management with back posture education (n=20)	1) NRS (Pain Intensity) 2) ROM (Active) 3) Muscle strength (N-m) 4) Walking capacity (seconds) **Follow-up:** 3 and 6 months	**Between group MD** **NRS (leg)** Preoperative: -2.1, p<0.05 Postoperative: 1.1, p>0.05 3 months: 1.1, p>0.05 6 months: 0.3, p>0.05 **ROM (active)** Preoperative: 5, p<0.05 Postoperative: -6, p>0.05 **Muscle Strength** Preoperative: 45.7, p<0.001 Postoperative: 5.1, p>0.05 **Walking Duration** Preoperative: 90, p<0.05 Postoperative: -14.5, p>0.05
Kim 2019	34 subjects, mean age 64 (5.3), women 24 (66.7) **Setting:** Hospital in Seoul, South Korea	1) MT1 group: 110 g of Gang-Chuk Tang was administered 3 times a day (Gang-Chuk Tang is an herbal concoction consisting of Eucommiae Cortex, Achyranthis Radix, Rhizoma Cibotii, Sorbus commixta, G. thunbergii, Saposhnikovia Radix, and Acanthopanacis Cortex in equal portions) Daily Mokhuri Chuna therapy (relaxation and mobilization of lumbar joint and back muscle) Daily acupuncture treatment on LI4, ST36, LV3, BL22, BL23, BL24, BL25, and Ashi points. Consultation on precautions related to daily	1) VAS for leg pain 2) VAS for low back pain 3) Oxford Claudication Scoring 4) Walking distance **Follow-up:** 3 and 6 months	**All between group comparisons** **VAS leg pain (post treatment)** MT2 (28.82±27.46) vs CMT (51.82±25.34) groups: P=0.04 **VAS leg pain (6 months)** MT1 (48.91±23.08) vs CMT (72.27±16.72) groups: P=0.01 MT2 (42.36±21.29) vs CMT groups: P=0.003 **VAS low back pain (6 months):** MT2 (30.00±13.48) vs CMT (60.82±18.62) groups: P=0.001 **Oxford Claudication Scoring (3 months)** MT1 (18.75±6.52) vs CMT (25.82±6.24) groups: p=0.02 **Walking distance (3 months)** MT1 vs CMT: p=0.03 **Walking distance (6 months)** MT1 vs CMT: p=0.01

		activity and stepwise walking training for the entire 4 weeks of therapy. (n=12) 2) MT2 group: Mokhuri Chuna, acupuncture, and physician consultation were offered in the same manner and dosage as the MT1 group with the exception that all herbal medications were withheld. (n=11) 3) CMT group: Oral analgesic therapy (aceclofenac 100 mg twice daily and eperisione hydrochloride 50 mg three times daily for 28 days) and three interlaminar epidural steroid injections (5 mg of dexamethasone per injection) at the level of the affected spinal region over a 4-week period were administered. Physiotherapy including heating pad, and transcutaneous electrical nerve simulator, and deep tissue heating therapy five times per week for 4 weeks. (n=11)		The primary outcome of this pilot study was safety as measured by the type and incidence of adverse events (AEs).
Spinal Manipulation				
Passmore 2017	14 patients with degenerative LSS (n=14); Swiss Spinal Stenosis score of M=63.2, standard deviation [SD] = 15.9) (mean age 59.0 (10.6)), 7 in the SM group (4	1) Spinal manipulation group: received bilateral high-velocity; low-amplitude spinal manipulation directed toward the lumbar region (by a licensed chiropractor with more than 10 years of clinical experience) (n=7) 2) Non Intervention Group: Waited 5 minutes if they were assigned to the	1) Movement time 2) NPS (Back) 3) NPS (leg) 4) ROM **Follow-up:** Immediately after intervention	There was no significant difference between groups for all outcomes. 1. Grp 1 vs. Grp 2, p=0.739 2. Grp 1 vs. Grp 2, p> 0.05 3. Grp 1 vs. Grp 2, p> 0.05 4. Grp 1 vs. Grp 2, p> 0.05

	female, 3 male) (mean age 59.1 (9.3)), 7 in the NI group (3 female, 4 male) (mean age 58.9 (12.6)) **Setting:** rehabilitation hospital in Winnipeg, Manitoba	no intervention group (n=7)		
Acupuncture				
Kim 2016	50 participants mean age of 62.0±9.8 years, acupuncture (n=26), age 65.0±8.7, male / female 12/14, control (n=24), age 58.9±10.2, male / female 10/14. Mean duration of symptoms 33m **Setting:** Hospital in Yangsan, South Korea	1) Acupuncture: 269 acupuncture sessions were administered during the study. 81% (n=21) of patients received at least 10 acupuncture sessions. Electrical acupuncture was applied at least once and bilaterally at back shu points (BL23, BL24, BL25 or BL26) or Jiaji points at L2–L5 spinal levels. Other frequently used points were BL57, BL60, GB39, GB34 and tender points located in the lower extremities (n=26) 2) Control: In total, 255 physical therapy sessions were provided to patients in the control group at their request. 92% (n=22) of patients received at least 10 physical therapy sessions (median 11, range 1–13). (n=24)	1) ODI 2) SF-36 bodily pain 3) SF-36 physical function 4) LBP bothersomeness 5) LBP intensity 6) Leg pain bothersomeness 7) Leg pain intensity 8) Self-reported pain-free walking distance (m) **Follow-up:** 6 weeks, 3 months	**Between group MD, 95% CI** **ODI** 6 wk: -2.2 (-7.0 to 2.6) 3 mo: -2.5 (-8.9 to 3.8) **SF-36 BP** 6 wk: -8.6 (-18.6 to 1.3) 3 mo: 3.2 (-8.3 to 14.7) **SF-36 PF** 6 wk: 0.1 (-7.6 to 7.9) 3 mo: 1.3 (-8.3 to 10.9) **LBP bothersomeness** 6 wk: -0.6 (-11.4 to 10.1) 3 mo: -7.4 (-19.6 to 4.8) **LBP intensity** 6 wk: -5.1 (-15.5 to 5.3) 3 mo: -13.5 (-26.2 to -0.7) **Leg pain bothersomeness** 6 wk: -7.4 (-18.4 to 3.7) 3 mo: -9.2 (-21.6 to 3.2) **Leg pain intensity** 6 wk: -11.5 (-0.9 to -22.0) 3 mo: -12.6 (-24.6 to -0.6)

				None statistically significant
Qin 2020	80 participants assigned with 70 completing the 8-week treatment course (38 in acu group and 32 in sham acu group). Mean age of 61.5±7.9 years with 34 males and 46 females. Duration of symptoms <3mo =14 (17.5%), 3-12 mo = 1(1.3%), 1 to 5 y = 24 (30%), >5 y =41 (51.3%) **Setting:** 2 Clinical Sites - Department of Acupuncture and Neurology, Guang'anmen Hospital Department of Acupuncture and Neurology, Beijing Fengtai Hospital of Integrated Traditional and Western Medicine.	1) Acupuncture: Applied by acupuncturists with 5 years of Chinese medical university program and at least 2 year of clinical experience. Sterile disposable steel needles (Hwato Acupuncture, Suzhou, China; 0.30 £ 40 mm/0.30 £ 75 mm) were inserted through adhesive pads. Participants underwent 3 treatments weekly over 8 weeks, and each session persisted for 30 minutes. To maintain "De qi," a sensation of numbness and soreness, acupuncture manipulation (twirling, lifting, and thrusting on needles) was performed every 10 minutes during the treatment. 2) Sham acupuncture: Chosen acupoints, treatment duration, and frequency of sessions were the same as in the acupuncture group. Participants in the sham cohort were treated using a pragmatic placebo needle on the same acupoints, which is similar to the Streitberger needle design (Supplementary Materials). Acupuncturists pretended to manipulate the needle every 10 minutes, but "De qi" was not sought.	1) RMDQ 2) NRS back 3) NRS Leg 4) SSS Symptoms subscale 5) SSS physical function subscale 6) SSS satisfaction subscale 7) Self-paced walk test **Follow-up:** 4 weeks, 8 weeks (end of treatment), 3 months, 6 months	**RMDQ** 4 wk: -3.6 (-5.2 to -1.9): p<0.001 8 wk: -2.6 (-3.7 to -1.4): p<0.001 3 mo: -2.3 (-3.9 to -0.7): p=0.005 6 mo: -1.8 (-3.6 to -0.3): p=0.086 **NRS Back** 4 wk: -1.7 (-2.4 to -0.9): p<0.001 8 wk: -2.3 (-3.0 to -1.5): p<0.001 3 mo: -1.7 (-2.6 to -0.8): p<0.001 6 mo: -1.2 (-2.1 to -0.3): p=0.007 **NRS Leg** 4 wk: -2.0 (-2.6 to -1.3): p<0.001 8 wk: -2.9 (-2.6 to -1.3): p<0.001 3 mo: -2.4 (-3.3 to -1.4): p<0.001 6 mo: -2.1 (-3.0 to -1.2): p<0.001 **SSS Symptoms Subscale** 4 wk: -0.6 (-0.8 to -0.4): p<0.001 8 wk: -0.9 (-1.2 to -0.6): p<0.001 3 mo: -0.9 (-1.2 to -0.6): p<0.001 6 mo: -1.0 (-1.3 to 0.6): p<0.001 **SSS Physical Function Subscale** 4 wk: -0.5 (-0.8 to -0.3): p<0.001 8 wk: -0.8 (-1.1 to -0.5): p<0.001 3 mo: -0.7 (-1.0 to -0.4): p<0.001 6 mo: -0.7 (-1.1 to -0.4): p<0.001 **Self-Paced Walk Test** 4 wk: p=0.648 8 wk: p=0.29 3 mo: p=030 6 mo: p=0.133 **Adverse events:** 3 participants in group 1 reported pain after needle insertion and 1 had a hematoma. 3 participants in group 2 reported back pain and 2 reported fatigue. All adverse events were reported as mild or moderate, and none required medical intervention.

Epidural injections				
Cuckler 1985	73 subjects in total, 37 with spinal stenosis, 36 with acute herniated nucleus pulposus, 37 males, 36 female, average age of 48.5 years in the experimental group and 49.5 years in the placebo group. Experimental group average 36.6 months in symptom duration, placebo group averaged 29.4 months. **Setting:** Orthopaedic surgery department in the United States	1) Steroid group: 2ml of sterile water containing 80mg of methylprednisolone acetate combined with 5ml of 1% procaine was injected into the epidural space in the region between the 3rd and 4th lumbar vertebrae with the patient in the lateral decubitus position lying on the side of the painful limb (n=42), 20 with stenosis). 2) Placebo group: 2ml of saline combined with 5ml of 1% procaine was injected into the epidural space in the region between the 3rd and 4th lumbar vertebrae with the patient in the lateral decubitus position lying on the side of the painful limb. (n=31, 17 with stenosis) All patients were advised to take mild analgesics (aspirin or acetaminophen) during the post-injection period. Second injection given if less than 50% improvement after 24 hours - considered treatment failure	1) Subjective percentage of improvement with 75% required to be considered a treatment improvement, if less than 50% after 24 hours was considered a treatment failure 2) Re-injection rates 3) Surgery rates **Follow-up:** 24 hours, every 3 months up to 30 months, averaging 20.2 months in the steroid group and 21.5 months in the control group.	**Patient Global Assessment (improved by at least 75%)** 24 hours: 33% (steroid) vs. 21% (saline) p>0.05 Long term: 33% (saline) vs. 14% (saline) p>0.05
Fukusaki 1988	53 subjects, 38 males and 15 female. Group 1 averaged 70 years of age and 79 days of symptoms on average, group 2 averaged 69 years of age and	1) Epidural injection with 8 ml of saline, repeated twice in the first week (n=16) 2) Epidural injection with 8 ml of 1% mepivacaine, repeated twice in the first week. (n=18) 3) Epidural injection with a mixture of 8 ml of 1% mepivacaine and 40 mg	1) Walking distance which was graded according to distance (excellent, good, or poor) **Follow-up:** 1 week, 1 month, 3	**Walking distance** Percent excellent effect = mean of > 100m in walking distance 1 week: 12.5 % (saline) vs. 55% (block) vs. 63.2% (block + steroid); block or block + steroid > saline, p< 0.05; 1 mo: 6.3% (saline) vs. 16.7% (block) vs. 15.8% (block + steroid) p > 0.05 3 mo: 6.3 (saline) vs. 5.6% (block) vs. 5.3% (block +steroid) p> 0.05 No significant difference between block vs. block + steroid at

	an average of 82 days of symptoms, group 3 averaged 72 years of age and 94 days of symptoms on average **Setting:** Anaesthesia department in Japan	of methylprednisone, repeated twice in the first week. (n=19)	months	all follow-up periods, p>0.05 **Adverse events:** no reported complications
Zahaar 1991	30 subjects, 37 male and 26 female. Steroid group averaged 46.5 years of age and 36.6 months of symptoms, control group averaged 49 years of age and 29.4 months of symptoms **Setting**: Medical facility in Egypt	1) Steroid injection: 5ml of hydrocortisone acetate suspension, 2x2ml carbocaine, 4% Volume completed with sterile saline to 30ml (n=18) 2) Control: 2x2ml of carbocaine, 4% injected into epidural space. Volume completed with sterile saline to 30ml. (n=12)	1) Subjective percentage of improvement where 75% or more was deemed successful and surgery after injection was considered a failure. **Follow-up:** 24 hours, then every three months up to 36 mo averaging 20.2 mo in the steroid group and 21.5 mo control group.	**Patient Global Assessment** (improved by at least 75%) 24 hours: 55% (steroid injection) vs. 50% (control) p> 0.05 Up to 36 mo: 38% (steroid injection) group vs. 33.3% (control) p>0.05 **Failures (%)** (required surgery) Up to 36 mo: 61% (steroid injection) vs. 66.6% (control) p>0.05
Friedly 2014, 2017 Makris 2016	400 patients, 221 females and 179 males, 200 in the lidocaine group	1) Lidocaine + glucocorticoid (1-3 mL of 0.25-1% lidocaine followed by 1-3 mL triamcinolone (60-120mg), betamethasone (6-12mg),	1) RMDQ 2) NRS (Leg Pain)	**Between group MD, 95% CI, p values** **RMDQ** 3 weeks: -1.8 (-2.8 to -0.9): p<0.001 6 weeks: -1.0 (-2.1 to 0.1): p=0.07

	with an average age of 68.1 years old and 200 gluocorticoid-lidocaine group with an average age of 68 years old, LSS by CT or MRI. 26% patients symptoms greater than 5 years. **Setting:** 16 medical centers across the United States	dexamethasone (8-10mg) or methylprednisone (60-120mg)) (n=200) 2) Lidocaine group (0.25-1% lidocaine alone) (n=200) Physician option for intralaminar and/or transformaminal techniques	**Follow-up:** 3, 6, and 12 weeks, 6 and 12 months Makris 2016 subgroup 1) RMDQ using SIP Weights 2) RMDQ patient-prioritized (LESSER) **Follow-up:** 3 and 6 weeks	12 wk: 0.1 (-1.0 to 1.3): p=0.784 6 mo -0.00 (-1.1 to 1.1): p=0.99 12 mo: -0.4 (-1.6 to 0.9): p=0.55 **NRS (Leg pain)** 3 weeks: -0.6 (-1.2 to -0.1): p=0.02 6 weeks: -0. (=0.8 to 0.4): p=0.48 12 wk: 0.1 (-0.5 to 0.7): p=0.70 6 mo: -0.2 (-0.8 to 0.4): p=0.47 12 mo: 0.1 (-0.5 to 0.7): P=0.75 Subgroup Analysis **RMDQ using SIP weight** 3 wks: -1.9 (-2.9 to -0.7): p=0.001 6 wks: -1.1 (-2.2 to -0.1): p=0.04 **RMDQ patient prioritized (LESSER)** 3 wks: -1.8 (-2.8 to -0.8): p=0.001 6 wks: -1.0 (-2.0 to 0.1): p=0.08 **Adverse events:** A total 21.5% of patients in group 1 and 15.5% in group 2 reported one or more adverse events (p=0.08) that included headaches, fever, infection, dizziness, cardiovascular/lung problems, leg swelling and dural puncture.
Song 2016	29 subjects, 14 males and 15 women with an average age of 58.3 and 61.7 between groups, history of intermittent claudication and lower limb radicular pain or paresthesia	1) Lidocaine spinal injection, 40 mg triamcinolone mixed with 10 mL 0.5% lidocaine was used under the guide of fluoroscopy (n=15) 2) Saline spinal injection using same volume (n=14)	1) VAS 2) FRI **Follow-up:** 1 and 3 months	No significant difference between groups. **VAS** 1-month p= 0.696, 3 months p= 0.891 **FRI** 1-month p=0.983, 3 months p=0.743

	Setting: Rehabilitation clinic in Korea			
Milburn 2014	57 patients met inclusion criteria, agreed to participate, and were enrolled. 20 patients were male; 37 were female. Mean patient age was 65.3 years (range, 32-88 years). Average duration of symptomatology (pain and/or disability) was 42 months. The mean degree of canal narrowing at the most stenotic level was 6.1 mm (range, 2.5-9.1 mm). The most common maximally stenotic intervertebral level was L4-L5	Fluoroscopically guided lumbar ILESI performed either at: 1) The level of maximal stenosis (n=30) 2) Two intervertebral levels cephalad, corresponding to a less stenotic level (n=27) Injection was performed with a 20-gauge Tuohy needle using a loss of resistance technique. The injectate consisted of 2 mL of 40 mg/mL methylprednisolone (Pfizer), 2 mL of bupivacaine 0.25% (Hospira), and 2 mL of normal saline for a total injectate volume of 6 mL.	1) NRS - Pain with Ambulation 2) RMDQ **Follow-up:** 1, 4 and 12 weeks	**All between group comparisons** **NRS (pain with ambulation)** 1 wk: Grp 1 lower pain compared to Grp 2, p=0.045 4 wk: Grp 1 lower pain compared to Grp 2, p=0.049 12 wk: Grp 1 lower pain compared to Grp 2, p=0.08 **RMDQ** 1 wk: Grp 1 lower compared to Grp 2, p=0.001 4 wk: Grp 1 lower compared to Grp 2, p=0.009 12 wk: Grp 1 lower compared to Grp 2, p=0.003

	(n¼42) followed by L3-L4 (n¼11) and L5-S1 (n¼4). **Setting:** Clinic in New Orleans, Louisiana			
Brown 2012	38 patients, 21 males and 17 females, 21 in mild group with an average age of 74.2 years and 17 in ESI group with an average age of 78.7 years, symptomatic LSS patients with painful lower limb neurogenic claudication, able to walk at least 10 feet unaided, (ODI) score > 20 **Setting:** Pain management clinic in Florida	1) Epidural steroid (80 mg triamcinolone acetate) (n=17) 2) Mild lumbar decompression (n=21)	1) VAS 2) ODI 3) ZCQ 4) Patient Satisfaction (0-10) **Follow-up:** 6 and 12 weeks	**VAS** 6 and 12 weeks P=0.54 **ODI** p=0.86 **ZCQ** p>0.05 **Patient satisfaction** p>0.05
Hammerich 2019	54 patients total, age 67.2 ± 9.7, 27 male, 27 female, 31 in ESI group, 23 in ESI plus PT. Mean duration of	1) ESI (n=31) 2) ESI + PT (n=23) ESI: 1.5 mL of steroid at each site injected with maximal involvement using transforaminal approach.	1) ODI 2) NRS current 3) SF-36 emotional role 4) SF-36 emotional well-being	**Between group MD, 95% CI, p values** **ODI** 10 wks: -1.08 (-8.10 to 5.94) p=0.80 6 mo: -4.70 (-11.72 to 2.32) p=0.27 12 mo: -2.72 (-9.74 to 4.30) p=0.52 **NRS** 10 wks: -1.68 (-3.08 to -0.29) p=0.07

	symptoms 14 m **Setting:** Clinics in Colorado, Texas, South Carolina and New Hampshire	PT: 8-10 sessions PT manual therapy and exercise. Walking program and/or stationary bike, stretching and strengthening exercises.	5) SF-36 general health perception **Follow-up**: 10 weeks, 6 and 12 months	6 mo: -1.99 (-3.38 to -0.60) p=0.04 12 mo:-2.44 (-3.80 to -1.08) p=0.00 **SF-36 Emotional role** 10 wks: -28.53 (-49.05 to -8.01) p=0.03 6 mo: -11.25 (-31.77 to 9.27) p=0.39 12 mo: -10.67 (-31.19 to 9.85) p-0.41 **SF-36 Emotional well-being** 10 wks: -11.26 (-19.52 to -2.99) p=0.02 6 mo: 2.69 (-5.57 to 10.95) p=0.59 12 mo: -5.76 (-14.02 to 2.50) p=0.24 **SF-36 General Health Perception** 10 wks: -8.99 (-17.20 to -0.78) p=0.05 6 mo: -5.56 (-13.77 to 2.65) p=0.23 12 mo: -5.10 (-13.31 to 3.11) p=0.27
Sencan 2020	67 patients. The median age 62.5 years with 18 males and 49 females. Median duration of symptoms was 29 and 24 months in the ILESI and bilateral TFESI groups, respectively **Setting:** University department Pain Medicine, Istanbul Turkey	1) Interlaminar: ILESI, fluoroscopy guided with 1 to 2 mL contrast dye with mixture of 80 mg methylprednisolone acetate, 2 mL saline solution, and 2 mL (0.5%) bupivacaine solution 2) Transforaminal: TFESI, fluoroscopy guided with 1 to 2 mL contrast dye with mixture of 80 mg methylprednisolone acetate, 2 mL saline solution, and 2 mL (0.5%) bupivacaine solution	1) NPS 2) ODI 3) Beck depression scale 4) Walk distance **Follow-up:** after treatment, 3 weeks and 3 months	**Between Group Median Differences (data not provided), p values** **NPS** after treatment: p=0.14 3 wks: p=0.28 3 mo: p=0.047 **ODI** 3 wks: p=0.93 3 mo: p=0.65 **Beck Depression Scale** 3wks: p=0.048 3 mo: p=0.03 Walking Distance 3 wks: p=0.23 3 mo: p= 0.048
Wei 2020	90 patients. Mean age about 65 years, 45 females, 45	1) Epidural injection with 2.0mL of lidocaine and 10 mg of TNF-a inhibitor (etanercept) on the affected spinal nerves.	1) VAS (leg) 2) ODI **Follow-up:** after	**Between Group Mean Differences (data not provided), p values** **Grp 1 vs Grp 2** **VAS**

	males, mean duration of symptoms about 2.8 months **Setting:** University Hospital Jiangsu China	2) Epidural administration with 2mL of lidocaine mixed with 2mL of steroid (diprospan) 3) Epidural injection 4.0mL of lidocaine only.	treatment, 1,3, 6 months	after treatment, 1, 3 and 6 mo, Grp 1 greater reduction, p<0.05 **ODI** 1, 3 and 6 mo, Grp 1 greater reduction, p<0.05 **Grp 1 vs Grp 3** **VAS** after treatment, 1, 3 and 6 mo, Grp 1 greater reduction, p<0.05 **ODI** 1, 3 and 6 mo, Grp 1 greater reduction, p<0.05 **Grp 2 vs Grp 3** **VAS** after treatment, 1, 3 and 6 mo, no significant difference, p>0.05 **ODI** 1, 3 and 6 mo, no significant difference, p>0.05
Karm 2018	44 patients total, 20 in the RACZ group (age 66.1 +-12.2, male 9 (45.0%), and 24 in the ZiNeu group (Age 65.5 +-6.4 18 females, 26 males. **Setting:** Single-center, academic, outpatient interventional pain management clinic in Korea	1) PEA Using a Balloon-less Catheter (Racz) (n = 20) 2) Percutaneous Epidural Decompression and Adhesiolysis Using an Inflatable Balloon Catheter (ZiNeu) (n = 24)	1) NRS (back pain) 2) NRS (leg pain) 3) ODI **Follow-up:** 1, 3 and 6 months	**Between group MD, 95% CI, p values** **NRS-11 (Back pain)** 1 mo:-0.38 (-1.81 to 1.06): p=0.61 3 mo: -1.13 (-2.63 to 0.38): p=0.14 6 mo: -2.02 (-3.58 to 0.45) p=0.01 **NRS-11 (Leg pain)** 1 mo: 0.73 (-0.40 to 1.85): p=0.21 3 mo: -0.69 (-1.89 to 0.52): p=0.26 6 mo: -1.88 (-3.15 to 0.61) p=0.00 **ODI (%)** 1 mo: -6.13 (-13.88 to 1.61): p=0.12 3 mo: -6.63 (-14.75 to 1.48): p=0.11 6 mo: -13.74 (-22.18 to 5.30): p=0.00 **Adverse events:** Minor and transient adverse events were reported equally in both groups (no data provided), mostly pain and paresthesia at the injection site.
Surgery				
Zucherman 2004, 2005, 2006	191 subjects, 57% male and 43% female in the X STOP group. 52% male	1) X STOP Interspinous Process Decompression System (n=100) 2) Non-operative treatment: Subjects received an epidural steroid injection	1) SF-36 2) ZCQ 3) Worker's compensation claims	**Patient global assessment (Good result)** 2 yrs: 73.1% (surgery) vs. 36.9% (control) (P< 0.001) **Symptoms Severity score**

