Facet Neurotomy:
Assessing Signals for Update

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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 a limited electronic literature of Medline for systematic reviews (SRs) with meta-analysis during the period January 1, 2018 to March 5, 2020 using terms used for the original report. A previous signal search was completed in March of 2018, which conducted a similar search for SRs published between July 1, 2013 and March 2, 2018. Appendix A includes the search methodology and results for the 2018 signal update. In addition, we searched the FDA website to determine if there was approval of new devices or indications for facet neurotomy (see Table 1).

3.2 Study selection

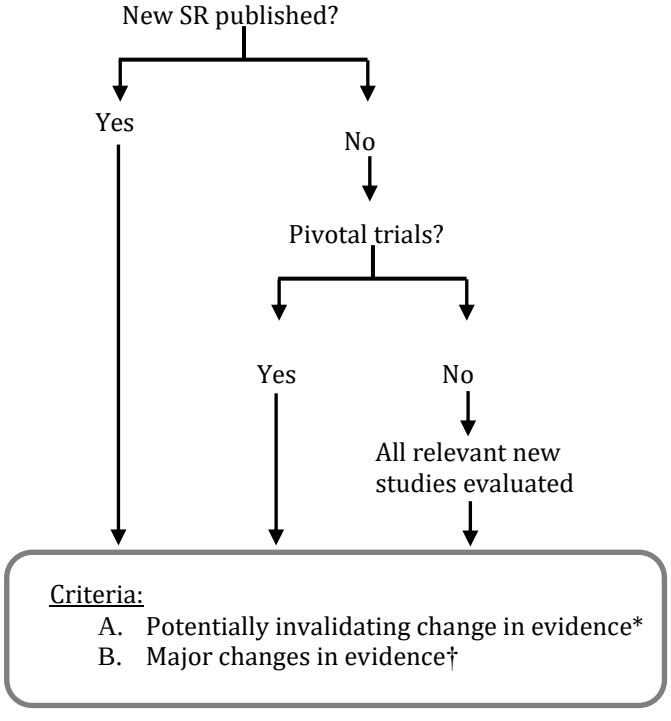
We sought SRs of randomized controlled trials (RCTs) of efficacy and safety with meta-analysis that included articles that met inclusion and exclusion criteria similar to the original report. In addition, we sought SRs reflecting updates or new advances for the technology. Although quality of SRs was not formally evaluated for this report, we chose SRs 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 SRs of RCTs were included for efficacy. SRs focused on longer-term safety outcomes may include nonrandomized studies. A summary of the included SRs and studies 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 (e.g., the risk of harm outweighs the benefits, identification of new serious adverse events)

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 (e.g., to new conditions or subgroups of subjects or additional FDA indications)

B-3. Clinically important caveat

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

Additional general criterion to consider:

- Quantitative signals include a change in statistical significance in which a statistically significant result in the original report is now NOT statistically significant or vice versa which is substantial and/or a change in effect size of at least 50%.

4. Results

4.1 Search

The literature search identified 92 citations. After title and abstract review, 78 articles were excluded and 14 articles that addressed in part or in full the key questions were reviewed at full text. A total of four 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 one SR that addressed in part or in full the key questions. SRs 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. The included SR investigated whether the use of diagnostic blocks for patient selection improves clinical outcomes following facet neurotomy (Key Question 1). No SRs for efficacy (Key Question 2) or safety (Key Question 3) and no full health technology assessments were identified. No SR described results for differential efficacy or safety (Key Question 4). We found no cost-effectiveness studies (Key Question 5); there were none in the previous report. Two new RCTs and one comparative cohort study were identified. No follow-up publications of RCTs included in the previous report were identified. With the exception of the cohort study, which was in the cervical spine, all included studies evaluated facet neurotomy in the lumbar spine. Clinicaltrials.gov was searched for currently ongoing comparative clinical trials, Appendix D.

The FDA has approved three new lesion probe devices 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
Relievant Medsystems, Inc. Sunnyvale, CA	Intracept Intraosseous Nerve Ablation System Relievant Medsystems radiofrequency Generator	K190504	Intended to be used in conjunction with radiofrequency (RF) generators for the ablation of basivertebral nerves of the L3 through S1 vertebrae for the relief of chronic low back pain of at least six months duration that has not responded to at least six months of conservative care	2019	None
Relievant Medsystems, Inc. Sunnyvale, CA	Intracept Intraosseous Nerve Ablation System	K180369	Intended to be used in conjunction with radiofrequency generators for the ablation of basivertebral nerves of the L3 through S1 vertebrae for the relief of chronic low back pain of at least six months duration that has not responded to at least six months of conservative care	2018	None

*Included in 2018 Signal Update

Table 2. Summary of available RCT evidence

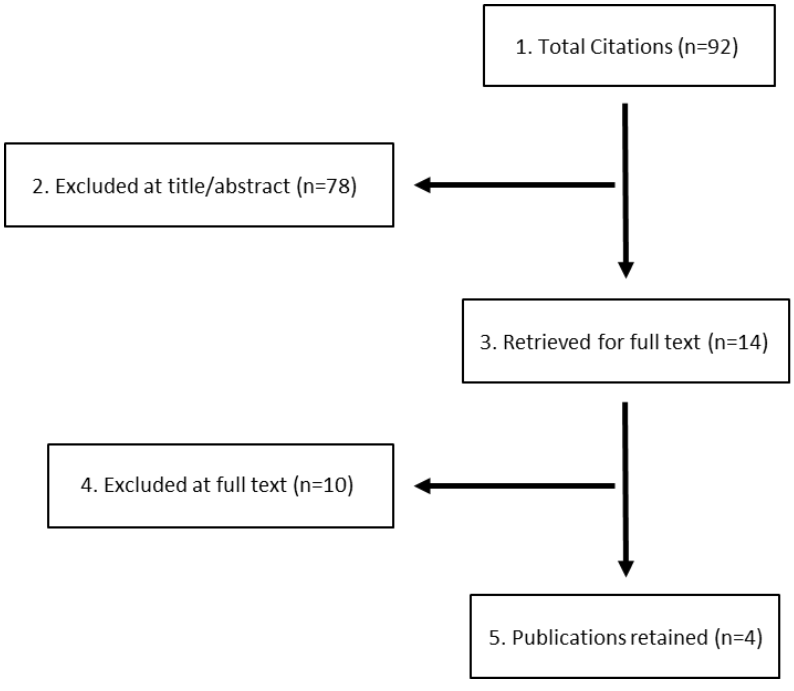
Key Question	Original Report	2018 Signal Search	2020 Signal Search
Key Question 1			
KQ1a. Diagnostic block vs. alternative diagnostic test (e.g., physical examination, radiological examination)	1 RCT (lumbar)	0 RCTs	0 RCTs
KQ1b. Type of diagnostic block (i.e., medial branch block vs. intra-articular injection) for patient selection	1 RCT (lumbar)	0 RCTs	1 RCT (lumbar)†
KQ1c. Use of a single diagnostic block vs. two or more controlled diagnostic blocks	1 RCT (lumbar)	0 RCTs	1 RCT (lumbar)†
KQ1d. Degree of pain reduction from diagnostic block	0 RCTs	3 RCTs (lumbar)*	1 RCT (lumbar)†
KQ1e. Unilateral vs. bilateral diagnostic block	0 RCTs	0 RCTs	1 RCT (lumbar)†
KQ1e. Diagnostic block of single vs. multiple levels	0 RCTs	0 RCTs	1 RCT (lumbar)†
Key Question 2			
KQ2. Radiofrequency Neurotomy vs. Sham Neurotomy	6 RCTs (lumbar) 1 RCT (cervical)	2 RCTs (lumbar)	0 RCTs
KQ2. Radiofrequency Neurotomy vs. Spinal Injections/Epidural Block	2 RCTs (lumbar) 1 RCT (cervical)	3 RCTs (lumbar) 1 RCT (cervical)	0 RCTs
KQ2. Radiofrequency Neurotomy+ exercise vs. Exercise alone	0 RCTs	1 RCT (lumbar)	0 RCTs
KQ2a. Conventional (i.e., continuous) vs. Pulsed Radiofrequency Neurotomy (RFN)	2 RCTs (lumbar)	0 RCTs	0 RCTs
KQ2a. Radiofrequency Neurotomy vs. Alcohol Ablation:	1 RCT (lumbar)	0 RCTs	0 RCTs
KQ2a: Thermal Radiofrequency (TRF) Ablation alone vs. Pulsed Radiofrequency ablation + TRF ablation	0 RCTs	1 RCT (lumbar)	0 RCTs
KQ2a: Cooled vs. Conventional Radiofrequency Neurotomy	0 RCTs	0 RCTs	1 RCT (lumbar)
KQ2b. Repeat Neurotomy	0 RCTs	0 RCTs	0 RCTs
KQ2c. Unilateral vs. Bilateral Neurotomy	0 RCTs	0 RCTs	0 RCTs
KQ2d. Single vs. Multi-level neurotomy	0 RCTs	0 RCTs	0 RCTs

