Facet Neurotomy:
Assessing Signals for Update

Provided by:

Aggregate Analytics, Inc.

Prepared by:

Andrea C. Skelly, PhD, MPH
Erika D. Brodt, BS
Cassandra Winter, BS
Aaron Ferguson, BA

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1. Previous Coverage Decision

A Health Technology Assessment titled: *Facet Neurotomy*, was published on February 21st, 2014 by the Health Care Authority. Findings and Coverage Decision was adopted on May 16th, 2014. The Committee's Coverage Decision is summarized below.

HTCC Coverage Determination

Facet Neurotomy is a **covered benefit with conditions** consistent with the criteria identified in the reimbursement determination.

HTCC Reimbursement Determination

Lumbar Facet Neurotomy is a **covered benefit with the following conditions:**

- Patient(s) must be over 17 years of age, and:
- Has at least six months of continuous low back pain referable to the facet join
- The pain is non-radicular pain
- Condition is unresponsive to other therapies including conservative care
- There are no other clear structural cause of back pain
- There is no other pain syndrome affecting the spine
- For identification, diagnosis, and treatment:
    - Patient must be selected by at least 80% improvement in pain after each of two differential medial branch blocks, one short-acting; on long-acting
    - One or two joints per each intervention, with documented, clinically significant improvement in pain and/or function for six months before further neurotomy at any level

Cervical Facet Neurotomy for cervical pain is a **covered benefit with the following conditions:**

- Limited to C3–4, through C6–7
- Patient(s) over 17 years of age, and:
- Has at least six months of continuous neck pain referable to the facet joint
- The pain is non-radicular
- Condition is unresponsive to other therapies including conservative care
- There are no other clear structural cause of neck pain
- No other pain syndrome affecting the spine
- For identification, diagnosis and treatment:
    - Patients must be selected by 100% improvement in pain after each of two differential medial branch blocks, one short-acting; one long-acting
    - One joint per each intervention, with documented, clinically significant improvement in pain and/or function for size months before further neurotomy at any level

Facet Neurotomy for the thoracic spine **is not covered.**

Facet Neurotomy for headache **is not covered.**

Committee Decision

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, and agency and state utilization information. The committee concluded that the current evidence on Facet Neurotomy demonstrates that there is sufficient evidence to cover with conditions. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable. Based on these findings, the committee voted to cover with conditions Facet Neurotomy.

The committee reviewed selected payer coverage policies from Aetna, Cigna and Health Net. The committee also reviewed practice guidelines from The American Pain Society, National Institute for Health and Clinical Excellence/ National Collaborating Centre for Primary Care, American College of Occupational and Environmental Medicine; American Society of Interventional Pain Physicians; Colorado Division of Workers' Compensation, American College of Occupational and Environmental Medicine, Institute of Health Economics, Work Loss Data Institute, Institute for Clinical Systems Improvement and American Society of Regional Anesthesia and Pain Medicine.

The committee Chair directed HTA staff to prepare a Findings and Decision document on Facet Neurotomy reflective of the majority vote for final approval at the next public meeting.

Medicare Decision and Expert Treatment Guidelines

CMS does not have a national coverage determination (NCD) for Facet Neurotomy, but has a decision on nerve ablation. The committee considered this decision and determined there was no data shown supporting the decision, and HTCC's determination did not conflict with this NCD.

2. Purpose of Report

The purpose of this literature update is to determine whether or not there is sufficient evidence published after the original report to conduct a re-review of this technology based on the presence of preset signal criteria (see Figure 1). The key questions in the included original report are listed below.

Key question 1

1. What is the evidence that the use of diagnostic blocks (i.e., medial branch blocks or intraarticular injections with local anesthetic) to select patients for facet neurotomy improves clinical outcomes following facet neurotomy? Consider each of the following:
    a. Diagnostic block versus alternative diagnostic test (e.g., physical examination, radiological examination)
    b. Type of diagnostic block (i.e., medial branch block versus intra-articular injection) for patient selection
    c. Use of a single diagnostic block versus two or more controlled diagnostic blocks (i.e., use of a short- versus a long-acting local anesthetic, or use of a local anesthetic versus saline)
    d. Degree and duration of pain reduction from diagnostic block (e.g., pain relief of ≥ 30% versus ≥ 50%, or ≥ 50% versus ≥80%)
    e. Unilateral versus bilateral diagnostic block
    f. Diagnostic block of single versus multiple levels

Key Question 2

2. With different regions of the spine (lumbar, thoracic, and cervical) considered separately, what is the evidence of short- and long-term comparative efficacy and effectiveness of facet neurotomy (FN) compared with alternatives (e.g., sham neurotomy, therapeutic intra-articular injections, etc.)?
    a. What is the evidence of the short- and long-term comparative efficacy and effectiveness of different types of facet neurotomy (e.g., radiofrequency, pulsed (cooled), chemical, cryoablation, laser)
    b. What is the evidence of the short- and long-term comparative efficacy of repeat neurotomy procedures at the same level and the same side as the initial successful procedure?
    c. Is there evidence of differential effectiveness when conducting unilateral versus bilateral facet neurotomy?
    d. Is there evidence of differential effectiveness when conducting facet neurotomy on single versus multiple spinal levels?

Key Question 3

3. With different regions of the spine (lumbar, thoracic, and cervical) considered separately, what is the comparative evidence regarding adverse events and complications during the periprocedural period and longer term for facet neurotomy?

Key Question 4

4. With different regions of the spine (lumbar, thoracic, and cervical) considered separately, is there evidence of differential efficacy or safety compared with other treatment options in subpopulations? Include consideration of age, gender, race, ethnicity, disability, and workers compensation.

Key Question 5

5. What is the evidence of cost effectiveness of facet neurotomy compared with other treatment options?

3. Methods

3.1 Literature Searches

We conducted an electronic literature search for the period July 1, 2013 to the present using identical search terms used for the original report for key questions 1 through 5. This search included 3 main databases: PubMed, Cochrane Library, and EMBASE. Additional electronic databases were searched; see Appendix A for search methodology and additional details. In addition, we searched the FDA website for updated information on such products.

3.2 Study selection

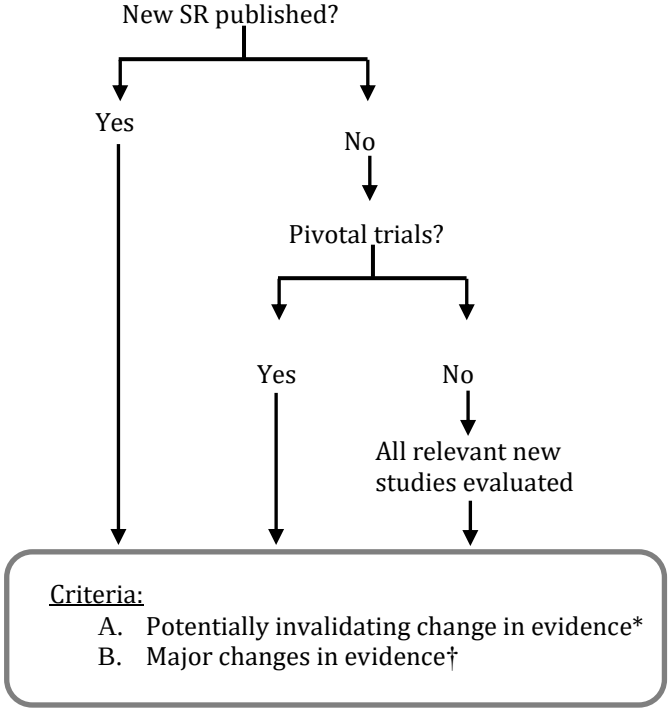
We sought systematic reviews (SR) of randomized controlled trials (RCTs) of efficacy and safety with meta-analysis that included articles that met inclusion and exclusion criteria similar to the original report. In addition we sought systematic reviews reflecting updates or new advances for the technology. Although quality of systematic reviews was not formally evaluated for this report, we chose systematic reviews of head to head trials for efficacy that were the most comprehensive and of higher quality based on the following: report of search strategies (two or more databases and description of dates searched), number of included relevant RCTs, pre-stated inclusion and exclusion criteria,

information on methodologies used for synthesis of data, inclusion of patient reported or safety outcomes and evaluation of the strength of the body of literature using GRADE or another analogous system. Only systematic reviews of RCTs were included for efficacy. Systematic reviews focused on longer-term safety outcomes may include nonrandomized studies. A summary of the included SRs and RCTs is found in Appendix B.

3.3 Compilation of Findings and Conclusions

For this assessment we constructed a summary table that included the key questions, the original conclusions, new sources of evidence, new findings, and conclusions based on available signals. To assess whether the conclusions might need updating, we used an algorithm based on a modification of the Ottawa method, Figure 1.

Figure 1. Algorithm of the modified Ottawa Method of Identifying Signals for SR Updates



*A-1. Opposing findings: Pivotal trial or SR including at least one new trial that characterized the treatment in terms opposite to those used earlier

A-2. Substantial harm: Pivotal trial or SR whose results called into question the use of the treatment based on evidence of harm or that did not proscribe use entirely but did potentially affect clinical decision making

A-3. Superior new treatment: Pivotal trial or SR whose results identified another treatment as significantly superior to the one evaluated in the original review, based on efficacy or harm.

†B-1. Important changes in effectiveness short of "opposing findings"

B-2. Clinically important expansion of treatment

B-3. Clinically important caveat

B-4. Opposing findings from discordant meta-analysis or nonpivotal trial

4. Results

4.1 Search

The literature search identified 269 citations. After title and abstract review, 249 articles were excluded and 20 articles that addressed in part or in full the key questions were reviewed at full text. A total of 10 articles were retained for the signal update, Figure 2. A full list of excluded studies and the reasons for exclusions can be found in Appendix C.

We identified two systematic reviews that addressed in part or in full the key questions. Systematic reviews were excluded if they did not include study types of interest and/or if they were not the most comprehensive and of the highest quality, Appendix B. Two systematic reviews related to efficacy were retained. No systematic reviews for safety and no full health technology assessments were identified. No systematic review described results for differential safety (key question 3). We found no cost-effectiveness studies (Key Question 5); there were none in the previous report. Eight new RCTs were identified. No follow-up publications of RCTs included in the previous report were also identified. Clinicaltrials.gov was searched for currently ongoing comparative clinical trials, Appendix D.

The FDA has approved one new lesion probe device for facet neurotomy since the publication of the initial report (Table 1).