	and 48% female in the non-operative group. Average age of 70 years in the X STOP group and 69.1 years in the non-operative group. Average of 3.5 year symptom duration in the X STOP group and 4.7 years in the non-operative group. **Setting:** Spine center in the United States	on enrolment and were eligible for additional injections as needed, as well as NSAIDS, analgesic agents, and physical therapy. Physical therapy consisted of education on back care and modalities such as ice packs, heat packs, massage, stabilization exercises, and pool therapy. Braces such as abdominal binders and corsets were permitted, but body jackets and chair back braces were not. (n=91)	4) ODI 5) Radiographic changes **Follow-up:** Surgery: 7 (2 yr) Control: 19 (2 yr)	Surgery better at 6 w, 6 mo, 1 and 2 yr (graphs) (P<0.001) 2 yrs: MPC 45.4% (surgery) vs. 7.4% (control) (P < 0.001) **"Clinically relevant improvement (patients)":** 2 yrs: 60.2% (surgery) vs. 18.5% (control) (P< 0.001) **Symptoms Severity score** Surgery better at 6 w, 6 mo, 1 and 2 yr (graphs) (P<0.001) 2 yrs: MPC 44.3% (surgery) vs. -0.4% (control) (P < 0.001) **"Clinically relevant improvement (as measured by patients)":** 2 yrs: 57% (surgery) vs. 14.3% (control) (P < 0.001) **ZCQ (global success)** 6 mo: 52% (surgery) vs. 9% (control) (P value not reported) 1 yr: 59% vs 12% (P value not reported) 2 yrs: 48.4% (surgery) vs. 4.9% (control) (P < 0.001) **Quality of life (SF-36)** At all post treatment time points (6 w, 6 mo, 1 yr, 2 yr), the mean domain scores documented in the X STOP group were significantly greater than those in the non operative group, with the exception of the mean General Health, Role Emotional, and Mental Component *Summary scores at 2 years* **Adverse events:** No complications were reported in group 2. In group 1, complications were reported in 11% of subjects including spinous process fracture, coronary ischemia, respiratory distress, hematoma, and 1 death (pulmonary edema)
Weinstein 2007, 2009, Abdu 2018	Subjects with image-confirmed degenerative spondylolisthesis: 304 subjects in the RCT, 303 in the observational cohort, 31% male in the surgical group, 33% male in the surgical group. Average	1) Assigned to surgery (standard laminectomy with or without fusion) (n=159) 2) Assigned to non-surgical treatment: Usual non-operative care (n=145)	1) SF-36 bodily pain 2) SF-36 bodily function 3) low back pain bothersomeness scale 4) Leg pain bothersomeness scale 5) ODI 6) Subjective self-	**All between group comparisons using Intention-to-Treat analysis** **SF-36 Bodily Pain, DMC, 95% CI** 2 yrs: 1.5 (-4.2 to 7.3) 4 yrs: -2 (-8.6 to 4.6) 8 yrs: p=0.85 **SF-36 Bodily Function, DMC, 95% CI** 2 yrs: 1.9 (-3.7 to 7.5) 4 yrs: -3.1 (-9.2 to 3.0) 8 yrs: p=0.31 **Disability (ODI), DMC, 95% CI** 2 yrs: 2.2 (-2.3 to 6.8)

	age of 64.7 years in the surgical group and 68.2 years in the non-surgical group. Subjects had symptoms for at least 12 weeks **Setting:** multi-centred orthopaedic departments in the United States		reported improvement, satisfaction with current symptoms and care 7) Stenosis bothersomeness index **Follow-up**: 6 weeks, 3 and 6 months, 1, 2, 4 and 8 years	4 yrs: 4.1 (-0.8 to 9.1) 8 yrs: p=0.039 Other outcomes (patient's satisfaction; Stenosis Bothersomeness Index, Leg Pain Bothersomeness Scale; and Low Back Pain Bothersomeness Scale) were not provided separately for the randomized cohort. **Adverse events:** group 1 reported 14% intraoperative complication mostly and dural tears and 19% postsurgical complications including 1 death, 11% required additional surgeries at 2 years,
Amundsen 2000	100 subjects, 54 male, 46 female, median age of 59 (males were 1.5 years higher than females). Median back pain duration was 14 years, median duration of sciatica was 2 years. **Setting:** Neurology department in a hospital in Norway	1) Surgery: Partial or total laminectomy, medial facetectomy, discectomy, and/or removal of osteophytes from the vertebral margins or facet joints. No fusions. (n=13) 2) Conservative therapy: Lumbar orthosis use for 1 month worn during the day for all activities plus instruction and back school." (n=18)	1) VAS 2) Verbal Rating Scale 3) Subjective change (better, worse, or unchanged) 4) Work status 5) Subjective rating from evaluating physician and study team (Excellent, Fair, Unchanged, Worse) **Follow-up:** 6 months, 1, 4 and 10 years	**Patient global assessment (Good result)** 1 yr: RR 2.07 (0.98 to 4.38) 4 yrs*: RR 1.94 (1.14 to 3.31)* 10 yrs: RR 3.18 (0.97 to 10.41) **Pain (none or mild)** 1 yr: NR 4 yrs: RR 3.33 (0.77 to 14.39) 10 yrs: RR 1.59 (0.55 to 4.55) Other outcomes (claudication or walking distance; level of daily activity; and neurologic deficits) were not reported separately for the randomized cohort.
Malmivaara 2007	94 subjects, 22% of surgical	1) Segmental decompressive surgery with facetectomy (n=50)	1) 11 point numerical pain	**All between group comparisons** **Leg pain, MD, 95% CI**

	subjects were male, 45% of non-operative subjects were male. Nonoperative group had average age of 62.9 years, surgical group had average age of 63.9 years. Surgical group averaged 14 years since onset of symptoms, nonsurgical group average 16 years since onset of symptoms. Minimum of 6 months of symptoms for study inclusion. **Setting:** Research Center in Finland	2) Non-operative treatment: NSAIDS when indicated and seen one to three times by a physiotherapist, in addition to the standard visit at each follow-up. The physiotherapist gave all patients educational brochure. The patients were encouraged to use their back in a normal way. Pain-relieving body postures were taught as well as basic ergonomics related to lifting and carrying. Individually structured programs included trunk muscle endurance and stretching-type exercises. Additional individual physiotherapy consisting of passive treatment methods (such as ultrasound and transcutaneous nerve stimulation). (n=44) The patients in the surgical group also received the brochure and the instructions described above.	rating scale for back and leg pain 2) Walking ability (distance without a break) also via treadmill test 3) General health status on a 5 point scale (very good, quite good, average, quite poor or very poor. 4) ODI 5) Ability to complete certain activities of daily 6) living without difficulty, some difficulty, marked difficulties or not at all 7) Radiographic examination **Follow-up:** 6 months, 1 and 2 years	1 yr: 1.69 (0.41 to 2.96) 2 yr: 1.51(0.25 to 2.77) **Back pain, MD, 95% CI** 1 yr: 2.33 (1.12 to 3.55) 2 yrs: 2.13(0.98 to 3.28) **Disability (ODI), MD, 95% CI** 1yr: 11.3 (4.3to 18.8) 2 yrs: 7.8 (0.8 to14.9) **> 10 points reduction (ODI): RR, 95% CI** 1 yr: 2.16 (1.31to 3.57) 2 yrs: 1.36 (0.88 to 2.10) **Walking disability (walking distance <1.250 m), RR, 95% CI** 1 yr: 0.93 (0.61 to 2.03) 2 yrs: 1.08 (0.70 to 2.42) **Walking disability (walking distance <400 m), RR, 95% CI** 1 yr: 0.91 (0.51 to 4.24) 2 yrs: 1.18 (0.67 to 4.72)

Weinstein 2008, 2010, Lurie 2015	289 in the RCT, 365 in the observational cohort. 62% male in the surgical groups, 59% male in the non-surgical groups. Average age of 63.8 in the surgical group, 66.1 in the non-surgical group. 60% in the surgical group and 55% in the non-surgical group had symptoms for over 6 months. **Setting:** multi-centred-orthopaedic departments in the United States.	1) Assigned to surgery: Standard laminectomy with or without fusion (n=138) 2) Assigned to non-surgical treatment: Usual non-operative care - recommended to include at least active physical therapy, education or counseling with home exercise instruction, and the administration of NSAIDs, if tolerated (n=151)	1) SF-36 bodily pain 2) SF-36 bodily function 3) Low back pain bothersomeness scale 4) Leg pain bothersomeness scale 5) ODI 6) Subjective self-reported improvement, satisfaction with current symptoms and care, 7) Stenosis bothersomeness index **Follow-up**: 6 weeks, 3 and 6 months, 1, 2, 4, 8 years	**All between group comparisons using Intention-to-Treat Analysis** **SF-36 Bodily Pain, DMC, 95% CI** 2 yrs: 7.8 (1.5to 14.1) 4 yrs: 0.3 (-6.4 to 7) 8 yrs: p=0.25 **SF-36 Bodily Function, DMC, 95% CI** 2 yrs: 0.1 (-6.4 to 6.5) 4 yrs: -3.2 (-9.9 to 3.6) 8 yrs: p=0.89 **Disability (ODI), DMC, 95% CI** 2 yrs: -3.5 (-8.7 to 1.7) 4 yrs: 0.2 (-5.2 to 5.7) 8 yrs: p=0.87 Other outcomes (patient's satisfaction; Stenosis Bothersomeness Index, Leg Pain Bothersomeness Scale; and Low Back Pain Bothersomeness Scale) were not provided separately for the randomized cohort. **Adverse events:** In group 1 10% of patients required transfusions intraoperatively and 5% postoperatively. The most common surgical complication was dural tear, in 9% of patients. At 2 years, reoperation had occurred in 8% of subjects.
Delitto 2015	169 patients, 88 males and 81 females, 87 surgical group with an average age of 66.6 years old and 82 PT group with an average age of 69.8 years old, LSS by computed	1) Surgical decompressive laminectomies, partial facet resection, and neuroforaminotomies (n=87) 2) PT program: lumbar flexion exercises, exercises and education (n=82)	1) SF-36 physical function **Follow-up:** 2 years	**2 years -SF-36 Physical Function, MD and 95% CI** 0.9 (7.9 to 9.6) **Adverse events:** 9 out of 82 participants in group 2 reported adverse events consisting of worsening of symptoms whereas 33 out 87 participants in group 1 reported surgery related complications, mainly attributable to reoperation, delay in wound healing and surgical site infection.

	tomography - criteria of Wiesel and colleagues (18) or magnetic resonance imaging - criteria of Boden and colleagues (2) **Setting:** Neurologic and orthopedic surgery departments and physical therapy clinics in western Pennsylvania			

ADLs = Activities of Daily Living, AUC = Area under the pain-intensity curve, BTX = Botox, CI = Confidence Interval, DMC = Difference in mean change from baseline, ESI = Epidural Steroid Injection, FRI = Functional Rate Index, GRP = Group, HADS =Hospital Anxiety and Depression Scle, IU = International Units, JOABPEQ = Japanese orthopaedic association back pain evaluation questionnaire, LBOS = Low Back Outcome Score, LBP = Low Back Pain, m = Meters, MCS = Mental Component Score, MD = Mean Difference, mm = Millimeters, Mo = Months, MPC = Mean Percent Change, NRS = Numerical Pain Rating Scale, NR = Not Reported, ODI = Oswestry Disability Index, OR = Odds Ratio, PASS-20 = Pain Anxiety Symptoms Scale, PCS = Physical Component Score, RCT = Randomized Controlled Trial, RMDI = Roland Morris Disability Index, ROM = Range of Motion, RR = Relative Risk, SBI = Stenosis Bothersomeness Index, SPWT = Self-Paced Walking Test, SSS = Spinal Stenosis Questionnaire, TSK-11 = Tampa Scale-11, VAS = Visual Analogue Scale, WMD = Weighted Mean Difference, ZCQ = Zurich Claudication Questionnaire

Supplemental Table 2. Non operative interventions for neurogenic claudication due to lumbar spinal stenosis: A summary of GRADE assessment and outcomes (60 comparisons)

						Walking ability/pain/function/quality of life measures				GRADE
Studies	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Selective Reporting**	**Immediate up to 1w**	**Short-term >1w - 3m**	**Intermediate 3m – 1yr**	**Long term >1yr**	
Calcitonin										
Calcitonin injection vs. placebo injection										
Eskola 1992	High	No No	Yes Yes	No No	Yes		= TWT = VAS	= TWT = VAS	= TWT = VAS	+000 +000
Porter 1983	High	No	Yes	No	Yes		? Distance walked	? Distance walked		+000
Porter 1988	High	No No	Yes Yes	No No	Yes		= Distance walked = VAS			+000 +000
Calcitonin nasal spray vs. placebo injection										
Podichetty 2004	High	No No No No	Yes Yes Yes Yes	No No No No	Yes		= Distance walked = Time walked = SF-36 = VAS			+000 +000 +000 +000
Tafazal 2007	High	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No		= Shuttle walk = VAS leg = VAS back = ODI = Global			+000 +000 +000 +000 +000
Calcitonin nasal spray plus physical therapy vs. paracetamol plus physical therapy										
Sahin 2009	High	No No No	Yes Yes Yes	No No No	No		= Distance walked = VAS = RMDI			+000 +000 +000
Oral Medication										
Oral prostaglandin vs. Etodlac (NSAID)										
Matsudaira 2009	Low	No No No No No	Yes Yes Yes Yes Yes	No No No No No	Yes		> Distance walked # ? SF-36 = LBP > Leg pain > Global #			++00 +000 ++00 ++00 ++00
Methylocobalamin (vit B12) plus conservative care vs. conservative care										
Waikakul 2000	High	No	Yes	No	No			> Distance walked #	> Distance walked #	+000

Gabapentin plus physical therapy, corset & NSAIDS vs. placebo plus physical therapy, corset & NSAIDS										
Yaksi 2007	High	No No No	Yes Yes Yes	No No No	No		= VAS	> Distance walked > VAS	> Distance walked # > VAS #	+000 +000
Pregabalin vs. active placebo										
Markman 2015	High	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No	= NPS rest/final = Distance walked = Recovery time = Global < RMDQ				+000 +000 +000 +000 +000
Gabapentin plus conservative vs. conservative plus botulinum										
Park 2017	High	No No No	Yes Yes Yes	No No No	No		= NPS (Back/leg) = ODI = Global			0000 0000 0000
Oxymorphone hydrochloride vs. placebo										
Markman 2015 - 2	High	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No	= NPS rest/final = Distance walked = Recovery Time = ZCQ (s) = ZCQ (f) = Global				0000 0000 0000 0000 0000 0000
Propoxyphene/acetaminophen vs. placebo										
Markham 2015 – 2	High	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No	= NPS rest/final = Distance walked = Recovery Time = ZCQ (s) < ZCQ (f) # = Global				0000 0000 0000 0000 0000 0000
Oxymorphone hydrochloride vs. propoxyphene/acetaminophen										
Markham 2015 - 2	High	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No	= NPS rest/final = Distance walked = Recovery Time = ZCQ (s) > ZCQ (f) # = Global				0000 0000 0000 0000 0000 0000
Oral corticoid vs. placebo										

Rodrigues 2014	High	No No No No	Yes Yes Yes Yes	No No No No	No		= SF-36 = RMDQ = 6 min walk < VAS #			0000 0000 0000 0000
Rehabilitation Therapy and Multimodal Care										
Exercise plus ultrasound vs. exercise plus sham ultrasound										
Goren 2010	low	No No No No	Yes Yes Yes Yes	No No No No	No		= TWT = VAS back = VAS leg = ODI			++00 ++00 ++00 ++00
Exercise plus ultrasound vs. no treatment										
Goren 2010	Low	No No No No	Yes Yes Yes Yes	No No No No	No		= TWT = VAS back > VAS leg # > ODI			++00 ++00 ++00 ++00
Exercise plus sham ultrasound vs. no treatment										
Goren 2010	Low	No No No No	Yes Yes Yes Yes	No No No No	No		= TWT = VAS back > VAS leg # > ODI #			++00 ++00 ++00 ++00
In-patient physical therapy vs. home exercise program plus oral diclofenac										
Koc 2009	High	No No No No	Yes Yes Yes Yes	No No No No	Yes		= TWT = VAS = RMDI = NHP	= TWT = VAS = RMDI = HNP		+000 +000 +000 +000
Unweighted treadmill walking plus exercise vs. cycling plus exercise										
Pua 2007	Low	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No		= Distance walked = ODI = RMDI = VAS = Global			++00 ++00 ++00 ++00 ++00
Manual therapy, exercise and unweighted treadmill vs. flexion exercise, walking and sham ultrasound										
Whitman 2006	High	No No No No	Yes Yes Yes Yes	No No No No	No		= TWT > Global # = ODI = NPRS			+000 +000 +000 +000
Supervised physical therapy vs home exercises										

Minetama 2019	High	No No No No No No No No	Yes Yes Yes Yes Yes Yes Yes Yes	No No No No No No No No	No		> ZCQ (F) # >ZCQ (S) # > Distance walked # > NPS (leg) > SF-36 PF > SF-36 BP = Daily Steps			+000 +000 +000 +000 +000 +000 +000
Manual therapy & exercise vs medical care										
Schneider 2019	Low	No No No	Yes Yes Yes	Yes Yes Yes	No		> ZCQ # = SPWT = PA	= ZCQ = SPWT = PA		+++0 +++0 +++0
Manual therapy & exercise vs. community exercise										
Schneider 2019	Low	No No No	Yes Yes Yes	Yes Yes Yes	No		> ZCQ # = SPWT = PA	= ZCQ = SPWT = PA		+++0 +++0 +++0
Community exercise vs. medical care										
Schneider 2019	Low	No No No	Yes Yes Yes	Yes Yes Yes	No		= ZCQ = SPWT > PA	= ZCQ = SPWT = PA		+++0 +++0 +++0
Comprehensive therapy and exercise vs. self-directed exercise										
Ammendolia 2018	Low	No No No No No No No No	Yes Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes Yes	No	> SPWT # > 30% SPWT > 50% SPWT > ZCQ (s) = ZCQ (f) = ODI > NPS (back) # = NPS (leg) = SF-36 BP = SF-36 PF	> SPWT # > 30% SPWT = 50% SPWT = ZCQ (s) = ZCQ (f) = ODI = NPS (back) = NPS (leg) = SF-36 BP > SF-36 PF #	> SPWT # > 30% SPWT = 50% SPWT = ZCQ (s) = ZCQ (f) > ODI (walk) = NPS (back) = NPS (leg) = SF-36 BP = SF-36 PF	> SPWT # >30% SPWT > 50% SPWT > ZCQ (f) # > ZCQ (s) + ZCQ (f) = ODI = NPS (back) > SF-36 BP # >SF-36 PF #	+++0 +++0 +++0 ++00 ++00 ++00 ++00 ++00 ++00 ++00
Standard exercise vs. isokinetic exercises										
Oğuz 2013	High	No No No	Yes Yes Yes	No No No	Yes	= VAS = ODI = TWT	= VAS = ODI = TWT	= VAS = ODI = TWT		0000 0000 0000
Standard exercise vs. unloaded exercise										
Oğuz 2013	High	No No No	Yes Yes Yes	No No No	Yes	< VAS < ODI = TWT	< VAS = ODI = TWT	= VAS = ODI = TWT		0000 0000 0000

Isokinetic exercises vs. unloaded exercises										
Oğuz 2013	High	No No No	Yes Yes Yes	No No No	Yes	< VAS < ODI < TWT #	= VAS < ODI < TWT	= VAS = ODI = TWT		0000 0000 0000
Aquatic physical therapy exercise vs. physical therapy										
Homayouni 2015	High	No No	Yes Yes	No No	Yes	> VAS # > Distance walked	= VAS = Distance walked			0000 0000
Pre-surgical exercise program vs. routine preoperative hospital management										
Marchand 2019	High	No No	Yes Yes	No No	Yes	> NPS (leg) # > Duration walked #	= NPS (leg) = Duration walked	= NPS (leg) = Duration walked		0000 0000
Gang-Chuk Tang (herbal concoction), daily Mokuri Chuna therapy, daily acupuncture, physician consultation vs. oral aceclofenac, epidural steroid injection, physical therapy										
Kim 2019	Low	No No No No	Yes Yes Yes Yes	No No No No	Yes		= VAS (leg) = VAS (back) > OCS > Distance walked	= VAS (leg) > VAS (back) # = OCS > Distance walked		+000 +000 +000 +000
Mokhuri Chuna, acupuncture, and physician consultation vs. oral aceclofenac, epidural steroid injection, physical therapy										
Kim 2019	Low	No No No No	Yes Yes Yes Yes	No No No No	Yes	>VAS (low back)#	= VAS (leg) = VAS (back) = OCS = Distance walked	> VAS (leg) # > VAS (back) # = OCS = Distance walked		+000 +000 +000 +000
Spinal Manipulation										
Lumbar spinal manipulation vs. waiting										
Passmore 2017	High	No No	Yes Yes	No No	No	= NPS (Back) = NPS (Leg)				0000 0000
Acupuncture										
Acupuncture with usual care vs. usual care										

Kim 2016	High	No No No No No No No No No No No No	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	No No No No No No No No No No No No	No		6 weeks: = ODI = SF-36 BP = SF-36 PF = LBP = Leg pain = Distance walked 3 months: = ODI = SF-36 BP = SF-36 PF = LBP = Leg pain = Distance walked			0000 0000 0000 0000 0000 0000 0000 0000 0000 0000 0000 0000
Acupuncture vs. sham acupuncture										
Qin 2020	Low	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No	> RMDQ > NRS (back) # > NRS (leg) # > SSS-S # > SSS-F # = SPWT	> RMDQ > NRS (back) # > NRS (leg) # > SSS-S # > SSS-F # = SPWT	> RMDQ > NRS (back) # > NRS (leg) # > SSS-S # > SSS-F # = SPWT		++00 ++00 ++00 ++00 ++00 ++00
Epidural Injection										
Translaminar epidural steroid injections vs. placebo injections										
Cuckler 1985	High	No	Yes	No	No	= Global			=global	+000
Translaminar epidural steroids plus epidural block vs. placebo injections										
Fukusaki 1988	High	No	Yes	No	No	> Distance walked #	= Distance walked			+000
Translaminar epidural steroids plus epidural block vs. epidural block injections										
Fukusaki 1988	High	No	Yes	No	No	= Distance walked	= Distance walked			+000
Translaminar epidural block vs. placebo										
Fukusaki 1988	High	No	Yes	No	No	> Distance walked #	= Distance walked			+000
Intralaminar epidural steroid plus epidural block vs. home exercise program plus oral diclofenac										
Koc 2009	High	No No No	Yes Yes Yes	No No No	Yes Yes Yes		= TWT > VAS # > RMDI #	= TWT = VAS = RMDI		+000 +000 +000

		No	Yes	No	Yes		> NHP	= HNP		+000
Intralaminar epidural steroid plus epidural block vs. in-patient physical therapy										
Koc 2009	High	No No No No	Yes Yes Yes Yes	No No No No	Yes Yes Yes Yes		= TWT = VAS = RMDI = NHP	= TWT = VAS = RMDI = HNP		+000 +000 +000 +000
Caudal epidural steroids vs. placebo injections										
Zahaar 1991	High	No	Yes	No	No	= Global			= Global	+000
Mild lumbar decompression vs. epidural steroid injection										
Brown 2012	High	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No		= VAS = ODI = ZCQ 12 weeks: = VAS = ODI = ZCQ			0000 0000 0000 0000 0000 0000
Lidocaine vs. glucocorticoid–lidocaine										
Friedly 2014, 2017	Low	No No No No	Yes Yes Yes Yes	Yes Yes Yes Yes	No		3 weeks: < RMDQ < NPS (leg) 6 weeks: = RMDQ = NPS (leg)	12 weeks: = RMDQ = NPS (leg) 6 months: = RMDQ = NPS (leg)	12 months: = RMDQ = NPS (leg)	 +++0 +++0 +++0 +++0
Makris 2016	Low	No No No No	Yes Yes Yes Yes	No No No No	Yes Yes Yes Yes		Makris 2016 3 weeks: < RMDQ using SIP Weights < RMDQ Patient-Prioritized (LESSER) 6 weeks: < RMDQ using SIP Weights = RMDQ Patient-Prioritized (LESSER)			 0000 0000 0000 0000

