Systematic Review

A Best-Evidence Systematic Appraisal of the Diagnostic Accuracy and Utility of Facet (Zygapophysial) Joint Injections in Chronic Spinal Pain

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Background: Spinal zygapophysial, or facet, joints are a source of axial spinal pain and referred pain in the extremities. Conventional clinical features and other noninvasive diagnostic modalities are unreliable in diagnosing zygapophysial joint pain.

Study Design: A systematic review of the diagnostic accuracy of spinal facet joint nerve blocks.

Objective: To determine the diagnostic accuracy of spinal facet joint nerve blocks in chronic spinal pain.

Methods: A methodological quality assessment of included studies was performed using Quality Appraisal of Reliability Studies (QAREL). Only diagnostic accuracy studies meeting at least 50% of the designated inclusion criteria were utilized for analysis.

The level of evidence was classified as Level I to V based on the grading of evidence utilizing best evidence synthesis.

Data sources included relevant literature identified through searches of PubMed and other electronic searches published from 1966 through March 2015, Cochrane reviews, and manual searches of the bibliographies of known primary and review articles.

Outcome Measures: Studies must have been performed utilizing controlled local anesthetic blocks. The criterion standard must have been at least 50% pain relief from baseline scores and the ability to perform previously painful movements.

Results: The available evidence is Level I for lumbar facet joint nerve blocks with the inclusion of a total of 17 studies with dual diagnostic blocks, with at least 75% pain relief with an average prevalence of 16% to 41% and false-positive rates of 25% to 44%.

The evidence for diagnosis of cervical facet joint pain with cervical facet joint nerve blocks is Level II based on a total of 11 controlled diagnostic accuracy studies, with significant variability among the prevalence in a heterogenous population with internal inconsistency. The prevalence rates ranged from 36% to 67% with at least 80% pain relief as the criterion standard and a false-positive rate of 27% to 63%.

The level of evidence for the diagnostic accuracy of thoracic facet joint nerve blocks is Level II with 80% or higher pain relief as the criterion standard with a prevalence ranging from 34% to 48% and false-positive rates ranging from 42% to 48%.

Limitations: The shortcomings of this systematic review include a paucity of literature related to the thoracic spine, continued debate on an appropriate gold standard, appropriateness of diagnostic blocks, and utility.

Conclusion: The evidence is Level I for the diagnostic accuracy of lumbar facet joint nerve blocks, Level II for cervical facet joint nerve blocks, and Level II for thoracic facet joint nerve blocks in assessment of chronic spinal pain.

Key words: Chronic spinal pain, lumbar facet or zygapophysial joint pain, cervical facet or zygapophysial joint pain, thoracic facet or zygapophysial joint pain, facet joint nerve blocks, medial branch blocks, controlled comparative local anesthetic blocks

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Despite the exponential growth of treatments, disability secondary to spinal pain continues to escalate resulting from multiple factors, including the inherent difficulty in obtaining an accurate diagnosis (1-15). An inaccurate or incomplete diagnosis may lead not only to treatment failure and unnecessary testing, but also may increase disease prevalence falsely, resulting in fiscal waste and the diversion of health care resources (6,7,10,11,16). The tests used to make a diagnosis are fundamental to an accurate diagnosis (7,17-26). Spinal pain without radiculitis is a common complaint in primary and tertiary care and coming up with a definitive diagnosis can be challenging (7,17-26).

Based on the literature, intervertebral discs, facet joints, nerve root dura, and sacroiliac joints have all been shown as potential sources of spinal pain and extremity pain (7,27). Controlled studies have established intervertebral discs, facet joints, and sacroiliac joints as sources of spinal pain (7,17,18,22-26). Despite recent advances and multiple publications (28-34), apparently facet joint pain is not being diagnosed accurately utilizing conventional clinical and radiological techniques (7-18,22-26,28-37). Consequently, controlled diagnostic blocks have been utilized (7,17,18,22-26). However, debate continues on the accuracy and appropriateness of diagnostic interventions and subsequent treatments (7,17,18,22-26,28-61).