Key Question	Original Report	2018 Signal Search	2020 Signal Search
Key Question 3			
KQ3. Neurotomy vs. Sham	4 RCTs (lumbar)* 1 RCT (cervical)*	1 RCT (lumbar)*	0 RCTs
KQ3. RFN vs. Spinal Injections	2 RCTs (lumbar)*	2 RCTs (lumbar)* 1 RCT (cervical)*	0 RCTs
Key Question 4			
KQ4. Heterogeneity of treatment effect	1 RCT (lumbar)*	0 RCTs	0 RCTs
KQ4. Patients selected on the basis of ≥50% pain relief following medial branch block	3 RCTs (lumbar)* 1 RCT (cervical)*	0 RCTs	0 RCTs
Key Question 5			
KQ4. Heterogeneity of treatment effect	0 RCTs	0 RCTs	0 RCTs
TOTAL RCTs:	14 RCTs (lumbar) 2 RCTs (cervical)	7 RCTs (lumbar) 1 RCT (cervical)	2 RCTs (lumbar) 0 RCTs (cervical)

*Accounted for in the count for KQ2.

†One trial (Cohen 2018) addressed subquestions 1b to 1e.

Figure 2. Flow chart showing results of literature search



4.2 Identifying signals for re-review

Tables 3-8 show the original key questions, the conclusions of the original report, the conclusions from the 2018 signal search, the new sources of evidence, the new findings, and the recommendations of Aggregate Analytics, Inc. (AAI) regarding the need for update (Figure 1).

Table 3. Summary Table for Key Question 1.

Conclusions from CER Executive Summary	Conclusions from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
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:				
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	This section of the report is still valid and does not need updating (Criteria A1, B-1-4). (No SRs or RCTs)	No SRs 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.	This section of the report is still valid and does not need updating (Criteria A1, B-1-4). (No SRs or RCTs)	No SRs 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%	This section of the report is still valid and does not need updating (Criteria A1, B-1-4). (No SRs or RCTs)	***Lumbar spine:*** 1 RCT (Cohen 2018)[3] included in one SR, (Schneider 2020)[5]	***Lumbar spine***: • One poor quality SR (Schneider 2020) reported RFN "success" (defined variably across studies) by patient selection criteria based diagnostic block thresholds (e.g. ≥50% pain relief) and strategies (e.g. single,	Findings from one new RCT suggest that patient outcomes following RFN are similar for IAB and MBB as diagnostic blocks at a ≥50% pain relief threshold. These findings are are consistent with those from the original HTA. This section

Conclusions from CER Executive Summary	Conclusions from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
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		**Cervical or thoracic spine**: No SRs or RCTs	dual) as well as placement of conventional RFN electrodes (e.g. parallel, perpendicular). Data from 2 RCTs identified for the 2018 signal report and one new RCT (Cohen 2018) were included. Comparison of RFN vs. sham or other comparators was not reported. Based on indirect comparisons for combinations of patient selection criteria and electrode placement, the authors concluded that the best outcomes were achieved when patients were selected based on high degrees of pain relief from dual medial branch blocks with a [conventional thermal RFN] technique that employed parallel electrode placement. (See data abstraction • One new RCT (Cohen 2018) compared outcomes following conventional RFN (parallel electrode placement) between patients who met ≥50% pain relief for IAB versus MBB. ○ Mean pain scores at follow-up scores and change scores from baseline for NRS pain and ODI scores were similar between diagnostic strategies at 1, 3 and 6 months. (see data abstraction) ○ "Success" (termed positive outcome by the authors and defined as 2-point or greater reduction in average pain score from baseline combined with a satisfaction score of greater than 3 out of 5) following RFN was somewhat less common for patients who had IAB injection versus MBB at 1 month (67% vs. 73%), 3 months (51% vs. 56%) and 6 months (31% vs. 42%), but differences were not statistically significant. The	of the report is still valid and does not need updating (Criteria A1, B-1-4).

Conclusions from CER Executive Summary	Conclusions from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
			proportions of patients reporting success decreased substantially between 1 and 6 moths in both groups.	
Other diagnostic block comparators: • ***Cervical, Lumbar or Thoracic Spine:*** No evidence	This section of the report is still valid and does not need updating (Criteria A1, B-1-4). (No SRs or RCTs)	No SRs 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)	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	No SRs 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).
Lumbar spine: No RCTs compared diagnostic blocks versus placebo	No SRs or RCTs identified.	***Lumbar spine:*** 1 RCT (Cohen 2018)[3] ***Cervical or Thoracic Spine:*** No SRs or RCTs	• One new RCT (Cohen 2018) compared outcomes following conventional RFN (parallel electrode placement) between patients who met ≥50% pain relief **IAB versus saline (placebo) injection**. Large standard deviations across outcomes were noted, estimate precision into question. ○ Differences in mean scores at 1, 3 and 6 months were not statistically significant, however differences in change scores at 1 and 3 months did reach statistical significance. Differences for each group may not be clinically meaningful (<2 points).	Findings from 1 new RCT suggest that when compared to placebo (saline injection) that either IAB and MBB for may improve patient selection, (using a ≥50% pain relief threshold) for RFN based on success defined as 2-point or greater reduction in average pain score from baseline combined with a satisfaction score of greater than 3 out of 5 following RFN. While these findings could be used to update this review section, they don't signal a need for re-review (Criterion B-1).

Conclusions from CER Executive Summary	Conclusions from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
			○ Differences between groups on mean ODI scores at 1, 3 and 6 months were not statistically significant; difference in changes scores from baseline were significant, however. ○ Success (defined above) following RFN was significantly more common in the IAB group versus the placebo group at 1 month (67% vs. 38%), 3 months (51% vs. 24%) and 6 months 31% vs. 17%). • The same RCT compared post RFN outcomes in patients who met ≥50% pain relief for **MBB versus saline (placebo) injection** ○ Mean NRS pain and ODI scores at 1, 3 and 6 months were similar. While differences between groups on NRS change scores at 1 and 3 months were statistically significant, changes from baseline in the groups may not be clinically important. ○ Success (defined previously) following RFN was significantly more common in the MBB group versus the placebo group at 1 month (73% vs.38%), 3 months (56% vs. 24%) and 6 months (42% vs. 17%).	
Key Question 1d. Duration and degree of pain reduction from diagnostic block (i.e., pain relief of ≥30% versus ≥50%, or ≥50% versus ≥80%)				
Lumbar spine (Insufficient evidence) • No studies were identified in which patients were selected for facet neurotomy based on different durations of pain relief following the diagnostic block. • 4 cohort studies: diagnostic groups based on the pain relief thresholds	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.	***Lumbar spine:*** 1 RCT (Cohen 2018)[3] ***Cervical Spine:*** No SRs or RCTs, 1 observational	***Lumbar spine:*** 1 new RCT (Cohen 2018) • One new RCT does not directly assess the impact of pain relief thresholds (degree of pain reduction from diagnostic block). Findings suggest that among patients who had diagnostic IAB or MBB, there was no difference in mean percent pain relief between those who achieved "success"	***Lumbar spine:*** Findings from the new RCT for this 2020 report do not signal re-review (Criteria A1, B1-4). These data support the previous HTA's conclusions. A re-review may not be warranted (Criterion B-1).