Lidocaine spinal injection vs. saline spinal injection										
Song 2016	High	No No No No	Yes Yes Yes Yes	No No No No	No		1 month: = VAS = FRI 3 months: = VAS = FRI			0000 0000 0000 0000
Fluoroscopically guided lumbar ILESIS at the level of maximal stenosis vs. two intervertebral levels cephalad										
Milburn 2014	High	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No	1 week: > NPS (walking) # > RMDQ #	4 weeks: > NPS (walking) # > RMDQ 12 weeks: = NPS (walking) > RMDQ			0000 0000 0000 0000
Epidural steroid injection (ESI) Vs. ESI & physiotherapy										
Hammerich 2019	High	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No		= ODI = NPS > SF-36 ER # > SF-36 EWB > SF-36 GH	= ODI > NPS # = SF-36 ER = SF-36 EWB = SF-36 GH	= ODI > NPS # = SF-36 ER = SF-36 EWB = SF-36 GH	0000 0000 0000 0000 0000
Interlaminar vs. transforaminal epidural steroid injection										
Sencan 2020	High	No No No No No No No No	Yes Yes Yes Yes Yes Yes Yes Yes	No No No No No No No No	Yes	= NPS	3 weeks: = NPS = ODI > BDS = Distance walked	3 months: > NPS = ODI > BDS > Distance walked #		0000 0000 0000 0000 0000 0000 0000 0000
TNF alpha inhibitor (Etanercept) vs. steroid injection										
Wei 2020	Low	No No No	Yes Yes Yes	No No No		> VAS #	1, 3 months: > VAS # > ODI #	6 months: > VAS # > ODI #		++00 ++00 ++00
TNF alpha inhibitor (Etanercept) vs. lidocaine										

Wei 2020	Low	No No No	Yes Yes Yes	No No No		> VAS #	1, 3 months: > VAS # > ODI #	6 months: > VAS # > ODI #		++00 ++00 ++00
Steroid vs. lidocaine injection										
Wei 2020	Low	No No No	Yes Yes Yes	No No No		= VAS	1, 3 months: = VAS = ODI	6 months: = VAS = ODI		++00 ++00 ++00
Percutaneous Epidural Adhesiolysis										
Balloon-less catheter (Racz) vs. inflatable balloon catheter (ZiNeu)										
Karm 2018	High	 No No No No No No	 Yes Yes Yes Yes Yes Yes	 No No No No No No	No		1 month: = NPS (back) = NPS (leg) = ODI 3 months: = NPS (back) = NPS (leg) = ODI	6 months: < NPS (back)# < NPS (leg) # < ODI		 0000 0000 0000 0000 0000 0000
Surgery vs. Physical Therapy										
Interspinous spacer (X_Stop) vs. non operative care										
Zucherman 2004, 2005, Hsu 2006	High	No No	Yes Yes	No No	No		> ZCQ(S)# > ZCQ(F)# > SF-36 PF > SF-36 BP > SF-36 GH > SF-36 ER	> ZCQ(S)# > ZCQ(F)# > SF-36 PF > SF-36 BP > SF-36 GH > SF-36 ER	> ZCQ(S)# > ZCQ(F)# > SF-36 PF# > SF-36 BP# > SF-36 GH > SF-36 ER#	+000 +000 +000 +000 +000 +000
Laminectomy +/- fusion vs. non operative care for degenerative spondylolisthesis										

Weinstein 2007, 2009 Abdu 2018	High	No No No No No No No No No No No No No No No	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	No No No No No No No No No No No No No No No	No		= SF-36 BP, PF = ODI = LBPBS = LPBI = SBS	= SF-36 BP, PF = ODI = LBPBS = LPBI = SBS	2 years: = SF-36 BP, PF = ODI = LBPBS = LPBI = SBS 4 years: = SF-36 BP, PF = ODI = LBPBS = LPBI = SBS 8 years: = SF-36 BP, PF = ODI = LBPBS = LPBI = SBS	+000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000
Laminectomy +/- fusion vs. non operative care										
Amundsen 2000	High	No No	Yes Yes	No No	No		?* Pain severity	?* Global	?* Pain severity ? Global	+000 +000
Malmivaara 2007 N= 94	Low	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No			= TWT = SW > VAS leg walk # > VAS LB walk # > ODI	= TWT = SW > VAS leg walk # > VAS LB walk # > ODI	++00 ++00 ++00 ++00 ++00 ++00
Weinstein 2008, 2010, Lurie 2015	High	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No		= SF-36 BP = SF-36 PF = LBPBS = LPBI = SBS = ODI	= SF-36 BP = SF-36 PF = LBPBS = LPBI = SBS = ODI	2 years: > SF-36 BP ** # = SF-36 PF = LBPBS = LPBI = SBS = ODI 4 years: =SF-36 BP ** = SF-36 PF = LBPBS = LPBI	+000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000

									= SBS 8 years: = SF-36 BP = SF-36 PF = ODI = Stenosis Index	+000 +000 +000 +000
Laminectomy, facet resection, neuroforaminotomy vs. physical therapy										
Delitto 2015	High	No No	Yes Yes	No No	No				2 years: = SF-36 = ODI	+000 +000

> favours intervention (first comparison), < favours control (second comparison), = no difference between intervention and control groups, TWT= Treadmill Walking Test, VAS= Visual Analog Scale for Pain Intensity, RMDI= Roland-Morris Back Disability Index, NHP= Nottingham Health Profile, Global= Patient Perceived Improvement, SR= Selective Reporting, ODI= Oswestry Back Disability Index, ?= insufficient data, LBP= Low back Pain Severity Scale, Leg pain= Leg Pain Severity Scale, ? SF-36=No data on overall score, improvement in some subscales, NPRS= Numeric Pain Rating Scale, SF-36 BP= SF-36 Bodily Pain Subscale, SF-36- PF= SF-36 Physical Function Subscale, SF-36 ER= SF-36 emotional role subscale, SF-36 EWB= SF-36 emotional well-being subscale, SF-36 GH= SF-36 General health subscale, LBPBS= Low Back Pain Bothersome Scale, LPBI= Leg Pain Bothersome Index, SBS= Stenosis Bothersome Scale, SW= Subjective Walking, VAS leg= Visual Analog Scale for Leg Pain, VAS LB= Visual Analog Scale for Low Back Pain, VAS leg walking= Visual Analog Scale for Leg pain while walking, SIP= sickness index profile, BDS= Beck Depression Score, LESSER= Lumbar Epidural Steroid Injection for Spinal Stenosis Extended Research, PA= Physical Activity, FRI= Functional Rating Index, TWT= Total Walking Time, SSS= Spinal Stenosis Questionnaire, ?*= no between group statistical comparisons, **= SF-36 BP significantly better at 2 years but not 4 years.

GRADE evidence; +000= Very low GRADE evidence, ++00= Low GRADE, +++0= Moderate GRADE evidence, ++++= High GRADE evidence

between group difference meeting the MCID. The MCID used were: ≥1.25 points for back pain and ≥1.5 points for leg pain on 0- to 100-point Visual Analogue Scale (VAS) and 0 to 10-point Numerical Rating Scale (NRS) for back pain (58), ≥5 points on 0- to 24-point Roland-Morris Disability Questionnaire (RMDQ) (59), ≥8 points for conservative treatment and ≥12 points for surgery on 0- to 100-points for Oswestry Disability Index (ODI) (60), ≥ 0.1 points for the functional component and 0.36 points for symptom component of the Zurich Claudication Questionnaire (ZCQ) (58), ≥ 0.38 points for combined symptoms and functional scores of the ZCQ (92), ≥ 30% between-group difference for walking distance, global improvement and SF36 subscales (61).

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 6-7
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 7
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 9
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 8-9
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 8-9
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 9
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 9
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 8 & 10
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 8-10 Supplemental Table 1
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 9-10
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 11-12
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 11-12
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 11-12
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Supplemental Table 2
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 10
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Supplemental Table 1
Risk of bias	18	Present assessments of risk of bias for each included study.	Table 1
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplemental Table 1 & 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Table 2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Supplemental Table 2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	NA
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Supplemental Table 2
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 25-26
	23b	Discuss any limitations of the evidence included in the review.	Page 28-29
	23c	Discuss any limitations of the review processes used.	Page 28-29
	23d	Discuss implications of the results for practice, policy, and future research.	Page 28
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 7
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	NA
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 30
Competing interests	26	Declare any competing interests of review authors.	Page 30
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	NA

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Nonoperative treatment for lumbar spinal stenosis with neurogenic claudication: An updated systematic review.

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ABSTRACT

Objectives: Neurogenic claudication due to lumbar spinal stenosis (LSS) is a growing health problem in older adults. We updated our previous Cochrane review (2013) to determine the effectiveness of nonoperative treatment of LSS with neurogenic claudication.

Design: A systematic review.

Data Sources: CENTRAL, MEDLINE, EMBASE, CINAHL, and ICL databases were searched and updated to July 22nd, 2020.

Eligibility criteria: We only included randomized controlled trials published in English where at least 1 arm provided data on nonoperative treatment and included participants diagnosed with neurogenic claudication with imaging confirmed LSS.

Data Extraction and synthesis: Two independent reviewers extracted data and assessed risk of bias using the Cochrane Risk of Bias Tool One. Grading of Recommendations Assessment, Development, and Evaluation (GRADE) was used for evidence synthesis.

Results: Of 15,200 citations screened, 156 were assessed and 23 new trials were identified.

There is moderate quality evidence from 3 trials that: Manual therapy and exercise provides superior and clinically important short-term improvement in symptoms and function compared to medical care or community-based group exercise; Manual therapy, education and exercise delivered using a cognitive-behavioural approach, demonstrates superior and clinically important improvements in walking distance in the immediate to long-term compared to self-directed home exercises; Glucocorticoid plus lidocaine injection is more effective than lidocaine alone in improving statistical, but not clinically important, improvements in pain and function in the short-term.

The remaining 20 new trials demonstrated low or very low-quality evidence for all comparisons and outcomes, like the findings of our original review.

Conclusions: There is moderate quality evidence that a multimodal approach which includes manual therapy and exercise, with or without education is an effective treatment, and that epidural steroids are not effective for the management of LSS with neurogenic claudication. All other nonoperative interventions provided insufficient quality evidence to make conclusions on their effectiveness.

This systematic review was registered with PROSPERO registration number CRD42020191860.

ARTICLE SUMMARY

Strengths and limitations of this study

- This systematic review included a wide range of nonoperative interventions commonly used in clinical practice.
- This review used consistent inclusion and exclusion criteria for neurogenic claudication, which included the corroboration of a diagnosis of lumbar spinal stenosis with imaging.
- This review used rigorous methods recommended by the Cochrane Back and Neck Pain Review Group including the use of Grading of Recommendations, Assessment, Development and Evaluation (GRADE) to synthesize and summarize the quality of the evidence.
- Only English studies were included in this review.

- Most studies had small samples sizes with heterogeneity in interventions tested, limiting ability to pool data.

Key words: neurogenic claudication, lumbar spinal stenosis, systematic review, nonoperative treatment, elderly

INTRODUCTION

Lumbar spinal stenosis (LSS) causing neurogenic claudication is a highly prevalent and rapidly growing public health problem among older adults (1). It is characterized by bilateral or unilateral buttock pain and/or lower extremity discomfort, pain, weakness, or heaviness precipitated by walking and prolonged standing and relieved by stooping forward and sitting (2, 3). The underlying etiology is usually age-related osteoarthritic changes to lumbar intervertebral discs, facets joints and ligaments leading to narrowing of the central and/or lateral spinal canals and compression and/or ischemia of the spinal nerves (2, 4).

Limited walking ability is the dominant impairment in neurogenic claudication and the most common reason for seeking care (5). Limited walking ability due to LSS is associated with a significant decline in functional status, quality of life and independence in this population (2, 5).

Although lumbar spinal stenosis is the most common reason for spine surgery in older adults, most people with neurogenic claudication receive nonoperative care (6). A course of nonoperative care is also recommended prior to receiving surgical intervention (7). However, what constitutes effective nonoperative care remains unknown. In 2013 we published a Cochrane review evaluating

nonoperative treatment for LSS causing neurogenic claudication (8, 9). This review identified 21 randomized controlled trials assessing a variety of nonoperative treatments. However, the quality of the evidence was deemed low or very low and therefore no conclusions could be made on the effectiveness of nonoperative treatment for neurogenic claudication. The purpose of this study is to update this systematic review and the evidence for nonoperative treatments for neurogenic claudication. Our specific research question was: What nonoperative interventions are effective in improving outcomes in patients with neurogenic claudication due to lumbar spinal stenosis?

METHODS

This systematic review was registered with PROSPERO registration number CRD42020191860 and was conducted and reported according to the PRISMA guidelines (10). We used methods recommended by the Cochrane Back Review Group (11).

Ethics Approval Statement

Ethics approval was not required for conducting this systematic review.

Patient and Public Involvement Statement

Patients or the public were not involved in the conduct of this systematic review.

Population, Interventions, Comparison and Outcomes (PICO Criteria)

The population of interest was individuals with imaging confirmed LSS (central or foraminal, with or without spondylolisthesis) and neurogenic claudication. Neurogenic claudication is a clinical diagnosis and was defined as buttock or leg pain and/or aching, numbness, tingling, weakness, or fatigue with or without back pain, precipitated by standing or walking. There were no age restrictions. The interventions of interest included all nonoperative treatments and the comparison was any treatment including surgery. Outcomes included at least one of the following measures: walking ability, pain intensity, physical function, quality of life, or global improvement.

Search and Study Selection

We replicated and updated our original electronic database search (from 1966 to January 2011) to July 22nd 2020. The search was performed by an experienced librarian in CENTRAL (Cochrane Library 2011 issue1), Medline, EMBASE, CINAHL and Index to Chiropractic Literature. The terms “spinal stenosis,” “lumbar spinal stenosis,” “neurogenic claudication,” “lumbar radicular pain,” "cauda equina," and “spondylosis” were combined with a highly sensitive search strategy to identify randomized controlled trials (RCTs). Reference lists of selected studies and previous reviews were also searched to identify additional articles. Supplemental file 1 provides details on the full search strategies used for all databases.

Studies were included if they were RCTs published in peer reviewed English journals, at least one arm of the trial provided data on effectiveness of a nonoperative treatment and at least 80% of subjects had neurogenic claudication with imaging confirmed LSS. Studies evaluating subjects with radiculopathy caused by disc herniations without neurogenic claudication were excluded.

Studies with mixed populations were only included if separate data for subjects with neurogenic claudication due to lumbar spinal stenosis were provided.

Two pairs of reviewers independently screened all titles and abstracts identified by the search strategy. Full text of articles deemed to be potentially relevant were independently assessed by two reviewers who made the final decision for inclusion. A third reviewer was consulted if consensus was not reached.

Risk of Bias Assessment and Data Analysis

Two reviewers independently assessed methodological risk of bias and performed data extraction. Safety data (intervention side effects and/or complications) when available were also collected. The Cochrane Risk of Bias Tool 1 was used that included the 12-item criteria recommended by the Cochrane Back Review Group (11). Discrepancies in risk of bias scoring and data extraction were resolved with discussion and if necessary, with a third reviewer until consensus was reached. Reviewers who were authors of any of

the included studies were recused from performing risk of bias assessment, data extraction, data analysis or synthesis of their own studies.

Low risk of bias was defined as fulfilling 6 or more of the 12 criteria including clearly described and appropriate randomization (Item A), and allocation concealment (Item B), and with no severe flaws. A severe flaw was defined *a priori* as a serious methodological deficiency not captured by the 12-item criteria that significantly increases the risk of bias such as very high dropout or cross-over rates and sample sizes less than 30 subjects per treatment arm.

For each comparison, outcomes were analyzed according to these follow-up time periods: immediate (up to one week following the intervention); short-term (between one week and three months); intermediate (between three months and one year) and; long-term (one year or longer). Outcome data were pooled, and meta-analyses were performed when trials were judged to be sufficiently homogeneous, both clinically and statistically.

Rehabilitation therapy was defined as treatment that utilized any combination of education, exercise instruction, manual therapy, heat and cold applications, electrotherapy, other physical therapy modalities, orthosis, and other assistive devices. Multimodal treatment included various combinations of rehabilitation therapy treatments, oral and other mediations, and spinal injections, but not surgery.

Data Synthesis

The quality of the evidence for each outcome and for each comparison was evaluated using GRADE (Grades of Recommendations, Assessment, Development and Evaluation (12, 13) Overall quality of the evidence was based on performance against five domains: 1) risk of bias; 2) consistency of findings; 3) directness of comparisons; 4) precision of estimates; and 5) other considerations such as selective reporting.

The quality of the evidence starts at high when there are consistent findings among at least 75% of RCTs with low risk of bias and consistent, direct, and precise data and with no known or suspected publication bias. It downgrades a level for each domain not met. Treatment effects between comparators (more effective, less effective or no difference) were based on statistically significant and clinically important differences in outcomes.

High quality evidence - all five domains are met; further research is very unlikely to change the confidence in the estimate of effect.

Moderate quality evidence - one of the domains is not met; further research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate.

Low quality evidence - two domains are not met; further research is very likely to have an important impact on the confidence of the estimate of effect and is likely to change the estimate.

Very low-quality evidence - three or more domains are not met; there is great uncertainty about the estimate of effect.

Evidence provided by a single small trial was considered inconsistent and imprecise and thus provide "low" or "very low" quality evidence, depending on whether it was assessed as having a low or high risk of bias, respectively, and there were no other limitations. Studies with both low risk of bias and inappropriate or unclear randomization and/or treatment allocation techniques were downgraded by two levels for the "risk of bias" domain.

The results below are reported based on statistically significant differences between comparators for each outcome using data reported by authors. Differences considered clinically important will be specified when the quality of the evidence is moderate or higher. The MCIDs we used are listed in Supplemental Table 2. Adverse events for the new studies are detailed when reported by the authors.

RESULTS

Selection and Description of Included Trials

We screened 15,200 titles and abstracts and assessed 156 full-text articles. This resulted in 44 RCTs meeting the inclusion criteria, including 23 new trials. Figure 1 summarizes original and updated screening results. Supplemental Table 1 describes the characteristics of all included trials. In total, 3,792 participants (1,765 males, 1836 females and 191 participants of undisclosed gender (14, 15) were randomized to one of 60 comparison groups. Seventeen studies evaluated rehabilitation therapy or multimodal care (14, 16-31), 11 assessed epidural injections (32-42), 7 evaluated oral medications (15, 43-48), 6 assessed calcitonin (49-54), 2 evaluated

acupuncture (55, 56) and 1 assessed spinal manipulation (57). Thirty-eight trials were conducted at tertiary care or university affiliated centres and 6 at medical/rehabilitation clinics (18, 24, 35-38). The mean age of participants was 63.3 years. The duration of symptoms varied considerably amongst the studies with a mean ranging from 12 weeks to 15 years. Follow-up periods also varied significantly ranging from immediately following the intervention to 10-year post intervention.

Risk of Bias of Included Studies

The median and mean number of criteria met was 7 of 12 (range 2-11), see Table 1.

Table 1. Risk of bias assessment for studies on non-operative treatment for lumbar spinal stenosis with neurogenic claudication

Author	A	B	C	D	E	F	G	H	I	J	K	L	Total
Calcitonin													
Eskola 1992	?	?	+	+	+	?	+	-	?	?	?	+	5
Porter 1983	?	?	-	?	?	+	+	?	-	?	+	+	4
Porter 1988	?	?	+	?	?	-	+	+	?	?	?	+	4
Podichetty 2004	?	?	+	+	+	-	+	-	+	?	?	+	6
Tafazal 2007	?	?	+	+	+	+	+	+	-	?	?	+	7
Sahin 2009	?	?	-	-	+	-	?	+	+	?	?	+	4
Oral Medications													
Prostaglandin													
Matsudaria 2009	+	+	-	-	+	+	+	?	+	?	?	+	7*
Methylcabalin													
Waikakul 2000	-	?	-	-	+	+	+	?	+	?	?	+	5
Gabapentin													
Yaksi 2007	?	?	-	-	-	?	+	+	?	?	?	+	3
Pregabalin													
Markman 2015	+	+	+	+	+	+	+	+	?	+	-	+	10 ****

Gabapentin													
Park 2017	+	?	+	+	+	+	+	+	?	?	-	+	8 *****
Oxymorphone Hydrochloride													
Markman 2015 (2)	+	+	+	+	+	-	?	+	?	+	+	+	9 **** #
Oral Corticoid													
Rodrigues 2014	+	+	?	?	?	+	+	?	?	?	?	+	5
Rehabilitation Therapy or Multimodal													
Goren 2010	+	+	-	-	+	+	-	+	+	?	?	+	7 *
Koc 2009	?	?	-	-	+	+	+	-	+	?	?	+	5
Pua 2007	+	+	-	-	+	-	+	+	+	?	-	+	7 *
Whitman 2006	+	?	-	-	+	+	+	+	+	?	?	+	7
Minetama 2019	+	?	-	-	+	+	+	+	?	+	+	+	8 *****
Schneider 2019	+	+	-	-	+	-	+	+	+	?	+	+	8 *
Ammendolia 2018	+	+	-	-	+	+	+	+	+	+	+	+	10 *
Oğuz 2013	?	?	-	-	?	?	+	-	?	?	?	+	2
Homayouni 2015	+	+	-	-	+	+	+	-	-	+	?	+	7 ****
Marchand 2019	+	+	-	-	+	?	+	+	?	-	+	+	7 ****
Kim 2019	+	+	+	+	+	+	+	+	?	+	+	+	11 *
Spinal Manipulation													
Passmore 2017	-	+	-	-	+	+	+	-	+	+	+	+	8 ****
Acupuncture													
Kim 2016	+	+	-	-	-	-	+	+	-	+	+	+	7 ****
Qin 2020	+	+	+	-	+	+	+	+	+	-	+	+	10 *
Epidural Injections													
Cuckler 1985	?	?	+	+	+	+	+	+	+	?	+	+	9
Fukusaki 1988	?	?	?	?	+	+	+	+	+	?	+	+	7
Zahaar 1991	?	?	+	?	+	+	+	+	+	-	?	-	6
Brown 2012	+	-	+	-	?	+	+	-	?	?	-	+	5
Friedly 2014, 2017, Makris 2016	+	+	+	+	+	+	+	+	?	+	+	+	11 *
Song 2016	?	?	?	?	?	+	+	-	?	+	+	+	5

Milburn 2014	?	?	+	-	+	-	+	-	?	-	-	+	4
Hammerich 2019	+	+	-	-	+	-	+	?	?	-	+	+	6 ****
Sencan 2020	+	?	+	-	+	+	?	+	+	+	?	+	8 *****
Wei 2020	+	+	+	-	-	+	-	+	?	+	+	+	8 *
Percutaneous Epidural Adhesiolysis													
Karm 2018	+	?	+	-	+	-	+	+	?	-	-	+	6 *****
Surgery vs Physical Therapy													
Zucherman 2004, 2005, 2006	?	+	-	-	+	+		+	+	?	+	+	>6 **
Weinstein 2007, 2009, Abdu 2018	+	+	-	-	+	+	+	+	?	?	-	+	>6 *** ^
Amundsen 2000	+	?	-	-	-	+	+	+	-	?	-	?	4
Malmivaara 2007	+	+	-	-	+	+	+	+	+	?	?	+	8 *
Weinstein 2008, 2010, Lurie 2015	+	+	-	-	+	-	+	+	?	?	-	+	6 ^
Delitto 2015	+	+	-	-	+	?	+	-	+	-	+	+	7 ^

A Was the method of randomization adequate?, B Was the treatment allocation concealed?, C Was the patient blinded to the intervention?, D Was the care provider blinded to the intervention?, E Was the outcome assessor blinded to the intervention?, F Was the drop-out rate described and acceptable?, G Were all randomized participants analyzed in the group to which they were allocated?, H Are reports of the study free of suggestion of selective outcome reporting?, I Were the groups similar at baseline regarding the most important prognostic indicators?, J Were co-interventions avoided or similar?, K Was the compliance acceptable in all groups?, L Was the timing of the outcome assessment similar in all groups?, + Yes, - No, ? Unclear, * Low risk of bias if 6 or more items met, including valid randomization and treatment allocation techniques and no severe flaws, ** 2 year follow-up drop out rate 30%, 1 year < 20%; intention to treat inconsistent at 2 year f/u, *** Drop out rate <20% at 1 year, >20% at 4 years, **** < 30 participants per treatment arm, ***** Treatment allocation unclear, ^ Severe flaw due to high crossover rates, # Premature end of study

Although 31 studies met 6 or more criteria, only 9 were considered to have low risk of bias (19, 20, 24, 27, 28, 31, 37, 42, 43, 56). Among the remaining 22 studies that met 6 or more criteria, 13 failed to explicitly describe and/or use appropriate randomization procedures, allocation concealment, or both (16-18, 30, 32-34, 39, 41, 48, 52, 54, 57); three had severe flaws due to high crossover rates (21, 22, 25), which made the intention-to-treat analyses uninterpretable and 6 had other serious flaws including premature

stopping of the trial (47), large number of participants lost to follow-up (40) and small sample size (less than 30 participants per arm) (26, 29, 46, 55).