It has been postulated that facet joint degeneration can result from abnormal motion associated with spondylolisthesis, vertical loading from disc degeneration as well as arthritis, similar to that seen in other synovial joints (50-53,62-68). The following have been put forth to be the basis for pain: an osteophyte impinging on a nerve, a capsule being stretched, synovial villi being trapped within articular surfaces, and chemicals that cause an inflammatory reaction (64,66,68-77). Facet joints also have been shown to be richly innervated by the medial branches of the dorsal rami (35,70,78-91). In addition to this innervation, neuroanatomic, neurophysiologic, and biomechanical studies have shown that facet joints have both free and encapsulated nerve endings and that they also have nerves that contain substance *P* as well as calcitonin gene-related peptide (CGRP) (62,64,74,75,80,81,92-113).

Based on postulates of Bogduk (114), spinal facet joints have been shown to have an abundant nerve supply (35,70,78-91); to be capable of causing persistent pain (33,115-127); to be affected by osteoarthritis, rheumatoid arthritis, spondylitis, degeneration, inflammation, and injury which in turn leads to a restriction of motion and pain upon motion (7,53,63-74,128,129); and using reliable and valid diagnostic techniques have been determined to be a source of pain (7,17,18,22-24,26,34,36,37,39,41,42,130,131). Consequently, controlled local anesthetic blocks of spinal facet joints or medial branch blocks are employed to diagnose facet joint pain.

The reasoning behind this is that a painful joint will cease being painful for the local anesthetic's duration of action, whereas anesthetic blockade of a nonpainful joint will not alter the pain report. By repeating the block with an anesthetic agent that has a different duration of action reproducing the analgesic response, it increases the probability that the blocked joint is the actual source of pain. Thus, to ensure accuracy and validity, these blocks must be controlled and verified for delivery of a local anesthetic agents and eliminate placebo response (7,18,22-24,26,35). A single facet joint injection is not recommended, since it cannot control for a false-positive response (7,18,22-24,36,37,41,42,130), even though some have advocated therapeutic interventions without any diagnostic blocks (130). The diagnostic accuracy of facet joint nerve blocks has been demonstrated with long-term follow-up (7,131). However, multiple manuscripts have been published supporting and opposing the accuracy of diagnostic facet joint nerve blocks (7,18,22-24,26,35-42,44-49,131).

A true placebo control for nerve blocks has been extremely difficult to achieve and thus far, true placebo control trials have not been performed. Further issues have arisen from those who oppose diagnostic interventions in general (7,38,40,47-49), as well as those who oppose any positive clinical trials those including the Database of Abstracts of Reviews of Effects (DARE), often without appropriate analysis and interpretation (132-135).

Recent systematic reviews have shown the accuracy for diagnostic facet joint nerve blocks with controlled diagnostic blocks to have a prevalence of 15% to 45% in the low back with a false-positive rate of 27% to 49% (22); a prevalence of 36% to 60% with a false-positive rate of 27% to 63% for cervical facet joint pain (23); and a prevalence of 40% in the thoracic spine with a false-positive rate of 42% (24). This systematic review was undertaken to update the accuracy and utility of diagnostic facet joint nerve blocks in managing chronic spinal pain of facet joint origin.

1.0 Methods

The methodology utilized in this systematic review followed the review process derived from evidence-

based systematic reviews and diagnostic accuracy studies (17,19,20,21,22,26,136-138).

1.1 Criteria for Considering Studies for This Review

1.1.1 Types of Studies

Diagnostic accuracy studies evaluating spinal facet joint pain of cervical, thoracic, and lumbar facet joints.

1.1.2 Types of Participants

Patients suffering with chronic neck pain, mid back pain, upper back pain, and low back pain.

1.1.3 Types of Interventions

Diagnostic cervical, thoracic, and lumbar facet joint injections.

1.1.4 Types of Outcome Measures

- The primary outcome parameter was pain relief.
- The secondary outcome measure was functional status improvement.

1.2 Literature Search

All available trials in all languages from all countries providing appropriate management with outcome evaluations were considered for inclusion. Searches were performed from the following sources without language restrictions:

1. PubMed from 1966
   www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed
2. Cochrane Library
   www.thecochranelibrary.com/view/0/index.html
3. US National Guideline Clearinghouse (NGC)
   www.guideline.gov/
4. Previous systematic reviews and cross references
5. Clinical Trials
   clinicaltrials.gov/
6. All other sources including non-indexed journals and abstracts

The search period was from 1966 through March 2015.