Table 1. FDA-Approved Neurotomy Devices approved since the publication of the original report

Manufacturer	Device Name	510(k) Number	Indications for Use	Year of Approval	Recalls?
Stryker Instruments, Kalamazoo, MI, USA	MultiGen 2 RF Generator System	K170242	Intended for coagulation of soft tissues in orthopedic, spinal, and neurosurgical applications. Examples include but are not limited to: Facet Denervation, Trigeminus Neuralgia, Peripheral Neuralgia, and Rhizotomy.	2017	None

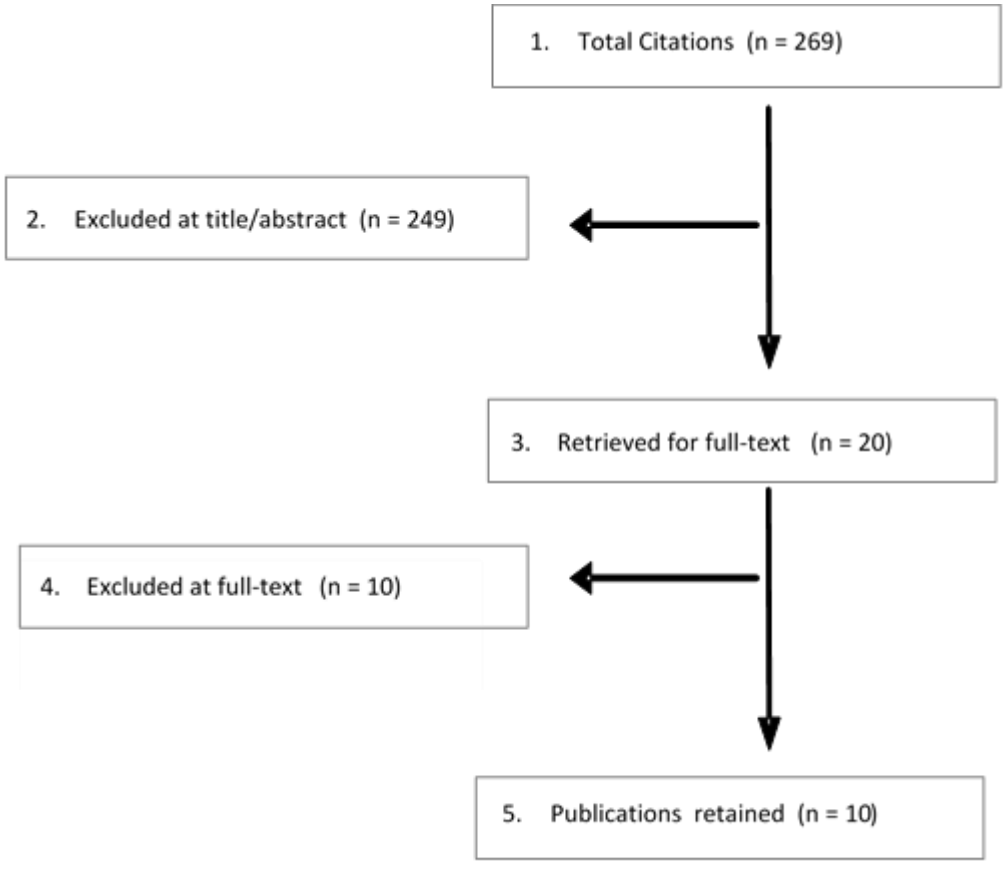


Figure 2. Flow chart showing results of literature search

4.2 Identifying signals for re-review

Tables 2-7 show the original key questions, the conclusions of the original report, the new sources of evidence, the new findings, and the recommendations of Aggregate Analytics, Inc. (AAI) regarding the need for update (Figure 1).

Table 2. Summary Table for Key Question 1.

Key Question 1. What is the evidence that the use of diagnostic blocks (i.e., medial branch blocks or intra-articular injections with local anesthetic) to select patients for facet neurotomy improves clinical outcomes following facet neurotomy? Consider each of the following:			
Conclusions from CER Executive Summary	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
Key Question 1a. Diagnostic block versus alternative diagnostic test (e.g., physical examination, radiological examination)			
Diagnostic block versus physical examination: ***Lumbar spine (LOW evidence)*** • 1 RCT: Neurotomy selection based on clinical exam (n = 51) or one medial branch block ≥50% pain (n = 19) relief and positive GPE • 1 and 3 months: No difference between diagnostic groups in the percentage of patients who achieved "success" (≥50% pain relief and a positive global perceived effect). ***Cervical or Thoracic Spine:*** No evidence	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)
Diagnostic block versus radiological examination: • No evidence in the cervical, lumbar or thoracic spine.	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)
Key Question 1b. Type of diagnostic block (i.e., medial branch block versus intra-articular injection) for patient selection			
Diagnostic medial branch block versus pericapsular block: ***Lumbar spine: (LOW evidence)*** • 1 RCT: Cryodenervation selection based on positive response (≥50% pain relief) to either a diagnostic medial branch block (n = 13) or pericapsular block (n = 13) • No difference between groups in the mean improvement in back pain or function ***Cervical or Thoracic Spine:*** No evidence	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)

Key Question 1. What is the evidence that the use of diagnostic blocks (i.e., medial branch blocks or intra-articular injections with local anesthetic) to select patients for facet neurotomy improves clinical outcomes following facet neurotomy? Consider each of the following:			
Conclusions from CER Executive Summary	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
Other diagnostic block comparators: • ***Cervical, Lumbar or Thoracic Spine:*** No evidence	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)
Key Question 1c. Use of a single diagnostic block versus two or more controlled diagnostic blocks (i.e., use of a short- versus a long-acting local anesthetic, or use of a local anesthetic versus saline)			
Lumbar spine: (LOW evidence) • 1 RCT: RF Neurotomy selection based on positive response (≥50% pain relief) to single diagnostic medial branch block (n=19) or two comparative diagnostic medial branch blocks (n=14). • Short term (1, 3 months): No difference between groups on "success" (≥50% pain relief and a positive global perceived effect)	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)
Key Question 1d. Degree of pain reduction from diagnostic block (i.e., pain relief of ≥30% versus ≥50%, or ≥50% versus ≥80%)			
Lumbar spine (Insufficient evidence) • 4 cohort studies: diagnostic groups based on the pain relief thresholds required to proceed with neurotomy of 50-79% and ≥80% • Taken together, the suggested that pain relief and function may be better following RF neurotomy in those patients who achieved a minimum of 80% pain relief following diagnostic media; branch block though this was not consistently shown across all studies. • Pain at 3 months, 6 months: one study showed no difference between groups, another reported more "success" (≥50% pain relief and a positive global perceived effect) in the higher diagnostic pain relief threshold (≥80%) group. • Function (≥50% improvement in activity level) at 6 months: One retrospective study reported significantly better function in the higher diagnostic pain relief threshold (≥80%) group.	**Lumbar Spine** ***Systematic Review:*** Lee 2017[5] (7 trials) ***RCTs:*** Do 2017,[2] Moussa 2016,[7] Zhou 2016[10] **Cervical or Thoracic Spine**: No systematic reviews or RCTs	***SR*:** Lee et al.'s analysis of equivocal diagnostic block response (≥50% pain relief) and best response (≥80% pain relief, "significant relief" or "near complete relief") indicates that best responders demonstrated better pain relief versus controls at all time points. Meta regression suggests modification by diagnostic block responder type, suggesting that equivocal responders show no difference versus controls or better pain relief with control treatment. A formal test of interaction is not provided. ***RCTs:***	New SR and RCT data suggest that response to diagnostic block may impact pain outcome; additional new trials allow for pooling. These data support the previous HTA's conclusions. A re-review may not be warranted. (Criteria B-1).

Key Question 1. What is the evidence that the use of diagnostic blocks (i.e., medial branch blocks or intra-articular injections with local anesthetic) to select patients for facet neurotomy improves clinical outcomes following facet neurotomy? Consider each of the following:			
Conclusions from CER Executive Summary	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
Cervical or Thoracic Spine: No evidence		Preliminary pooled effect estimates combining data from 3 new RCTs (Do, Moussa, Zhou) with data from trials included in the previous HTA (See Appendix E) provide RCT support for the conclusion of the previous report: • Regardless of the comparator (sham or steroid), trials requiring ≥80% relief (to include "complete or near complete" or "significant" relief) with diagnostic block generally showed better pain improvement compared with those requiring ≥50% relief (to include "good" relief"). • A formal test of interaction is not done.	
Key Question 1e. Unilateral versus bilateral diagnostic block			
No studies were identified which met our inclusion criteria.	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)
Key Question 1f. Single versus multiple level diagnostic block			
No studies were identified which met our inclusion criteria.	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)

GPE: global perceived effect; RCT: randomized controlled trial; RF: radiofrequency

Table 3. Summary Table for Key Questions 2.

Key Question 2. What is the evidence of short- and long-term comparative efficacy and effectiveness of facet neurotomy compared with alternatives (e.g., sham neurotomy, therapeutic intraarticular injections, etc.)?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
KQ 2. Radiofrequency Neurotomy (RFN) versus Sham Neurotomy			
Efficacy: Lumbar spine (LOW Evidence) • Six RCTs; Neurotomy selection criteria varied. Three studies performed diagnostic medial branch block(s) and required ≥50% (2 trials) or ≥80% (1 trial pain relief following the block(s) the three remaining studies employed one or two intraarticular block(s); one specified the percentage of pain relief required. Taken together, the results suggest that outcomes *may* be better following RF neurotomy compared with sham neurotomy, though in many instances there were no differences between treatment groups. Measures of pain and function varied across trials. • Pain, Short-term (1-6 months): ○ Success: One RCT (N = 81) reported no difference for VAS back pain between groups at three months when defined as ≥50% pain relief but marginally significant improvement when defined as (≥50% improvement in GPE of back pain ○ Mean change from baseline, VAS back pain: Four RCTs found no difference between groups in VAS back pain, 1 found no difference in McGill Pain scores at 3-6 months; however, two RCTs favored neurotomy, describing improvement in VAS back pain. ○ Leg and generalized pain; difference in mean change from baseline on leg pain, favored neurotomy in two trials, one of which reported no difference in "success" (≥50% improvement in VAS Scores) ○ The one small trial (N=40) which used 2 MBBs and ≥80% pain relief as a criteria for neurotomy selection consistently reported improve pain with RFN across measures. • Pain, Long-term (12 months) (1 RCT N = 40): significantly improved VAS back pain following RF neurotomy	**Lumbar Spine** ***Systematic Review:*** Lee 2017[5] (7 trials) ***RCTs*** Moussa 2016[7] (N = 120) (in Lee 2017 SR) van Tilburg 2016[9] (N = 60)	***SRs*:** Lee reported results for pain only and pooled across studies of RF neurotomy vs. any comparator (sham or steroid injection). Authors did not report pooled estimates separately for the comparison of RFN versus sham alone. Across comparators for 6 trials (7 publications, N =454 patients), RF neurotomy was not associated with improvement in VAS pain at 1-3 months. At 6 months, RFN was associated with a small improvement in pain (5 trials pooled MD 1.5 95% CI 0.15, 2.8) compared with sham or steroid injection but the difference is not likely to be clinically significant. There was substantial heterogeneity at both time periods. At 12 months, one new study (Moussa) favored RF neurotomy over sham (MD 5.1, 95% CI 4.8, 5.4). Analysis of RF neurotomy groups only suggests that point estimates for pain improvement generally meet an MCID (≥ 3 point improvement in 0-10 VAS), however the lowest confidence interval bound did not exceed the MCID at 3 or 6 months.	Findings from new trials and one systematic review are consistent with the previous report with respect to mean difference in pain improvement, and function for RF neurotomy vs. sham. Additional data on pain success at 6 and 12 months from one new trial significantly favored RF neurotomy versus sham that would update the report. (Criteria B1)

Key Question 2. What is the evidence of short- and long-term comparative efficacy and effectiveness of facet neurotomy compared with alternatives (e.g., sham neurotomy, therapeutic intraarticular injections, etc.)?

Conclusions from CER Executive Summary (Strength of Evidence)	New Sources of Evidence	New Findings	Conclusion from AAI
• Function, short-term (1-6 months): Across 3 trials, ODI scores were improved favoring RFN, however no differences in other functional outcomes were seen in two other trials. • Function, long-term (12 months): Improved ODI scores favoring RFN were reported in 1 trial. • Success on composite scores: No differences between RFN and sham were identified. ***No evidence for any of the following:*** • Efficacy or effectiveness of other types of neurotomy versus sham neurotomy in the lumbar spine. • Effectiveness of neurotomy versus sham neurotomy in the lumbar spine		***RCTs*:** Preliminary pooled effect estimates combining data from two new RCTs (Moussa 2016 and van Tilburg 2016) with data from trials included in the previous HTA (See Appendix E) suggest results were generally consistent with those of the previous report for mean back and leg pain and function. For pain success at 6 and 12 month pooled estimates including one new trial provide additional evidence favoring RFN at 6 and 12 months: • Back pain (improvement in VAS scores): no difference between RF neurotomy and sham at 3 months (1 new trial, van Tilburg) but at 6 months, the pooled estimate tended to favor RF neurotomy but did not reach statistical significance and heterogeneity was substantial (1 new trial, Moussa). One new trial with 12 month data is consistent with the old trial showing statistically greater improvement with RF neurotomy versus sham. • Leg pain (improvement in VAS scores): no difference between groups at 3 months and a tendency to favor RF neurotomy vs. sham at 6 months (1 new trial, Moussa). Longer-term data is available at 24 and 36 months from one new trial also showing a tendency	

Key Question 2. What is the evidence of short- and long-term comparative efficacy and effectiveness of facet neurotomy compared with alternatives (e.g., sham neurotomy, therapeutic intraarticular injections, etc.)?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
		to favor RF neurotomy versus sham but the differences did not reach statistical significance. • Pain "success" (various definitions): the addition of one new trial (Moussa) provides additional evidence. While there was no difference between groups at 3 months (consistent with the previous report), RF neurotomy was substantially favored at both 6 months (RR 2.9, 95% CI 1.6, 5.1) and 12 months (5.0, 95% CI 2.1 to 12.1) compared with sham. • Function (improvement in ODI scores): pooled estimates at 6 and 12 months with the addition of one new trial (Moussa) tended to favor RFN but did not reach statistical significance. Moussa was significant at both time points but due to substantial heterogeneity, pooled estimates are not reliable. Moussa required "complete or near complete" reduction of pain following diagnostic block; van Tilberg required only a decrease ≥ 2 on a 0 to 10 point NRS scale.	