Evidence of Effect of Interventions

Fifty-three of the 60 comparisons were examined in a single trial, most with small sample sizes. It was only possible to combine data from 2 trials (assessing surgery vs. multimodal treatment) for 1 outcome in a meta-analysis (19, 22). The 5 other studies (all assessing calcitonin) (49-52, 54) were combined qualitatively. The results of these pooled analyses were published in our previous reviews (8, 9). Heterogeneity in source population, intervention, and outcome instruments precluded pooling of data from other trials. Supplemental Table 2, a summary of GRADE assessment and outcomes, summarizes the quality of the evidence for outcomes for each comparison.

Calcitonin

There were no new studies assessing calcitonin. The conclusion from our previous review was that there is very low-quality evidence from 6 trials (49-54) (N= 231) that calcitonin is no better than placebo or paracetamol regardless of mode of administration or outcome assessed.

Oral Medication

We identified 4 new studies assessing 5 oral medications. There is low-quality evidence based on 1 small cross-over trial (46) (N=29), that pregabalin does not improve pain, distance walked, function or global health status immediately following the intervention compared to placebo. Adverse events were reported in 64% of the pregabalin group, the most common being dizziness, compared to 35% in the placebo group.

A small trial evaluating gabapentin plus conservative care (48) (N=45) provides very low-quality evidence demonstrating no significant improvement in back/leg pain, disability scores or global health in the short-term compared to conservative care plus botulinum toxin injection. Five patients (20.8%) reported mild to moderate pain at injection sites for a few days after botulinum toxin injections.

There is very low-quality evidence from 1 small trial (47) (N=24) that oxymorphone hydrochloride or propoxyphene and acetaminophen is no better than placebo in the immediate term for all outcomes assessed.

A single small trial provided very low-quality evidence (15) (N=61) that oral corticoids do not improve outcomes in the short-term compared to placebo.

The original review identified 3 studies assessing oral medications and concluded that there is low-quality evidence that prostaglandins improves walking distance and leg pain in the short-term compared with etodolac (a nonsteroidal anti-inflammatory drug) (43); very low-quality evidence that gabapentin improves walking distance and pain compared with placebo in the intermediate and long-term(45) and that methylcobalamin (vitamin B 12) plus conservative treatment improves walking distance in the intermediate and long-term compared with conservative treatment alone (44).

Rehabilitation Therapy and Multi-modal Treatment

We identified 8 new studies evaluating 13 rehabilitation therapy and/or multimodal treatment approaches, with one study being compared to surgery.

There is moderate quality evidence from 1 trial (31) (N=259) that manual therapy and exercise provides superior and clinically important short-term improvement in symptoms and function compared to medical care or community-based group exercise and that community-based group exercise improves physical activity in the short-term compared to medical care. There were no reported serious adverse events in any group. There was a significantly greater rate of transient joint soreness associated with the manual therapy and exercise group (49%) compared with the community-based group exercise (31%) and medical care (6%) groups.

Another trial provides moderate quality evidence (27) (N=104) that comprehensive care (manual therapy, education and exercise delivered using a cognitive-behavioural approach) demonstrates superior and clinically important improvements in walking distance in the immediate, short, intermediate, and long-term and compared to self-directed home exercise. This study also provides low-quality evidence that comprehensive care improves overall pain and function in the long-term compared to self-directed home exercises. At 12 months, none of the 43 participants in the comprehensive group and 2 of the 46 participants in the self-directed group experienced adverse events. These adverse events were mostly attributed to a temporary increase in low back and/or leg pain.

There is low-quality evidence from 1 trial (28) (N=34) that a form of manual therapy (Mokuri Chuna), acupuncture and physician care, with or without a herbal remedy (Gang-Chuk Tang), improves low back pain in the intermediate term compared to oral aceclofenac, epidural steroids and physical therapy (heat and TENS).

A single study assessing supervised physical therapy (manual therapy, exercise, and body weight-supported treadmill) (30) (N= 86) provides low-quality evidence for improved symptoms, function and walking distance in the short-term compared to home exercises.

There is very low-quality evidence from 1 study (14) (N=120) that heat, TENS and home exercise instruction is no better than isokinetic exercise in the immediate, short and intermediate term for all outcomes and less effective than unloaded exercises in the immediate and short-term. Unloaded exercise was also found to be superior to isokinetic exercise in the immediate and short-term.

One small single study (26) (N=47) provides very low-quality evidence that aquatic exercise is more effective than physical therapy (exercise, ultrasound, heat and TENS) in improving pain and walking distance in the immediate term.

Another small single trial (29) (N=40) provides very low-quality evidence that a pre-surgical exercise program improves post-surgical outcomes in the immediate, but not in the short or intermediate terms.

There is low-quality evidence from 1 study (25) (N=169) that a structured physical therapy program (education and exercises) provides similar outcomes to decompression surgery in the long-term (2 years follow-up). Nine out of 82 participants receiving physical therapy reported adverse events consisting of worsening of symptoms whereas 33 out 87 participants reported surgery related complications, mainly attributable to reoperation, delay in wound healing and surgical site infection.

Our original review identified 9 rehabilitation therapy/multi-modal trials of which 5 were compared to surgical interventions. A meta-analysis was conducted for 2 of the surgical trials. Two of the original surgical trials have since published 8-year follow-up results (see below). All studies provide either low or very low-quality evidence.

A meta-analysis (8, 9) that includes 2 trials (22) (19) shows that laminectomy improves outcomes only at the 2 year follow-up compared to conservative care. One of these studies shows no difference in outcomes after an 8-year follow-up (58).

An interspinous surgical implant (17, 59, 60) was found to be superior to multi-modal treatment (epidural injections, pain medication, education, exercise, back brace, heat/ice, and massage). Another trial (16) provided inconclusive evidence when comparing laminectomy with or without fusion to lumbar orthosis and education.

Among patients with degenerative spondylolisthesis, 1 study (21) shows no difference in outcomes with laminectomy when compared to conservative care including after an 8-year follow-up (61).

One study showed that exercise plus ultrasound is no better than exercise plus sham ultrasound but better than no treatment, and exercise plus sham ultrasound is better than no treatment (24). Other studies demonstrated that in-patient physical therapy (ultrasound, heat and TENS) is more effective than home exercise plus oral diclofenac (23), unweighted treadmill walking plus exercise is no better than cycling plus exercise (20), and manual therapy, exercise and unweighted treadmill is more effective than flexion exercises, walking and sham ultrasound (18).

Epidural Injections

We identified 6 new studies evaluating epidural injections. There is moderate quality evidence from 1 study (57, 62) (N=400) that glucocorticoid plus lidocaine injection is better than lidocaine alone in improving pain and function at 3 weeks (short-term) but not at

6-weeks (short-term), 12 weeks (intermediate-term) or 12 months (long-term). The improved outcomes at 3 weeks were statistically significant but not considered to be of clinical importance (63). A follow-up subgroup analysis (64) using patient-prioritized Roland-Morris Disability Questionnaire (RMDQ) items, did not change the results. A total 21.5% of patients in the glucocorticoid-lidocaine group and 15.5% in the lidocaine alone group reported one or more adverse events (p=0.08). Adverse events included headaches, fever, infection, dizziness, cardiovascular/lung problems, leg swelling and dural puncture.

A small study (36) (N=29) provided very low-quality evidence that an injection of lidocaine is no better than a saline injection for all outcomes in the short-term.

There is very low-quality evidence from 1 study (38) (N=57) that steroid injections at the level of maximal stenosis improve pain and function in the immediate and short-term compared to steroid injections at 2 levels cephalad to the maximum level of stenosis.

A small trial (40) (N=54) provided very low-quality evidence that steroid injections are no better than steroid injections combined with physical therapy (manual therapy and exercise) in improving pain or function in the short-term but are more effective in improving pain in the intermediate and long-term.

There is very low-quality evidence from 1 study (41) (N=67) that interlaminar steroid injection improves pain and walking distance in the intermediate but not in the short-term compared to transforaminal steroid injection.

A 3-arm trial (42) (N=30) provided low-quality evidence that TNF alpha inhibitor (Etanercept) injections improved pain and function in the immediate, short and intermediate term compared to steroid or lidocaine injections and that steroid injections were no better than lidocaine for all outcomes and follow-up periods.

There is very low-quality evidence from 1 small trial (35) (N=38) that minimally invasive lumbar decompression surgery (MILD) is no better than epidural steroid injections for all outcomes in the short-term.

One small trial (39) (N=44) provided very low-quality evidence that an epidural inflatable balloon catheter (ZyNeu) improves pain and function in the intermediate term but not the short-term compared to a balloon-less catheter (Racz). Minor and transient adverse events were reported equally in both groups (no data provided), mostly pain and paresthesia at the injection site.

Our original review identified 4 trials evaluating 7 epidural injection approaches, all with very low-quality evidence for all outcomes. Two trials demonstrated that translaminar (32) or caudal (33) steroid injections were no better than placebo. Two other trials showed that translaminar epidural steroid plus a block was better than placebo or an epidural block alone (34), that translaminar epidural block

was better than placebo (34), and that interlaminar epidural steroid plus a block was better than home exercise plus diclofenac or in-patient physical therapy (ultrasound, heat and TENS) (23).

Acupuncture

We identified 2 new studies assessing acupuncture. There is low quality evidence from 1 trial (56) (N=80) that acupuncture improves back and leg pain, symptoms and function in the immediate, short, and intermediate term compared to sham acupuncture. Three out of 40 participants in the acupuncture group reported short-term pain at the insertion site (1 also had a hematoma) and 5 out of the 40 participants in the sham group reported non-serious back pain or fatigue. There is very low-quality evidence from a small trial (55) (N=50) that acupuncture plus usual care is no better than usual care alone in the short-term for all outcomes.

Spinal Manipulation

We identified 1 study assessing spinal manipulation. There is very low-quality evidence from a very small trial (57) (N=14) that spinal manipulation alone is no better than a wait list control in the immediate term for all outcomes

DISCUSSION

We updated our systematic review on nonoperative treatments for LSS causing neurogenic claudication and identified 23 new trials that were added to the previous 21 studies. The highest number of studies, 17/44, evaluated rehabilitation therapy/multimodal treatment, 11 assessed epidural interventions, 7 oral medications, 6 calcitonin, 2 evaluated acupuncture and 1 assessed spinal

manipulation. Of the 60 comparisons that were evaluated, 5 comparisons from 3 trials (27, 31, 37) provided moderate quality evidence. The remaining comparisons provide either low or very low-quality evidence. In our original review, all comparisons for all the interventions assessed were of low or very low-quality evidence. This lack of moderate or high-quality evidence limited our ability to make conclusions on the effectiveness of most nonoperative treatments.

There is now moderate evidence that a multimodal structured 6-week program consisting of manual therapy and exercise with or without education is an effective treatment approach (27, 31) for neurogenic claudication and that epidural steroid injections do not provide clinically important improvements in short or long-term outcomes compared to epidural lidocaine injections. However, given that these respective findings came from single studies, this evidence lacks consistency and therefore there is a possibility that replicating these trials in the future might result in substantially different conclusions. However, a recent clinical practice guideline for the management of LSS leading to neurogenic claudication concurred with our findings and recommended, based on moderate quality evidence, multimodal care consisting of education with home exercises and manual therapy (65). These guidelines also recommended against the use of epidural steroid injections, based on high quality evidence. A recent systematic review and meta-analysis of RCTs evaluating conservative nonpharmacological therapies for degenerative LSS also concluded, based on low to moderate evidence, that manual therapy and supervised exercises significantly improves outcomes compared to self-directed or group exercises (66). A recent clinical update published in the British Medical Journal recommended supervised exercise and manual therapy as a first line treatment for LSS and recommended against the use of epidural steroid injections (67). More dated systematic reviews did not recommend a

combination of education, exercise, manual therapy as an effective treatment for LSS (7, 68, 69). However, these reviews did not include the more recent higher quality trials (27, 31) evaluating this multimodal approach.

A multimodal approach to the treatment of LSS would appear to be a rational approach given the complexity of neurogenic claudication with underlying physical, functional, and psychosocial factors impacting recovery (70). There is also a plausible rationale for the lack of effectiveness of epidural steroid injections for neurogenic claudication since the dominant underlying pathophysiological mechanism appears to be neuro-ischemia rather than neuro-inflammation (4).

Although we cannot make firm conclusions about the effectiveness of nonoperative treatments for neurogenic claudication, this review is important because it provides important information regarding the state of current evidence regarding nonoperative treatments. This can be used to inform clinical practice guidelines and aid clinicians and patients in making clinical decisions regarding treatment options. This is particularly important with respect to interventions that have higher risk and costs such as epidural injections and surgery. About 25% of all epidural injections are performed for LSS (71, 72) yet the evidence from our current review and those of others (73-75) do not support their use. The number and associated costs of surgical procedures for degenerative LSS is growing, especially decompression surgery with complex fusion (76, 77). LSS continues to be the most common reason for spine surgery in older adults (6, 76). High quality evidence for the effectiveness of surgery is also lacking based on our current review and the findings of other systematic reviews (78, 79). Clinical trials evaluating surgery for LSS are difficult to conduct due to

challenges in recruitment and blinding (patient and practitioner) and high costs (80). One ongoing clinical trial is comparing decompression surgery with sham surgery which should help to evaluate the potential role of the placebo effect of surgery for LSS (81).

Oral medication is often the first line treatment in primary care management of LSS (5). Pregabalin and gabapentin are commonly prescribed medications for LSS despite the growing evidence that these medications are not effective for back-related leg symptoms and may cause more harm than good (82-84).

New to this updated review are clinical trials on acupuncture and spinal manipulation, however, the quality of the evidence was insufficient to make conclusions on their effectiveness. A systematic review and meta-analysis of RCTs and controlled clinical trials published in Chinese, found no conclusive evidence for the effectiveness and safety of acupuncture for LSS (85). Passive unimodal treatments such as acupuncture and spinal manipulation are unlikely to provide long-term benefit but more likely to provide benefit when combined with a comprehensive approach to managing LSS (27), not unlike recommendations for managing chronic low back pain (86).

This review is also important because it provides a comprehensive assessment and identification of significant knowledge gaps in this area to guide future research. This includes the need for higher quality studies that assess commonly used non-operative treatments

particularly in primary care settings, that are adequately powered and have low risk of bias and long-term follow-up. Future RCTs should follow the CONSORT guideline (87) when planning trials and reporting study findings in an attempt to improve transparency and reduce bias.

The strengths of this review include the evaluation of a wide range of nonoperative interventions and the use of consistent inclusion and exclusion criteria for neurogenic claudication, which included the corroboration of a diagnosis of LSS with imaging. The use of these criteria to define the study population increases the likelihood that participants in the included studies had the diagnosis of neurogenic claudication due to narrowing of the central canal or lateral foraminae (88-90). Other strengths of this review include the use of rigorous methods recommended by The Cochrane Collaboration, the World Health Organization, and the Cochrane Back and Neck Pain Review Group.(13) This included the use of the GRADE method to synthesize and summarize the quality of the evidence. Limitations of this review include the potential for language bias because only English articles were accepted. We also included studies with small samples sizes which are more prone to high risk of bias (91). Over half of the included studies had less than 30 subjects per arm at baseline, and none of these studies could be pooled because of high heterogeneity across studies. However, the exclusion of studies with small samples sizes in this review would not have changed our conclusions. The definition of a severe flaw and the cut-off point of 6 or more to differentiate trials of low from high risk of bias were arbitrary, therefore alternative definitions and cut-off points or the use of other risk of bias tools could have impacted the findings and conclusions of this review. The validity of MCIDs used in this review is unknown. Although most were derived from studies with neurogenic claudication (63, 92, 93) others

were based on an arbitrary improvement of at least 30% (94). There are no agreed upon MCIDs in LSS and therefore different MCIDs thresholds could have potentially altered our conclusions. The location and severity of the stenosis on imaging was not deemed important in this review. Imaging findings often do not correlate with patient symptoms or severity and therefore imaging by itself is a not reliable diagnostic tool in this population (67, 95, 96). Neurogenic claudication is the clinical entity of interest in this review and, although usually caused by LSS, the diagnosis is made clinically without imaging (97). Neurogenic claudication symptoms, by definitions improve with flexion, due to the increased volume around the involved nerve roots irrespective of where the stenosis is located (e.g., centrally or at the lateral recess). However, it is uncertain whether the effectiveness of some interventions, such as epidural steroid injections is dependent on location of the spinal stenosis. This is a different research question requiring future research.

CONCLUSIONS

There is moderate quality evidence that a multimodal approach that includes manual therapy and exercise, with or without education is a safe and effective treatment, and that epidural steroids are not effective for the management of LSS causing neurogenic claudication. All other studies evaluating nonoperative interventions provided insufficient quality evidence, limiting the ability to make conclusions about their effectiveness. With the growing prevalence and significant personal, social, and economic burden of LSS, more high-quality evidence for nonoperative interventions is urgently needed to guide clinical practice.

CONTRIBUTORSHIP STATEMENT

CA was involved in the conception and design of the study, screening of articles, risk of bias assessment, Grade analysis, writing the first draft of the manuscript, revision of the manuscript and administrative support. AB, MS, AF, CC, JO were involved in screening of articles, risk of bias assessment, Grade analysis and critical revision of the manuscript. CH, JP, AA, KS, JJY, AA participated in screening of articles, risk of bias assessment, data extraction and critical revision of the manuscript.

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Figure Legend

Figure 1. Study Flow Diagram

Table Legend

Table 1. Risk of Bias Assessment

Supplemental Files

Supplemental File 1. Search Strategy

Supplemental Table 1. Characteristics of Included Studies

1 Supplementals Table 2. Summary of Grade Assessment and Outcomes

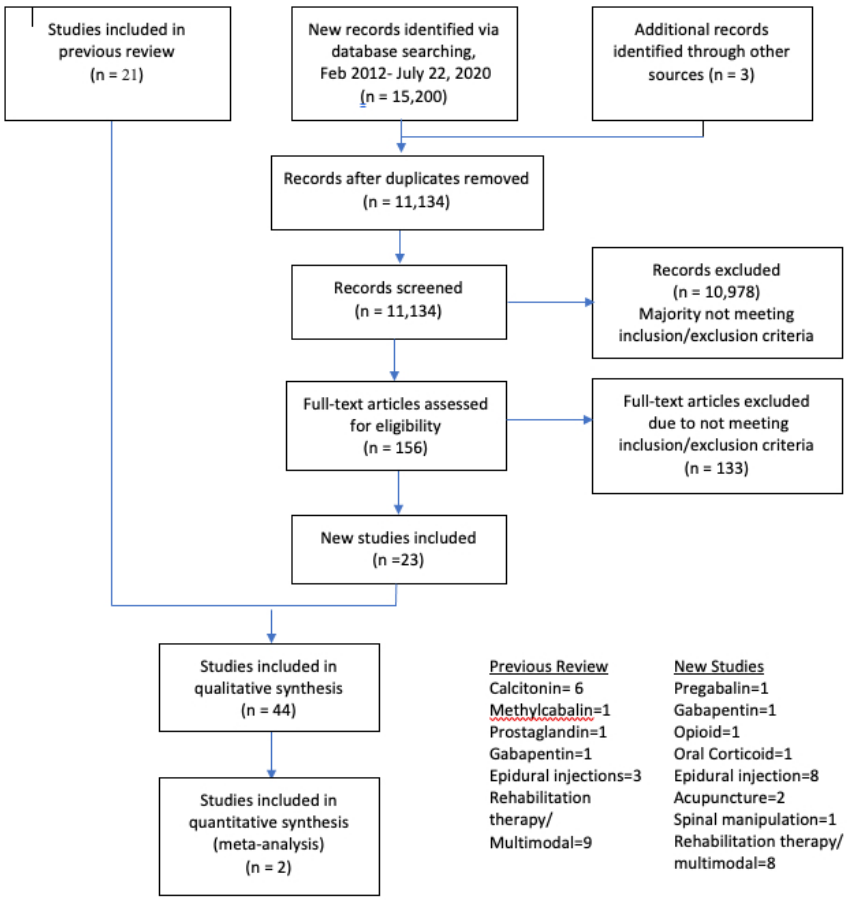

Figure 1. Study Flow Diagram

Figure 1. Study Flow Diagram

258x285mm (72 x 72 DPI)

Nonoperative treatment for lumbar spinal stenosis – 22 July 2020 update

Database: Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® <1946-Present>
Search Strategy:

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1 randomized controlled trial.pt. (509927)
2 controlled clinical trial.pt. (93770)
3 Pragmatic clinical trial.pt. (1444)
4 random*.ti,ab. (1145458)
5 placebo.ab,ti. (215288)
6 drug therapy.fs. (2221199)
7 trial.ab,ti. (599425)
8 groups.ab,ti. (2097678)
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (5031369)
10 (animals not (humans and animals)).sh. (4686362)
11 9 not 10 (4375594)
12 exp Constriction, Pathologic/ (30449)
13 limit 12 to yr="1976 - 1982" (1906)
14 exp Lumbar Vertebrae/ (52505)
15 limit 14 to yr="1966 - 1982" (4472)
16 exp Spinal Canal/ (7519)
17 limit 16 to yr="1966 - 1982" (1172)
18 exp Spinal Diseases/ (123399)
19 limit 18 to yr="1966 - 1982" (18365)
20 exp Spinal Stenosis/ (6116)
21 spinal stenosis.ti,ab. (5088)
22 (lumbar adj5 stenosis).ti,ab. (4268)
23 (spin* adj5 stenosis).ti,ab. (6620)
24 neurogenic claudication.ti,ab. (633)
25 exp Spinal Osteophytosis/ (4018)
26 exp Spondylosis/ (7484)
27 (lumb* adj5 spondyl*).ti,ab. (2886)
28 exp Cauda Equina/ (3250)
29 lumbar radicular pain.ti,ab. (218)
30 13 or 15 or 17 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 (44520)
31 9 and 30 (6508)
32 limit 31 to ed=20190920-20200731 (275)
33 limit 31 to yr=2019-2020 (545)
34 32 or 33 (583)

Database: Embase Classic+Embase <1947 to 2020 July 21>
Search Strategy:

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1 Randomized Controlled Trial/ (613507)
2 exp Controlled clinical trial/ (800817)
3 Controlled Study/ (7533843)
4 Double Blind Procedure/ (176652)

5 Single Blind Procedure/ (39549)
6 crossover procedure/ (64054)
7 placebo/ (362923)
8 Randomization/ (87513)
9 random*.ti,ab. (1563918)
10 placebo?.ti,ab. (314621)
11 allocat*.ti,ab. (155448)
12 assign*.ti,ab. (400691)
13 blind*.ti,ab. (436413)
14 (cross-over or crossover).ti,ab. (107060)
15 (compare or compared or comparing or comparison or comparative).ti,ab. (6802913)
16 (controlled adj7 (study or design or trial)).ti,ab. (355549)
17 ((singl* or doubl* or trebl* or tripl*) adj7 (blind* or mask*)).ti,ab. (250201)
18 trial.ti,ab. (878032)
19 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (12682849)
20 exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/ (29761121)
21 human/ or normal human/ or human cell/ (22533987)
22 20 and 21 (22470134)
23 20 not 22 (7290987)
24 19 not 23 (9386132)
25 exp vertebral canal stenosis/ (12543)
26 (spin* adj5 stenosis).ti,ab. (9011)
27 (lumbar adj5 stenosis).ti,ab. (5728)
28 (neurogenic adj2 claudication).ti,ab. (1047)
29 (Spin* adj2 Osteophytosis).ti,ab. (26)
30 exp cauda equina/ (4498)
31 lumbar radicular pain.ti,ab. (316)
32 (lumb* adj5 spondyl*).ti,ab. (4037)
33 exp spondylosis/ (9560)
34 spondylolisthesis/ (9419)
35 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 (36443)
36 24 and 35 (11296)
37 limit 36 to yr=2019-2020 (1405)
38 limit 36 to dd=20190920-20200731 (282)
39 37 or 38 (1426)

CENTRAL via CRS Web

1 MESH DESCRIPTOR Spinal Stenosis EXPLODE ALL AND CENTRAL:TARGET 423
2 (spin* NEAR5 stenosis) AND CENTRAL:TARGET 1189
3 lumb* NEAR5 stenosis AND CENTRAL:TARGET 871
4 neurogenic claudication AND CENTRAL:TARGET 168
5 MESH DESCRIPTOR Spinal Osteophytosis EXPLODE ALL AND CENTRAL:TARGET 86
6 MESH DESCRIPTOR Spondylosis EXPLODE ALL AND CENTRAL:TARGET 374
7 lumb* NEAR5 spondyl* AND CENTRAL:TARGET 400
8 MESH DESCRIPTOR Cauda Equina EXPLODE ALL AND CENTRAL:TARGET 15
9 lumbar radicular pain AND CENTRAL:TARGET 93

10 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 AND CENTRAL:TARGET 1932
11 2019:YR AND CENTRAL:TARGET 105034
12 2020:YR AND CENTRAL:TARGET 30634
13 #11 OR #12 135668
14 #13 AND #10 209

CINAHL
S43 S41 OR S42 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 242
S42 S40 AND EM 20190919-20200731 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 192
S41 S40 Limiters - Published Date: 20190901-20200731
Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
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S40 S28 AND S39 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
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S39 S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 6,262
S38 lumb* W5 spondyl* Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
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S37 MH "Spondylolysis" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 486
S36 MH "Spondylolisthesis" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 1,438
S35 "lumbar radicular pain" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 125
S34 MH "Cauda Equina" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 368
S33 MH "Spinal Osteophytosis" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search