1.3 Search Strategy

The search strategy emphasized chronic cervical, mid back, and low back pain, facet or zygapophysial joint pain, cervical, thoracic, and lumbar facet injections, and cervical, thoracic, and lumbar facet joint nerve blocks.

The key words searched were: ((((((((((spinal pain, chronic low back pain) OR chronic back pain) OR chronic neck pain) OR facet joint pain) OR lumbosciatic pain) OR postlaminectomy) OR lumbar surgery syndrome) OR cervical post surgery syndrome OR spinal stenosis) OR zygapophysial)) AND ((((((facet joint) OR zygapophyseal) OR zygapophysial) OR medial branch block) OR diagnostic block) OR intraarticular).

This systematic review focused only on the diagnostic accuracy of facet joint injections. Only cervical, thoracic, and lumbar facet joint nerve blocks performed under fluoroscopy or computed tomography imaging techniques were evaluated. If the blocks were performed with any other imaging method, or if performed blindly, the study was excluded. All studies using controlled diagnostic blocks in all languages from all sources describing appropriate outcome evaluations with proper statistical evaluations were reviewed. Reports without an appropriate diagnosis, nonsystematic reviews, book chapters, and case reports were excluded.

1.4 Data Collection and Analysis

The quality of each individual article used in this assessment was based on the Quality Appraisal of Reliability Studies (QAREL) checklist (Table 1) (19,139). This checklist has been validated and utilized in multiple systematic reviews (22-24). The final selected studies had their quality and applicability assessed with a 12-item checklist. Expert methodologists signed off on the checklist's face validity (19,139). It was compared to other checklists for diagnostic reliability used in other systematic reviews (139-142). This checklist was also developed in accordance to the Standards for Reporting Studies of Diagnostic Accuracy (STARD) (20) and the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) (138) appraisal tool. Each checklist item was assessed independently and given a grade of "yes," "no," "unclear," or "not applicable."

1.4.1 Inclusion and Exclusion Criteria

Only studies utilizing controlled diagnostic blocks either with placebo, comparative local anesthetic blocks or single blocks, with appropriate assessment and statistical evaluation were utilized. Further, studies scoring at least 4 on a scale of 12 on the Quality Appraisal Tool for Studies of Diagnostic Reliability (QAREL) were utilized for diagnostic accuracy analysis (19,22-24,139).

1.4.2 Data Extraction and Management

Two review authors working independently, in an unblinded standardized manner, developed search criteria, searched for relevant literature, selected the

Table 1. *Quality Appraisal of Diagnostic Reliability (QAREL) checklist.*

Item	Yes	No	Unclear	N/A
1. Was the test evaluated in a spectrum of subjects representative of patients who would normally receive the test in clinical practice?				
2. Was the test performed by examiners representative of those who would normally perform the test in practice?				
3. Were raters blinded to the reference standard for the target disorder being evaluated?				
4. Were raters blinded to the findings of other raters during the study?				
5. Were raters blinded to their own prior outcomes of the test under evaluation?				
6. Were raters blinded to clinical information that may have influenced the test outcome?				
7. Were raters blinded to additional cues, not intended to form part of the diagnostic test procedure?				
8. Was the order in which raters examined subjects varied?				
9. Were appropriate statistical measures of agreement used?				
10. Was the application and interpretation of the test appropriate?				
11. Was the time interval between measurements suitable in relation to the stability of the variable being measured?				
12. If there were dropouts from the study, was this less than 20% of the sample.				
TOTAL				

Source: Lucas NP, Macaskill P, Irwing L, Bogduk N. The development of a quality appraisal tool for studies of diagnostic reliability (QAREL). J Clin Epidemiol 2010; 63:854-861 (19).

manuscripts and extracted the data from the included studies. Disagreements were resolved by discussion between the 2 reviewers; if needed, another author would resolve the dispute.

1.5 Methodological Quality Assessment

Methodological quality assessment was performed by multiple review authors with groups of 2 authors reviewing 4 to 6 manuscripts apiece. The assessment was carried out independently in an unblinded standardized manner to assess the methodological quality and internal validity of all the studies considered for inclusion. The methodological quality assessment was performed in a manner to avoid any discrepancies, but if any occurred, they were evaluated by a third reviewer and settled by consensus. Continued issues were also discussed with the entire group and resolved.