Key Question 2. What is the evidence of short- and long-term comparative efficacy and effectiveness of facet neurotomy compared with alternatives (e.g., sham neurotomy, therapeutic intraarticular injections, etc.)?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
		Intermediate and long term: Moussa reported sustained pain relief at 6, 12, 24 and 36 months	
Efficacy: Cervical spine (Insufficient Evidence) • 1 RCT; Neurotomy selection criteria, 100% pain relieve with anesthetics; 3 MBBs used • More FN patients achieved "Freedom from accustomed pain" compared with sham at 6 months ***No evidence for the following:*** • Effectiveness of neurotomy versus sham neurotomy in the cervical spine • Efficacy or effectiveness of other types of neurotomy compared with sham neurotomy in the cervical spine	**Cervical Spine** No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)
KQ 2. RF Neurotomy versus Spinal Injections/Epidural Block			

Efficacy: Lumbar spine (LOW Evidence)
Taken together, the results suggest that outcomes are similar following RF neurotomy and spinal injections
• Two RCTs; Neurotomy selection, one RCT ≥50% pain relief following a diagnostic medial branch block, other RCT used intra-articular injection, pain relief threshold not described.
• Pain relief
  ○ Success (≥50% pain relief from baseline, 1 RCT): more RFN patients achieved success at 6 and 12 months vs. spinal injections.
  ○ VAS score improvement (2 RCTs): No difference between groups at 6 or 12 months.
• Function (1 RCT): No differences between treatment groups on ODI or Roland-Morris scores at 6 months.
	Lumbar Spine
	
	Systematic Reviews: Lee 2017[5] (7 trials); Piso 2016[8] (4 trials)
	
	RCTs:
	Zhou 2016[10] (N = 80) (in Lee 2017 SR)
	Do 2017[2] (N = 60)
	Hashemi 2014[3] (in Piso 2016 SR) (N = 80)
		SRs:
		Two SRs were identified which included one new trial each.
		
		As stated above, Lee et al. did not provide pooled estimates separately by comparator. One included new trial (Zhou 2016; N=80) reported pain improvement with RFN at 3 months (MD 2.3, 95%CI 1.8, 2.8) and 6 months (4.2, 95% CI 3.7, 4.8) versus injections.
		
		Piso et al. reported significant improvement in VAS pain scores across three trials over all timepoints measured: ≤1 month (pooled MD -1.8, 95% CI -3.1 to -0.6, 2 trials), ≥6 months to <12 months (pooled MD -2.1, 95% CI -3.5 to -0.8, 3
			There are new data that would update the report. New evidence suggests that RF neurotomy may be associated with improved pain relief versus steroid injections. A re-review may be warranted. (Criteria B-1).

Key Question 2. What is the evidence of short- and long-term comparative efficacy and effectiveness of facet neurotomy compared with alternatives (e.g., sham neurotomy, therapeutic intraarticular injections, etc.)?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
		trials), and ≥12 months (pooled MD -2.7, 95% CI -3.4 to -1.9, 2 trials); two of the trials were included in our previous report and one trial was excluded from our previous report. The included new trial (Hashemi 2014; N=80) did not provide detailed data and therefore was not included in the pooled analyses above. This trial reported improvement in both pain (MD in NRS change scores -5) and function (MD in ODI change scores -56.3%) favoring pulsed RFN at 6 months; results were also significant at 3 months but not at 1.5 months. ***RCTs*** None reported on long-term pain. Pain relief: Across the three new trials, results were mixed. Short-term, Do reported significant improvement in back pain favoring intra-articular steroid injection over RFN. Hashemi reports improvement in back pain at 3 months and Zhou reports improvement in leg pain at 1 month. At 6 months, Do reports no difference between RFN and steroid injection; Hashemi and Zhou report sustained improvement in pain compared with steroid injection. Zhou required ≥ 80% pain relief from diagnostic block, Hashemi didn't specify and Do used ≥ 50% pain relief as a threshold.	

Key Question 2. What is the evidence of short- and long-term comparative efficacy and effectiveness of facet neurotomy compared with alternatives (e.g., sham neurotomy, therapeutic intraarticular injections, etc.)?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
		Function: Hashemi reports no improvement in ODI at 1.5 months, but statistically significant improvement at 3 and 6 months. The others did not report on function.	
Efficacy: Cervical spine (LOW Evidence) Taken together, results suggest no difference between RFM and occipital nerve injection. • One RCT, no diagnostic blocks used; RFN compared with occipital nerve injection in patients with cervicogenic headache. • At 2 months, no difference in headache relief (VAS score improvement) or a composite measure 20% reduction in pain (as measured on the VAS scale) or a global perceived effect (GPE) score of +2 or +3 ("much better" or "complete relief"). ***No evidence for any of the following*** • Efficacy or effectiveness of other types of neurotomy compared with spinal injections in the cervical spine. • Neurotomy compared with spinal injections in the thoracic spine	**Cervical spine** No new SRs; ***RCTs*:** Lim 2017[6] (N = 40)	Lim 2017 reports no difference in pain relief between intraarticular RFN and steroid injection in patients with cervical *facet joint pain* at either 3 or 6 months; ≥50% pain relief following diagnostic block was required.	There is limited new evidence that would update the report; however the findings from this small trial are not sufficient to trigger an updated report. (Criterion B1)
KQ 2. RF Neurotomy Plus exercise versus Exercise			
No studies in previous report	**Lumbar spine** No new SRs; ***RCT*:** Juch 2017[4] (N=251)	Radiofrequency denervation combined with a standardized exercise program resulted in either no improvement or no clinically important improvement in chronic low back pain compared with a standardized exercise program alone. There were no differences between treatment groups in mean NRS pain scores at any time up to 12 months and no statistical differences between groups in the proportion of patients achieving	There are new data that would update the report. New evidence suggests that RF neurotomy combined with exercise is not associated with improved pain or function compared with exercise alone. A re-review may be warranted (Criteria B-1).

Key Question 2. What is the evidence of short- and long-term comparative efficacy and effectiveness of facet neurotomy compared with alternatives (e.g., sham neurotomy, therapeutic intraarticular injections, etc.)?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
		>30% pain reduction. There was no difference between groups for function measured via ODI or for Global Perceived Effect.	

CI: confidence interval; GPE: Global Perceived Effect; HTA: Health Technology Assessment; MBB: medial branch block; MCID: minimal clinically important difference; MD: mean difference; NRS: numerical rating scale; ODI: Oswestry Disability Index; RCT: randomized controlled trial; RF: radiofrequency; RFN: radiofrequency neurotomy; VAS: visual analog scale.

Table 4. Summary Table for Key Questions 2a - d.

Conclusions from CER Executive Summary (Strength of Evidence)	New Sources of Evidence	New Findings	Conclusion from AAI
Key Question 2a. What is the evidence of the short- and long-term comparative efficacy and effectiveness of different types of facet neurotomy (e.g., radiofrequency, pulsed (cooled), chemical, cryoablation, laser			
KQ 2a. Conventional versus Pulsed RF Neurotomy:			
Efficacy: Lumbar spine (LOW Evidence) Taken together, results suggest that outcomes are similar with conventional and pulsed RFN • Two RCTs; Neurotomy selection based on ≥50% pain relief following diagnostic MBB. • Pain, short-term (3, 6 months, 2 RCTs): No difference between groups for improvement on VAS scores. Long term, (12 months) 1 RCT favored conventional RFN • Function, short-term (3, 6 months, 2 RCTs) and long term (12 months, 1RCT): No difference between groups for improvement on ODI. ***No evidence for any of the following:*** • Effectiveness of conventional versus pulsed RF neurotomy in the lumbar spine • Efficacy or effectiveness of conventional versus pulsed RF neurotomy in the cervical or thoracic spine	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)
KQ 2a. RF Neurotomy versus Alcohol Ablation:			
Efficacy: Lumbar spine (LOW Evidence) Long-term, outcomes *may* favor alcohol ablation, though there was no difference between treatment groups in the short-term results. • One RCT (N = 40); Neurotomy selection based on 2 diagnostic blocks, degree of pain relief NR. • Composite "success" outcome (VAS score <7 and a revised ODI score <22%) no differences between ablation types at 9 months; alcohol ablation favored between 12 and 24 months. ***No evidence for any of the following:*** • Effectiveness of RF neurotomy vs. alcohol ablation in the lumbar spine • Efficacy or effectiveness of RF neurotomy vs. alcohol ablation in the cervical or thoracic spine	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)

Conclusions from CER Executive Summary (Strength of Evidence)	New Sources of Evidence	New Findings	Conclusion from AAI
KQ 2a: OTHER COMPARISONS			
• No studies meeting the inclusion criteria were identified	***RCTs:*** Aranious 2016[1]; thermal radio-frequency ablation (TRF) alone vs. pulsed dose radio-frequency (PDRF) immediately followed by TRF (N = 55)	Aranious et al.: Although patients receiving PDFR followed TRF demonstrated statistically significant pain scores the morning post-procedure Day 1, there were no differences between groups the evening of Day 1 or on Day 2. An improvement of ≥ 80% following diagnostic block was required for inclusion. Function was not reported.	There is limited new evidence that would update the report; however the findings from this small trial comparing combined use of TRF (continuous) and PDRF with TRF alone is not sufficient to trigger an updated report. (Criterion A1, B1).
KQ 2b. What is the evidence of the short- and long-term comparative efficacy of repeat neurotomy procedures at the same level and the same side as the initial procedure?			
Repeat neurotomy: Lumbar spine (Insufficient evidence) • Six case series; Taken together, results suggest that patients undergoing a second or third procedure may have similar results to those achieved during the first procedure. ***Repeat neurotomy: Cervical spine (Insufficient evidence)*** • Two case series; Taken together, results suggest that patients undergoing a second or third procedure may have similar results to those achieved during the first procedure. ***Repeat neurotomy: Thoracic spine (Insufficient evidence)*** • No studies met inclusion criteria.	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)
KQ2c: Is there evidence of differential effectiveness when conducting unilateral versus bilateral facet neurotomy?			
Unilateral vs. bilateral RF neurotomy effectiveness: Lumbar spine (LOW Evidence) • One retrospective cohort: No difference between treatment groups for the percentage of procedures that resulted in back	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)

Conclusions from CER Executive Summary (Strength of Evidence)	New Sources of Evidence	New Findings	Conclusion from AAI
pain "success" (≥50% pain relief or complete elimination of pain) at a mean of 5.6 months			
KQ2d: Is there evidence of differential effectiveness when conducting facet neurotomy on single versus multiple spinal levels?			
• No studies meeting the inclusion criteria were identified	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)

ODI: Oswestry Disability Index; PDRF: pulsed dose radiofrequency; RCT: randomized controlled trial; RF: radiofrequency; TRF: thermal radiofrequency; VAS: visual analog scale.