Database - CINAHL Plus with Full Text 310
S32 "neurogenic claudication" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 243
S31 lumb* W5 stenosis Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 1,768
S30 spin* W5 stenosis Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 3,656
S29 MH "Spinal Stenosis" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 2,741
S28 S26 NOT S27 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 2,433,818
S27 MH "Animals" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 87,894
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Search Screen - Advanced Search
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Search Screen - Advanced Search
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Search Screen - Advanced Search
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S23 prospectiv* Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
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S22 control* Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
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S13 MH "Random Sample" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
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S8 MH "Placebo Effect" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
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S4 double blind Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 58,644
S3 clinical W3 trial Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL Plus with Full Text 250,481
S2 "randomi?ed controlled trial*" Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases
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Database - CINAHL Plus with Full Text 169,418
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Search Screen - Advanced Search
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PEDro
Yield: 12
Abstract and title: stenosis
AND
Body part: lumbar spine, sacroiliac joint or pelvis
AND
Method: clinical trial
Year: Since 2012

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S16 , Peer Review only, Publication Type:Clinical Trial OR , Peer Review only, Publication Type:Controlled Clinical Trial OR , Peer Review only, Publication Type:Randomized Controlled Trial OR All Fields:random* OR All Fields:placebo* OR All Fields:sham, Peer Review only OR All Fields:\"clinical trial\" OR All Fields:\"controlled trial\", Peer Review only OR All Fields:versus OR All Fields:vs., Peer Review only OR All Fields:double-blind OR All Fields:\"double-blind\", Peer Review only OR All Fields:single-blind OR All Fields:\"single-blind\", Peer Review only AND Subject:\"spinal stenosis\" OR All Fields:\"spinal stenosis\", Peer Review only OR Subject:\"Spinal Osteophytosis\" OR Subject:\"Spondylosis\" OR Subject:\"Spondylolisthesis\", Peer Review only OR Subject:\"Cauda equina\" OR All Fields:\"lumbar radicular pain\", Peer Review only AND , Year: from 2019 to 2020, Peer Review only

Supplemental Table 1. Characteristics of included studies

Study	Participants and Settings	Interventions	Outcomes/Follow-up	Results (Group 1 is reference group)
Calcitonin				
Eskola 1992	39 subjects with an average of 6 years of pain, average age of 56.6 years of age, 20 males and 19 females. **Setting:** Orthopaedic hospital in Finland.	1) 100IU Calcitonin injection every other day for 4 weeks (n=20) 2) Placebo treatment (Miacalcic Sandoz 100IU) every other day for 4 weeks (n=19)	1) VAS 2) Treadmill test 3) Coping with ADLs 4) Digitest Ergojump 5) Blood tests **Follow-up:** 1, 3, 4, 6 and 12 months	**Between group WMD and 95% CI** **Pain (VAS) (mm):** -0.050 (-0.053 to -0.047) **Walking distance (meters):** -18.5 (-240.37 to 203.37) **Adverse events:** The calcitonin injection group reported minor nausea and rash in 8% of the subjects.
Podichetty 2004	55 subjects with an average age of 68.5 years and an average of 36.2 weeks of the condition in the intervention group and 29.8 weeks in the placebo group, 33 males and 22 females. **Setting:** Spinal center in the United States	1) 400 IU intranasal calcitonin daily for 6 weeks followed by open label 6-week extension (n=36) 2) Placebo nasal spray daily for 6 weeks, followed by open label 6-week extension, during which all patients received 400IU calcitonin (n=19)	1) VAS 2) Walking capacity 3) ODI 4) Stenosis specific questionnaire 5) Satisfaction with pain levels, functional status, and treatment received 6) SF-36 7) Symptom diary **Follow-up:** 12 weeks	**Between group MD, 95% CI, p values** **12 weeks:** **Pain VAS (mm):** 0.5 (-0.85 to 1.93): p=0.44, **Walking time (seconds)**: 42.2 (-86.9 to 170.4): p=0.5 **Walking distance (feet)**: 163.3 (-311.16 to637.84); p=0. 0.49 **SF-36 MCS:** -4.22 (-10.41 to1.97) ; p=0.18 **SF-36 PCS:** 0.43 (-3.73 to 4.59); p= 0.84
Porter	41 subjects with	1) 100 IU salmon calcitonin injection	1) Walking chart	Insufficient data provided to calculate mean difference in

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1983	10 in a double blind RCT crossover, 37 males and 4 females with mean age of 55.4 years. **Setting:** Infirmary in England	four times per week, sometimes with Maxalon for nausea (n=5) 2) Matching placebo (n=5) Only responders randomized	and ability to walk more than 1 mile 2) ODI **Follow-up:** 10 weeks	walking distance or ODI among the 10 patients enrolled in RCT. **Adverse events:** The calcitonin injection group reported minor nausea and rash in 4% of the subjects.
Porter 1988	42 subjects, 35 male, 7 female, average age of 53.6 years in 20 subjects and 56.7 years in 22 subjects, median duration of back pain reported was 11 years for 19 subjects, and 14 years for 22 subjects. Median duration of claudication was 1.25 years for 20 subjects and 4.5 years for 22 subjects. **Setting:** Infirmary in England	1) 100 IU of salmon calcitonin injected subcutaneously 4 times per week for 8 weeks (n=20) 2) 1 ml of saline injected 4 times per week for 8 weeks (n=22)	1) VAS 2) Claudication threshold 3) 3 level mobility assessment 4) Analgesic requirements 5) 3 level sleep disturbance 6) Treatment success defined as 100% improvement in walking distance and able to walk 800 m. **Follow-up**: 4 and 8 weeks	**Difference in median score from baseline between groups** **Pain score (VAS) (mm):** 4 weeks: -9 8 weeks: -5.5 **Walking distance until symptoms onset (meters):** 4 weeks: -14 8 weeks: 42 **Walking distance until pain prevents walking (meters):** 4 weeks: -41 8 weeks: -99 No significant between group differences. No p values or 95% CI provided.
Sahin 2009	45 subjects 31 males and 14 females, average	1) 200 IU intranasal calcitonin daily for 8 weeks (n=23)	1) VAS 2) Walking capacity	**Percent change between groups:** **8 weeks:** **VAS at rest:** 4.7%, p>0.05

	ages of 57.65 years in calcitonin group and 54.45 years in paracetamol group. **Setting:** Physical and Rehabilitation Medicine Department in Turkey	2) Up to 1500mg of paracetamol daily for 8 weeks (n=22) Both groups took part in a physical therapy and exercise program 5 times per week for 15 sessions.	3) RMDI 4) Ranges of motion **Follow-up:** 8 weeks	**VAS with motion:** -7.9%, p>0.05 **Roland Morris**: 8.2%, p>0.05 **Walking distance**: -15.4%, p>0.05
Tafazal 2007	40 subjects, 30 males, 10 females, average of 67 years in the intervention group and 70.2 years in the placebo group, average of 38.7 months with symptoms in the calcitonin group and 30.9 months in the placebo group. **Setting:** University hospital in England	1) Placebo nasal spray NaCl for 4 weeks (n=20) 2) 200 IU nasal salmon calcitonin for 4 weeks (n=20)	1) VAS 2) Shuttle walking test 3) 4-point subjective outcome of overall assessment (excellent, good, fair, poor) 4) ODI 5) Modified Somatic Perception Questionnaire 6) Modified Zung Depression Score **Follow-up:** Baseline, 4, 10, 16 weeks	**4 weeks: Between group MD 95% CI** **ODI:** -0.7 (1.7 to -3.5) **LBOS**: -3.0 (-0.6 to -4.7) **VAS leg (mm):** -10 (-4.0 to -13) **VAS back (mm)**: -6.0 (-6 to -12) **Shuttle walk distance (m)**: -13 (-7 to -35) **16 weeks: between group MD, p values** **ODI**: 0.1, p=0.44; **LBOS**: 0.7, p=0.93; **VAS leg (mm):** -4, p=0.66; **VAS back (mm):** 16, p=0.08; **Shuttle walking distance (m):** -11, p=0.39

Oral Medication				
Matsudaira 2009	79 subjects, 24 males and 24 females, with an average age of 69.6 years in the Limaprost group and 72.2 in the Etodolac group. **Setting:** Orthopaedic surgery in a medical faculty in Japan	1) Oral prostaglandin E1 derivative (15 g Limaprost) 3 times daily for 8 weeks (n=39) 2) 400 mg of etodolac (NSAID) twice daily for 8 weeks (n=40)	1) SF-36 2) Verbal pain rating scales 3) Walking distance 4) LBP severity 5) Leg pain severity 6) Leg numbness severity 7) Treatment satisfaction **Follow-up:** 8 weeks	**SF-36 subscales MD, p values** 8 weeks: **physical function:** 9.4, p=0.01, **role physical:** 13.7, p=0.03, **bodily pain**: 15.5, p<0.01: **General health**: 6.6, p=0.08; **vitality**: 11.3, p=0.02; **social functioning**: 8.0, p=0.17; **role emotional:** 10.2, p=0.07; **mental health:** 12.2, p<0.01. **Secondary outcomes** not provided in a way that MD can be extracted: 8 weeks: **low back pain:** p=0.77; leg pain p=0.08; **Leg numbness:** p<0.01; **walking distance** p<0.01; **patient subjective improvement** p<0.01; **patient satisfaction** p<0.01 all in favor of limaprost **Adverse events:** 5% of subjects in both groups reported gastrointestinal upset.
Waikakul 2000	152 subjects, 68 males and 84 females with an average age of 66.8 years. 44 of the subjects had symptoms for less than one month, 98 had symptoms for more than one month. **Setting:** Hospital in Thailand	1) Conservative treatment consisting of education, activity modification, exercise and physical therapy. NSAIDs, muscle relaxants, and analgesics as necessary. Vitamin B1, B6, and B12 3 times per day (n=82) 2) Conservative treatment plus Methlcobalin ESAI, 1.5mg per day in 3 divided doses after meals for 6 months (n=70)	1) Presence of pain on spinal motion 2) Claudication distance 3) Medication intake (NSAIDs, muscle relaxants, and steroids) **Follow-up:** every month for two years	**Walking distance** **Percent able to walk > 1000 meters** 6 mo: 71.3% vs. 88.6%, p<0.05 12 mo: 81.3% vs. 97.1%, p< 0.05 18mo: 83.8% vs. 97.1% p <0.05 **Adverse events:** There were no reported adverse effects in subjects in methylocabalin group
Yaksi 2007	55 subjects, 22 males, 33 females, average age of 50.8 years. **Setting:** Hospital	1) 900 mg of gabapentin per day increased weekly by 300 mg to a maximum of 2400 mg (n=28) 2) Placebo (n=27)	1) VAS – low back and leg pain during movement 2) Walking distance	**Between group difference, p values** **Pain (VAS) (mm) no raw data** 3rd mo 3.4 vs. 1.9, p =0.039 4th mo 4.1 vs.2.0, p =0.006 **Walking Ability, no raw data**

	department of physical medicine and rehabilitation in Turkey	Both groups received physical therapy exercises, a lumbosacral corset with steel bracing and NSAID treatments	3) Presence or absence of motor and/or sensory deficits **Follow-up:** 15 days, 1, 2, 3, 4 months	Grp 1: longer walking distance at end of 2nd mo ($p < 0.05$), 3rd mo ($p < 0.05$) and 4th mo ($p < 0.005$) **Adverse events:** some subjects randomized to the gabapentin group (no data specified) experienced mild to moderate drowsiness and/or dizziness.
Markman 2015	29 participants, 20 males, 9 females, Eligible subjects were older than 50 years (mean 70 .1 years) with at least one level of radiographically confirmed lumbar spinal stenosis and symptoms of neurogenic claudication for at least 3 months. **Setting:** Hospital in Rochester, New York	1) Pregabalin group (n=14) 2) Active placebo (Diphenhydramine) (n=15) Cross over study after 7 day wash out period. Pregabalin was started at 75 mg PO twice daily or diphenhydramine, 6.25 mg) and increased on day 4 to 150 mg PO twice daily (12.5 mg diphenhydramine) for 7 days. Pregabalin was decreased to 75 mg PO twice daily (6.25 mg diphenhydramine) on day 11 for 3 days of tapering.	1) NRS - time to first moderate pain symptom during a 15-minute treadmill test (Tfirst) (NRS - greater than 4) **Follow-up:** day 10 of intervention period	**Between group MD, 95% CI, p values** **Treadmill testing pain at rest (NRS)** 0.29 (0.41 to 0.98): p=0.40 **Treadmill testing final pain (NRS)** 0.25 (-0.44 to 0.94): p=0.46 **Treadmill testing distance walked (m)** -24.06 (-75.63 to 27.52): p=0.35 **Treadmill testing recovery time (min)** -0.79 (-1.86 to 0.28): p=0.1 **Treadmill testing patient global assessment of pain** -0.08 (-0.45 to 0.29): p=0.6 **Treadmill testing RMDQ** 1.50 (0.38 to 2.62): p=0.01 **Adverse events:** Complications were reported in 64% of subjects in group 1, the most common being dizziness, compared to 35% in group 2.
Park 2017	45 subjects, 21 in GPN Group (17 female, 4 males, mean age 66.1± 10.5), and 24 in BTX group (15 female and 9 males, mean age	1) Conservative treatments plus gabapentin (group GPN): Gabapentin 300 to 1200mg/d - titrated to patient characteristics, comorbidities, and reported side effects (n=21) 2) Conservative treatments plus BTX	3) NRS - back/leg pain intensity 4) Cramp frequency (no./wk) 5) Cramp severity (0-4	No statistically significant difference between groups and lack of reporting of quantitative data **Adverse events:** Five patients (20.8%) in group 2 reported mild to moderate pain at injection sites for a few days.

	66.2±8.2) **Setting:** Outpatient department for interventional pain management in Korea	injection (group BTX): The BTX (botulinum toxin type A [Nabota]) dose was 100U in 5mL of 0.9% saline injected into the gastrocnemius medialis and lateralis. (n=24) Conservative treatments: education, exercise, analgesic medication, injection therapy including epidural injections, and physical therapy	criteria) 6) Insomnia severity – (ISI 0-28) 7) ODI 8) Patient global impression of change **Follow-up:** 2 weeks, 1 and 3 months.	
Markman 2015 - 2	24 participants, 12 males and 12 females, (mean age 72 years) LSS by imaging with symptoms of neurogenic claudication **Setting:** Translational Pain Research Center at a University in Rochester, New York	1) Oxymorphone hydrochloride (Opana IR, 5 mg) (n=8) 2) Propoxyphene/acetaminophen (Darvocet, 100 mg/650 mg) (n=8) 3) Placebo: 3 separate visits (random order with at least 3 day washout periods) (n=8)	1) NRS (at rest) 2) NRS (final pain rating) 3) AUC 4) 4) Distance walked (m) 5) Recovery time (min) 6) ZCQ 7) Patient global assessment of pain 8) RMDQ 9) ODI **Follow-up:** Study was prematurely terminated	**Between group MD, 95% CI, p values** **Treadmill testing pain at rest (NRS)** Grp 1 vs Grp 3: -0.04 (-0.72 to 0.65): p-0.89 Grp 2 vs Grp 3: -0.27 (-0.95 to 0.41): p=0.32 Grp 1 vs Grp 2: 0.23 (-0.45 to 0.92): p=0.40 **Treadmill testing final pain (NRS)** Grp 1 vs Grp 3: 0.2 (-0.74 to 1.14): p=0.60 Grp 2 vs Grp 3: 0.53 (-0.40 to 1.46): p=0.16 Grp 1 vs Grp 2: -0.33 (-1.26 to 0.61): p=0.39 **Treadmill testing distance walked (m)** Grp 1 vs Grp 3: -12.41 (-63.01 to 38.20): p=0.54 Grp 2 vs Grp 3: -23.41 (-73.60 to 26.79): p=0.25 Grp 1 vs Grp 2: 11 (-39.53 to 61.54): p=0.59 **SSSQ symptom severity score** Grp 1 vs Grp 3: -0.03 (-0.19 to 0.13): p=0.61 Grp 2 vs Grp 3: 0.01 (-0.15 to 0.17): p=0.85 Grp 1 vs Grp 2: -0.04 (-0.20 to 0.11): p=0.49 **SSSQ physical function score** Grp 1 vs Grp 3: 0.04 (-0.16 to 0.09): p=0.47 Grp 2 vs Grp 3: 0.11 (-0.01 to 0.23): p=0.03 Grp 1 vs Grp 2: -0.15 (-0.27 to -0.02): p=0.01 **Patient global assessment of pain** Grp 1 vs Grp 3: -0.03 (-0.52 to 0.47): p=0.90 Grp 2 vs Grp 3: 0.13 (-0.36 to 0.61): p=0.52

				Grp 1 vs Grp 2: -0.15 (-0.64 to 0.34): p=0.44 **The study was prematurely terminated because of the removal of propoxyphene acetaminophen from the US market.**
Rodrigues 2014	61 patients with lumbar canal stenosis (50–75 years; canal area < 100 mm^2 at L3/L4, L4/L5, and/or L5/S1on MRI; and claudication within 100 m). 31 in the corticoid group (mean age 58.23 (6.38), and 30 in the placebo group (mean age 58.33 (6.19)) **Setting:** Hospital in São Paulo, Brazil	1) Oral corticoid group received 1 mg/kg of oral corticoids daily, with a dose reduction of one-third per week for 3 weeks (n=31) 2) Control group was administered placebo for the same period (n=30)	1) SF-36 2) RMDQ 3) 6-min walk test 4) VAS 5) Likert scale **Follow-up:** 3, 6 and 12 weeks	**Between group comparison** **VAS (6 weeks)** Corticoid vs Placebo: 1.53 (-0.02 (in favour of placebo)
Rehabilitation Therapy and Multimodal Care				
Goren 2010	45 subjects, 13 males, 32 females, average ages in groups of 57.4, 49.13, and 53.06. 7 subjects with pain duration of 3-6 months, 7 with pain duration of 6-12 months, and	1) Stretching and strengthening exercises for lumbar, abdominal, leg muscles as well as low intensity cycling exercises were given as therapeutic exercises. Ultrasound was applied with 1mHz, 1.5W/cm2 intensity, in continuous mode on the back muscle for 10 minutes (n=17) 2) Same as group 1 with Ultrasound on off- mode (n=17)	1) VAS (out of 10) 2) Treadmill test at 3 km/h for maximum of 15 minutes or 750m. 3) ODI 4) Analgesic consumption 5) Physiatrist	**Pain (VAS) (mm) within group MD** 3 weeks: Grp 1: -2.2 for **back pain;** -1.47 for **leg pain** Grp 2: -1.94 for **back pain;** -2.47 for **leg pain** Grp 3: 0.40 for **back pain;** -0.54 for **leg pain** Between groups differences: Leg pain: Grp 1> Grp 3 (p<0.01), Grp 2> Grp 3 (p<0.01) **Walking Ability (within group MD)** 3 weeks: Grp 1: 94.30 seconds

	31 with pain duration of greater than 12 months. **Setting:** Rehabilitation center in Turkey	3) No exercise-no treatment (n=16)	assessment **Follow-up:** End of 3-week treatment period only	Grp 2: 114.94 seconds Grp 3: -66.10 seconds No significant change between groups **Disability (ODI) (within group MD)** 3 weeks: Grp 1: -3.94 Grp 2: -7.8 Grp 3: -3.6 ODI between groups differences Grp 1> Grp 3 (p<0.05), Grp 2> Grp 3 (p<0.05)
Koc 2009	29 subjects, 21 male, 8 female, average ages of 62.6, 61.1, and 53.1 years in the three groups, average pain duration of 5.7 years, 5.0 years, and 5.7 years in the three groups. **Setting**: Medical school department of physical medicine and rehabilitation in Turkey	1) Conservative inpatient physical therapy program 5 days a week for 2 weeks. PT included applications of ultrasound 1.5 W/cm2 for 10min, hot pack for 20min, and TENS for 20min to the lumbar region (n=13) 2) Lumbar epidural steroid injections, 10 ml of solution containing 60mg of triamcinolon acetonide (1.5 mL), 15 mg of 0.5% bupivacain hydrochloride (3 mL), and 5.5 mL of physiologic saline (0.9%NaCl) was injected in 3.5minutes. (n=10) 3) Control group (n=10) All patients included were trained to pursue a home-based therapeutic exercise program performed twice daily for a period of 6 months, and oral diclofenac sodium 75mg was administered to all patients twice daily for 2 weeks	1) VAS 2) Treadmill walk test 3) Nottingham Health Profile 4) RMDI 5) Functional testing including finger to floor distance, sit-to-stand, and a weight carrying test **Follow-up:** 2 weeks, 1, 3 and 6 months	No raw data provided. No significant between group differences for all outcomes and follow-ups except: **Pain (VAS)** 2 weeks: Grp 2 less pain than Grp 3 p= 0.008 **Disability (RMDI)** 2 weeks: Grp 2 less disability than Grp 3 p= 0.007 **Quality of Life (Nottingham Health Profile) (no data provided)** Grp 2 had significantly higher improvement than Grp 3 at 2 weeks in mobility subgroup scores. **Adverse events:** 1 subject reported angina pectoralis and 1 reported gastric complaints (group not specified).
Pua 2007	68 subjects, 35 males, 33	1) Unweighted treadmill training: Weeks 1 and 2, participants walked	1) VAS for pain over past	**Pain (VAS) (mm) MD and 95% CI** 6 weeks: 2 (-5 to 10)

	females, average age of 58 years, 12 week median pain duration **Setting:** Hospital in Singapore	with a relatively pain-free gait which translated to 30–40% of body weight. In weeks 3 to 6, participants were encouraged to walk at a moderate intensity. The duration of each treadmill session was limited by participant tolerance or to a maximum of 30 minutes. 2x per week for 6 weeks = 12 sessions (n=33) 2) Cycling on upright bicycle: During weeks 1 and 2, participants cycled at their comfortable pace at 50 to 60 rpm. Participants were instructed to assume a flexed posture. In weeks 3 to 6, participants were encouraged to exercise at a moderate intensity and the duration of each cycling session was limited by participant tolerance or to a maximum of 30 minutes. 2x per week for 6 weeks for 12 sessions (n=35)	week 2) Patient perceived benefit on a 6-point scale 3) ODI 4) RMDI 5) Walking ability **Follow-up:** 3 and 6 weeks	**Disability (ODI), OR, 95% CI** 6 weeks: OR 1.10 (0.41 to 2.98) **Patient perceived benefit, OR, 95% CI** 6 weeks: OR 0.50 (0.17 to 1.48) **Walking ability** (≥800 m), **OR, 95% CI** 6 weeks: OR 1.14 (0.44 to 2.94) **Adverse events:** 1 subject in treadmill group reported increase in pain.
Whitman 2006	58 subjects, 31 males, 27 female, 29 (group 1) with an average age of 70 years, 29 (group 2) with an average age of 68.9, median low back pain duration of 108 months in Group 1's 29 subjects and 60 months in Group 2's 29	1) Flexion Exercise and Walking Group: 45-60 minutes twice per week for 6 weeks. Lumbar flexion exercises along with self-pace treadmill walking program, and sub-therapeutic ultrasound. The duration of each treadmill session was based on that patient's tolerance on that specific day and could extend up to 45 minutes. (n=29) 2) Manual Therapy, Exercise and Walking Group: 45-60 minutes twice per week for 6 weeks - Manual	1) Global Rating of Change (15-point scale) 2) NPRS for lower limb 3) Walking Tolerance test 4) ODI 5) Medication consumption 6) Satisfaction subscale of the Spinal	**Patient Global Assessment (somewhat better or greater)** 6 weeks: 41% vs. 79% p<0.001 1 year: 21% vs. 38% p>0.05 **Number needed to treat for benefit for perceived recovery and 95% CI** 6 weeks: 2.6 (1.8 to 7.8) 1 year: 4.8 (-2.3 to 21.3) long term: 4.4 (- 2.1 to 22.7) **Pain (NPRS lower extremity)** **Within group MD, 95% CI** 6 weeks: 1.1 (0.2 to 2.0) vs. 1.5 (0.5 to 2.5) 1 year: 1.2 (0.4 to 1.9 vs. 1.0 (-0.2 to 2.2);

	subjects, lower extremity median pain duration of 48 months in Group 1's 29 subjects and 24 months in Group 2's 29 subjects. **Setting:** University in the United States	physical therapy (thrust and non thrust) to the thoracic and lumbar spine, pelvis, and lower extremities and specific exercises at discretion based on the underlying impairments. Patients received specific exercises to address impairments in mobility, strength, and/or coordination. Exercises were performed in the clinic and as part of a home exercise program. Patients also underwent a bodyweight supported treadmill ambulation program using a cable and trunk harness system to unload a specific amount of weight from the patient while the patient walks as comfortably as possible on a treadmill (n=29).	Stenosis Scale 7) Additional use of health care resources **Follow-up:** 6 weeks, 1 year, long term mail survey (averaging 29 months)	Long term: 1.8 (0.6 to 3.0) vs. 2.0 (0.7 to 3.4) Between group MD not statistically significant at any follow-up period **Walking Ability (improvement in meters) within group MD, 95% CI** 6 weeks: 176.5 (-9.5 to 362.4) vs. 339.7 (218.4 to 461) 1 year: 130.4 (-55.3 to 316.2) vs. 209.8 (67.5 to 352.1) Between group improvement not statistically significant at any follow-up **Disability (ODI) within group MD** 6 weeks: 6.55 (1.87 to 11.23) vs. 10.48 (6.5 to 14.4) 1 year: 5.03 (1.71 to 8.35) vs. 7.14 (1.5 to 12.8) Between group differences not statistically significant at any follow-up
Minetama 2019	86 patients, 39 men and 47 women, average age 72.7 years 43 patients (20 men and 23 women, average age 72.3 years to the PT group 43 patients (19 men and 24 women, average age 73.2 years) to the HE group. Duration symptoms 20 months	1) Physical therapy + home exercise program (n=43) 2) Home exercise (HE) program alone (n=43) Supervised physical therapy twice a week for 6 weeks, including manual therapy, individually tailored stretching and strengthening exercises, cycling, and body weight-supported treadmill walking. The manual therapy included manipulation, stretching, and massaging of the thoracic and lumbar spine, pelvis, and lower extremities. The individually tailored muscle exercises included those for the trunk (eg, abdominal planks, side bridge, and/or back extension) and lower	1) ZCQ 2) Satisfaction 3) SPWT (m) 4) NRS 5) JOABPEQ-acquired points 6) SF-36 7) HADS 8) PCS 9) PASS-20 10) TSK-11 11) Daily steps **Follow-up:** 6 weeks	**Between group MD, 95% CI** **ZCQ - Symptom severity** −0.4 (−0.6 to −0.2): statistically significant **ZCQ - Physical function** −0.4 (−0.6 to −0.2): statistically significant **SPWT (m)** 455.9 (308.5 to 603.2): statistically significant **NRS - Leg pain** −1.4 (−2.5 to −0.3): statistically significant **SF-36 - Physical functioning** 9.2 (2.1 to 16.3): statistically significant **SF-36 - Bodily pain** 10.4 (3.3 to 17.5): statistically significant **Daily steps** 723.4 (199.1 to 1,283.5): statistically significant