Conclusions from CER Executive Summary	Conclusions from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
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. ***Cervical or Thoracic Spine:*** No evidence	A re-review may not be warranted (Criterion B-1). Evidence from 1 SR and new RCTs identified in the 2018 report suggested that patients experienced better pain relief when a higher diagnostic threshold for block pain relief (≥80% vs. ≥50%) was used.	study (Burnham 2020)[2] ***Thoracic Spine:*** No SRs or RCTs	follow RFN (previously defined) and those who did not (73% and 74% pain relief from block) at 3 months. Across the IAB, MBB and placebo groups, percent pain relief from the block in patients who achieved success (70%) was substantially greater than those who did not (56%). • The same RCT reported that the duration of pain relief from the IAB and MBB were the same (0.4 months) as was the duration of paint relief following RFN (2.8 months vs. 3.1 months). In contrast, the duration of pain relief for the saline placebo was 0.1 month and 1.4 months following RFN; this was significantly different compared to either IAB or MBB. Authors do not report the magnitude of pain relief that corresponds to durations reported; thus, the impact on clinical outcomes following RFN are not known. ***Cervical Spine:*** • One small poor-quality retrospective observational study (N=50) of RFN compared outcomes in patients whose dual diagnostic block pain relief was 80%–99% to those reporting a 100% pain relief after dual diagnostic block. There were no differences in mean NRS (0–10 scale) pain scores following RFN between these groups (3.2 vs. 3.7) or in the proportion of patients achieving ≥50% pain relief following RFN (54% for both groups)	Conclusions from evidence identified in the 2018 review support those of the previous HTA and re-review may not be warranted (Criterion B-1). ***Cervical Spine***: One new observational study does not alter the conclusions prior HTA.
Key Question 1e. Unilateral versus bilateral diagnostic block				

Conclusions from CER Executive Summary	Conclusions from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
No studies were identified which met our inclusion criteria.	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	***Lumbar spine:*** 1 RCT (Cohen 2018)[3] ***Cervical or Thoracic Spine:*** No SRs or RCTs	***Lumbar spine:*** One new RCT reported that the proportion of patients achieving "success" (previously defined) was not different in patients receiving bilateral blocks and that unilateral vs. bilateral treatment was not significantly associated with radiofrequency ablation outcomes at 3 months.	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.	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	***Lumbar spine:*** 1 RCT (Cohen 2018)[3] ***Cervical or Thoracic Spine:*** No SRs or RCTs	***Lumbar spine:*** One new RCT reported that the number of levels treated was not significantly associated with radiofrequency ablation outcomes at 3 months.	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).

CER = Comparative effectiveness review; GPE = global perceived effect; HTA = health technology assessment; IAB = intra-articular block; MBB = medial branch block; NRS = numeric rating scale; ODI = Oswestry disability index; RCTs = randomized controlled trial; RF = radiofrequency; RFN = radiofrequency neurotomy; SR = systematic review.

Table 4. Summary Table for Key Questions 2.

Conclusions from CER Executive Summary (Strength of Evidence)	Conclusion from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
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.)?				
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 • 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.	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. (Criterion B1) (1 SR with 7 trials, 1 additional RCT)	No SRs or RCTs	No studies meeting inclusion criteria were identified.	Findings from 2018 suggested that pain success and function was improved at 6 and 12 months for RFN versus sham and that these data could be used to update the report (Criterion B1).

Conclusions from CER Executive Summary (Strength of Evidence)	Conclusion from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
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.)?				
• 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				
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	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	No SRs 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.
	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 (Criterion B-1).	No SRs 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)	Conclusion from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
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.)?				
• Function (1 RCT): No differences between treatment groups on ODI or Roland-Morris scores at 6 months.				
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	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 B1).	No SRs or RCTs	No studies meeting inclusion criteria were identified.	Conclusions from the 2018 signal update report are still valid.
KQ 2. RF Neurotomy Plus exercise versus Exercise				
No studies in previous report	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 (Criterion B-1).	No SRs 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).

CER = comparative effectiveness review; 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; SR = systematic review; VAS = visual analog scale.

Table 5. Summary Table for Key Questions 2a – d.

Conclusions from CER Executive Summary (Strength of Evidence)	Conclusion from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
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, 1 RCT): 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	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	No SRs 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: Pulsed plus Conventional versus Conventional RF Neurotomy				
• No studies meeting the inclusion criteria were identified	There is limited new evidence from 1 RCT (Arsanious 2016)[1] that would update the report; however, the findings from this small trial comparing combined use of conventional (continuous) TRF and pulsed TRF with conventional TRF alone is not sufficient to trigger	No SRs 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)	Conclusion from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
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				
	an updated report (Criteria A1, B1).			
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	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	No SRs 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: Cooled vs. Conventional RFN				
• No studies meeting the inclusion criteria were identified	No studies meeting the inclusion criteria were identified.	***Lumbar spine:*** 1 RCT (N=39) (McCormick 2019)[4] ***Cervical or Thoracic Spine:*** No SRs or RCTs	**Success (6 months)**: No statistically significant differences between cooled vs. conventional RFN in **function success** (i.e., ≥30% or ≥15 points reduction in ODI; 61.9% vs. 44.4%, p=0.28) or **pain success** (i.e., ≥50% reduction in NRS; 52.4% vs. 50.0%, p=0.89). **ODI and NRS pain scores (6 months)**	There is limited new evidence from 1 RCT that would update the report; however, the findings from this small trial comparing cooled vs. conventional RFN is not sufficient to trigger an updated report (Criterion A1, B1). Findings are similar to other previously included studies comparing types of neurotomy.

Conclusions from CER Executive Summary (Strength of Evidence)	Conclusion from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
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				
			No statistically significant differences between cooled vs. conventional RFN in *function* [**mean ODI** scores (17.8 ± 10.0 vs. 18.6 ± 11.6) or **mean change in ODI** from baseline (–11.3 ± 11.2 vs. –8.1 ± 12.3; p=0.40)] and *pain* [**mean NRS** scores (3.6 ± 2.4 vs. 3.9 ± 3.4) or **mean change in NRS** from baseline (–3.8 ± 2.5 vs. –3.0 ± 3.2; p=0.41)]	
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.	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	No SRs 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)	This section of the report is still valid and does not	No SRs or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not

Conclusions from CER Executive Summary (Strength of Evidence)	Conclusion from 2018 Signal Update	New Sources of Evidence	New Findings	AAI Conclusions 2020 Signal Update
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				
• One retrospective cohort: No difference between treatment groups for the percentage of procedures that resulted in back pain "success" (≥50% pain relief or complete elimination of pain) at a mean of 5.6 months	need updating (Criteria A1, B-1-4).			need updating (Criteria A1, B-1-4).
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	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	No SRs 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).

NRS = numeric rating scale; ODI = Oswestry disability index; RCT = randomized controlled trial; RF = radiofrequency; RFN = radiofrequency neurotomy; TRF = thermal radiofrequency; SR = systematic review; VAS = visual analog scale.

Table 6. 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)	**Conclusion from 2018 Signal Update**	**New Sources of Evidence**	**New Findings**	**AAI Conclusions 2020 Signal Update**
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	This section of the report is still valid and does not need updating (Criteria A1, B-1-4). Findings from the new trial are consistent with the previous report with respect to frequency of adverse events.	***Lumbar, Cervical or Thoracic Spine:*** No SRs or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating (Criteria A2, B-1-4).
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	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 of adverse events following neurotomy in the lumbar spine. For the cervical spine, there is limited new evidence that would update the report;	No SRs or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating (Criteria A2, B-1-4).

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)	**Conclusion from 2018 Signal Update**	**New Sources of Evidence**	**New Findings**	**AAI Conclusions 2020 Signal Update**
Safety: Cervical and Thoracic spine • No evidence	however, the findings from one small trial are not sufficient to trigger an updated report (Criteria A2, B).			