Table 5. Summary Table for Key Question 3

Key Question 3: What is the comparative evidence regarding adverse events and complications during the periprocedural period and longer term for facet neurotomy?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
KQ 3: RF Neurotomy versus Sham Neurotomy			
Safety: Lumbar spine (LOW Evidence) • 1 RCT (N=81): no differences between treatment groups in treatment-related pain, change of sensibility, or loss of motor function during the periprocedural period. • 4 RCTs (N=191 total) stated only that no adverse events or complications occurred in either treatment group during the periprocedural period. • No nonrandomized comparative studies or case series met inclusion criteria. ***Safety: Cervical spine (LOW Evidence)*** • 1 RCT (N=24): significantly higher frequency of procedure-related numbness following RF neurotomy vs. sham neurotomy (38% vs. 0%); no differences between groups for all other safety outcomes reported. • No nonrandomized comparative studies or case series met inclusion criteria. ***Safety: Thoracic spine*** • No evidence	**Lumbar spine** ***RCTs:*** van Tilburg 2016[9] (N = 60) **Cervical and Thoracic spine:** no new evidence	van Tilburg 2016 stated that no serious adverse events were encountered during the trial. Four patients withdrew for the following reasons: increased pain after diagnostic test (n=1) and painful procedure despite local anesthetic (n=3); however, the group to which patients were randomized was not reported.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4) Findings from the new trial and are consistent with the previous report with respect to frequency of adverse events.
KQ 3: RF Neurotomy versus Spinal Injections			
Safety: Lumbar spine (LOW Evidence) • 1 RCT (N=100), vs. medial branch block: no difference between treatment groups in any of the following adverse events over 6 months: infection, new motor deficit, new sensory deficit, superficial burns, and increase in lower back pain; a second RCT reported vaguely on adverse events but did not define which specific outcomes they examined. • No harms data in one retrospective cohort; no case series met inclusion criteria	**Lumbar spine** ***RCTs:*** Do 2017,[2] pulsed RF neurotomy (N=60); Zhou 2016,[10] RF neurotomy	**Lumbar spine** Do 2017 reported no adverse events in the pulsed RF group vs. one event (hyperglycemia) in the steroid injection group; Zhou 2016 reported no adverse events in either group.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4) Findings from the new trials and are consistent with the previous report with respect to frequency

Key Question 3: What is the comparative evidence regarding adverse events and complications during the periprocedural period and longer term for facet neurotomy?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
Safety: Cervical and Thoracic spine • No evidence	(N = 80) (in Lee 2017 SR); **Cervical spine:** ***RCTs:*** Lim 2017,[6] pulsed RF neurotomy (N = 40) **Thoracic spine:** no new evidence	**Cervical spine** Lim 2017 reported no adverse events in the pulsed RF group vs. two events in the steroid injection group (1 case each of facial flushing and hyperglycemia).	of adverse events following neurotomy in the lumbar spine. For the cervical spine, there is limited new evidence that would update the report; however the findings from one small trial are not sufficient to trigger an updated report. (Criterion A2, B)

RCT: randomized controlled trial; RF: radiofrequency.

Table 6. Summary Table for Key Question 4

Key Question 4: Is there evidence of differential efficacy or safety compared with other treatment options in subpopulations? Include consideration of age, gender, race, ethnicity, disability, and workers compensation?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
KQ 4: Heterogeneity of treatment effect			
Lumbar spine (LOW evidence) • 1 RCT (N=81); RF neurotomy vs. sham neurotomy; patient selection by either diagnostic medial branch block or clinical exam alone. • None of the following subgroups had differential treatment effect in terms of the composite outcome "success" or GPE pain relief "success": sex, age (18-40 versus >40), duration of pain (≤5 versus > 5 years), employment status (unemployed versus employed), and previous low back surgery. ***Cervical and Thoracic spine*** • No evidence	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating.(Criteria A1, B-1-4)
KQ 4: Comparative efficacy of RF Neurotomy: patients selected on the basis of ≥50% pain relief following medial branch block *In Key Question 1, no direct evidence was identified that type of diagnostic block (i.e., medial branch block versus intra-articular block) affected patient outcomes following facet neurotomy. As a result, no restrictions were placed on type of diagnostic block used for patient selection for studies included in Key Question 2. However, during the public comment period, a peer reviewer (Paul Dreyfuss, MD) indicated that the methods by which patients are selected for facet neurotomy affects the efficacy of the procedure. Specifically, he suggested that patients should be selected on the basis of ≥50% pain relief following one or more diagnostic medial branch block(s). In order to address this concern, we provided the results from on a subgroup studies included in Key Question 2 that selected patients on the basis of ≥50% pain relief following medial branch block.*			
RF Neurotomy vs. Sham Neurotomy: efficacy following medial branch block			
Lumbar spine (LOW evidence) Taken together, the results suggested that outcomes favored RF neurotomy over sham neurotomy. • 3 RCTs (N=111 total); patient selection based on ≥50% or ≥80% pain relief following diagnostic medial branch block. • Pain, Short-term (2-6 months): ○ VAS back pain, mean change from baseline: Two RCTs (N=71 total) favored RF neurotomy, describing significant	**Lumbar Spine** ***Systematic Review:*** Lee 2017[5] **Cervical and Thoracic Spine:**	Lee reported results for pain only and pooled across studies of RF neurotomy vs. any comparator (sham or steroid injection) (6 trials [7 publications], N=454 patients). Authors did not report pooled estimates separately for the comparison of RF neurotomy versus sham alone, or	This section of the report is still valid and does not need updating. (Criteria A1, B-1-4)

Key Question 4: Is there evidence of differential efficacy or safety compared with other treatment options in subpopulations? Include consideration of age, gender, race, ethnicity, disability, and workers compensation?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
improvement in back pain VAS scores over 2-6 months; the third RCT (N=40) found no difference between groups. ○ VAS leg and generalized pain, mean change from baseline (1 RCT, N=40); significantly improved leg and generalized pain VAS scores following RF neurotomy at 6 months. ○ The one small trial (N=40) which used two medial branch blocks and ≥80% pain relief as a criteria for neurotomy selection consistently reported improve pain with RFN across measures. • Pain, Long-term (12 months) (1 RCT, N = 40): significantly improved VAS back pain scores following RF neurotomy • Function, Short-term (2-6 months): Two RCTs (N=71 total) reported significant improvement in ODI scores favoring RF neurotomy. A third trial (N=31) found no difference between groups for improvement in Waddell scores at 2 months. • Function, Long-term (12 months) (1 RCT, N=40): significant improvement in ODI scores favoring RF neurotomy ***Cervical spine (INSUFFICIENT evidence)*** • 1 RCT (N=24); patient selection based on three medial branch blocks and 100% pain relief following diagnostic blocks (i.e. anesthetic) and 0% pain relief when saline was injected. • Back pain, Short-term (6 months): significantly more patients in the RF neurotomy group had achieved freedom from "accustomed pain" compared with those in the sham group. ***Thoracic spine*** • No evidence	no new evidence	for the type of diagnostic block used (medial branch, intraarticular). Authors' analysis of equivocal diagnostic block response (≥50% pain relief) and best response (≥80% pain relief, "significant relief" or "near complete relief") indicates that best responders demonstrated better pain relief versus controls at all time points. Meta regression suggests modification by diagnostic block responder type, suggesting that equivocal responders show no difference versus controls or better pain relief with control treatment. A formal test of interaction is not provided. As stated above, results were not reported by type of diagnostic block.	
RF Neurotomy vs. Spinal injection: efficacy following medial branch block			
Lumbar spine (LOW evidence) • 1 RCT (N=56); patient selection based on ≥50% pain relief following diagnostic medial branch block.	**Lumbar Spine** ***RCT***: Zhou 2016[10] (N =	Zhou selected patients based on ≥80% pain relief following diagnostic medial branch block *or* intraarticular injection;	This section of the report is still valid and does not need updating. (Criteria A1, B-1-4)

Key Question 4: Is there evidence of differential efficacy or safety compared with other treatment options in subpopulations? Include consideration of age, gender, race, ethnicity, disability, and workers compensation?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
• Pain and Function, Short-term (6 months): no difference between treatment groups for improvement in VAS back pain scores and ODI or Roland Morris scores. ***Cervical and Thoracic spine*** • No evidence	80) (in Lee 2017 SR) **Cervical and Thoracic Spine:** no new evidence	however, results were not reported by type of diagnostic block. Authors report results for pain only. Greater improvement in VAS pain scores was seen with RF neurotomy at 3 months (MD 2.3, 95% CI 1.8, 2.8) and 6 months (MD 4.2, 95% CI 3.7, 4.8) versus injections. A formal test of interaction is not provided. As stated above, results were not reported by type of diagnostic block.	

CI: confidence interval; GPE: Global Perceived Effect; MD: mean difference; ODI: Oswestry Disability Index; RCT: randomized controlled trial; RF: radiofrequency; RF: radiofrequency; VAS: visual analog scale.

Table 7. Summary Table for Key Question 5

Key Question 5: What is the evidence of cost effectiveness of facet neurotomy compared with other treatment options?			
Conclusions from CER Executive Summary (Strength of Evidence)	**New Sources of Evidence**	**New Findings**	**Conclusion from AAI**
• No studies meeting the inclusion criteria were identified	No systematic reviews or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating. (Criteria A1, B-1-4)

RCT: randomized controlled trial

5. Conclusions

Tables 2-7 show the original key questions, the conclusions of the original report, the new sources of evidence, the new findings, and the conclusions of Aggregate Analytics, Inc. (AAI) with respect to the criteria that identify a trigger for an update (Figure 1).

5.1 Key Question 1 (Diagnostic):

- 1a-c, e-f: Comparisons of diagnostic block versus alternative diagnostic test; type of diagnostic block; use of a single versus two or more controlled diagnostic blocks; unilateral versus bilateral diagnostic block; and single versus multiple level diagnostic block:
    - No new systematic reviews or RCTs published since the previous HTA that evaluated whether the use of diagnostic blocks (considering the above comparisons) to select patients for facet neurotomy improves clinical outcomes following facet neurotomy were identified (Criteria A-1, A-3, B-1-4). These sections do not need updating.
- 1d: Comparison of response to diagnostic block:
    - New SR and RCT evidence suggest that response to diagnostic block (e.g., ≥50% vs. ≥80% relief) may impact pain outcome; additional new trials allowed for a preliminary pooled analysis. These data support the previous HTA's conclusions that pain relief may be better in patients achieving a greater degree (e.g., ≥80%) of relief with diagnostic block. A re-review may not be warranted. (Criteria B-1).

5.2 Key Question 2 (Efficacy): For the comparison of RF neurotomy versus sham in the lumbar spine, findings from new trials and one systematic review are consistent with the previous report with respect to mean pain improvement and function, however, additional evidence from pooled estimates that include one new trial significantly favored RF neurotomy versus sham on pain success at 6 and 12 months and would update the report (Criteria B-1). There is new evidence (from 2 SRs, 3 RCTs) suggesting that RF neurotomy may be associated with improved pain relief versus steroid injections in the lumbar spine. Additionally, a new comparator was identified for the lumbar spine: new evidence from one RCT suggests that RF neurotomy combined with a standardized exercise program is not associated with improved pain or function compared with exercise alone. There are new data that would update this section of the report. A re-review may be warranted. (Criterion B-1).

No new evidence was identified for the comparison of RF neurotomy versus sham in the cervical spine. There is limited new evidence that would update the report for the comparison of RF neurotomy versus steroid injection; however the findings from this small trial alone are not sufficient to trigger an updated report (Criterion B-1).

5.3 Key Question 2a-d (Efficacy):

- 2a: Comparison of different types of facet neurotomy
    - Conventional versus pulsed RF neurotomy and RF neurotomy versus alcohol ablation: no new systematic reviews or RCTs published since the previous HTA were identified which met inclusion criteria. (Criteria A-1, A-3, B-1-4)

    - One new RCT compared thermal RF neurotomy alone versus pulsed dose RF neurotomy immediately followed by thermal RF and showed no difference in pain between groups the evening of Day 1 or on Day 2 (function was not reported). However, findings from one small trial alone are not sufficient to trigger an updated report (Criterion B-1). This section does not need updating.
- 2b-d: Comparisons of repeat neurotomy procedures (same level and side as initial successful procedure); unilateral versus bilateral facet neurotomy; and facet neurotomy on single versus multiple spinal levels.
    - No new systematic reviews or RCTs published since the previous HTA that evaluated the above comparisons were identified which met inclusion criteria. (Criteria A-1, A-3, B-1-4). These sections do not need updating.