	Setting: Spine care center at a university hospital in Japan	extremities (eg, unloading hip and/or knee exercise with ankle weight and/or standing squats). The typical dosage for strengthening exercises was a total of 2 to 3 sets with 10 repetitions, each of 6-second contraction. The typical duration of stretching was three repetitions of 30 seconds. All patients in both groups were asked to take a daily walk that did not exacerbate their lower extremity symptoms using a pedometer and walking diary and to perform a HE program consisting of lumbar flexion exercises including three 30-second bouts of both single and double knee-to-chest exercises, ten 6-second bouts of trunk raises and bridging in the supine position, and a 4-point kneeling exercise at least twice daily.		
Schneider 2019	259 subjects, 122 males and 137 women with an average age of 72.4, 68 patients had symptoms for less than 6 months, 191 had symptoms for greater than 6 months **Setting:** Outpatient research clinic in Pittsburgh	1) Medical care (MC) (n=88) 2) Group exercise (GE) (n=84) 3) Manual therapy + exercise (MTE) (n=87) **Medical Care:** 3 visits to a physical medicine physician over 6 weeks. Primarily prescription of oral medications in any combination of nonnarcotic analgesics, anticonvulsants, antidepressants. Optional referral for epidural steroid injections if inadequate pain relief by oral medication, severe neurogenic claudication, and/or patient preference.	1) SSS 2) SPWT 3) Physical Activity **Follow-up:** 2 and 6 months	**Between group MD, 95% CI** **SSS (2 months)** GE vs MC: 0.4 (-1.3 to 2.1) MTE vs MC: -2.0 (-3.6 to -0.4) MTE vs GE: -2.4 (-4.1 to -0.8) **SPWT (2 months)** GE vs MC: 79.9 (-74.5 to 234.5) MTE vs MC: 122.9 (-25.7 to 271.6) MTE vs GE: 43.0 (-111.8 to 197.9) **Physical activity (2 months)** GE vs MC: 28.7 (2.7 to 54.8) MTE vs MC: 20.4 (-4.5 to 45.3) MTE vs GE: -8.3 (-34.5 to 17.6) **SSS (6 months)** GE vs MC: -0.5 (-2.3 to 1.3) MTE vs MC: -1.1 (-2.8 to 0.6) MTE vs GE: -0.6 (-2.4 to 1.2)

		Physician rendered general guide and on gentle stretching and advice to stay active. **Group Exercise:** Supervised exercise classes at 2 local senior community centers. 2x 45-min classes/week, 6 weeks. Taught by senior fitness instructors. Participants self-select level of exercise based on fitness level (easy to medium) **Manual Therapy + Exercise:** 2x 45minute sessions per week, 6 weeks by either 2 chiropractors or 2 physiotherapists. Sessions included 3 interventions: 1. Warm-up procedure on stationary bicycle 2. Manual therapy procedures (lumbar distraction, hip, lumbar/sacroiliac joint and neural mobilizations 3. Individualized instruction in spinal stabilization exercises and home stretching Practitioner determined what muscles required stretch/strengthening and appropriate exercises added to program.		**SPWT (6 months)** GE vs MC: 86.5 (-75.7 to 248.8) MTE vs MC: 73.8 (-84.1 to 231.7) MTE vs GE: -12.7 (-175.6 to 150.1) **Physical activity (6 months)** GE vs MC: 21.3 (-6.9 to 49.4) MTE vs MC: -2.9 (-30.1 to 24.3) MTE vs GE: -24.2 (-52.5 to 4.0) **Adverse events:** There were no reported serious adverse events in any group. There was a significantly greater rate of transient joint soreness associated with group 3 (49%) compared with group 2 (31%) and group 1 (6%).
Ammendolia 2018	104 patients, 45 males and 59 females, 48 in comprehensive group and 51 in self-directed group, with an average age of 69.4	1) Comprehensive (n=48) 2) Self-directed (n=51) **Comprehensive:** Chiropractor providing 2x/week of 15-20-minute treatment sessions over a 6-week period followed by a single (booster) session, 4 weeks later.	1) SPWT Distance 2) Clinical Significance - 30% improvement in SPWT no. (%) 3) Clinical	**Between group MD, 95% CI, p values** **SPWT** 8 wks: 345.4 (150.0 to 540.7): p=0.00 3 mo: 304.1 (77.9 to 530.3): p=0.01 6 mo: 421.0 (181.4 to 660.6): p=0.00 12 mo: 473.2 (203.9 to 742.4): p=0.00 **30% improvement in SPWT** 8 wks: 24 (6-40): p=0.01 3 mo: 21 (4-38): p=0.02

	(comprehensive) and 71.7 (self-directed) neurogenic claudication >3 months, imaging-confirmed canal narrowing, walk >20m and not surgical candidates in next 12 months **Setting:** Academic hospital outpatient clinic in Toronto	Education: Self-management strategies via cognitive behavioral approach. Body repositioning (pelvic tilt) when standing and walking. Exercises: Standardized set of exercises demonstrated gradually over 6 weeks and was a part of structured home exercise program. Cycling, muscle stretching, strengthening, conditioning for back and lower extremity fitness and to facilitate lumbar flexion Manual therapy: Spinal manipulation; joint, soft tissue and neural mobilization; lumbar flexion-distraction; and manual muscle stretching applied each visit. Participants received an instructional video and workbook and pedometer. **Self-directed:** Instructional Video, workbook, pedometer and a single 15-to 30-minute training session with an experienced independent licensed chiropractor, independent of the comprehensive program, Training session: Describe 6-week program, review workbook, explain pedometer use and recording of weekly walking steps. Video and workbook: Educational information and the same exercise instruction and self-management strategies received by the comprehensive group	Significance - 50% improvement in SPWT no. (%) 4) ZCQ-S 5) ZCQ-F 6) ZCQ-S + ZCQ-F 7) ODI 8) ODI walk 9) NRS Back 10) NRS Leg **Follow-up:** 8 weeks, 3, 6, and 12 months	6 mo: 19 (2-35): p=0.02 12 mo: 22 (4-39): p=0.02 **50% improvement in SPWT** 8 wks: 26 (8-42): p=0.01 3 mo: 19 (-1.0 to 36): p=0.06 6 mo: 17 (-2 to 35): p=0.09 12 mo: 24 (5-40): p=0.01 **ZCQS** 8 wks: -0.19 (-0.37 to -0.02): p=0.03 3 mo: -0.15 (-0.37 to 0.08): p=0.19 6 mo: -0.02 (-0.22 to 0.19): p=0.87 12 mo: -0.22 (-0.47 to 0.02): p=0.07 **ZCQF** 8 wks: -0.02 (-0.22 to 0.17): p=0.81 3 mo: -0.18 (-0.39 to 0.03): p=0.09 6 mo: -0.11 (-0.33 to 0.11): p=0.34 12 mo: -0.27 (-0.49 to 0.04): p=0.02 **ZCQS+ZCQF** 8 wks: -0.24 (-0.56 to 0.07): p=0.13 3 mo: -0.36 (-0.75 to 0.03): p=0.07 6 mo: -0.23 (-0.58 to 0.12): p=0.20 12 mo: -0.48 (-0.90 to -0.06): p=0.03 **ODI** 8 wks: -0.02 (-0.07 to 0.02): p=0.30 3 mo: -0.04 (-0.09 to 0.01): p=0.13 6 mo: -0.02 (-0.07 to 0.02): p=0.34 12 mo: -0.03 (-0.08 to 0.02): p=0.30 **ODI Walk** 8 wks: -0.2 (-0.6 to 0.1): p=0.14 3 mo: -0.4 (-0.9 to 0.03): p=0.07 6 mo: -0.9 (-1.3 to -0.4): p<0.001 12 mo: -0.2 (-0.7 to 0.2): p=0.32 **NRS Back** 8 wks: -1.4 (-2.2 to -0.5): p=0.002 3 mo:-0.6 (-1.4 to 0.3): p=0.03 6 mo: -0.7 (-1.7 to 0.3): p=0.16 12 mo: -0.4 (-1.3 to 0.4): p=0.32

				NRS Leg 8 wks: -0.7 (-1.5 to 0.1): p=0.09 3 mo: 0.05 (-0.85 to 0.96): p=0.91 6 mo: -0.9 (-1.9 to 0.003): p=0.58 12 mo: -0.5 (-1.6 to 0.6): p=0.37 **SF-36 Bodily Pain** 8 wks: 2.0 (-4.9 to 8.9: p=0.57 3 mo: -4.5 (-12.4 to 3.5): p=0.27 6 mo: -3.3 (-10.2 to 3.6): p=0.35 12 mo: 10 (2.1 to 17.9): p=0.013 **SF-36 Physical Function** 8 wks: 4.2 (-3.9 to 12.4): p=0.31 3 mo: 9.2 (1.1 to 17.3): p=0.027 6 mo: 5.8 (-2.1 to 13.6): p=0.15 12 mo: 8.2 (0.2 to 16.2): p=0.045 **Adverse events:** At 12 months, 0 participants out of 43 in group 1 and 2 out of 46 participants in group 2 experienced adverse events that were mostly attributed to a temporary increase in low back and/or leg pain.
Oğuz 2013	120 patients, 30 in group 1 with an average age of 57.1 years old, 30 in group 2 with an average age of 55.8 years old and group 3 with an average age of 57.4 years old, LSS symptoms, narrowing by MRI **Setting:** University	1) Standard exercise group (n=30) 2) Isokinetic exercise program (n=30) 3) Unloading exercise group (n=60) All groups physician-guided (5x/week for 3 weeks) then at-home (3x/week) **Standard Exercise:** 15 sessions of TENS, hot packs with home exercise instruction. **Isokinetic exercise:** 20 minutes/day, 5 sessions/week for a total of 15 sessions with a physician. Isokinetic exercises:	1) VAS 2) ODI 3) Beck Depression Inventory **Follow-up:** 4, 12 and 24 weeks	**Between group MD, p value** **VAS** After treatment: Grp 1 vs Grp 2:0.37, p>0.05 Grp 1 vs Grp 3: 1.36, p<0.05 Grp 2 vs Grp 3: 0.99, p<0.05 4th week: Grp 1 vs Grp 2: 1.43, p>0.05 Grp 1 vs Grp 3: 1.17, p<0.05 Grp 2 vs Grp 3: -0.26, p>0.05 12th week: Grp 1 vs Grp 2: 0.93, p>0.05 Grp 1 vs Grp 3: 0.71, p>0.05 Grp 2 vs Grp 3: -0.22, p>0.05 24th week: Grp 1 vs Grp 2: 1.08, p>0.05

	department of physical medicine and rehabilitation in Turkey	rates of 60°/sec, 120°/sec, 180°/sec with 70° of body movement (50° flexion to 20° extension) Each session had 3 sets, each set had 5 repetitions at described velocity, with 20s rest between each set. **Unloaded exercise:** 5 sessions of unloading exercise per week, for a total of 15 sessions with a physician. Walking with unloading exercise devise: session 1-5 = 45% body weight, session 6-15 = 30% body weight. Treadmill walking at 1.2 km/hr for 20 minutes, or until pain due to neurogenic claudication was felt. Subjects advised to follow exercise program s at home at least 3x/week after discharge.		Grp 1 vs Grp 3: 0.46, p>0.05 Grp 2 vs Grp 3: -0.62, p>0.05 **ODI** After treatment: Grp 1 vs Grp 2: -0.8, p>0.05 Grp 1 vs Grp 3: 1.8, p<0.05 Grp 2 vs Grp 3: 2.6, p<0.05 4th week: Grp 1 vs Grp 2: 1.5, p>0.05 Grp 1 vs Grp 3: 2.6, p>0.05 Grp 2 vs Grp 3: 1.1, p<0.05 12th week: Grp 1 vs Grp 2: 1, p>0.05 Grp 1 vs Grp 3: 1.3, p>0.05 Grp 2 vs Grp 3: 0.3, p>0.05 24th week: Grp 1 vs Grp 2: 0.4, p>0.05 Grp 1 vs Grp 3: 0.5, p>0.05 Grp 2 vs Grp 3: 0.1, p>0.05 **Total Gait Duration** After treatment: Grp 1 vs Grp 2: 64.6, p>0.05 Grp 1 vs Grp 3: -50.5, p>0.05 Grp 2 vs Grp 3: -115.1, P<0.05 4th week: Grp 1 vs Grp 2: 45.9, p>0.05 Grp 1 vs Grp 3: -18.4, p>0.05 Grp 2 vs Grp 3: -64.3, p<0.05 12th week: Grp 1 vs Grp 2: 52.23 p>0.05 Grp 1 vs Grp 3: -0.67 p>0.05 Grp 2 vs Grp 3: -52.9 p>0.05 24th week: Grp 1 vs Grp 2: 35.2, p>0.05 Grp 1 vs Grp 3: 1.9, p>0.05 Grp 2 vs Grp 3: -33.3, p>0.05

Homayouni 2015	47 subjects, 23 male, 24 female, 24 in group one, mean age 55.56, 12 male, 12 female, 23 in group two, mean age 55.68, 11 male, 12 female **Setting:** University-based pain clinics in Iran	1) Treatment in therapeutic pools with water temperature of 29–30 degrees Celsius. Every aquatic session started with warm up and ended with cool down, with duration of 10–15 min for each of them. Participants should have attended aquatic physical therapy sessions every other day for a total duration of 24 sessions. Each session included ambulation, side walking, chain walking, forward walking with kickboard, stretching of each muscle group including adductors, abductors, flexors and extensors of the hip, knee flexors and ankle plantar flexors and dorsiflexors. Other interventions were mini-squat, pelvic curl, pelvic tilt, and knee to chest, double knee lift, and deep-water exercise. (n=25) 2) Passive modalities by physical therapists including continuous mode ultrasound (US) 1.5W/ cm2 for 10 min and hot pack and trans-electrical nerve stimulation (TENS) for 20 min to the lumbar region. Also, the therapists instructed the patients in this group to perform trunk muscle endurance, William's and stretching exercises. The patients were treated using these passive modalities and were given exercises under supervision of physiotherapists for 10 sessions. They were instructed to perform the learned exercises 30 min	1) VAS 2) Walking ability **Follow-up:** Immediately after therapy, 3 months	**All between group comparisons** **Walking ability** Grp 1 > Grp 2: p=0.02 **VAS** Grp 1 > Grp 2 p=0.001

		a day at home in the following weeks until the end of the eighth week. (n=25)		
Marchand 2019	40 participants, 17 females and 23 males, 20 in the intervention group with an average age of 66.7 years old and 20 in the control group with an average age of 71.5 years old, with history and diagnostic imaging of LSS **Setting:** Regional hospital in Quebec	1) Exercise 3x week / 6 weeks prior to surgery (n=20) 2) Regular hospital preoperative management with back posture education (n=20)	1) NRS (Pain Intensity) 2) ROM (Active) 3) Muscle strength (N-m) 4) Walking capacity (seconds) **Follow-up:** 3 and 6 months	**Between group MD** **NRS (leg)** Preoperative: -2.1, p<0.05 Postoperative: 1.1, p>0.05 3 months: 1.1, p>0.05 6 months: 0.3, p>0.05 **ROM (active)** Preoperative: 5, p<0.05 Postoperative: -6, p>0.05 **Muscle Strength** Preoperative: 45.7, p<0.001 Postoperative: 5.1, p>0.05 **Walking Duration** Preoperative: 90, p<0.05 Postoperative: -14.5, p>0.05
Kim 2019	34 subjects, mean age 64 (5.3), women 24 (66.7) **Setting:** Hospital in Seoul, South Korea	1) MT1 group: 110 g of Gang-Chuk Tang was administered 3 times a day (Gang-Chuk Tang is an herbal concoction consisting of Eucommiae Cortex, Achyranthis Radix, Rhizoma Cibotii, Sorbus commixta, G. thunbergii, Saposhnikovia Radix, and Acanthopanacis Cortex in equal portions) Daily Mokhuri Chuna therapy (relaxation and mobilization of lumbar joint and back muscle) Daily acupuncture treatment on LI4, ST36, LV3, BL22, BL23, BL24, BL25, and Ashi points. Consultation on precautions related to daily	1) VAS for leg pain 2) VAS for low back pain 3) Oxford Claudication Scoring 4) Walking distance **Follow-up:** 3 and 6 months	**All between group comparisons** **VAS leg pain (post treatment)** MT2 (28.82±27.46) vs CMT (51.82±25.34) groups: P=0.04 **VAS leg pain (6 months)** MT1 (48.91±23.08) vs CMT (72.27±16.72) groups: P=0.01 MT2 (42.36±21.29) vs CMT groups: P=0.003 **VAS low back pain (6 months):** MT2 (30.00±13.48) vs CMT (60.82±18.62) groups: P=0.001 **Oxford Claudication Scoring (3 months)** MT1 (18.75±6.52) vs CMT (25.82±6.24) groups: p=0.02 **Walking distance (3 months)** MT1 vs CMT: p=0.03 **Walking distance (6 months)** MT1 vs CMT: p=0.01

		activity and stepwise walking training for the entire 4 weeks of therapy. (n=12) 2) MT2 group: Mokhuri Chuna, acupuncture, and physician consultation were offered in the same manner and dosage as the MT1 group with the exception that all herbal medications were withheld. (n=11) 3) CMT group: Oral analgesic therapy (aceclofenac 100 mg twice daily and eperisione hydrochloride 50 mg three times daily for 28 days) and three interlaminar epidural steroid injections (5 mg of dexamethasone per injection) at the level of the affected spinal region over a 4-week period were administered. Physiotherapy including heating pad, and transcutaneous electrical nerve simulator, and deep tissue heating therapy five times per week for 4 weeks. (n=11)		The primary outcome of this pilot study was safety as measured by the type and incidence of adverse events (AEs).
Spinal Manipulation				
Passmore 2017	14 patients with degenerative LSS (n=14); Swiss Spinal Stenosis score of M=63.2, standard deviation [SD] = 15.9) (mean age 59.0 (10.6)), 7 in the SM group (4	1) Spinal manipulation group: received bilateral high-velocity; low-amplitude spinal manipulation directed toward the lumbar region (by a licensed chiropractor with more than 10 years of clinical experience) (n=7) 2) Non Intervention Group: Waited 5 minutes if they were assigned to the	1) Movement time 2) NPS (Back) 3) NPS (leg) 4) ROM **Follow-up:** Immediately after intervention	There was no significant difference between groups for all outcomes. 1. Grp 1 vs. Grp 2, p=0.739 2. Grp 1 vs. Grp 2, p> 0.05 3. Grp 1 vs. Grp 2, p> 0.05 4. Grp 1 vs. Grp 2, p> 0.05

	female, 3 male) (mean age 59.1 (9.3)), 7 in the NI group (3 female, 4 male) (mean age 58.9 (12.6)) **Setting:** rehabilitation hospital in Winnipeg, Manitoba	no intervention group (n=7)		
Acupuncture				
Kim 2016	50 participants mean age of 62.0±9.8 years, acupuncture (n=26), age 65.0±8.7, male / female 12/14, control (n=24), age 58.9±10.2, male / female 10/14. Mean duration of symptoms 33m **Setting:** Hospital in Yangsan, South Korea	1) Acupuncture: 269 acupuncture sessions were administered during the study. 81% (n=21) of patients received at least 10 acupuncture sessions. Electrical acupuncture was applied at least once and bilaterally at back shu points (BL23, BL24, BL25 or BL26) or Jiaji points at L2–L5 spinal levels. Other frequently used points were BL57, BL60, GB39, GB34 and tender points located in the lower extremities (n=26) 2) Control: In total, 255 physical therapy sessions were provided to patients in the control group at their request. 92% (n=22) of patients received at least 10 physical therapy sessions (median 11, range 1–13). (n=24)	1) ODI 2) SF-36 bodily pain 3) SF-36 physical function 4) LBP bothersomeness 5) LBP intensity 6) Leg pain bothersomeness 7) Leg pain intensity 8) Self-reported pain-free walking distance (m) **Follow-up:** 6 weeks, 3 months	**Between group MD, 95% CI** **ODI** 6 wk: -2.2 (-7.0 to 2.6) 3 mo: -2.5 (-8.9 to 3.8) **SF-36 BP** 6 wk: -8.6 (-18.6 to 1.3) 3 mo: 3.2 (-8.3 to 14.7) **SF-36 PF** 6 wk: 0.1 (-7.6 to 7.9) 3 mo: 1.3 (-8.3 to 10.9) **LBP bothersomeness** 6 wk: -0.6 (-11.4 to 10.1) 3 mo: -7.4 (-19.6 to 4.8) **LBP intensity** 6 wk: -5.1 (-15.5 to 5.3) 3 mo: -13.5 (-26.2 to -0.7) **Leg pain bothersomeness** 6 wk: -7.4 (-18.4 to 3.7) 3 mo: -9.2 (-21.6 to 3.2) **Leg pain intensity** 6 wk: -11.5 (-0.9 to -22.0) 3 mo: -12.6 (-24.6 to -0.6)

				None statistically significant
Qin 2020	80 participants assigned with 70 completing the 8-week treatment course (38 in acu group and 32 in sham acu group). Mean age of 61.5±7.9 years with 34 males and 46 females. Duration of symptoms <3mo =14 (17.5%), 3-12 mo = 1(1.3%), 1 to 5 y = 24 (30%), >5 y =41 (51.3%) **Setting:** 2 Clinical Sites - Department of Acupuncture and Neurology, Guang'anmen Hospital Department of Acupuncture and Neurology, Beijing Fengtai Hospital of Integrated Traditional and Western Medicine.	1) Acupuncture: Applied by acupuncturists with 5 years of Chinese medical university program and at least 2 year of clinical experience. Sterile disposable steel needles (Hwato Acupuncture, Suzhou, China; 0.30 £ 40 mm/0.30 £ 75 mm) were inserted through adhesive pads. Participants underwent 3 treatments weekly over 8 weeks, and each session persisted for 30 minutes. To maintain "De qi," a sensation of numbness and soreness, acupuncture manipulation (twirling, lifting, and thrusting on needles) was performed every 10 minutes during the treatment. 2) Sham acupuncture: Chosen acupoints, treatment duration, and frequency of sessions were the same as in the acupuncture group. Participants in the sham cohort were treated using a pragmatic placebo needle on the same acupoints, which is similar to the Streitberger needle design (Supplementary Materials). Acupuncturists pretended to manipulate the needle every 10 minutes, but "De qi" was not sought.	1) RMDQ 2) NRS back 3) NRS Leg 4) SSS Symptoms subscale 5) SSS physical function subscale 6) SSS satisfaction subscale 7) Self-paced walk test **Follow-up:** 4 weeks, 8 weeks (end of treatment), 3 months, 6 months	**RMDQ** 4 wk: -3.6 (-5.2 to -1.9): p<0.001 8 wk: -2.6 (-3.7 to -1.4): p<0.001 3 mo: -2.3 (-3.9 to -0.7): p=0.005 6 mo: -1.8 (-3.6 to -0.3): p=0.086 **NRS Back** 4 wk: -1.7 (-2.4 to -0.9): p<0.001 8 wk: -2.3 (-3.0 to -1.5): p<0.001 3 mo: -1.7 (-2.6 to -0.8): p<0.001 6 mo: -1.2 (-2.1 to -0.3): p=0.007 **NRS Leg** 4 wk: -2.0 (-2.6 to -1.3): p<0.001 8 wk: -2.9 (-2.6 to -1.3): p<0.001 3 mo: -2.4 (-3.3 to -1.4): p<0.001 6 mo: -2.1 (-3.0 to -1.2): p<0.001 **SSS Symptoms Subscale** 4 wk: -0.6 (-0.8 to -0.4): p<0.001 8 wk: -0.9 (-1.2 to -0.6): p<0.001 3 mo: -0.9 (-1.2 to -0.6): p<0.001 6 mo: -1.0 (-1.3 to 0.6): p<0.001 **SSS Physical Function Subscale** 4 wk: -0.5 (-0.8 to -0.3): p<0.001 8 wk: -0.8 (-1.1 to -0.5): p<0.001 3 mo: -0.7 (-1.0 to -0.4): p<0.001 6 mo: -0.7 (-1.1 to -0.4): p<0.001 **Self-Paced Walk Test** 4 wk: p=0.648 8 wk: p=0.29 3 mo: p=030 6 mo: p=0.133 **Adverse events:** 3 participants in group 1 reported pain after needle insertion and 1 had a hematoma. 3 participants in group 2 reported back pain and 2 reported fatigue. All adverse events were reported as mild or moderate, and none required medical intervention.