CER = comparative effectiveness review; RCT = randomized control trial; SR = systematic review.

*Cohen 2018 RCT does not compare RFN to sham or other treatment but, four patients reported serious adverse events, only one of which was considered related to the procedure (suspected medial branch neuritis).

Table 7. 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)	**Conclusion from 2018 Signal Update**	**New Sources of Evidence**	**New Findings**	**AAI Conclusions 2020 Signal Update**
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 (uack surgery. ***Cervical and Thoracic spine*** • No evidence	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	No SRs 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 ba nemployed versus employed), and previous low b **sis 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 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.
	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	No SRs or RCTs	No studies meeting inclusion criteria were identified.	This section of the report is still valid and does not need updating (Criteria A, B-1-4).

• 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				
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. • 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	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	No SRs 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).

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

Table 8. 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)	**Conclusion from AAI**	**New Sources of Evidence**	**New Findings**	**AAI Conclusions 2020 Signal Update**
• No studies meeting the inclusion criteria were identified	This section of the report is still valid and does not need updating (Criteria A1, B-1-4).	No new economic studies	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).

5. 5. Conclusions

Tables 3-8 show the original key questions, the conclusions of the original report, the conclusions from the 2018 signal search, the new sources of evidence, the new findings, and the recommendations of Aggregate Analytics, Inc. (AAI) regarding the need for update (Figure 1).

5.1 Key Question 1 (Diagnostic):

One new poor-quality SR, 1 moderate-quality RCT reporting on diagnostic blocks prior to lumbar radiofrequency neurotomy (RFN) and 1 poor-quality observational study reporting on diagnostic blocks in the cervical spine do not substantially change the findings of the original HTA.

- 1a. No new SRs or RCTs published since the previous HTA compared use of diagnostic block with other diagnostic methods (e.g. physical examination, radiographic examination) for any spinal segment.
- 1b and c. Evidence from one new RCT suggest that patient outcomes following lumbar RFN are similar for intra-articular block (IAAB) and medial branch block (MBB) as diagnostic blocks at a ≥50% pain relief threshold. Based in indirect evaluation, the SR suggests that patient selection prior to conventional RFN that is based on high degrees of pain relief from dual medial branch blocks may lead to the best outcomes. These findings are consistent with those from the original HTA. This section of the report is still valid and does not need updating (Criteria A1, B-1-4).
- 1c**.** Both IAAB and MBB were more effective than saline injection in identifying patients for lumbar RFN who may experience a 2-point or greater reduction in average pain score from baseline combined with a satisfaction score of greater than 3 out of 5 following RFN using a ≥50% pain relief threshold for diagnostic block in one new RCT. This finding in and of itself does not signal a need for re-review (Criteria B-1).
- 1d: Comparison of response to diagnostic block:
    - Findings from the new RCT in the lumbar spine do not signal re-review (Criteria A1, B1-4). New SR and RCT evidence identified in the 2018 signal update suggested that response to lumbar 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).
    - Limited evidence from one poor-quality observational study do not alter the conclusions of the HTA report and do not warrant re-review (Criteria B-1).
- 1 e, f; Unilateral versus bilateral block, single versus multiple blocks: The new RCT in the lumbar spine reports no statistically significant differences in post-RFN outcomes for unilateral versus bilateral blocks or based on the number of levels. These sections do not need updating (Criteria A1, B-1-4).

5.2 Key Question 2 (Efficacy):

No new SRs or RCTs were identified for this 2020 signal update report. For the comparison of RFN versus sham in the lumbar spine, findings reported in the 2018 signal report from new trials and one SR 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 RFN versus sham on pain success at 6 and 12 months and would update the report (Criteria B-1). This evidence (from 2 SRs, 3 RCTs) suggested that RFN 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 RFN versus sham in the cervical spine. Limited new evidence identified in the 2018 signal update would update the report for a comparison of RFN 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: While new RCTs identified via the current and the 2018 signal update reports would update the available evidence, findings from these small trials are not sufficient to signal an updated report (Criterion A1, B1).
    - One new RCT identified for this signal report compared conventional RFN with water-cooled RFN. No difference between RFN types for pain or function outcomes were identified. Findings were consistent with from the prior HTA and signal update report for comparisons of neurotomy types.
    - One new RCT identified in the 2018 signal update report compared thermal RFN alone versus pulsed dose RFN immediately followed by thermal RFN 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 SRs 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): No new SR or RCT evidence was identified for this 2020 signal update. This section does not need updating. The 2018 report described new evidence from three RCTs of the lumbar spine (1 comparing RFN with sham neurotomy and 2 comparing conventional or pulsed RFN with steroid injections) did 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 RFN vs. steroid injection); however, the findings from one trial are not sufficient to trigger an updated report (criteria B-2, 3).

5.5 Key Question 4 (Differential efficacy or safety): No new SRs 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 SRs (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.

6. REFERENCES

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APPENDIX A. SEARCH STRATEGIES

Search strategy for PubMed—Search dates: 01/01/2018 to 03/05/2020

	Search terms	Number of articles
#1	Facet OR Zygapophyseal OR "Zygapophyseal Joint"[Mesh] OR “medial branch”	2401
#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	24,037
#3	#1 AND #2	107
#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	92
#6	Additional references identified from hand searching	0

Search strategy for Cochrane—Search dates: 01/01/2018 to 03/05/2020

	Search terms	Number of articles
#1	Facet OR Zygapophyseal OR "Zygapophyseal Joint"(Mesh) OR “medial branch”	916
#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	915
#3	#1 AND #2	905
#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	8

*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

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. The updated search goes from January 1, 2018 to March 5, 2020.

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
Schneider 2020 *Search dates: May 2017 and October 2018 (start dates of searches NR)*	To determine the effectiveness of lumbar medial branch thermal radiofrequency neurotomy based on different selection criteria and procedural techniques	Back pain, disc pain, sacroiliac pain, tumors	Comparisons evaluated are indirect. Authors do not present data for comparisons of direct comparison of diagnostic block strategies or comparison of RFN with sham or other treatments except in rare instances; "success" is presented for combinations of diagnostic strategy and RFN electrode placement.	Treatment success (e.g. ≥50% reduction in pain; the definition of treatment success could be defined differently by each study)	Unclear (includes a mix of RCTs and observational studies); reports SOE using Grade (ROB and application detail not provided)	**Proportion of patients achieving treatment success 6 months after lumbar medial RFN based on how patients are selected and procedural techniques, % (95% CI)** When treatment success = 50% relief of pain • Perpendicular placement of electrodes in patients who get 50% relief from a single diagnostic block: 26% (12% to 40%) • Parallel placement of electrodes in patients who get 50% relief from a single diagnostic block: 57% (52% to 62%) • Parallel placement of electrodes in patients who get 80% relief from a single diagnostic block: 64% (51% to 77%) • Parallel placement of electrodes in patients who get 50% relief from two diagnostic blocks: 49% (26% to 62%) • Parallel placement of electrodes in patients

Assessment *Search dates*	Purpose	Condition	Treatment vs. comparators	Primary Outcomes	Evidence-base Used	Primary Conclusions
						who get 80% relief from two diagnostic blocks: 58% (54% to 62%) <u>When treatment success = 80% relief of pain</u> • Parallel placement of electrodes in patients who get 80% relief from two diagnostic blocks: 36% (32% to 40%) <u>When treatment success = 100% relief of pain</u> • Parallel placement of electrodes in patients who get 80% relief from two diagnostic blocks: 23% (20% to 26%) • Parallel placement of electrodes in patients who get 100% relief from two diagnostic blocks: 56% (47% to 65%) In general, authors consider SOE to be "High", but details of ROB and methods for considering RCTs versus observational studies for determination of SOE are not clear. **Author conclusions**: The best outcomes were achieved when patients

Assessment *Search dates*	Purpose	Condition	Treatment vs. comparators	Primary Outcomes	Evidence-base Used	Primary Conclusions
						were selected based on high degrees of pain relief from dual medial branch blocks with a [conventional thermal RFN] technique that employed parallel electrode placement.