5.4 Key Question 3 (Safety): New evidence from three RCTs of the lumbar spine (1 comparing RF neurotomy with sham neurotomy and 2 comparing conventional or pulsed RF with steroid injections) does not change the conclusions from the previous report (criteria A-1-3); there are not any major changes in the evidence base (criteria B-1-4). For the cervical spine, there is limited new evidence from one RCT (pulsed RF neurotomy vs. steroid injection); however the findings from one trial are not sufficient to trigger an updated report (criteria B-2, 3). This section does not need updating.

5.5 Key Question 4 (Differential efficacy or safety): No new systematic reviews or RCTs published since the previous HTA were identified which met inclusion criteria and evaluated heterogeneity of treatment effect for facet neurotomy compared with other treatment options in subpopulations (e.g., age, sex, race, ethnicity, disability, and workers compensation) (Criteria A-1, A-3, B-1-4). This section does not need updating.

5.6 Key Question 5 (Cost-effectiveness): No new systematic reviews (that included new studies) or RCTs published since the previous HTA were identified which met inclusion criteria that evaluated the cost effectiveness of facet neurotomy compared with other treatment options (Criteria A-1, A-3, B-1-4). This section does not need updating.

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APPENDIX A. SEARCH STRATEGIES

Search strategy for PubMed—Search dates: 07/01/13 to present

	Search terms	Number of articles
#1	Facet OR Zygapophyseal OR "Zygapophyseal Joint"[Mesh] OR "medial branch"	4,264
#2	Neurotomy OR "Rhizotomy"[Mesh] OR Rhizotomy OR "Articular rhizolysis" OR rhizolysis OR "Radiofrequency neurotomy" OR "Radiofrequency denervation" OR (radiofrequency AND "denervation"[MeSH Terms]) OR Denervation OR "Radiofrequency neurolysis" OR "Radiofrequency facet denervation" OR "Pulsed Radiofrequency Treatment"[Mesh] OR "Cooled radiofrequency ablation" OR "cooled ablation" OR ablat* OR chemodenervation OR "Chemical facet neurolysis" OR "cryosurgery"[MeSH Terms] OR Cryoablation OR radiofrequency	45,289
#3	#1 AND #2	222
#4	(In Vitro[TI] OR Cadaver*[TIAB] OR Case Reports[Publication Type] OR rat[TI] OR rats[TI] OR mouse[TI] OR mice[TI] OR dog[TI] OR dogs[TI] OR sheep[TI] OR rabbit[TI] OR "experimental model"[TI])	
#5	#3 NOT #4	189
#6	Additional references identified from hand searching	0

Search strategy for Cochrane—Search dates: 2013 to 03/02/18

	Search terms	Number of articles
#1	Facet OR Zygapophyseal OR "Zygapophyseal Joint"(Mesh) OR "medial branch"	565
#2	Neurotomy OR "Rhizotomy"(Mesh) OR Rhizotomy OR "Articular rhizolysis" OR rhizolysis OR "Radiofrequency neurotomy" OR "Radiofrequency denervation" OR (radiofrequency AND "denervation"(MeSH Terms)) OR Denervation OR "Radiofrequency neurolysis" OR "Radiofrequency facet denervation" OR "Pulsed Radiofrequency Treatment"(Mesh) OR "Cooled radiofrequency ablation" OR "cooled ablation" OR ablat* OR chemodenervation OR "Chemical facet neurolysis" OR "cryosurgery"(MeSH) OR Cryoablation OR radiofrequency	3870
#3	#1 AND #2	50
#4	(In Vitro(ti) OR Cadaver*(ab,ti) OR Case Reports(Publication Type) OR rat(ti) OR rats(ti) OR mouse(ti) OR mice(ti) OR dog(ti) OR dogs(ti) OR sheep(ti) OR rabbit(ti) OR "experimental model"(ti))	
#5	#3 NOT #4	46* (19 unique citations)

*Other reviews, technology assessments, and economic evaluations were not included in title abstract triage—all citations were abstracts and/or were not study types of interest

EMBASE search strategy—Search dates: 2013 to 03/02/2018

	Search terms	Number of articles
#1	'facet joint' OR 'zygapophyseal joint' OR 'medial branch'	1,759
#2	'neurotomy' OR 'rhizotomy' OR 'radiofrequency' OR 'denervation' OR ablation	71,137
#3	#1 AND #2	270
#4	Article/lit OR review/lit	
#5	#3 AND #4	151 (60 unique citations)

Additional electronic databases were searched using key words and included ClinicalTrials.gov, AHRQ, National Guideline Clearinghouse and INAHTA for eligible studies, including health technology assessments (HTAs), systematic reviews, primary studies and FDA reports. Original search was performed through October 4, 2013. The updated search goes from July 1, 2013 to the present.

The first twenty related PubMed articles of all newly included studies were evaluated for inclusion. Bibliographies of included systematic reviews were reviewed for relevant articles

APPENDIX B. SUMMARY OF INCLUDED STUDIES

Appendix Table B1. Summary of systematic reviews included for efficacy

Assessment *Search dates*	Purpose	Condition	Treatment vs. comparators	Primary Outcomes	Evidence-base Used	Primary Conclusions
Lee 2017 *Database inception to October 12, 2016*	To elucidate the precise effects of RF in patients with low back pain originating from the facet joints relative to those obtained using control treatments, with particular attention to consistency in the denervation protocol.	Facet joint disease of the lumbar spine	RF denervation vs sham or epidural nerve block	Pain VAS	7 RCTs (2 new RCTs: Moussa 2016, Zhou 2016)	**RFN vs control, pain:** At a short term follow-up (1-3 months), a pooled analysis across comparators for 6 trials reported no difference in pain VAS scores between RFN vs sham. At a 1 to 3 month follow-up across comparators for 6 trials, RFN was not associated with pain VAS improvement. At an intermediate follow-up at 6 months, RFN was associated with a small improvement in pain VAS (5 trials pooled; MD 1.5 95% CI 0.15, 2.8) compared to sham or steroid injection but the difference was not likely to be clinically significant. At both a short and intermediate term follow-up, there was substantial heterogeneity. At a long term follow-up of 12 months, one new study (Moussa 2016) found a statistically significant difference favoring RFN over sham (MD 5.1, 95% CI 4.8, 5.4). An analysis of the RN group suggested that point estimates for pain improvement generally meet an MCID (≥ 3 points improvement in 0-10 VAS), however the lowest confidence interval bound did not exceed MCID at either 3 or 6 months. **RFN equivocal diagnostic block response or best diagnostic block response vs control, success on pain VAS:** The authors' analysis of equivocal diagnostic block response (≥50% pain relief) and best response (≥80% pain relief, "significant relief", or "near complete relief") indicates that best responders demonstrated better pain relief compared to controls at all time points. A meta regression analysis suggests modification by diagnostic block responder type, suggesting that equivocal

Assessment *Search dates*	Purpose	Condition	Treatment vs. comparators	Primary Outcomes	Evidence-base Used	Primary Conclusions
						responders show no difference versus controls or better pain relief with control treatment. A formal test of interaction is not provided. **RFN vs spinal injections:** Authors did not provide pooled estimates separately by comparator. One included new trial (Zhou 2016) reported pain improvement with RFN over injections at 3 months (MD 2.3, 95% CI 1.8, 2.8) and 6 months (MD 4.2. 95% CI 3.7, 4.8).
Piso 2016	To compare RF denervation to placebo or other treatments in patients with chronic facet joint pain and a positive response to the diagnostic block.	Chronic facet joint pain	RFN vs steroid injections	Pain, functional status, global improvement, HR-QoL; ability to work, satisfaction with treatment, safety complications	RFN vs steroid injections: 4 RCTs	**RFN vs spinal injections/epidural blocks, pain:** Authors report improvement in VAS pain scores across three trials over all timepoints measured: ≤1 month (pooled MD -1.8, 95% CI -3.1 to -0.6, 2 trials), ≥6 months to <12 months (pooled MD -2.1, 95% CI -3.5 to -0.8, 3 trials), and ≥12 months (pooled MD -2.7, 95% CI -3.4 to -1.9, 2 trials); two of the trials were included in our previous report and one trial was excluded from our previous report. The included new trial (Hashemi 2014; N=80) did not provide detailed data and therefore was not included in the pooled analyses above

CI: confidence interval; HR-QoL: health-related quality of life; MCID: minimal clinically important difference; MD: mean difference; RF: radiofrequency; RFN: radiofrequency neurotomy; VAS: visual analog score

Appendix Table B2. Study characteristics and results of new RCTs

Author (Year)	Demographics	Results	Conclusions	Comments
RFN vs. sham neurotomy, lumbar				
Moussa 2016	N=80 *RFN vs sham neurotomy* Age, mean: 56.5 vs 55.9 years Female: 72.5% Mean duration of procedure: 35 minutes *Total* F/U: 3, 6, 12, 24, and 36 months RFN at facet joints procedure description (n=40): After sensory and motor tests, radiofrequency was delivered at 85°C for 90 seconds at both the medial and lateral sides of the facet joint *Device used:* RFG-1A Sham neurotomy procedure description (n=40): Same procedure but without delivering current to the electrode. *Device used:* RFG-1A	Pain: RFN vs sham neurotomy* VAS, mean improvement (SD): • Baseline: NR vs NR • 3 months: 6.0 (1.0) vs 5.4 (1.1), p=0.01 • 6 months: 6.0 (1.1) vs 2.1 (0.4), p<0.001 • 12 months: 5.8 (1.0) vs 0.7 (0.3), p<0.001 • 24 months: 2.3 (0.4) vs 0.5 (0.1), p<0.001 • 36 months: 2.2 (0.8) vs 0.4 (0.2), p<0.001 Pain reduction >50%, n/N (%): • 3 months: 30/40 (75%) vs 23/40 (57.5%), p=0.008 • 6 months: 24/40 (60%) vs 8/40 (20%), p<0.001 • 12 months: 18/40 (45%) vs 3/40 (7.5%), p<0.001 • 24 months: 7/40 (17.5%) vs 1/40 (2.5%), p=0.01 • 36 months: 5/40 (12.5%) vs 1/40 (2.5%), p=0.052 Function: RFN vs sham neurotomy ODI, mean change: • 3 months: 44.3 vs 39.8 • 6 months: 40.3 vs 10.3 • 12 months: 31.6 vs 5.9 • 24 months: 12.3 vs 3.2 • 36 months: 8.2 vs 2.9	**Pain:** Based on calculations performed by AAI using the reported data, RFN had a statistically significant better effect on pain VAS at all time points. The RFN group had a statistically significant higher percent of patients reaching >50% reduction in pain than the sham neurotomy group at all time points except 36 months. **Function:** The authors did not provide enough information to draw conclusions on the impact of RFN compared to sham neurotomy on functional outcomes.	Authors report no conflict of interest Authors report that no funding was received for the research
Van Tilburg 2016	N=60 *RFN group vs sham neurotomy group* Age, median (IQR): 65 (12) vs 58 (12) years	Pain: RFN vs sham neurotomy VAS, mean (SD): • Baseline: 7.2 (1.4) vs 7.4 (0.8) • 1 month: 5.3 (1.8) vs 5.5 (1.9), p NS	**Pain:** The authors reported no differences in pain VAS scores at a 1 month follow-up	Authors state that no benefits in any form have been received or will be received from a commercial part related