Epidural injections				
Cuckler 1985	73 subjects in total, 37 with spinal stenosis, 36 with acute herniated nucleus pulposus, 37 males, 36 female, average age of 48.5 years in the experimental group and 49.5 years in the placebo group. Experimental group average 36.6 months in symptom duration, placebo group averaged 29.4 months. **Setting:** Orthopaedic surgery department in the United States	1) Steroid group: 2ml of sterile water containing 80mg of methylprednisolone acetate combined with 5ml of 1% procaine was injected into the epidural space in the region between the 3rd and 4th lumbar vertebrae with the patient in the lateral decubitus position lying on the side of the painful limb (n=42), 20 with stenosis). 2) Placebo group: 2ml of saline combined with 5ml of 1% procaine was injected into the epidural space in the region between the 3rd and 4th lumbar vertebrae with the patient in the lateral decubitus position lying on the side of the painful limb. (n=31, 17 with stenosis) All patients were advised to take mild analgesics (aspirin or acetaminophen) during the post-injection period. Second injection given if less than 50% improvement after 24 hours - considered treatment failure	1) Subjective percentage of improvement with 75% required to be considered a treatment improvement, if less than 50% after 24 hours was considered a treatment failure 2) Re-injection rates 3) Surgery rates **Follow-up:** 24 hours, every 3 months up to 30 months, averaging 20.2 months in the steroid group and 21.5 months in the control group.	**Patient Global Assessment (improved by at least 75%)** 24 hours: 33% (steroid) vs. 21% (saline) p>0.05 Long term: 33% (saline) vs. 14% (saline) p>0.05
Fukusaki 1988	53 subjects, 38 males and 15 female. Group 1 averaged 70 years of age and 79 days of symptoms on average, group 2 averaged 69 years of age and	1) Epidural injection with 8 ml of saline, repeated twice in the first week (n=16) 2) Epidural injection with 8 ml of 1% mepivacaine, repeated twice in the first week. (n=18) 3) Epidural injection with a mixture of 8 ml of 1% mepivacaine and 40 mg	1) Walking distance which was graded according to distance (excellent, good, or poor) **Follow-up:** 1 week, 1 month, 3	**Walking distance** Percent excellent effect = mean of > 100m in walking distance 1 week: 12.5 % (saline) vs. 55% (block) vs. 63.2% (block + steroid); block or block + steroid > saline, p< 0.05; 1 mo: 6.3% (saline) vs. 16.7% (block) vs. 15.8% (block + steroid) p > 0.05 3 mo: 6.3 (saline) vs. 5.6% (block) vs. 5.3% (block +steroid) p> 0.05 No significant difference between block vs. block + steroid at

	an average of 82 days of symptoms, group 3 averaged 72 years of age and 94 days of symptoms on average **Setting:** Anaesthesia department in Japan	of methylprednisone, repeated twice in the first week. (n=19)	months	all follow-up periods, p>0.05 **Adverse events:** no reported complications
Zahaar 1991	30 subjects, 37 male and 26 female. Steroid group averaged 46.5 years of age and 36.6 months of symptoms, control group averaged 49 years of age and 29.4 months of symptoms **Setting**: Medical facility in Egypt	1) Steroid injection: 5ml of hydrocortisone acetate suspension, 2x2ml carbocaine, 4% Volume completed with sterile saline to 30ml (n=18) 2) Control: 2x2ml of carbocaine, 4% injected into epidural space. Volume completed with sterile saline to 30ml. (n=12)	1) Subjective percentage of improvement where 75% or more was deemed successful and surgery after injection was considered a failure. **Follow-up:** 24 hours, then every three months up to 36 mo averaging 20.2 mo in the steroid group and 21.5 mo control group.	**Patient Global Assessment** (improved by at least 75%) 24 hours: 55% (steroid injection) vs. 50% (control) p> 0.05 Up to 36 mo: 38% (steroid injection) group vs. 33.3% (control) p>0.05 **Failures (%)** (required surgery) Up to 36 mo: 61% (steroid injection) vs. 66.6% (control) p>0.05
Friedly 2014, 2017 Makris 2016	400 patients, 221 females and 179 males, 200 in the lidocaine group	1) Lidocaine + glucocorticoid (1-3 mL of 0.25-1% lidocaine followed by 1-3 mL triamcinolone (60-120mg), betamethasone (6-12mg),	1) RMDQ 2) NRS (Leg Pain)	**Between group MD, 95% CI, p values** **RMDQ** 3 weeks: -1.8 (-2.8 to -0.9): p<0.001 6 weeks: -1.0 (-2.1 to 0.1): p=0.07

	with an average age of 68.1 years old and 200 gluocorticoid-lidocaine group with an average age of 68 years old, LSS by CT or MRI. 26% patients symptoms greater than 5 years. **Setting:** 16 medical centers across the United States	dexamethasone (8-10mg) or methylprednisone (60-120mg)) (n=200) 2) Lidocaine group (0.25-1% lidocaine alone) (n=200) Physician option for intralaminar and/or transformaminal techniques	**Follow-up:** 3, 6, and 12 weeks, 6 and 12 months Makris 2016 subgroup 1) RMDQ using SIP Weights 2) RMDQ patient-prioritized (LESSER) **Follow-up:** 3 and 6 weeks	12 wk: 0.1 (-1.0 to 1.3): p=0.784 6 mo -0.00 (-1.1 to 1.1): p=0.99 12 mo: -0.4 (-1.6 to 0.9): p=0.55 **NRS (Leg pain)** 3 weeks: -0.6 (-1.2 to -0.1): p=0.02 6 weeks: -0. (=0.8 to 0.4): p=0.48 12 wk: 0.1 (-0.5 to 0.7): p=0.70 6 mo: -0.2 (-0.8 to 0.4): p=0.47 12 mo: 0.1 (-0.5 to 0.7): P=0.75 Subgroup Analysis **RMDQ using SIP weight** 3 wks: -1.9 (-2.9 to -0.7): p=0.001 6 wks: -1.1 (-2.2 to -0.1): p=0.04 **RMDQ patient prioritized (LESSER)** 3 wks: -1.8 (-2.8 to -0.8): p=0.001 6 wks: -1.0 (-2.0 to 0.1): p=0.08 **Adverse events:** A total 21.5% of patients in group 1 and 15.5% in group 2 reported one or more adverse events (p=0.08) that included headaches, fever, infection, dizziness, cardiovascular/lung problems, leg swelling and dural puncture.
Song 2016	29 subjects, 14 males and 15 women with an average age of 58.3 and 61.7 between groups, history of intermittent claudication and lower limb radicular pain or paresthesia	1) Lidocaine spinal injection, 40 mg triamcinolone mixed with 10 mL 0.5% lidocaine was used under the guide of fluoroscopy (n=15) 2) Saline spinal injection using same volume (n=14)	1) VAS 2) FRI **Follow-up:** 1 and 3 months	No significant difference between groups. **VAS** 1-month p= 0.696, 3 months p= 0.891 **FRI** 1-month p=0.983, 3 months p=0.743

	Setting: Rehabilitation clinic in Korea			
Milburn 2014	57 patients met inclusion criteria, agreed to participate, and were enrolled. 20 patients were male; 37 were female. Mean patient age was 65.3 years (range, 32-88 years). Average duration of symptomatology (pain and/or disability) was 42 months. The mean degree of canal narrowing at the most stenotic level was 6.1 mm (range, 2.5-9.1 mm). The most common maximally stenotic intervertebral level was L4-L5	Fluoroscopically guided lumbar ILESI performed either at: 1) The level of maximal stenosis (n=30) 2) Two intervertebral levels cephalad, corresponding to a less stenotic level (n=27) Injection was performed with a 20-gauge Tuohy needle using a loss of resistance technique. The injectate consisted of 2 mL of 40 mg/mL methylprednisolone (Pfizer), 2 mL of bupivacaine 0.25% (Hospira), and 2 mL of normal saline for a total injectate volume of 6 mL.	1) NRS - Pain with Ambulation 2) RMDQ **Follow-up:** 1, 4 and 12 weeks	**All between group comparisons** **NRS (pain with ambulation)** 1 wk: Grp 1 lower pain compared to Grp 2, p=0.045 4 wk: Grp 1 lower pain compared to Grp 2, p=0.049 12 wk: Grp 1 lower pain compared to Grp 2, p=0.08 **RMDQ** 1 wk: Grp 1 lower compared to Grp 2, p=0.001 4 wk: Grp 1 lower compared to Grp 2, p=0.009 12 wk: Grp 1 lower compared to Grp 2, p=0.003

	(n¼42) followed by L3-L4 (n¼11) and L5-S1 (n¼4). **Setting:** Clinic in New Orleans, Louisiana			
Brown 2012	38 patients, 21 males and 17 females, 21 in mild group with an average age of 74.2 years and 17 in ESI group with an average age of 78.7 years, symptomatic LSS patients with painful lower limb neurogenic claudication, able to walk at least 10 feet unaided, (ODI) score > 20 **Setting:** Pain management clinic in Florida	1) Epidural steroid (80 mg triamcinolone acetate) (n=17) 2) Mild lumbar decompression (n=21)	1) VAS 2) ODI 3) ZCQ 4) Patient Satisfaction (0-10) **Follow-up:** 6 and 12 weeks	**VAS** 6 and 12 weeks P=0.54 **ODI** p=0.86 **ZCQ** p>0.05 **Patient satisfaction** p>0.05
Hammerich 2019	54 patients total, age 67.2 ± 9.7, 27 male, 27 female, 31 in ESI group, 23 in ESI plus PT. Mean duration of	1) ESI (n=31) 2) ESI + PT (n=23) ESI: 1.5 mL of steroid at each site injected with maximal involvement using transforaminal approach.	1) ODI 2) NRS current 3) SF-36 emotional role 4) SF-36 emotional well-being	**Between group MD, 95% CI, p values** **ODI** 10 wks: -1.08 (-8.10 to 5.94) p=0.80 6 mo: -4.70 (-11.72 to 2.32) p=0.27 12 mo: -2.72 (-9.74 to 4.30) p=0.52 **NRS** 10 wks: -1.68 (-3.08 to -0.29) p=0.07

	symptoms 14 m **Setting:** Clinics in Colorado, Texas, South Carolina and New Hampshire	PT: 8-10 sessions PT manual therapy and exercise. Walking program and/or stationary bike, stretching and strengthening exercises.	5) SF-36 general health perception **Follow-up**: 10 weeks, 6 and 12 months	6 mo: -1.99 (-3.38 to -0.60) p=0.04 12 mo:-2.44 (-3.80 to -1.08) p=0.00 **SF-36 Emotional role** 10 wks: -28.53 (-49.05 to -8.01) p=0.03 6 mo: -11.25 (-31.77 to 9.27) p=0.39 12 mo: -10.67 (-31.19 to 9.85) p-0.41 **SF-36 Emotional well-being** 10 wks: -11.26 (-19.52 to -2.99) p=0.02 6 mo: 2.69 (-5.57 to 10.95) p=0.59 12 mo: -5.76 (-14.02 to 2.50) p=0.24 **SF-36 General Health Perception** 10 wks: -8.99 (-17.20 to -0.78) p=0.05 6 mo: -5.56 (-13.77 to 2.65) p=0.23 12 mo: -5.10 (-13.31 to 3.11) p=0.27
Sencan 2020	67 patients. The median age 62.5 years with 18 males and 49 females. Median duration of symptoms was 29 and 24 months in the ILESI and bilateral TFESI groups, respectively **Setting:** University department Pain Medicine, Istanbul Turkey	1) Interlaminar: ILESI, fluoroscopy guided with 1 to 2 mL contrast dye with mixture of 80 mg methylprednisolone acetate, 2 mL saline solution, and 2 mL (0.5%) bupivacaine solution 2) Transforaminal: TFESI, fluoroscopy guided with 1 to 2 mL contrast dye with mixture of 80 mg methylprednisolone acetate, 2 mL saline solution, and 2 mL (0.5%) bupivacaine solution	1) NPS 2) ODI 3) Beck depression scale 4) Walk distance **Follow-up:** after treatment, 3 weeks and 3 months	**Between Group Median Differences (data not provided), p values** **NPS** after treatment: p=0.14 3 wks: p=0.28 3 mo: p=0.047 **ODI** 3 wks: p=0.93 3 mo: p=0.65 **Beck Depression Scale** 3wks: p=0.048 3 mo: p=0.03 Walking Distance 3 wks: p=0.23 3 mo: p= 0.048
Wei 2020	90 patients. Mean age about 65 years, 45 females, 45	1) Epidural injection with 2.0mL of lidocaine and 10 mg of TNF-a inhibitor (etanercept) on the affected spinal nerves.	1) VAS (leg) 2) ODI **Follow-up:** after	**Between Group Mean Differences (data not provided), p values** **Grp 1 vs Grp 2** **VAS**

	males, mean duration of symptoms about 2.8 months **Setting:** University Hospital Jiangsu China	2) Epidural administration with 2mL of lidocaine mixed with 2mL of steroid (diprospan) 3) Epidural injection 4.0mL of lidocaine only.	treatment, 1,3, 6 months	after treatment, 1, 3 and 6 mo, Grp 1 greater reduction, p<0.05 **ODI** 1, 3 and 6 mo, Grp 1 greater reduction, p<0.05 **Grp 1 vs Grp 3** **VAS** after treatment, 1, 3 and 6 mo, Grp 1 greater reduction, p<0.05 **ODI** 1, 3 and 6 mo, Grp 1 greater reduction, p<0.05 **Grp 2 vs Grp 3** **VAS** after treatment, 1, 3 and 6 mo, no significant difference, p>0.05 **ODI** 1, 3 and 6 mo, no significant difference, p>0.05
Karm 2018	44 patients total, 20 in the RACZ group (age 66.1 +-12.2, male 9 (45.0%), and 24 in the ZiNeu group (Age 65.5 +-6.4 18 females, 26 males. **Setting:** Single-center, academic, outpatient interventional pain management clinic in Korea	1) PEA Using a Balloon-less Catheter (Racz) (n = 20) 2) Percutaneous Epidural Decompression and Adhesiolysis Using an Inflatable Balloon Catheter (ZiNeu) (n = 24)	1) NRS (back pain) 2) NRS (leg pain) 3) ODI **Follow-up:** 1, 3 and 6 months	**Between group MD, 95% CI, p values** **NRS-11 (Back pain)** 1 mo:-0.38 (-1.81 to 1.06): p=0.61 3 mo: -1.13 (-2.63 to 0.38): p=0.14 6 mo: -2.02 (-3.58 to 0.45) p=0.01 **NRS-11 (Leg pain)** 1 mo: 0.73 (-0.40 to 1.85): p=0.21 3 mo: -0.69 (-1.89 to 0.52): p=0.26 6 mo: -1.88 (-3.15 to 0.61) p=0.00 **ODI (%)** 1 mo: -6.13 (-13.88 to 1.61): p=0.12 3 mo: -6.63 (-14.75 to 1.48): p=0.11 6 mo: -13.74 (-22.18 to 5.30): p=0.00 **Adverse events:** Minor and transient adverse events were reported equally in both groups (no data provided), mostly pain and paresthesia at the injection site.
Surgery				
Zucherman 2004, 2005, 2006	191 subjects, 57% male and 43% female in the X STOP group. 52% male	1) X STOP Interspinous Process Decompression System (n=100) 2) Non-operative treatment: Subjects received an epidural steroid injection	1) SF-36 2) ZCQ 3) Worker's compensation claims	**Patient global assessment (Good result)** 2 yrs: 73.1% (surgery) vs. 36.9% (control) (P< 0.001) **Symptoms Severity score**

	and 48% female in the non-operative group. Average age of 70 years in the X STOP group and 69.1 years in the non-operative group. Average of 3.5 year symptom duration in the X STOP group and 4.7 years in the non-operative group. **Setting:** Spine center in the United States	on enrolment and were eligible for additional injections as needed, as well as NSAIDS, analgesic agents, and physical therapy. Physical therapy consisted of education on back care and modalities such as ice packs, heat packs, massage, stabilization exercises, and pool therapy. Braces such as abdominal binders and corsets were permitted, but body jackets and chair back braces were not. (n=91)	4) ODI 5) Radiographic changes **Follow-up:** Surgery: 7 (2 yr) Control: 19 (2 yr)	Surgery better at 6 w, 6 mo, 1 and 2 yr (graphs) (P<0.001) 2 yrs: MPC 45.4% (surgery) vs. 7.4% (control) (P < 0.001) **"Clinically relevant improvement (patients)":** 2 yrs: 60.2% (surgery) vs. 18.5% (control) (P< 0.001) **Symptoms Severity score** Surgery better at 6 w, 6 mo, 1 and 2 yr (graphs) (P<0.001) 2 yrs: MPC 44.3% (surgery) vs. -0.4% (control) (P < 0.001) **"Clinically relevant improvement (as measured by patients)":** 2 yrs: 57% (surgery) vs. 14.3% (control) (P < 0.001) **ZCQ (global success)** 6 mo: 52% (surgery) vs. 9% (control) (P value not reported) 1 yr: 59% vs 12% (P value not reported) 2 yrs: 48.4% (surgery) vs. 4.9% (control) (P < 0.001) **Quality of life (SF-36)** At all post treatment time points (6 w, 6 mo, 1 yr, 2 yr), the mean domain scores documented in the X STOP group were significantly greater than those in the non operative group, with the exception of the mean General Health, Role Emotional, and Mental Component *Summary scores at 2 years* **Adverse events:** No complications were reported in group 2. In group 1, complications were reported in 11% of subjects including spinous process fracture, coronary ischemia, respiratory distress, hematoma, and 1 death (pulmonary edema)
Weinstein 2007, 2009, Abdu 2018	Subjects with image-confirmed degenerative spondylolisthesis: 304 subjects in the RCT, 303 in the observational cohort, 31% male in the surgical group, 33% male in the surgical group. Average	1) Assigned to surgery (standard laminectomy with or without fusion) (n=159) 2) Assigned to non-surgical treatment: Usual non-operative care (n=145)	1) SF-36 bodily pain 2) SF-36 bodily function 3) low back pain bothersomeness scale 4) Leg pain bothersomeness scale 5) ODI 6) Subjective self-	**All between group comparisons using Intention-to-Treat analysis** **SF-36 Bodily Pain, DMC, 95% CI** 2 yrs: 1.5 (-4.2 to 7.3) 4 yrs: -2 (-8.6 to 4.6) 8 yrs: p=0.85 **SF-36 Bodily Function, DMC, 95% CI** 2 yrs: 1.9 (-3.7 to 7.5) 4 yrs: -3.1 (-9.2 to 3.0) 8 yrs: p=0.31 **Disability (ODI), DMC, 95% CI** 2 yrs: 2.2 (-2.3 to 6.8)

	age of 64.7 years in the surgical group and 68.2 years in the non-surgical group. Subjects had symptoms for at least 12 weeks **Setting:** multi-centred orthopaedic departments in the United States		reported improvement, satisfaction with current symptoms and care 7) Stenosis bothersomeness index **Follow-up**: 6 weeks, 3 and 6 months, 1, 2, 4 and 8 years	4 yrs: 4.1 (-0.8 to 9.1) 8 yrs: p=0.039 Other outcomes (patient's satisfaction; Stenosis Bothersomeness Index, Leg Pain Bothersomeness Scale; and Low Back Pain Bothersomeness Scale) were not provided separately for the randomized cohort. **Adverse events:** group 1 reported 14% intraoperative complication mostly and dural tears and 19% postsurgical complications including 1 death, 11% required additional surgeries at 2 years,
Amundsen 2000	100 subjects, 54 male, 46 female, median age of 59 (males were 1.5 years higher than females). Median back pain duration was 14 years, median duration of sciatica was 2 years. **Setting:** Neurology department in a hospital in Norway	1) Surgery: Partial or total laminectomy, medial facetectomy, discectomy, and/or removal of osteophytes from the vertebral margins or facet joints. No fusions. (n=13) 2) Conservative therapy: Lumbar orthosis use for 1 month worn during the day for all activities plus instruction and back school." (n=18)	1) VAS 2) Verbal Rating Scale 3) Subjective change (better, worse, or unchanged) 4) Work status 5) Subjective rating from evaluating physician and study team (Excellent, Fair, Unchanged, Worse) **Follow-up:** 6 months, 1, 4 and 10 years	**Patient global assessment (Good result)** 1 yr: RR 2.07 (0.98 to 4.38) 4 yrs*: RR 1.94 (1.14 to 3.31)* 10 yrs: RR 3.18 (0.97 to 10.41) **Pain (none or mild)** 1 yr: NR 4 yrs: RR 3.33 (0.77 to 14.33) 10 yrs: RR 1.59 (0.55 to 4.55) Other outcomes (claudication or walking distance; level of daily activity; and neurologic deficits) were not reported separately for the randomized cohort.
Malmivaara 2007	94 subjects, 22% of surgical	1) Segmental decompressive surgery with facetectomy (n=50)	1) 11 point numerical pain	**All between group comparisons** **Leg pain, MD, 95% CI**

	subjects were male, 45% of non-operative subjects were male. Nonoperative group had average age of 62.9 years, surgical group had average age of 63.9 years. Surgical group averaged 14 years since onset of symptoms, nonsurgical group average 16 years since onset of symptoms. Minimum of 6 months of symptoms for study inclusion. **Setting:** Research Center in Finland	2) Non-operative treatment: NSAIDS when indicated and seen one to three times by a physiotherapist, in addition to the standard visit at each follow-up. The physiotherapist gave all patients educational brochure. The patients were encouraged to use their back in a normal way. Pain-relieving body postures were taught as well as basic ergonomics related to lifting and carrying. Individually structured programs included trunk muscle endurance and stretching-type exercises. Additional individual physiotherapy consisting of passive treatment methods (such as ultrasound and transcutaneous nerve stimulation). (n=44) The patients in the surgical group also received the brochure and the instructions described above.	rating scale for back and leg pain 2) Walking ability (distance without a break) also via treadmill test 3) General health status on a 5 point scale (very good, quite good, average, quite poor or very poor. 4) ODI 5) Ability to complete certain activities of daily 6) living without difficulty, some difficulty, marked difficulties or not at all 7) Radiographic examination **Follow-up:** 6 months, 1 and 2 years	1 yr: 1.69 (0.41 to 2.96) 2 yr: 1.51(0.25 to 2.77) **Back pain, MD, 95% CI** 1 yr: 2.33 (1.12 to 3.55) 2 yrs: 2.13(0.98 to 3.28) **Disability (ODI), MD, 95% CI** 1yr: 11.3 (4.3to 18.8) 2 yrs: 7.8 (0.8 to14.9) **> 10 points reduction (ODI): RR, 95% CI** 1 yr: 2.16 (1.31to 3.57) 2 yrs: 1.36 (0.88 to 2.10) **Walking disability (walking distance <1.250 m), RR, 95% CI** 1 yr: 0.93 (0.61 to 2.03) 2 yrs: 1.08 (0.70 to 2.42) **Walking disability (walking distance <400 m), RR, 95% CI** 1 yr: 0.91 (0.51 to 4.24) 2 yrs: 1.18 (0.67 to 4.72)