If any conflict of interest arose, including a reviewer assigned to review a manuscript he had written, that reviewer was not allowed to assess the manuscript's methodological quality.

The minimum acceptable relief was considered to be ≥ 50% as the cutoff threshold for a positive block during the performance of previously painful movements.

1.6 Summary Measures

Summary measures included ≥ 50% pain relief with the ability to perform previously painful movements concordant with the duration of the local anesthetic used.

1.7 Analysis of Evidence

The analysis of the evidence was performed based on grading of evidence utilizing best evidence synthesis, developed with modification of multiple available criteria including those of the United States Preventive Services Task Force (USPSTF) criteria as illustrated in Table 2 (143).

The analysis was conducted using 5 levels of evidence ranging from Level I to V.

At least 2 of the review authors independently, in an unblinded standardized manner, analyzed the evidence. Any disagreements between reviewers were resolved by a third author and consensus. If there were any conflicts of interest (e.g., authorship), those reviewers were recused from assessment and analysis.

2.0 Results

Figure 1 shows the study selection flow diagram. There were numerous studies considered for inclusion. Among these, 61 met the inclusion criteria for assessing diagnostic facet joint injections for accuracy and outcomes (36,37,41-46,54-63,131,144-182). Studies assessing factors influencing the diagnostic accuracy were included with descriptions. Overall, 26 studies were considered for inclusion for diagnostic accuracy, with 17 studies of lumbar facet joint pain (42,43,54,55,57,58,146-154,176,177), 11 studies of cervical facet joint pain (36,150-152,155,157,158,160-163), and 3 studies of thoracic facet joint pain (151,152,164). Two studies (151,152) assessed prevalence and false-positive rates in all 3 regions.

Table 2. *Modified grading of qualitative evidence with best evidence synthesis for diagnostic accuracy and therapeutic interventions.*

Level I	Evidence obtained from multiple relevant high quality randomized controlled trials or Evidence obtained from multiple high quality diagnostic accuracy studies
Level II	Evidence obtained from at least one relevant high quality randomized controlled trial or multiple relevant moderate or low quality randomized controlled trials or Evidence obtained from at least one high quality diagnostic accuracy study or multiple moderate or low quality diagnostic accuracy studies
Level III	Evidence obtained from at least one relevant moderate or low quality randomized controlled trial study or Evidence obtained from at least one relevant high quality non-randomized trial or observational study with multiple moderate or low quality observational studies or Evidence obtained from at least one moderate quality diagnostic accuracy study in addition to low quality studies
Level IV	Evidence obtained from multiple moderate or low quality relevant observational studies or Evidence obtained from multiple relevant low quality diagnostic accuracy studies
Level V	Opinion or consensus of large group of clinicians and/or scientists.

Source: Manchikanti L, Falco FJE, Benyamin RM, Kaye AD, Boswell MV, Hirsch JA. A modified approach to grading of evidence. Pain Physician 2014; 17:E319-E325 (143).