Author (Year)	Demographics	Results	Conclusions	Comments
	Total Female: 57% BMI, mean (SD): 29.6 (5.3) Caucasian: 100% F/U: 1 and 3 months <u>RFN procedure description (n=30)</u>: 1 mL of 2% lidocaine was infiltrated into skin. After sensory and motor tests, RF heat lesion delivered at 80°C for 60 seconds per level. *Device used:* NT2000, Neurotherm <u>Sham neurotomy procedure description (n=30)</u> Sham group underwent the same procedure but without RF lesions *Device used:* NT2000, Neurotherm			directly or indirectly to the subject of this article. Funding NR
RFN vs spinal injections/epidural block, lumbar				
Do 2017	N=60 *PRF vs ICI* Age, mean (SD): 67 (9.6) vs 63 (10.9) years Female: 60% *Total* F/U: 2 weeks, 1, 3 and 6 mos. <u>PRF procedure description (n=30)</u>: Treatment was administered at 5Hz with a 5-millisesond pulsed width for 360 seconds, at 55V. Electrode tip temperature did not exceed 42°C. *Device used:* Cosman G4 radiofrequency generator	<u>Pain: PRF vs ICI</u> NRS, mean change (SD): • Baseline: 4.9 (0.8) vs. 5.0 (0.8) • 2 weeks: 2.3 (1.4) vs 1.4 (0.8), p<0.001 • 1 month: 2.5 (1.4) vs 1.8 (1.2), p=0.011 • 3 months: 2.5 (1.3) vs 2.9 (1.4), p=NS • 6 months: 2.7 (1.5) vs 3.2 (NR), p=NS <u>Percent of patients with pain relief of ≥50%, PRF vs ICI</u> • 6 months: 50.0% (15/30) vs 46.7% (14/30), p=NS	**Pain:** Authors report statistically significant improvement in pain VAS score for the PRF group over the ICI group at 2 weeks and 1 month. The difference was not significant at 3 and 6 months. There was no difference in the percent of patients with pain relief ≥50% at 6 months.	The authors declare no conflict of interest Funding NR

Author (Year)	Demographics	Results	Conclusions	Comments
	ICI procedure description (n=30): 10mg (0.25mL) of dexamethasone mixed with 0.25mL of 0.125% bupivacaine injected.			
Hashemi 2014	N=80 *PRF group vs steroid injection* Age: 64.3 (13.3) vs 63.9 (11.5) years Female: 42% vs 44% BMI: 23.4 (5.3) vs 22.6 (4.8) Duration of Low Back Pain: 3.4 (2.3) vs 3.8 (2.4) years History of Smoking: 34% vs 38% *Total* F/U: 1.5, 3 and 6 months PRF procedure description (n=40): Local anesthesia was administered. After sensor and motor tests were performed, radiofrequency was delivered in 2 x 20 ms/s duration 120 seconds with 45 v with silent time 480 ms. Skin temperature did not exceed 42°C. *Device used:* NeuroTherm radiofrequency generator Steroid injection procedure description (n=40): Injection of 1 mL (40 mg) of triamcinolone and 0.5 mL bupivacaine (0.5%)	Pain: PRF vs Steroid Injection NRS, mean (SD)*: • Baseline: 7.4 (1.1) vs. 8.1 (1.0) • 1.5 months: 2.5 (0.8) vs 3.2 (0.8), p NS • 3 months: 2.9 (0.9) vs 5.9 (0.8), p<0.05 • 6 months: 2.4 (1.9) vs 7.4, (1.2) p<0.05 Function: PRF vs Steroid Injection ODI%, mean (SD)†: • Baseline: 75.6 (14.3) vs. 74.0 (NR) • 1.5 months: 2.5 (NR) vs 3.2 (NR), p NS • 3 months: 2.9 (NR) vs 5.9 (NR), p=0.022 • 6 months: 19.3 (9.5) vs 7.4 (NR), p<0.03	**Pain:** Authors report no difference in pain VAS scores between groups at 1.5 months. At 3 and 6 months follow-up, authors report the PRF group had statistically significant better pain VAS scores than the steroid injection group. **Function:** Authors report no difference in ODI scores between groups at 1.5 mos. At 3 and 6 months follow-up, authors report the PRF group had statistically significant better ODI scores than the steroid injection group.	Conflict of interest NR Funding NR
Zhou 2016	N=80 *RF-T group vs spinal injection* Age, mean (SD): 56.5 (8.7) vs 54.6 (7.5) years	Pain: RFN vs spinal injection VAS, mean (SD‡): • Baseline: 6.7 (0.9) vs 6.8, p = NS • 1 week: 1.4 (0.3) vs 1.9 (0.2), p = NS	**Pain:** Authors report no difference in treatments at 1 week but found that the RFN had statistically	Authors declare no conflicts of interest Funding NR

Author (Year)	Demographics	Results	Conclusions	Comments
	Female: 42.5% vs 47.5% *Total* F/U: 1 week, 1 month and 6 months <u>RFN procedure description (n=40)</u>: 3 mL of 2% lidocaine was injected followed by sensory and motor tests. RF-T was delivered at 80°C was performed for 90 s. *Device used:* Smith-Nephew Electrothermal 20s Spine System Radiofrequency Device <u>Spinal injection procedure description (n=40)</u>: 5 mL solution containing 1 mL of betamethasone and 1 mL of 2% lidocaine (diluted with normal saline) into facet joint cavity and medial branch of the spinal nerve. Infiltration block was also performed around the facet joint.	• 1 month: 1.4 (1.2) vs 3.6 (0.9), p < 0.05 • 6 months: 1.7 (1.6) vs 5.8 (1.1), p < 0.01 <u>Efficacy: RFN vs spinal injection</u> Proportion of patients with 'excellent§' rating: • 6 months: 62.5% vs 12.5%, p<0.01	significant lower pain VAS scores compared to the spinal injection group at 1 and 6 months. **Efficacy:** The authors report that a statistically significant higher proportion of patients in the RFN group had an efficacy rating of excellent.	
RFN vs PRF neurotomy + RFN, lumbar				
Arsanious 2016	N=55 Age, mean (SD): 51.3 (10.5) years Female: 77% BMI, mean (SD): 36.0 (10.0) F/U: 1 day AM, 1 day PM, 2 days AM, 2 days PM <u>Procedure description, RFN</u>: After sensory and motor tests, RF heat lesions were delivered at 80°C for 90 seconds at each level treated.	<u>Pain: RFN vs PRF neurotomy + RFN</u> VAS, mean (SD): • Day 1 AM: 4.43 (2.9) vs 2.38 (2.4), p = 0.01 • Day 1 PM: 4.80 (3.2) vs 3.08 (2.8), p = 0.06 • Day 2 AM: 3.86 (2.8) vs 2.31 (2.7), p = 0.06 • Day 2 PM: 3.90 (2.7) vs 2.60 (2.4), p = 0.09	**Pain:** Authors reported a statistically significant difference favoring PRF neurotomy+RFN in pain VAS scores at post-procedure Day 1 AM, but no differences were observed in Day 1 PM or on Day 2.	Authors declare no conflicts of interest Funding: No external funding was provided

Author (Year)	Demographics	Results	Conclusions	Comments
	Device used: NeuroTherm NT2000iX Procedure description, PRF+RFN: After sensory and motor tests, RF heat lesions were delivered at 80°C for 90 seconds at each level treated. Immediately after, pulsed RF waves at 42°C at 2 Hz for 240 pulses were delivered. *Device used:* NeuroTherm NT2000iX			
RFN+exercise vs exercise, lumbar				
Juch 2017	N=251 *RFN+Exercise vs Exercise Alone* Age, mean (SD): 52.9(11.4) vs 52.6 (10.8) years Female: 55.5% vs 51.7% Pain Duration, median: 146 vs 100.3 months *Total* F/U: 1 week, 1 and 6 months Exercise alone procedure description (n=126): All patients received standardized 3 month (8-12 hours) exercise program based on Dutch physical therapy guidelines, focusing on quality of movement and behavior. RFN+exercise procedure description (n=125): Within 1 week of the first exercise session, patients underwent RFN. Sensory and motor tests were	Pain: RFN+Exercise vs. Exercise NRS, mean (95%CI): • Baseline, mean (SD): 7.14 (1.38) vs. 7.19 (1.29) • 3 weeks: 5.17 (4.73 to 5.61) vs. 5.92 (5.58 to 6.26); MD −0.41 (−1.02 to 0.19), p=0.18 • 1.5 months: 5.19 (4.76 to 5.61) vs 5.90 (5.53 to 6.26); MD −0.38 (−0.96 to 0.20), p=0.20 • 3 months: 5.01 (4.59 to 5.43) vs 5.44 (5.03 to 5.85); MD −0.18 (−0.76 to 0.40), p=0.55 • 6 months: 4.61 (4.18 to 5.04) vs 4.84 (4.38 to 5.30); MD −0.04 (−0.63 to 0.56) p=0.91 • 9 months: 4.66 (4.20 to 5.00) vs 4.73 (4.24 to 5.22); MD 0.19 (−0.41 to 0.80), p=53 • 12 months: 4.49 (4.00 to 4.97) vs 4.44 (3.94 to 4.94); MD 0.47(−0.14 to 1.07), p=0.13	**Pain:** The authors report no difference between groups in pain NRS scores or in the percentage of patients with a reduction of pain greater than 30% at any time point. **Function:** The authors report no difference between groups in function scores at any time point.	Conflict of interest: One author received grant funding from the Netherlands Organization for Scientific Research and Scientific Association Physiotherapy. One author received funding to his institution from professional organizations, travel expenses by the professional organizations when speaking at conferences, and honoraria for reviewing grant proposals from Swedish and Canadian governmental grant agencies. Funding: The study was funded by grant 171202013 from the

Author (Year)	Demographics	Results	Conclusions	Comments
	performed followed by a 1-2 mL injection of 2% lidocaine. RF was performed at 90°C for 90 seconds	<u>Pain Intensity Reduction >30%: RFN+Exercise vs. Exercise</u> NRS, %(n/N): • 3 weeks: 39% (40/102) vs 27% (27/100); RR 1.33 (0.80 to 1.97) p=0.25 • 1.5 months: 40% (45/112) vs 31.5% (36/114); RR 1.13(0.70 to 1.63) p=0.59 • 3 months: 45.6% (52/114) vs 36% (40/111); RR 1.16 (0.76 to 1.60), p=0.46 • 6 months: 55.5% (60/108) vs 50.4% (53/105) RR 1.02 (0.71 to 1.33) p=0.88 • 9 months: 51% (52/102) vs 49% (50/102) RR 1.09(0.75 to 1.42) p=0.60 • 12 months: 47% (47/100) vs 53.5% (53/99); RR 0.78 (0.50 to 1.09) p=.16 <u>Function: RFN+Exercise vs Exercise</u> ODI, mean (95%CI): • Baseline, mean (SD): 35.07 (14.66) 34.39 (12.24) • 3 months: 26.03(23.01 to 29.06) vs 28.67(26.06 to 31.84); MD −2.45 (−5.93 to 1.03), p=0.17 • 6 months: 25.38(22.45 to 28.30) vs 27.15(24.07 to 30.23); MD −0.60(−4.13 to 2.92), p=0.74 • 9 months: 25.74(22.74 to 28.73) vs 24.52(21.49 to 27.54); MD 2.26 (−1.29 to 5.82), p=0.21 • 12 months: 24.59(21.39 to 27.79) vs 25.04 (21.77 to 28.31); MD 1.48(−2.09 to 5.06), p=0.42		Netherlands Organization for Health Research and Development, by the Society for Anesthesiology, and the Dutch Health insurance companies.

Author (Year)	Demographics	Results	Conclusions	Comments
RFN vs spinal injections/epidural block, cervical				
Lim 2017	N=40 *Pulsed RF group vs ICI* Age, mean (SD): 52.8(12.1) vs 52.7(14.8) years Female: 65% vs 50% Pain Duration: 15.1(14.1) vs 11.1(10.8) months *Total* F/U: 1 week, 1 and 6 months <u>PRF procedure description (n=20)</u>: Treatment was administered at 5Hz with a 5-millisesond pulsed width for 360 seconds, at 55V. Electrode tip temperature did not exceed 42°C. *Device used:* Cosman G4 radiofrequency generator <u>ICI procedure description (n=20)</u>: 10mg (0.25mL) of dexamethasone mixed with 0.25mL of 0.125% bupivacaine injected.	<u>Pain: PRF vs ICI</u> NRS, mean (SD): • Baseline: 5.6 (1.3) vs. 5.8 (1.4), p=NS • 1.5 months*: 2.4 (1.6) vs 1.7 (0.9), p=NS • 3 months*: 3.0 (1.7) vs 2.4 (1.5), p=NS • 6 months: 3.2 (1.7) vs 2.7 (1.5), p=NS <u>Percent of patients with pain relief of ≥50%, PRF vs ICI</u> • 6 months: 50.0% (10/20) vs 60% (12/20), p=NS	**Pain:** The authors report no statistically significant differences between groups in pain VAS at any time point or in the percent of patients with pain relief ≥50%.	Authors report no conflict of interest Funding: 2016 Yeungnam University Research Grant (Level 2)

CI: confidence interval; F/U: follow-up; IA: intra-articular; ICI: intra-articular corticosteroid injection; IQR: interquartile range; MD: mean difference; NR: not reported; NRS: numerical rating scale; ODI: Oswestry Disability Index; PRF: pulsed radiofrequency; RF: radiofrequency; RFN: radiofrequency neurotomy; RR: risk ratio; SD: standard deviation; VAS: visual analog scale.