Weinstein 2008, 2010, Lurie 2015	289 in the RCT, 365 in the observational cohort. 62% male in the surgical groups, 59% male in the non-surgical groups. Average age of 63.8 in the surgical group, 66.1 in the non-surgical group. 60% in the surgical group and 55% in the non-surgical group had symptoms for over 6 months. **Setting:** multi-centred-orthopaedic departments in the United States.	1) Assigned to surgery: Standard laminectomy with or without fusion (n=138) 2) Assigned to non-surgical treatment: Usual non-operative care - recommended to include at least active physical therapy, education or counseling with home exercise instruction, and the administration of NSAIDs, if tolerated (n=151)	1) SF-36 bodily pain 2) SF-36 bodily function 3) Low back pain bothersomeness scale 4) Leg pain bothersomeness scale 5) ODI 6) Subjective self-reported improvement, satisfaction with current symptoms and care, 7) Stenosis bothersomeness index **Follow-up**: 6 weeks, 3 and 6 months, 1, 2, 4, 8 years	**All between group comparisons using Intention-to-Treat Analysis** **SF-36 Bodily Pain, DMC, 95% CI** 2 yrs: 7.8 (1.5to 14.1) 4 yrs: 0.3 (-6.4 to 7) 8 yrs: p=0.25 **SF-36 Bodily Function, DMC, 95% CI** 2 yrs: 0.1 (-6.4 to 6.5) 4 yrs: -3.2 (-9.9 to 3.6) 8 yrs: p=0.89 **Disability (ODI), DMC, 95% CI** 2 yrs: -3.5 (-8.7 to 1.7) 4 yrs: 0.2 (-5.2 to 5.7) 8 yrs: p=0.87 Other outcomes (patient's satisfaction; Stenosis Bothersomeness Index, Leg Pain Bothersomeness Scale; and Low Back Pain Bothersomeness Scale) were not provided separately for the randomized cohort. **Adverse events:** In group 1 10% of patients required transfusions intraoperatively and 5% postoperatively. The most common surgical complication was dural tear, in 9% of patients. At 2 years, reoperation had occurred in 8% of subjects.
Delitto 2015	169 patients, 88 males and 81 females, 87 surgical group with an average age of 66.6 years old and 82 PT group with an average age of 69.8 years old, LSS by computed	1) Surgical decompressive laminectomies, partial facet resection, and neuroforaminotomies (n=87) 2) PT program: lumbar flexion exercises, exercises and education (n=82)	1) SF-36 physical function **Follow-up:** 2 years	**2 years -SF-36 Physical Function, MD and 95% CI** 0.9 (7.9 to 9.6) **Adverse events:** 9 out of 82 participants in group 2 reported adverse events consisting of worsening of symptoms whereas 33 out 87 participants in group 1 reported surgery related complications, mainly attributable to reoperation, delay in wound healing and surgical site infection.

	tomography - criteria of Wiesel and colleagues (18) or magnetic resonance imaging - criteria of Boden and colleagues (2) **Setting:** Neurologic and orthopedic surgery departments and physical therapy clinics in western Pennsylvania			

ADLs = Activities of Daily Living, AUC = Area under the pain-intensity curve, BTX = Botox, CI = Confidence Interval, DMC = Difference in mean change from baseline, ESI = Epidural Steroid Injection, FRI = Functional Rate Index, GRP = Group, HADS =Hospital Anxiety and Depression Scle, IU = International Units, JOABPEQ = Japanese orthopaedic association back pain evaluation questionnaire, LBOS = Low Back Outcome Score, LBP = Low Back Pain, m = Meters, MCS = Mental Component Score, MD = Mean Difference, mm = Millimeters, Mo = Months, MPC = Mean Percent Change, NRS = Numerical Pain Rating Scale, NR = Not Reported, ODI = Oswestry Disability Index, OR = Odds Ratio, PASS-20 = Pain Anxiety Symptoms Scale, PCS = Physical Component Score, RCT = Randomized Controlled Trial, RMDI = Roland Morris Disability Index, ROM = Range of Motion, RR = Relative Risk, SBI = Stenosis Bothersomeness Index, SPWT = Self-Paced Walking Test, SSS = Spinal Stenosis Questionnaire, TSK-11 = Tampa Scale-11, VAS = Visual Analogue Scale, WMD = Weighted Mean Difference, ZCQ = Zurich Claudication Questionnaire

Supplemental Table 2. Non operative interventions for neurogenic claudication due to lumbar spinal stenosis: A summary of GRADE assessment and outcomes (60 comparisons)

						Walking ability/pain/function/quality of life measures				GRADE
Studies	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Selective Reporting**	**Immediate up to 1w**	**Short-term >1w - 3m**	**Intermediate 3m – 1yr**	**Long term >1yr**	
Calcitonin										
Calcitonin injection vs. placebo injection										
Eskola 1992	High	No No	Yes Yes	No No	Yes		= TWT = VAS	= TWT = VAS	= TWT = VAS	+000 +000
Porter 1983	High	No	Yes	No	Yes		? Distance walked	? Distance walked		+000
Porter 1988	High	No No	Yes Yes	No No	Yes		= Distance walked = VAS			+000 +000
Calcitonin nasal spray vs. placebo injection										
Podichetty 2004	High	No No No No	Yes Yes Yes Yes	No No No No	Yes		= Distance walked = Time walked = SF-36 = VAS			+000 +000 +000 +000
Tafazal 2007	High	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No		= Shuttle walk = VAS leg = VAS back = ODI = Global			+000 +000 +000 +000 +000
Calcitonin nasal spray plus physical therapy vs. paracetamol plus physical therapy										
Sahin 2009	High	No No No	Yes Yes Yes	No No No	No		= Distance walked = VAS = RMDI			+000 +000 +000
Oral Medication										
Oral prostaglandin vs. Etodlac (NSAID)										
Matsudaira 2009	Low	No No No No No	Yes Yes Yes Yes Yes	No No No No No	Yes		> Distance walked # ? SF-36 = LBP > Leg pain > Global #			++00 +000 ++00 ++00 ++00
Methylocobalamin (vit B12) plus conservative care vs. conservative care										
Waikakul 2000	High	No	Yes	No	No			> Distance walked #	> Distance walked #	+000

Gabapentin plus physical therapy, corset & NSAIDS vs. placebo plus physical therapy, corset & NSAIDS										
Yaksi 2007	High	No No No	Yes Yes Yes	No No No	No		= VAS	> Distance walked > VAS	> Distance walked # > VAS #	+000 +000
Pregabalin vs. active placebo										
Markman 2015	High	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No	= NPS rest/final = Distance walked = Recovery time = Global < RMDQ				+000 +000 +000 +000 +000
Gabapentin plus conservative vs. conservative plus botulinum										
Park 2017	High	No No No	Yes Yes Yes	No No No	No		= NPS (Back/leg) = ODI = Global			0000 0000 0000
Oxymorphone hydrochloride vs. placebo										
Markman 2015 - 2	High	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No	= NPS rest/final = Distance walked = Recovery Time = ZCQ (s) = ZCQ (f) = Global				0000 0000 0000 0000 0000 0000
Propoxyphene/acetaminophen vs. placebo										
Markham 2015 – 2	High	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No	= NPS rest/final = Distance walked = Recovery Time = ZCQ (s) < ZCQ (f) # = Global				0000 0000 0000 0000 0000 0000
Oxymorphone hydrochloride vs. propoxyphene/acetaminophen										
Markham 2015 - 2	High	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No	= NPS rest/final = Distance walked = Recovery Time = ZCQ (s) > ZCQ (f) # = Global				0000 0000 0000 0000 0000 0000
Oral corticoid vs. placebo										

Rodrigues 2014	High	No No No No	Yes Yes Yes Yes	No No No No	No		= SF-36 = RMDQ = 6 min walk < VAS #			0000 0000 0000 0000
Rehabilitation Therapy and Multimodal Care										
Exercise plus ultrasound vs. exercise plus sham ultrasound										
Goren 2010	low	No No No No	Yes Yes Yes Yes	No No No No	No		= TWT = VAS back = VAS leg = ODI			++00 ++00 ++00 ++00
Exercise plus ultrasound vs. no treatment										
Goren 2010	Low	No No No No	Yes Yes Yes Yes	No No No No	No		= TWT = VAS back > VAS leg # > ODI			++00 ++00 ++00 ++00
Exercise plus sham ultrasound vs. no treatment										
Goren 2010	Low	No No No No	Yes Yes Yes Yes	No No No No	No		= TWT = VAS back > VAS leg # > ODI #			++00 ++00 ++00 ++00
In-patient physical therapy vs. home exercise program plus oral diclofenac										
Koc 2009	High	No No No No	Yes Yes Yes Yes	No No No No	Yes		= TWT = VAS = RMDI = NHP	= TWT = VAS = RMDI = HNP		+000 +000 +000 +000
Unweighted treadmill walking plus exercise vs. cycling plus exercise										
Pua 2007	Low	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No		= Distance walked = ODI = RMDI = VAS = Global			++00 ++00 ++00 ++00 ++00
Manual therapy, exercise and unweighted treadmill vs. flexion exercise, walking and sham ultrasound										
Whitman 2006	High	No No No No	Yes Yes Yes Yes	No No No No	No		= TWT > Global # = ODI = NPRS			+000 +000 +000 +000
Supervised physical therapy vs home exercises										

Minetama 2019	High	No No No No No No No No	Yes Yes Yes Yes Yes Yes Yes Yes	No No No No No No No No	No		> ZCQ (F) # >ZCQ (S) # > Distance walked # > NPS (leg) > SF-36 PF > SF-36 BP = Daily Steps			+000 +000 +000 +000 +000 +000 +000
Manual therapy & exercise vs medical care										
Schneider 2019	Low	No No No	Yes Yes Yes	Yes Yes Yes	No		> ZCQ # = SPWT = PA	= ZCQ = SPWT = PA		+++0 +++0 +++0
Manual therapy & exercise vs. community exercise										
Schneider 2019	Low	No No No	Yes Yes Yes	Yes Yes Yes	No		> ZCQ # = SPWT = PA	= ZCQ = SPWT = PA		+++0 +++0 +++0
Community exercise vs. medical care										
Schneider 2019	Low	No No No	Yes Yes Yes	Yes Yes Yes	No		= ZCQ = SPWT > PA	= ZCQ = SPWT = PA		+++0 +++0 +++0
Comprehensive therapy and exercise vs. self-directed exercise										
Ammendolia 2018	Low	No No No No No No No No	Yes Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes Yes	No	> SPWT # > 30% SPWT > 50% SPWT > ZCQ (s) = ZCQ (f) = ODI > NPS (back) # = NPS (leg) = SF-36 BP = SF-36 PF	> SPWT # > 30% SPWT = 50% SPWT = ZCQ (s) = ZCQ (f) = ODI = NPS (back) = NPS (leg) = SF-36 BP > SF-36 PF #	> SPWT # > 30% SPWT = 50% SPWT = ZCQ (s) = ZCQ (f) > ODI (walk) = NPS (back) = NPS (leg) = SF-36 BP = SF-36 PF	> SPWT # >30% SPWT > 50% SPWT > ZCQ (f) # > ZCQ (s) + ZCQ (f) = ODI = NPS (back) > SF-36 BP # >SF-36 PF #	+++0 +++0 +++0 ++00 ++00 ++00 ++00 ++00 ++00 ++00
Standard exercise vs. isokinetic exercises										
Oğuz 2013	High	No No No	Yes Yes Yes	No No No	Yes	= VAS = ODI = TWT	= VAS = ODI = TWT	= VAS = ODI = TWT		0000 0000 0000
Standard exercise vs. unloaded exercise										
Oğuz 2013	High	No No No	Yes Yes Yes	No No No	Yes	< VAS < ODI = TWT	< VAS = ODI = TWT	= VAS = ODI = TWT		0000 0000 0000

Isokinetic exercises vs. unloaded exercises										
Oğuz 2013	High	No No No	Yes Yes Yes	No No No	Yes	< VAS < ODI < TWT #	= VAS < ODI < TWT	= VAS = ODI = TWT		0000 0000 0000
Aquatic physical therapy exercise vs. physical therapy										
Homayouni 2015	High	No No	Yes Yes	No No	Yes	> VAS # > Distance walked	= VAS = Distance walked			0000 0000
Pre-surgical exercise program vs. routine preoperative hospital management										
Marchand 2019	High	No No	Yes Yes	No No	Yes	> NPS (leg) # > Duration walked #	= NPS (leg) = Duration walked	= NPS (leg) = Duration walked		0000 0000
Gang-Chuk Tang (herbal concoction), daily Mokuri Chuna therapy, daily acupuncture, physician consultation vs. oral aceclofenac, epidural steroid injection, physical therapy										
Kim 2019	Low	No No No No	Yes Yes Yes Yes	No No No No	Yes		= VAS (leg) = VAS (back) > OCS > Distance walked	= VAS (leg) > VAS (back) # = OCS > Distance walked		+000 +000 +000 +000
Mokhuri Chuna, acupuncture, and physician consultation vs. oral aceclofenac, epidural steroid injection, physical therapy										
Kim 2019	Low	No No No No	Yes Yes Yes Yes	No No No No	Yes	>VAS (low back)#	= VAS (leg) = VAS (back) = OCS = Distance walked	> VAS (leg) # > VAS (back) # = OCS = Distance walked		+000 +000 +000 +000
Spinal Manipulation										
Lumbar spinal manipulation vs. waiting										
Passmore 2017	High	No No	Yes Yes	No No	No	= NPS (Back) = NPS (Leg)				0000 0000
Acupuncture										
Acupuncture with usual care vs. usual care										

Kim 2016	High	No No No No No No No No No No No No	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	No No No No No No No No No No No No	No		6 weeks: = ODI = SF-36 BP = SF-36 PF = LBP = Leg pain = Distance walked 3 months: = ODI = SF-36 BP = SF-36 PF = LBP = Leg pain = Distance walked			0000 0000 0000 0000 0000 0000 0000 0000 0000 0000 0000 0000
Acupuncture vs. sham acupuncture										
Qin 2020	Low	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No	> RMDQ > NRS (back) # > NRS (leg) # > SSS-S # > SSS-F # = SPWT	> RMDQ > NRS (back) # > NRS (leg) # > SSS-S # > SSS-F # = SPWT	> RMDQ > NRS (back) # > NRS (leg) # > SSS-S # > SSS-F # = SPWT		++00 ++00 ++00 ++00 ++00 ++00
Epidural Injection										
Translaminar epidural steroid injections vs. placebo injections										
Cuckler 1985	High	No	Yes	No	No	= Global			=global	+000
Translaminar epidural steroids plus epidural block vs. placebo injections										
Fukusaki 1988	High	No	Yes	No	No	> Distance walked #	= Distance walked			+000
Translaminar epidural steroids plus epidural block vs. epidural block injections										
Fukusaki 1988	High	No	Yes	No	No	= Distance walked	= Distance walked			+000
Translaminar epidural block vs. placebo										
Fukusaki 1988	High	No	Yes	No	No	> Distance walked #	= Distance walked			+000
Intralaminar epidural steroid plus epidural block vs. home exercise program plus oral diclofenac										
Koc 2009	High	No No No	Yes Yes Yes	No No No	Yes Yes Yes		= TWT > VAS # > RMDI #	= TWT = VAS = RMDI		+000 +000 +000

		No	Yes	No	Yes		> NHP	= HNP		+000
Intralaminar epidural steroid plus epidural block vs. in-patient physical therapy										
Koc 2009	High	No No No No	Yes Yes Yes Yes	No No No No	Yes Yes Yes Yes		= TWT = VAS = RMDI = NHP	= TWT = VAS = RMDI = HNP		+000 +000 +000 +000
Caudal epidural steroids vs. placebo injections										
Zahaar 1991	High	No	Yes	No	No	= Global			= Global	+000
Mild lumbar decompression vs. epidural steroid injection										
Brown 2012	High	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No		= VAS = ODI = ZCQ 12 weeks: = VAS = ODI = ZCQ			0000 0000 0000 0000 0000 0000
Lidocaine vs. glucocorticoid–lidocaine										
Friedly 2014, 2017	Low	No No No No	Yes Yes Yes Yes	Yes Yes Yes Yes	No		3 weeks: < RMDQ < NPS (leg) 6 weeks: = RMDQ = NPS (leg)	12 weeks: = RMDQ = NPS (leg) 6 months: = RMDQ = NPS (leg)	12 months: = RMDQ = NPS (leg)	 +++0 +++0 +++0 +++0
Makris 2016	Low	No No No No	Yes Yes Yes Yes	No No No No	Yes Yes Yes Yes		Makris 2016 3 weeks: < RMDQ using SIP Weights < RMDQ Patient-Prioritized (LESSER) 6 weeks: < RMDQ using SIP Weights = RMDQ Patient-Prioritized (LESSER)			 0000 0000 0000 0000

Lidocaine spinal injection vs. saline spinal injection										
Song 2016	High	No No No No	Yes Yes Yes Yes	No No No No	No		1 month: = VAS = FRI 3 months: = VAS = FRI			0000 0000 0000 0000
Fluoroscopically guided lumbar ILESIS at the level of maximal stenosis vs. two intervertebral levels cephalad										
Milburn 2014	High	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No	1 week: > NPS (walking) # > RMDQ #	4 weeks: > NPS (walking) # > RMDQ 12 weeks: = NPS (walking) > RMDQ			0000 0000 0000 0000
Epidural steroid injection (ESI) Vs. ESI & physiotherapy										
Hammerich 2019	High	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No		= ODI = NPS > SF-36 ER # > SF-36 EWB > SF-36 GH	= ODI > NPS # = SF-36 ER = SF-36 EWB = SF-36 GH	= ODI > NPS # = SF-36 ER = SF-36 EWB = SF-36 GH	0000 0000 0000 0000 0000
Interlaminar vs. transforaminal epidural steroid injection										
Sencan 2020	High	No No No No No No No No	Yes Yes Yes Yes Yes Yes Yes Yes	No No No No No No No No	Yes	= NPS	3 weeks: = NPS = ODI > BDS = Distance walked	3 months: > NPS = ODI > BDS > Distance walked #		0000 0000 0000 0000 0000 0000 0000 0000
TNF alpha inhibitor (Etanercept) vs. steroid injection										
Wei 2020	Low	No No No	Yes Yes Yes	No No No		> VAS #	1, 3 months: > VAS # > ODI #	6 months: > VAS # > ODI #		++00 ++00 ++00
TNF alpha inhibitor (Etanercept) vs. lidocaine										

Wei 2020	Low	No No No	Yes Yes Yes	No No No		> VAS #	1, 3 months: > VAS # > ODI #	6 months: > VAS # > ODI #		++00 ++00 ++00
Steroid vs. lidocaine injection										
Wei 2020	Low	No No No	Yes Yes Yes	No No No		= VAS	1, 3 months: = VAS = ODI	6 months: = VAS = ODI		++00 ++00 ++00
Percutaneous Epidural Adhesiolysis										
Balloon-less catheter (Racz) vs. inflatable balloon catheter (ZiNeu)										
Karm 2018	High	 No No No No No No	 Yes Yes Yes Yes Yes Yes	 No No No No No No	No		1 month: = NPS (back) = NPS (leg) = ODI 3 months: = NPS (back) = NPS (leg) = ODI	6 months: < NPS (back)# < NPS (leg) # < ODI		 0000 0000 0000 0000 0000 0000
Surgery vs. Physical Therapy										
Interspinous spacer (X_Stop) vs. non operative care										
Zucherman 2004, 2005, Hsu 2006	High	No No	Yes Yes	No No	No		> ZCQ(S)# > ZCQ(F)# > SF-36 PF > SF-36 BP > SF-36 GH > SF-36 ER	> ZCQ(S)# > ZCQ(F)# > SF-36 PF > SF-36 BP > SF-36 GH > SF-36 ER	> ZCQ(S)# > ZCQ(F)# > SF-36 PF# > SF-36 BP# > SF-36 GH > SF-36 ER#	+000 +000 +000 +000 +000 +000
Laminectomy +/- fusion vs. non operative care for degenerative spondylolisthesis										

Weinstein 2007, 2009 Abdu 2018	High	No No No No No No No No No No No No No No No	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	No No No No No No No No No No No No No No No	No		= SF-36 BP, PF = ODI = LBPBS = LPBI = SBS	= SF-36 BP, PF = ODI = LBPBS = LPBI = SBS	2 years: = SF-36 BP, PF = ODI = LBPBS = LPBI = SBS 4 years: = SF-36 BP, PF = ODI = LBPBS = LPBI = SBS 8 years: = SF-36 BP, PF = ODI = LBPBS = LPBI = SBS	+000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000
Laminectomy +/- fusion vs. non operative care										
Amundsen 2000	High	No No	Yes Yes	No No	No		?* Pain severity	?* Global	?* Pain severity ? Global	+000 +000
Malmivaara 2007 N= 94	Low	No No No No No	Yes Yes Yes Yes Yes	No No No No No	No			= TWT = SW > VAS leg walk # > VAS LB walk # > ODI	= TWT = SW > VAS leg walk # > VAS LB walk # > ODI	++00 ++00 ++00 ++00 ++00 ++00
Weinstein 2008, 2010, Lurie 2015	High	No No No No No No	Yes Yes Yes Yes Yes Yes	No No No No No No	No		= SF-36 BP = SF-36 PF = LBPBS = LPBI = SBS = ODI	= SF-36 BP = SF-36 PF = LBPBS = LPBI = SBS = ODI	2 years: > SF-36 BP ** # = SF-36 PF = LBPBS = LPBI = SBS = ODI 4 years: =SF-36 BP ** = SF-36 PF = LBPBS = LPBI	+000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000 +000

									= SBS 8 years: = SF-36 BP = SF-36 PF = ODI = Stenosis Index	+000 +000 +000 +000
Laminectomy, facet resection, neuroforaminotomy vs. physical therapy										
Delitto 2015	High	No No	Yes Yes	No No	No				2 years: = SF-36 = ODI	+000 +000

> favours intervention (first comparison), < favours control (second comparison), = no difference between intervention and control groups, TWT= Treadmill Walking Test, VAS= Visual Analog Scale for Pain Intensity, RMDI= Roland-Morris Back Disability Index, NHP= Nottingham Health Profile, Global= Patient Perceived Improvement, SR= Selective Reporting, ODI= Oswestry Back Disability Index, ?= insufficient data, LBP= Low back Pain Severity Scale, Leg pain= Leg Pain Severity Scale, ? SF-36=No data on overall score, improvement in some subscales, NPRS= Numeric Pain Rating Scale, SF-36 BP= SF-36 Bodily Pain Subscale, SF-36- PF= SF-36 Physical Function Subscale, SF-36 ER= SF-36 emotional role subscale, SF-36 EWB= SF-36 emotional well-being subscale, SF-36 GH= SF-36 General health subscale, LBPBS= Low Back Pain Bothersome Scale, LPBI= Leg Pain Bothersome Index, SBS= Stenosis Bothersome Scale, SW= Subjective Walking, VAS leg= Visual Analog Scale for Leg Pain, VAS LB= Visual Analog Scale for Low Back Pain, VAS leg walking= Visual Analog Scale for Leg pain while walking, SIP= sickness index profile, BDS= Beck Depression Score, LESSER= Lumbar Epidural Steroid Injection for Spinal Stenosis Extended Research, PA= Physical Activity, FRI= Functional Rating Index, TWT= Total Walking Time, SSS= Spinal Stenosis Questionnaire, ?*= no between group statistical comparisons, **= SF-36 BP significantly better at 2 years but not 4 years.

GRADE evidence; +000= Very low GRADE evidence, ++00= Low GRADE, +++0= Moderate GRADE evidence, ++++= High GRADE evidence

between group difference meeting the MCID. The MCID used were: ≥1.25 points for back pain and ≥1.5 points for leg pain on 0- to 100-point Visual Analogue Scale (VAS) and 0 to 10-point Numerical Rating Scale (NRS) for back pain (58), ≥5 points on 0- to 24-point Roland-Morris Disability Questionnaire (RMDQ) (59), ≥8 points for conservative treatment and ≥12 points for surgery on 0- to 100-points for Oswestry Disability Index (ODI) (60), ≥ 0.1 points for the functional component and 0.36 points for symptom component of the Zurich Claudication Questionnaire (ZCQ) (58), ≥ 0.38 points for combined symptoms and functional scores of the ZCQ (92), ≥ 30% between-group difference for walking distance, global improvement and SF36 subscales (61).

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 6-7
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 7
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 9
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 8-9
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 8-9 & Supplemental File 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 9
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 9
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 8 & 10
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 8-10 Supplemental Table 1
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 9-10
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 11-12
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 11-12
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 11-12
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Supplemental Table 2
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 10
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Supplemental Table 1
Risk of bias	18	Present assessments of risk of bias for each included study.	Table 1
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplemental Table 1 & 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Table 2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Supplemental Table 2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	NA
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Supplemental Table 2
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 25-26
	23b	Discuss any limitations of the evidence included in the review.	Page 28-29
	23c	Discuss any limitations of the review processes used.	Page 28-29
	23d	Discuss implications of the results for practice, policy, and future research.	Page 28
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 7
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	NA
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 30
Competing interests	26	Declare any competing interests of review authors.	Page 30
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	NA

PRISMA 2020 Checklist

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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