CI = confidence interval; RFN = radiofrequency ablation

Appendix Table B2. Study characteristics and results of new RCTs and cohort studies

Author (Year)	Demographics	Results	Author's Conclusions	Comments
Key Question 1				
KQ1b: Type of diagnostic block, lumbar				
Cohen 2018 RCT **[Also abstracted for KQ1c, KQ1d, KQ1e, KQ1f]**	N=182 *Intraarticular injection vs. medial branch block* • Age, mean (SD): 48 (15) vs. 46 (13) years • Female: 30% vs. 37% • Duration of pain, mean (SD): 8 (7) vs. 6 (6) years • Levels, mean (SD): 2.2 (0.6) vs. 2.0 (0.5) • Bilateral: 66% vs. 69% • Proportion of patients having a positive block in the immediate post-procedural period: 51% (46/91) vs. 55% (50/91), p=0.713 (Blocks were considered positive when patients had ≥50% pain relief sustained for at least 3h after administration of pain block or intraarticular injection). • F/U: 1, 3, and 6 months <u>Intraarticular injection description (n=91 randomized, 46 eligible for RFN (i.e. positive block), 45 received RFN)</u> • A 22-gauge needle was inserted into the joint using fluoroscopic imaging. • To confirm placement, 0.2 ml of contrast dye was injected. • Once needle placement was deemed acceptable, 0.5 ml of solution containing 0.25 ml of 0.5% bupivacaine mixed with 0.25 ml of 40 mg/ml depomethylprednisolone was injected.	<u>Pain, Intraarticular injection vs. medial branch block</u> **Proportion of patients with a positive outcome, % (n/N)**: • 1 month: 67% (30/45) vs. 73% (35/48) • 3 months: 51% (23/45) vs. 56% (27/48) • 6 months: 31% (14/45) vs. 42% (20/48) **NRS pain score (0 to 10; higher=worse pain), mean (SD)** • Pre-RFN (n = 45 vs. 48): 4.8 (1.6) vs. 5.0 (1.6) • 1 month raw score (n = 45 vs. 48): 2.6 (1.8) vs. 2.9 (3.2) • 3 months raw score (n = 29 vs. 33): 3.0 (2.0) vs. 3.2 (2.5) • 6 months raw score (n = 20 vs. 22): 3.6 (2.0) vs. 3.7 (2.6) • 1 month Δ from baseline (n = 45 vs. 48): -2.2 (2.1) vs. -2.1 (2.0) • 3 months Δ from baseline (n = 29 vs. 33): -1.8 (2.3) vs. -1.8 (2.4) • 6 months Δ from baseline (n = 20 vs. 22): -1.2 (2.1) vs. -1.3 (2.3)	The higher responder rates in the treatment groups suggest a hypothesis that facet blocks might provide prognostic value before radiofrequency ablation.	Funding: Center for Rehabilitation Sciences Research, Bethesda, Maryland. COI: Dr. Cohen has served as a consultant to Halyard, Alpharetta, Georgia, Boston Scientific, Natick, Massachusetts, and Abbott, Abbott Park, Illinois, within the past 3 yr.

Author (Year)	Demographics	Results	Author's Conclusions	Comments
	Medial branch block description (n=91 randomized, 50 eligible for RFN (i.e. positive block), 48 received RFN) • L5 dorsal rami blocks were performed by placing a 22-gauge needle in the groove between the sacral ala and articular process, while higher level lumbar medial branch blocks were done by inserting 22-gauge needles in an oblique trajectory at a point several millimeters below the junction of the upper transverse process and the superior articular process. • After confirmation of needle placement, contrast was injected to ascertain appropriate spread and absence of intravascular uptake. • When needle placement was deemed appropriate, 0.5 ml of solution containing 0.25 ml of 0.5% bupivacaine mixed with 0.25 ml of 40 mg/ml depomethylprednisolone was administered. RFN description • 18- or 20-gauge curved radiofrequency needles with 10-mm active tips were inserted in coaxial views until bone was contacted. • For each nerve, needles were adjusted to optimize sensory and motor stimulation. For each nerve lesion, electrodes were inserted and adjusted until correct placement was confirmed by electrostimulation at 50 Hz, with the goal being concordant sensation at 0.5 V or less. • Ablation was then commenced at 90°C for 135 s with a radiofrequency generator.	Function, Intraarticular injection vs. medial branch block **ODI score (0 to 100; higher=greater disability), mean (SD)** • Pre-RFN (n = 45 vs. 48): 35 (15) vs. 32 (12) • 1 month raw score (n = 45 vs. 48): 25 (15) vs. 25 (16) • 3 months raw score (n = 29 vs. 33): 26 (16) vs. 26 (18) • 6 months raw score (n = 20 vs. 22): 26 (16) vs. 26 (18) • 1 month Δ from baseline (n = 45 vs. 48): -10 (12) vs. -7 (13) • 3 months Δ from baseline (n = 29 vs. 33): -9 (13) vs. -7 (13) • 6 months Δ from baseline (n = 20 vs. 22): -6 (14) vs. -6 (13) Safety, Intraarticular injection vs. medial branch block **RFN complications, % (n/N)**** • 7% (3/45) vs. 4% (2/48)		

Author (Year)	Demographics	Results	Author's Conclusions	Comments
KQ1c: Single vs. controlled or comparative diagnostic blocks, lumbar				
Cohen 2018 RCT **[Also abstracted for KQ1b, KQ1d, KQ1e, KQ1f]**	N=138 *Intraarticular injection vs. saline injection* • Age, mean (SD): 48 (15) vs. 48 (15) • Female: 30% vs. 36% • Duration of pain, mean (SD): 8 (7) vs. 5 (5) years • Levels, mean (SD): 2.2 (0.6) vs. 2.1 (0.4) • Bilateral: 66% vs. 57% • Proportion of patients having a positive block in the immediate post-procedural period: 51% (46/91) vs. 30% (14/47), p=0.006 (Blocks were considered positive when patients had ≥50% pain relief sustained for at least 3h after administration of pain block or intraarticular injection). • F/U: 1, 3, and 6 months <u>Intraarticular injection description (n=91 randomized, 46 eligible for RFN (i.e. positive block), 45 received RFN)</u> • A 22-gauge needle was inserted into the joint using fluoroscopic imaging. • To confirm placement, 0.2 ml of contrast dye was injected. • Once needle placement was deemed acceptable, 0.5 ml of solution containing 0.25 ml of 0.5% bupivacaine mixed with 0.25 ml of 40 mg/ml depomethylprednisolone was injected. <u>Saline injection description (n=47 randomized, 47 eligible for RFN (i.e. positive block), 42 received RFN)</u>	<u>Pain, Intraarticular injection vs. saline (placebo) injection</u> **Proportion of patients with a positive outcome, % (n/N)**: • 1 month: 67% (30/45) vs. 38% (16/42) • 3 months: 51% (23/45) vs. 24% (10/42) • 6 months: 31% (14/45) vs. 17%(7/42) **NRS pain score (0 to 10; higher=worse pain), mean (SD)** • Pre-RFN (n = 45 vs. 42): 4.8 (1.6) vs. 4.3 (1.5) • 1 month raw score (n = 45 vs. 42): 2.6 (1.8) vs. 3.2 (1.9) • 3 months raw score (n = 29 vs. 16): 3.0 (2.0) vs. 3.5 (1.9) • 6 months raw score (n = 20 vs. 10): 3.6 (2.0) vs. 3.8 (1.9) • 1 month Δ from baseline (n = 45 vs. 42): -2.2 (2.1) vs. -1.0 (1.6) • 3 months Δ from baseline (n = 29 vs. 16): -1.8 (2.3) vs. -0.7 (1.5) • 6 months Δ from baseline (n = 20 vs. 10): -1.2 (2.1) vs. -0.5 (1.5)	The higher responder rates in the treatment groups suggest a hypothesis that facet blocks might provide prognostic value before radiofrequency ablation.	See above