*P values calculated by AAI

†NRS means and SDs for both groups at 1.5 and 3 months, and for ICI at baseline and 6 months were estimated from graphs

‡All SD's estimated from graph

§Excellent rating defined as patient's pain disappearing, lumbar range of motion partly restored, and the patient returning to normal work and life

Appendix Table B3. Safety information from new RCTs

Author (Year)	Safety outcomes
RFN vs sham neurotomy, lumbar	
Moussa 2016	NR
Van Tilburg 2016	Withdrawals*, reason (n of patients): • increased pain after diagnostic test (1) • painful procedure despite local anesthetic (3) No serious adverse events were encountered during the trial
RFN vs spinal injections/epidural block, lumbar	
Do 2017	No adverse events in PRF group, 1 event of hyperglycemia in ICI
Hashemi 2014	NR
Zhou 2016	No adverse events reported
RFN vs P RF neurotomy + RFN, lumbar	
Arsanious 2016	NR
RFN+exercise vs exercise, lumbar	
Juch 2017	None reported
RFN vs spinal injections/epidural block, cervical	
Lim 2017	No adverse events in PRF group, 2 adverse events in ICI group (1 report of facial flushing, 1 report of hyperglycemia)

ICI: intra-articular corticosteroid injection; NR: not reported; PRF: pulsed radiofrequency; RFN: radiofrequency neurotomy
*Group that withdrawals were in was not reported

APPENDIX C. ARTICLES EXCLUDED AT FULL TEST REVIEW

Appendix Table C1. Excluded systematic reviews

Citation	Reason for exclusion
Al-Najjim M, Shah R, Rahuma M, Gabbar OA. Lumbar facet joint injection in treating low back pain: Radiofrequency denervation versus SHAM procedure. Systematic review. Journal of orthopaedics 2018;15:1-8.	No new RCTs included
Boswell MV, Manchikanti L, Kaye AD, et al. A Best-Evidence Systematic Appraisal of the Diagnostic Accuracy and Utility of Facet (Zygapophysial) Joint Injections in Chronic Spinal Pain. Pain physician 2015;18:E497-533.	No new RCTs included
Engel A, Rappard G, King W, Kennedy DJ. The Effectiveness and Risks of Fluoroscopically-Guided Cervical Medial Branch Thermal Radiofrequency Neurotomy: A Systematic Review with Comprehensive Analysis of the Published Data. Pain medicine (Malden, Mass) 2016;17:658-69.	No new RCTs included
Facchini G, Spinnato P, Guglielmi G, Albisinni U, Bazzocchi A. A comprehensive review of pulsed radiofrequency in the treatment of pain associated with different spinal conditions. The British journal of radiology 2017;90:20150406.	No new RCTs included
Leggett LE, Soril LJ, Lorenzetti DL, et al. Radiofrequency ablation for chronic low back pain: a systematic review of randomized controlled trials. Pain research & management 2014;19:e146-53.	No new RCTs included
Maas ET, Ostelo RW, Niemisto L, et al. Radiofrequency denervation for chronic low back pain. The Cochrane database of systematic reviews 2015:Cd008572.	No new RCTs included
Manchikanti L, Hirsch JA, Kaye AD, Boswell MV. Cervical zygapophysial (facet) joint pain: effectiveness of interventional management strategies. Postgraduate medicine 2016;128:54-68.	No new RCTs included
Manchikanti L, Hirsch JA, Falco FJ, Boswell MV. Management of lumbar zygapophysial (facet) joint pain. World journal of orthopedics 2016;7:315-37.	No new RCTs included
Poetscher AW, Gentil AF, Lenza M, Ferretti M. Radiofrequency denervation for facet joint low back pain: a systematic review. Spine 2014;39:E842-9.	No new RCTs included

RCTs: randomized controlled trials.

Appendix Table C2. Excluded observational studies

Citation	Reason for exclusion
Cohen SP, Moon JY, Brummett CM, White RL, Larkin TM. Medial Branch Blocks or Intra-Articular Injections as a Prognostic Tool Before Lumbar Facet Radiofrequency Denervation: A Multicenter, Case-Control Study. Regional anesthesia and pain medicine 2015;40:376-83.	Case-control design – previous report had RCT data to answer KQ1

KQ1: Key Question 1; RCT: randomized controlled trial.

APPENDIX D. ONGOING COMPARATIVE CLINICAL STUDIES ASSESSING RADIOFREQUENCY FACET NEUROTOMY

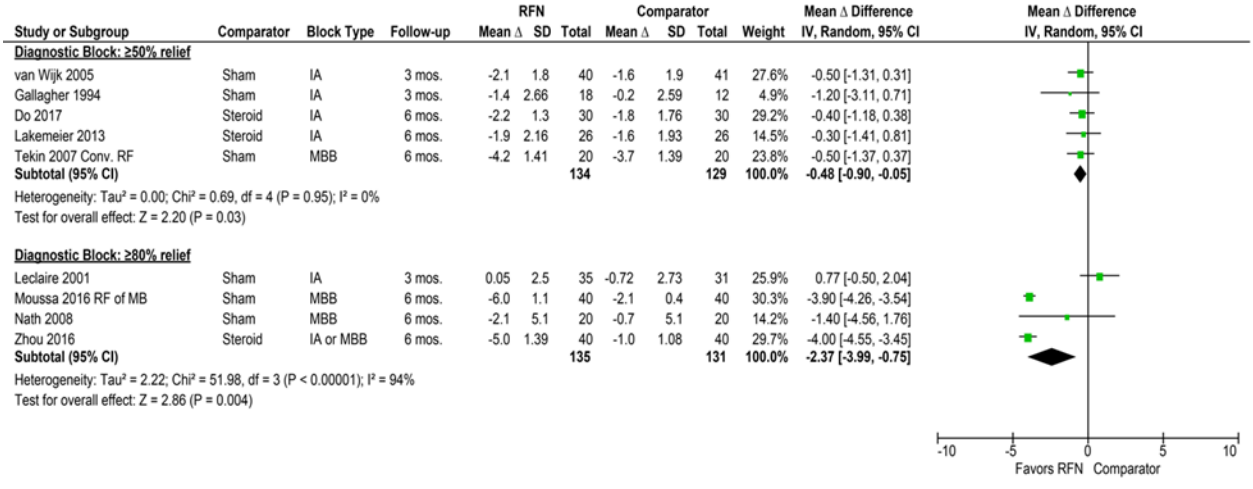
Appendix Table D1. Ongoing clinical trials evaluating facet neurotomy indexed in CLINICALTRIALS.GOV*

NCT number	Title	Status	Conditions	Study type (N)	Interventions	Comparator	Sponsor	State date	Estimated completion date
NCT01300715	An alternative technique for lumbar medial branch radiofrequency: Comparison with the empirical technique	Unknown	Low back pain, lumbar facet joint pain, arthropathy	RCT (N = 100)	Modified lumbar MBRF	Tunnel vision lumbar MBRF	Seoul National University Bundang Hospital	November 2010	May 2011
NCT01743326	RFD versus cervical medial branch blocks in chronic degenerative neck pain	Unknown	Facet joint arthritis	RCT (N = 84)	Radiofrequency denervation	Local anesthesia	Maastricht University Medical Center	November 2012	June 2015
NCT03066960	Radiofrequency neurotomy for chronic facet joint related neck pain	Not yet recruiting	Neck pain	RCT (N = 44)	Radiofrequency neurotomy	Sham radiofrequency neurotomy	Oslo University Hospital	August 2017	April 2019
NCT03039296	EuroPainClinics® Study IV	Recruiting	Low back pain, facet joint pain	Cohort (N = 150)	Unilateral endoscopic rhizotomy	Bilateral endoscopic rhizotomy	Europainclinics z.u.	February 2017	December 2021
NCT02478437	A trial of cooled radiofrequency ablation of medial branch nerves for the treatment of lumbar facet syndrome	Recruiting	Low back pain	RCT (N = 40)	Cooled radiofrequency ablation	Conventional radiofrequency ablation	Northwestern University	June 2015	September 2017
NCT02148003	Effect of the temperature used in thermal radiofrequency ablation	Recruiting	Low back pain	RCT (N = 237)	Radiofrequency ablation at 90°C	Radiofrequency ablation at 80°C	The Cleveland Clinic	May 2014	February 2018

*accessed March 8, 2018.

APPENDIX E. PRELIMINARY META-ANALYSES CONDUCTED BY AAI

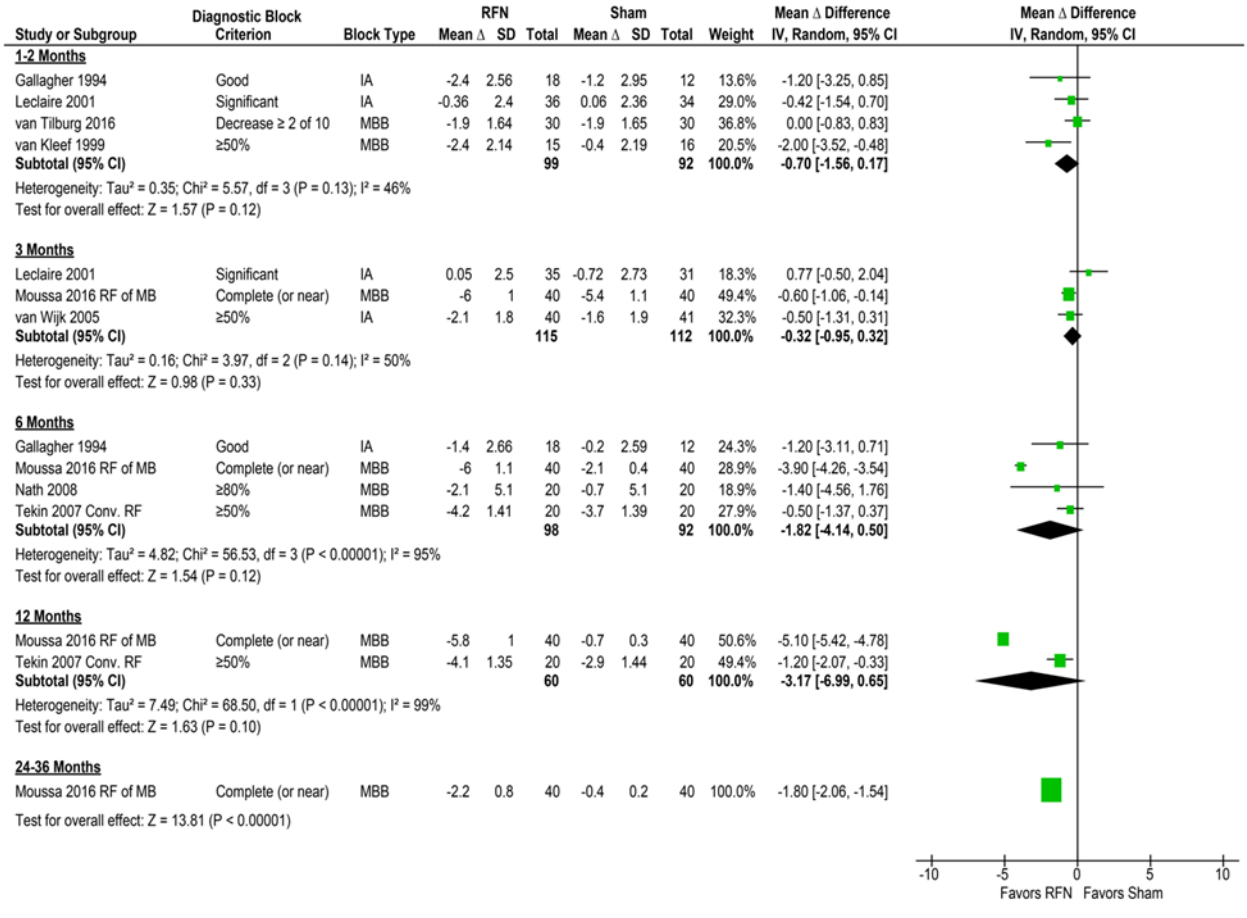
Appendix Figure E1. Improvement in VAS pain following RF neurotomy stratified by degree of pain relief achieved from diagnostic block*



CI: confidence interval; IA: intraarticular; MBB: medial branch block; RFN: radiofrequency neurotomy; SD: standard deviation; VAS: visual analog scale.