Author (Year)	Demographics	Results	Author's Conclusions	Comments
	All patients in the placebo group were eligible for radiofrequency ablation, regardless of whether or not they scored positively on the pain block. [For description of RFN procedure, see above data abstraction for this study]	Function, Intraarticular injection vs. saline (placebo) injection **ODI score (0 to 100; higher=greater disability), mean (SD)** • Pre-RFN (n = 45 vs. 42): 35 (15) vs. 31 (13) • 1 month raw score (n = 45 vs. 42): 25 (15) vs. 27 (17) • 3 months raw score (n = 29 vs.16): 26 (16) vs. 29 (18) • 6 months raw score (n = 20 vs. 10): 26 (16) vs. 29 (18) • 1 month Δ from baseline (n = 45 vs. 42): -10 (12) vs. -4 (13) • 3 months Δ from baseline (n = 29 vs. 16): -9 (13) vs. -3 (12) • 6 months Δ from baseline (n = 20 vs. 10): -6 (14) vs. -1 (12) Safety, Intraarticular injection vs. saline (placebo) injection **RFN complications, % (n/N)**** • 7% (3/45) vs. 19% (8/42)		
	N=138 *Medial branch block vs. saline injection* • Age, mean (SD): 46 (13) vs. 48 (15) • Female: 37% vs. 36% • Duration of pain, mean (SD): 6 (6) vs. 5 (5) years • Levels, mean (SD): 2.0 (0.5) vs. 2.1 (0.4)	Pain, Medial branch block vs. saline (placebo) injection **Proportion of patients with a positive outcome, % (n/N)**: • 1 month: 73% (35/48) vs. 38% (16/42)	The higher responder rates in the treatment groups suggest a hypothesis that facet blocks might provide prognostic value before radiofrequency ablation.	

Author (Year)	Demographics	Results	Author's Conclusions	Comments
	• Bilateral: 69% vs. 57% • Proportion of patients having a positive block in the immediate post-procedural period: 55% (50/91) vs. 30% (14/47), p=0.005 (Blocks were considered positive when patients had ≥50% pain relief sustained for at least 3h after administration of pain block or intraarticular injection). • F/U: 1, 3, and 6 months <u>Medial branch block description (n=91 randomized, 50 eligible for RFN (i.e. positive block), 48 received RFN)</u> • L5 dorsal rami blocks were performed by placing a 22-gauge needle in the groove between the sacral ala and articular process, while higher level lumbar medial branch blocks were done by inserting 22-gauge needles in an oblique trajectory at a point several millimeters below the junction of the upper transverse process and the superior articular process. • After confirmation of needle placement, contrast was injected to ascertain appropriate spread and absence of intravascular uptake. • When needle placement was deemed appropriate, 0.5 ml of solution containing 0.25 ml of 0.5% bupivacaine mixed with 0.25 ml of 40 mg/ml depomethylprednisolone was administered.	• 3 months: 56% (27/48) vs. 24% (10/42) • 6 months: 42% (20/48) vs. 17% (7/42) **NRS pain score (0 to 10; higher=worse pain), mean (SD)** • Pre-RFN (n = 48 vs. 42): 5.0 (1.6) vs. 4.3 (1.5) • 1 month raw score (n = 48 vs. 42): 2.9 (2.3) vs. 3.2 (1.9) • 3 months raw score (n = 33 vs. 16): 3.5 (1.9) vs. 3.5 (1.9) • 6 months raw score (n = 22 vs. 10): 3.8 (1.9) vs. 3.8 (1.9) • 1 month Δ from baseline (n = 48 vs. 42): -2.1 (2.0) vs. -1.0 (1.6) • 3 months Δ from baseline (n = 33 vs. 16): -1.8 (2.4) vs. -0.7 (1.5) • 6 months Δ from baseline (n = 22 vs. 10): -1.3 (2.3) vs. -0.5 (1.5) <u>Function, Medial branch block vs. saline (placebo) injection</u> **ODI score (0 to 100; higher=greater disability), mean (SD)** • Pre-FRA (n = 48 vs. 42): 32 (12) vs. 31 (13)		

Author (Year)	Demographics	Results	Author's Conclusions	Comments
	Saline injection description (n=47 randomized, 47 eligible for RFN (i.e. positive block), 42 received RFN) All patients in the placebo group were eligible for radiofrequency ablation, regardless of whether or not they scored positively on the pain block. [For description of RFN procedure, see above data abstraction for this study]	• 1 month raw score (n = 48 vs. 42): 25 (16) vs. 27 (17) • 3 months raw score (n = 33 vs.16): 26 (18) vs. 29 (18) • 6 months raw score (n = 22 vs. 10): 26 (18) vs. 29 (18) • 1 month Δ from baseline (n = 48 vs. 42): -7 (13) vs. -4 (13) • 3 months Δ from baseline (n = 33 vs. 16): -7 (13) vs. -3 (12) • 6 months Δ from baseline (n = 22 vs.10): -6 (13) vs. -1 (12) Safety, Medial branch block vs. saline (placebo) injection **RFN complications, % (n/N)**** • 4% (2/48) vs. 19% (8/42)		
KQ1d: Degree and duration of pain reduction from diagnostic blocks, lumbar				
Cohen 2018 RCT **[Also abstracted for KQ1b, KQ1c, KQ1e, KQ1f]**	See above for information regarding patient and treatment characteristics	**Degree of relief from diagnostic block** **Factors Associated with Treatment Outcome 3 months after Radiofrequency Denervation** *Negative outcome vs. positive outcome*†† • Mean percent pain relief from diagnostic block for patients in any of the three diagnostic block arms (intraarticular, medial branch, and saline), mean (SD); n: 56% (31%); n=74 vs. 70% (21%); n=60, p=0.004	The strongest predictor of a positive categorical outcome at 3 months after radiofrequency ablation was the presence of a positive diagnostic block. Patients with a positive block had a 6.87 (95% CI, 2.32 to 20.33; *P* < 0.001) times increased odds of a positive categorical outcome compared to those who had a negative block.	See above

Author (Year)	Demographics	Results	Author's Conclusions	Comments
		[The data above includes patients in the placebo saline group who were not required to meet any sort of pain relief threshold in order to qualify for RFN. Patients randomized to either of the two block groups were required to meet a ≥50% pain relief from diagnostic block threshold in order to qualify for RFN]. • Mean percent pain relief from diagnostic block for the patients in the intraarticular and medial branch block arms only, mean (SD); n: 74% (15%), n=42 vs. 73% (17%), n=50, p=0.864 [The data above includes only those patients who were randomized to either of the two block groups. These patients were required to meet a ≥50% pain relief from diagnostic block threshold in order to qualify for RFN]. **Duration (months) of pain relief, mean (SD)** *Intraarticular vs. Medial Branch vs. Saline* • Total duration of pain relief from block and RFN: 2.8 (2.7) vs. 3.4 (2.8) vs. 1.5 (2.3); p=0.540 for intraarticular vs. medial branch, p=0.016 for intraarticular vs. placebo,		

Author (Year)	Demographics	Results	Author's Conclusions	Comments
		p=0.001 for medial branch vs. saline. - Total duration of pain relief from block only: 0.4 (1.3) vs. 0.4 (1.3) vs. 0.1 (0.5) - Total duration of pain relief from RFN only: 2.6 (2.5) vs. 3.1 (2.6) vs. 1.4 (2.3)		
KQ1e: Unilateral vs. bilateral diagnostic blocks, lumbar				
Cohen 2018 RCT **[Also abstracted for KQ1b, KQ1c, KQ1d, KQ1f]**	See above for information regarding patient and treatment characteristics	**Factors Associated with Treatment Outcome 3 months after Radiofrequency Denervation** *Negative outcome vs. positive outcome*†† Mean (SD) number of levels treated: 2.1 (0.5) vs. 2.1 (0.4), p=0.816	Number of levels treated was not significantly associated with radiofrequency ablation outcomes at 3 months.	See above
KQ1f: Diagnostic block of single vs. multiple levels, lumbar				
Cohen 2018 RCT **[Also abstracted for KQ1b, KQ1c, KQ1d, KQ1e]**	See above for information regarding patient and treatment characteristics	**Factors Associated with Treatment Outcome 3 months after Radiofrequency Denervation** *Negative outcome vs. positive outcome*†† • Bilateral, % (n/N): 68% (51/74) vs. 60% (36/60), p=0.335	Unilateral vs. bilateral treatment was not significantly associated with radiofrequency ablation outcomes at 3 months.	See above
Cervical				
KQ1d: Degree and duration of pain reduction from diagnostic blocks, cervical				
Burnham 2020 Retrospective observational study	N=50 *80% to 99% (n=26) vs. 100% (n=24) symptom improvement*	Pain, 80% to 99% vs. 100% symptom improvement (n=26 vs. 24)	Cervical medial branch RFN is an effective treatment in patients who report ≥80% symptom relief with dual concordant MBBs. The	Funding: None COI: Zachary L. McCormick, MD, serves on the Board of