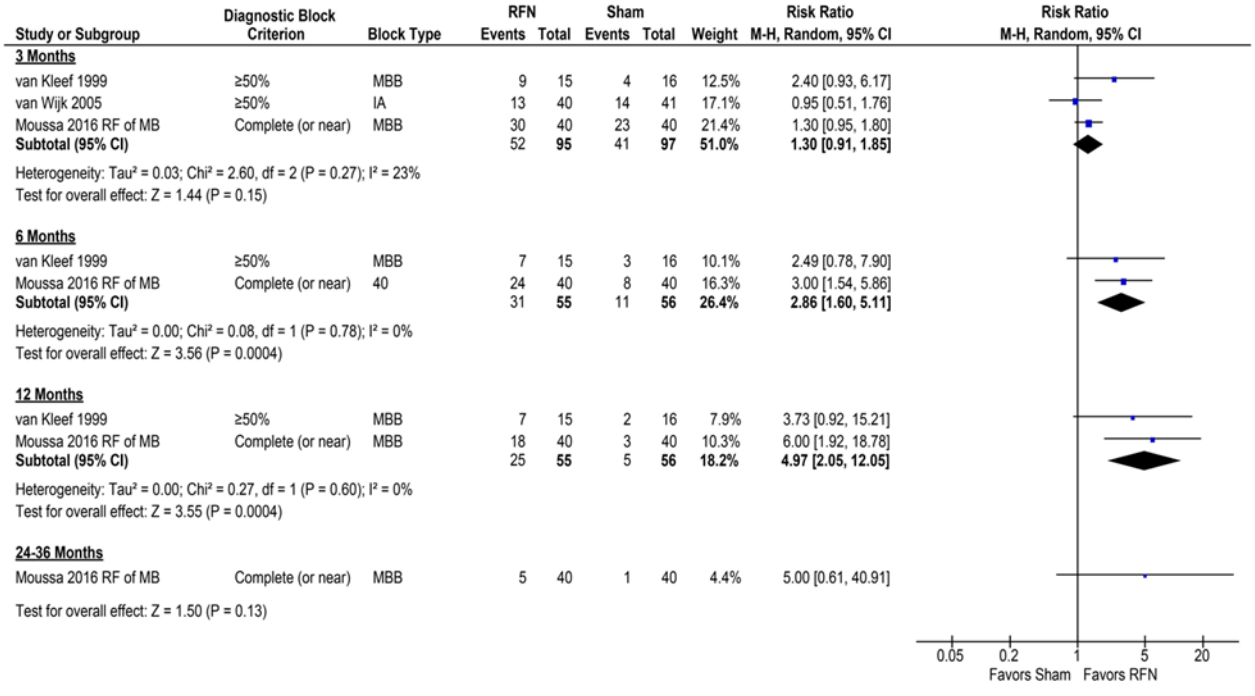
*Three trials did not describe the required response to diagnostic block using a % cut-off. Gallagher 1994 stated that a "good" response was required for inclusion; we decided it was most appropriate to group this trial with the "≥50% relief" trials. Leclaire 2001 require a "significant" response and Moussa 2016 required "a complete or near complete" response; we grouped these with the "≥80% relief" trials.

Appendix Figure E2. RF Neurotomy versus Sham: Back pain improvement (change in VAS scores)*



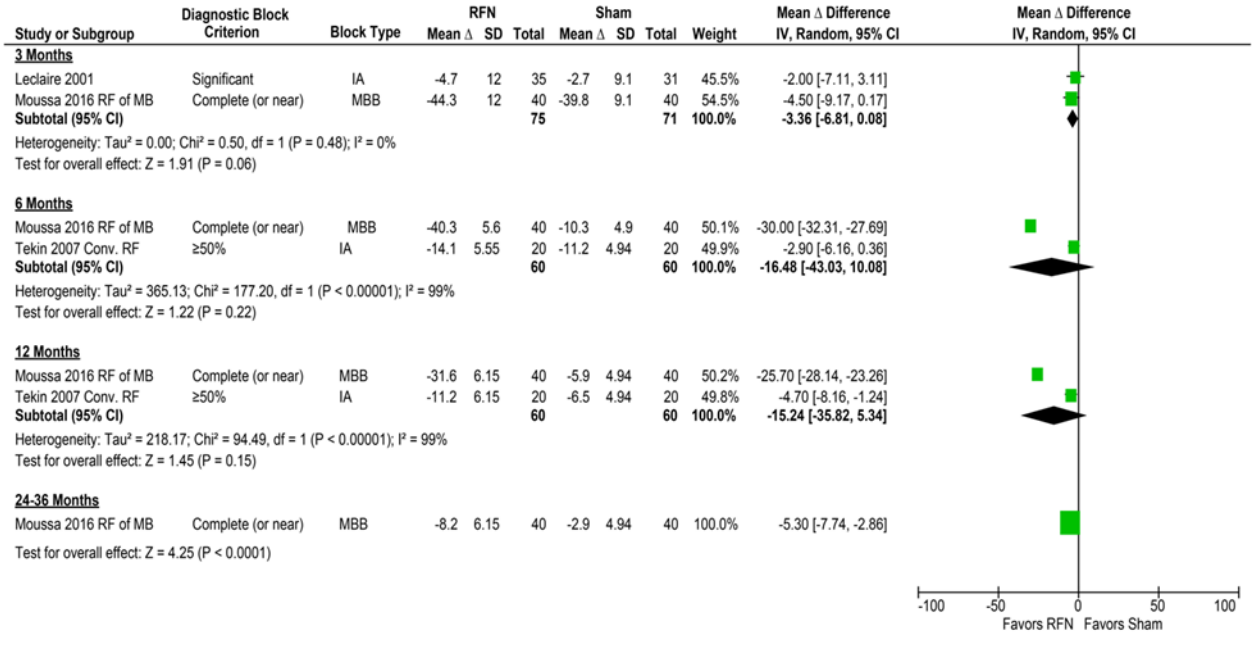
CI: confidence interval; IA: intraarticular; MBB: medial branch block; RFN: radiofrequency neurotomy; SD: standard deviation; VAS: visual analog scale.
*Van Tilburg 2016 and Moussa 2016 are new trials.

Appendix Figure E3. RF Neurotomy versus Sham: Pain relief "success"*



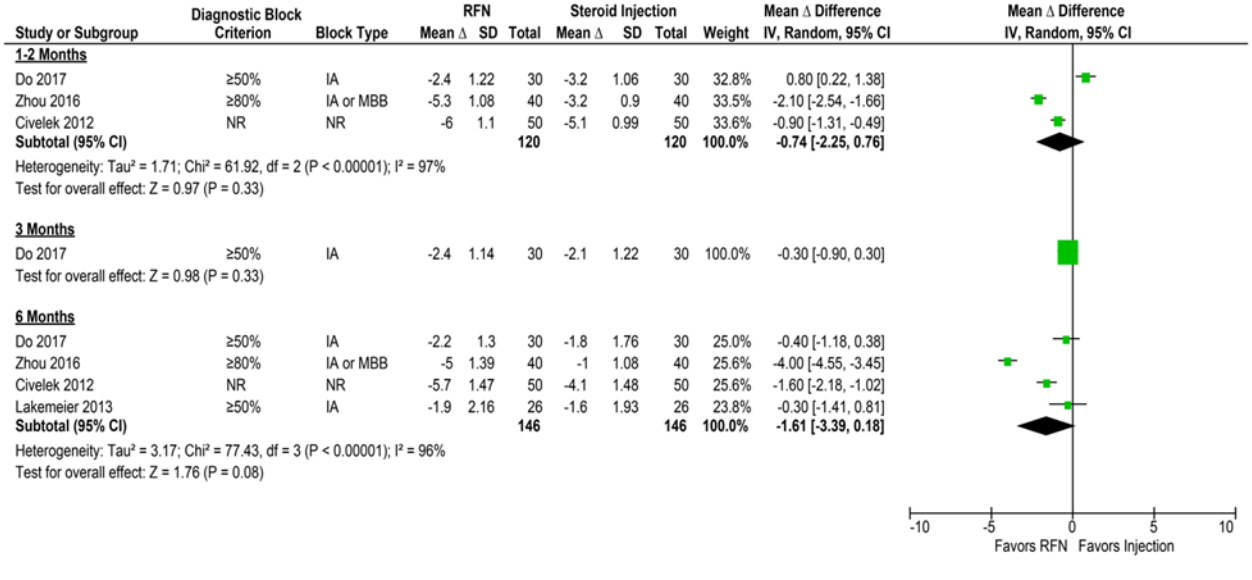
CI: confidence interval; IA: intraarticular; MBB: medial branch block; RFN: radiofrequency neurotomy; SD: standard deviation.
*Definitions of pain success included: 1) Visual analog scale (VAS) pain reduction of ≥50% (van Wijk 2005, Moussa 2016 [new trial]), and 2) Both 2-point reduction on VAS and ≥50% pain reduction on global perceived effect (van Kleef 1999).

Appendix Figure E4. RF Neurotomy versus Sham: Function improvement (change in ODI scores)*



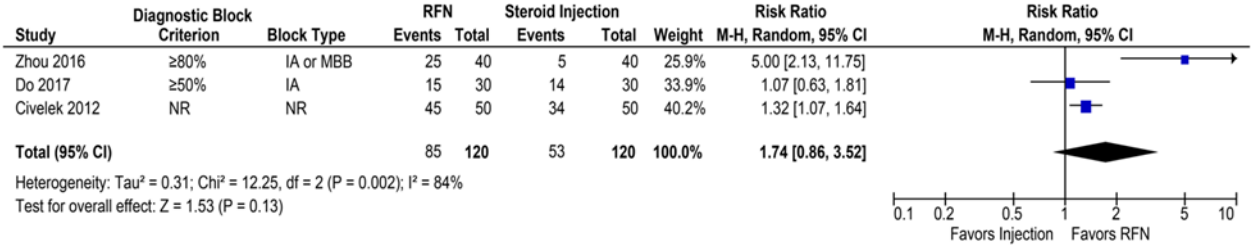
CI: confidence interval; IA: intraarticular; MBB: medial branch block; ODI: Oswestry Disability Index; RFN: radiofrequency neurotomy; SD: standard deviation.
*Moussa 2016 is a new trial.

Appendix Figure E5. RF Neurotomy versus Steroid Injection: Back pain improvement (change in VAS scores)*



CI: confidence interval; IA: intraarticular; MBB: medial branch block; NR: not reported; RFN: radiofrequency neurotomy; SD: standard deviation; VAS: visual analog scale.
*Do 2017 and Zhou 2016 are new trials.

Appendix Figure E6. RF Neurotomy versus Steroid Injection: Pain relief "success"*



CI: confidence interval; IA: intraarticular; MBB: medial branch block; NR: not reported; RFN: radiofrequency neurotomy; SD: standard deviation.

*Definitions of pain success included: 1) Visual analog scale (VAS) pain reduction of ≥50% (Civelek 2012, Do 2017 [new trial]), and 2) Complete relief of pain, lumbar range of motion restored, and patient returned to normal work life (Zhou 2016 [new trial])