Author (Year)	Demographics	Results	Author's Conclusions	Comments
[also abstracted for KQ2, below]	(patient data provided for all patients overall only) • Age, mean (SD): 57.5 years • BMI, mean (SD): 29.9 (8.6) • Female: 54% • Bilateral: 24% • Duration of pain - <1 year: 6% - 1 to 5 years: 50% - ≥5 years: 42% • Number of levels treated - 1: 54% - 2: 38% - 3: 2% - 4: 4% - 5: 0% - 6: 2% • Repeat RFN, yes: 16% • RFN type - Conventional: 20% - Cooled: 80% • Mean (SD) F/U: 16.9 (12.7) months <u>Description of block for all patients</u> • Using a lateral fluoroscopic approach, 25-gauge, 1.5–2.5-inch short bevel needles were advanced to the C2-C3 joint line for the third occipital nerve, to the centroid of the lateral mass for the C3-C6 medial branch nerves, and to the superior/anterior portion of the lateral mass for the C7 medial branch nerve, depending on which medial branch nerves were targeted.	**NRS (0 to 10; higher=worse pain), mean (SDs NR)** • Baseline: 6.9 vs. 6.3 • Post-RFN: 3.2 vs. 3.7 **Proportion of patients with pain relief by ≥50% after RFN, % (n/N)** • 54% (95% CI 35 to 73%) vs. 54% (95% CI 32% to 74%, RR 0.99 (95% CI 0.59 to 1.66), p=NS	present study demonstrated an overall ≥50% pain reduction rate of 54% and no significant difference between those selected by 80–99% vs. 100% symptom relief with dual concordant MBBs.	Directors of the Spine Intervention Society. There are no other potential conflicts of interest to disclose on the part of any of the other authors.

Author (Year)	Demographics	Results	Author's Conclusions	Comments
	• Correct needle placement was confirmed with anterior-posterior (AP) fluoroscopic imaging. • Next, 0.2mL of Omnipaque contrast was deposited at each injection site in order to further confirm appropriate needle placement and rule out vascular uptake. • Then, 0.3–0.5mL of either 4% lidocaine or 0.5% bupivacaine was injected.			
Key Question 2				
Conventional vs. cooled RFN, lumbar				
McCormick 2019 **RCT**	N=43 *Conventional RFN (n=18) vs. Cooled RFN (n=21)* • Age, mean (SD): 58.4 (13.5) vs. 53.6 (13.7) • Female: 55.6% vs. 61.9% • BMI, mean (SD): 28.1 (5.6) vs. 34.4 (9.0) • Percent relief from diagnostic block: mean (SD): 80% (20%) vs. 90% (10%) • Joints denervated - 1 (unilateral): 5.6% vs. 9.5% - 1 (bilateral): 11.1% vs. 4.8% - 2 (unilateral): 44.4% vs. 52.4% - 2 (bilateral): 27.8% vs. 28.6% - 3 (unilateral): 11.1% vs. 4.8% - 3 (bilateral): 0% vs. 0% • Mean (SD) F/U: 16.9 (12.7) months Patients were required to have >75% pain reduction with diagnostic block in order to qualify for RFN. In both groups, following ablation, 0.5 mL of 0.5% bupivacaine was injected at each MBN site to provide post-	<u>Pain, conventional RFN vs. cooled RFN (n=18 vs. 21)</u> **NRS (0 to 10; higher=worse pain), mean (SDs NR)** • Baseline: 6.9 (1.5) vs. 7.4 (1.7) • 6 months: 3.9 (3.4) vs. 3.6 (2.4) • 6 months Δ from baseline: -3.0 (3.2) vs. -3.8 (2.5), p=0.410 **Proportion of patients with ≥50% reduction in NRS from baseline, % (n/N)** 44.4% (8/18) vs. 52.4% (11/21), p=0.882 <u>Function, conventional RFN vs. cooled RFN (n=18 vs. 21)</u> **ODI score (0 to 100; higher=greater disability), mean (SD)** • Baseline: 26.7 (8.7) vs. 29.1 (7.0) • 6 months: 18.6 (11.6) vs. 17.8 (10.0)	No significant differences were observed between the two RFN modalities. When using a single diagnostic block paradigm with a threshold of >75% pain reduction, cooled RFN resulted in a treatment success rate greater than 50% when defined by pain reduction (NRS), and greater than 60% when defined by improvement in physical function (ODI). These treatment effects were maintained at 6-month follow-up.	Funding: Supported by the 2014 Addison Blonsky Research Grant from the Midwest Pain Society. COI: ZLMcC serves on the board of directors for the Spine Intervention Society. The authors otherwise declare no potential conflicts of interest.

Author (Year)	Demographics	Results	Author's Conclusions	Comments
	procedure analgesia. No corticosteroids were injected. <u>Description of conventional RFN</u> • 20-gauge T-RFN probes with 10 mm active tips (Baylis Medical, Montreal, Canada) were placed at each target MBN using parallel technique. • 18 Motor testing was performed. • Prior to lesioning, 1 mL of 2% lidocaine was injected through the introducer needle for anesthesia. T-RFN lesions were performed for 90 s at 80°C at each MBN target site. <u>Description of cooled RFN</u> • 17-gauge introducer needle was placed at the medial branch nerve target level, and an 18- gauge cooled RFN probe with a 4 mm active tip (Coolief Cooled Radiofrequency Kit, Halyard Health, Alpharetta, Georgia) was placed at the junction of the transverse process and the superior articular process. • Once the satisfactory needle position was confirmed motor testing was performed (2.0 V, 2 Hz) at each of the MBN target sites. • C-RFN lesions were performed for 165 s at each MBN site, with the RFN generator temperature set to 60°C (intralesional temperature >80°).	• 6 months Δ from baseline: -8.1 (12.3) vs. 11.3 (11.2), p=0.397 **Proportion of patients with ≥30% reduction in ODI from baseline, % (n/N)** 44.4% (8/18) vs. 61.9%% (13/21), p=0.276		
Conventional vs. cooled RFN, cervical				
Burnham 2020 Retrospective observational study	N=50 *Conventional (n=10) vs. cooled RFN (n=40)* (patient data provided for all patients overall only)	<u>Conventional vs. cooled RFN (n = 10 vs. 40)</u> **Proportion of patients with pain relief by ≥50% after RFN, % (n/N)**	No significant differences in conventional vs. cooled RFN in predicting pain reduction.	See above

Author (Year)	Demographics	Results	Author's Conclusions	Comments
[also abstracted for KQ2, below]	• Age, mean (SD): 57.5 years • BMI, mean (SD): 29.9 (8.6) • Female: 54% • Bilateral: 24% • Duration of pain - <1 year: 6% - 1 to 5 years: 50% - ≥5 years: 42% • Number of levels treated - 1: 54% - 2: 38% - 3: 2% - 4: 4% - 5: 0% - 6: 2% • Repeat RFN, yes: 16% • RFN type - Conventional: 20% - Cooled: 80% • F/U: 1, 3, and 6 months <u>Description of block for all patients</u> • Using a lateral fluoroscopic approach, 25-gauge, 1.5–2.5-inch short bevel needles were advanced to the C2-C3 joint line for the third occipital nerve, to the centroid of the lateral mass for the C3-C6 medial branch nerves, and to the superior/anterior portion of the lateral mass for the C7 medial branch nerve, depending on which medial branch nerves were targeted. • Correct needle placement was confirmed with anterior-posterior (AP) fluoroscopic imaging.	• NR vs. NR, OR 0.737 (95% CI 0.180 to 3.016), p=0.669		

Author (Year)	Demographics	Results	Author's Conclusions	Comments
	• Next, 0.2mL of Omnipaque contrast was deposited at each injection site in order to further confirm appropriate needle placement and rule out vascular uptake. • Then, 0.3–0.5mL of either 4% lidocaine or 0.5% bupivacaine was injected. <u>Description of cooled RFN</u> • For cooled RFN, the same sterile technique as the conventional RFN was implemented, but an 18-gauge probe with a 2–4-mm active tip (Coolief Cooled Radiofrequency Kit, Halyard Health, Alpharetta, GA, USA) was inserted perpendicular to the MBN in anticipation of forward projection of cooled RFN lesions beyond the active tip of the electrode.			

Δ: change; BMI: body mass index; CI: confidence interval; COI: Conflict of interest; F/U: follow-up; IA: intra-articular; 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
**A total of 11 patients (8%) developed adverse events after radiofrequency ablation, 7 of whom experienced minor events. Of the four serious adverse events reported, three were judged to be unrelated to the procedure, and one was a case of suspected medial branch neuritis resulting in an emergency department visit for worsening axial pain.
††A positive outcome was defined as a 2-point or greater reduction in average pain score from baseline combined with a satisfaction score of greater than 3 out of 5.

APPENDIX C. ARTICLES EXCLUDED AT FULL TEXT REVIEW

Appendix Table C1. Studies excluded at full text review

Citation	Reason for exclusion
Al-Najjim M, Shah R, Rahuma M, et al. Lumbar facet joint injection in treating low back pain: Radiofrequency denervation versus SHAM procedure. Systematic review. J Orthop. 2018 Mar;15(1):1-8. doi: 10.1016/j.jor.2017.10.001. PMID: 29167604.	SR; no new RCTs included
Boudier-Reveret M, Thu AC, Hsiao MY, et al. The Effectiveness of Pulsed Radiofrequency on Joint Pain: A Narrative Review. Pain Pract. 2019 Nov 29doi: 10.1111/papr.12863. PMID: 31782970.	SR; no new RCTs included
Chang MC. Effect of Pulsed Radiofrequency Treatment on the Thoracic Medial Branch for Managing Chronic Thoracic Facet Joint Pain Refractory to Medial Branch Block with Local Anesthetics. World Neurosurg. 2018 Mar;111:e644-e8. doi: 10.1016/j.wneu.2017.12.141. PMID: 29294395.	Case series
Chen CH, Weng PW, Wu LC, et al. Radiofrequency neurotomy in chronic lumbar and sacroiliac joint pain: A meta-analysis. Medicine (Baltimore). 2019 Jun;98(26):e16230. doi: 10.1097/md.0000000000016230. PMID: 31261580.	SR; no new RCTs included
Conger A, Burnham T, Salazar F, et al. The Effectiveness of Radiofrequency Ablation of Medial Branch Nerves for Chronic Lumbar Facet Joint Syndrome in Patients Selected by Guideline-Concordant Dual Comparative Medial Branch Blocks. Pain Med. 2019 Oct 14doi: 10.1093/pm/pnz248. PMID: 31609391.	Case series
Contreras Lopez WO, Navarro PA, Vargas MD, et al. Pulsed Radiofrequency Versus Continuous Radiofrequency for Facet Joint Low Back Pain: A Systematic Review. World Neurosurg. 2019 Feb;122:390-6. doi: 10.1016/j.wneu.2018.10.191. PMID: 30404055.	SR; no new RCTs included
Gomez Vega JC, Acevedo-Gonzalez JC. Clinical diagnosis scale for pain lumbar of facet origin: systematic review of literature and pilot study. Neurocirugia (Astur). 2019 May - Jun;30(3):133-43. doi: 10.1016/j.neucir.2018.05.004. PMID: 29910103.	SR; does not address a KQ; no new RCTs included
Hambraeus J, Hambraeus KS, Persson J. Radiofrequency Denervation Improves Health-Related Quality of Life in Patients with Thoracic Zygapophyseal Joint Pain. Pain Med. 2018 May 1;19(5):914-9. doi: 10.1093/pm/pnx142. PMID: 29741743.	Cohort study indirectly comparing thoracic and vs. cervical and lumbar RFN; is a case series for the purposes of this report
Mawe L, Thoren LM, Kvarstein G. Responses after spinal interventions in a clinical pain practice - a pragmatic observational study. Scand J Pain. 2020 Jan 24doi: 10.1515/sjpain-2019-0126. PMID: 31977310.	Cohort study of a comparison for which we have RCT data.
Paulsen RT, Carreon L, Busch F, et al. A pilot cohort study of lumbar facet joint denervation in patients with chronic low-back pain. Dan Med J. 2019 Mar;66(3) PMID: 30864544.	Case series

KQ = key question; RCTs: randomized controlled trials; SR: systematic review.

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	Start 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	Nov-10	May-11
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	Nov-12	Jun-15
NCT03066960	Radiofrequency neurotomy for chronic facet joint related neck pain	Recruiting	Neck pain	RCT (N=44)	Radiofrequency neurotomy	Sham radiofrequency neurotomy	Oslo University Hospital	Oct-8-18	Dec-14-22
NCT03039296	EuroPainClinics® Study IV	Recruiting	Low back pain, facet joint pain	Cohort (N=150)	Unilateral endoscopic rhizotomy	Bilateral endoscopic rhizotomy	Europainclinics z.u.	Feb-17	Dec-21
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-14	Feb-21

NCT03614793	A Prospective Trial of Cooled Radiofrequency Ablation of Medial Branch Nerves Versus Facet Joint Injection of Corticosteroid for the Treatment of Lumbar Facet Syndrome	Enrolling by invitation	Lumbar Facet Syndrome	RCT	Cooled Radiofrequency Ablation	Facet Joint Injection of Corticosteroid	University of Utah	Oct-18	Dec-24
NCT04124445	Pulsed vs Continuous Radiofrequency Neurotomy for Cervical Facet Joint Mediated Pain	Not yet recruiting	Chronic Cervical Faceto-genic Pain, Including Shoulder Pain and Cervicogenic Headache	RCT	Pulsed Radiofrequency Ablation	Continuous Radiofrequency Ablation	Allevio Pain Management Clinic	10-Dec-19	31-Dec-23
NCT02073292	Cooled Radiofrequency Ablation vs. Thermal Radiofrequency Ablation	Recruiting	Chronic Thoracic Back Pain	RCT	Cooled Radiofrequency Ablation	Therma Radiofrequency Ablation	The Cleveland Clinic|Kimberly-Clark Corporation	Mar-14	Dec-22
NCT03168802	MRgFUS and Radiofrequency Ablation for Treatment of Facet-joint Osteoarthritis Low Back Pain	Recruiting	Chronic Low Back Pain|Facet Joint Syndrome	RCT	Radiofrequency ablation	Magnetic Resonance-guided Focused Ultrasound	Taipei Medical University Hospital	24-Aug-18	1-Jun-21
NCT03651804	Radiofrequency Ablation: Treatment for Posterior	Recruiting	Vertebral Compression Fracture|Facet Joint Pain	RCT	Radiofrequency ablation	NSAIDs, Bisphosphonates, Acetaminophen,	University of California, Davis	10-Apr-19	1-Mar-20

	Element Pain From Vertebral Compression Fractures					Physical therapy, Opioids			
NCT03912519	Parallel Versus Perpendicular Technique for Lumbar Medial Branch Radiofrequency Neurotomy	Recruiting	Back Pain Without Radiation|Low Back Pain|Lumbar Radiofrequency Neurotomy	RCT	Parallel placement of 16 gauge electrodes	Perpendicular placement with 22 gauge electrodes	Vanderbilt University Medical Center|Spine Intervention Society	21-Aug-19	May-22

*accessed May 27, 2020