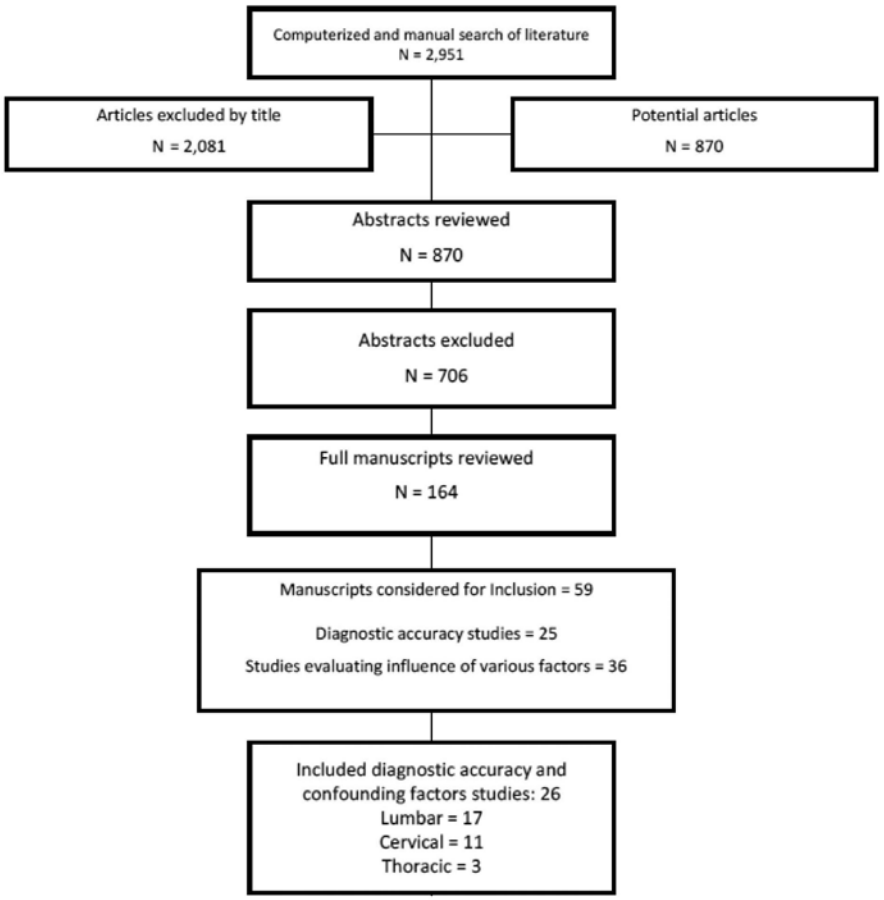

Fig. 1. *Flow diagram illustrating published literature evaluating the accuracy of spinal facet joint nerve blocks in the diagnosis of chronic facet joint pain.*

2.1 Methodological Quality Assessment

Table 1 lists the QAREL criteria for carrying out the methodological quality assessment of included studies. Studies achieving at least 4 of 12 or higher scores were included. Scores of 8 of 12 or higher were considered to be high quality, while 4 to 7 were considered to be moderate quality.

The methodological quality assessment performed is detailed in Tables 3 and 4. A total of 26 studies meeting inclusion criteria were assessed (36,42,43,54,55,57,58,146-155,157,158, 160-164,176,177).

One study was of moderate quality (160); the remaining studies were of high quality.

Table 3. *Quality appraisal of the diagnostic accuracy of lumbar facet joint nerve block diagnostic studies.*

	Manchikanti et al (42)	Pang et al (43)	Schwarzer et al (54,55)	Schwarzer et al (57)	Manchikanti et al (58)	DePalma et al 2011 (154)	Manchikanti et al (176)
1. Was the test evaluated in a spectrum of subjects representative of patients who would normally receive the test in clinical practice?	Y	Y	Y	Y	Y	Y	Y
2. Was the test performed by examiners representative of those who would normally perform the test in practice?	Y	Y	Y	Y	Y	Y	Y
3. Were raters blinded to the reference standard for the target disorder being evaluated?	N	N	N	N	N	N	N
4. Were raters blinded to the findings of other raters during the study?	Y	Y	Y	Y	Y	Y	Y
5. Were raters blinded to their own prior outcomes of the test under evaluation?	N	N	N	N	N	N	N
6. Were raters blinded to clinical information that may have influenced the test outcome?	N	N	N	N	N	N	N
7. Were raters blinded to additional cues, not intended to form part of the diagnostic test procedure?	Y	N	Y	Y	Y	Y	Y
8. Was the order in which raters examined subjects varied?	Y	Y	Y	Y	Y	Y	Y
9. Were appropriate statistical measures of agreement used?	Y	Y	Y	Y	Y	Y	Y
10. Was the application and interpretation of the test appropriate?	Y	Y	Y	Y	Y	Y	Y
11. Was the time interval between measurements suitable in relation to the stability of the variable being measured?	Y	Y	Y	Y	Y	Y	Y
12. If there were dropouts from the study, was this less than 20% of the sample.	Y	Y	Y	Y	Y	Y	Y
TOTAL	9/12	8/12	9/12	9/12	9/12	9/12	9/12

Y=yes; N=no; U=unclear; N/A=not applicable
Source: Lucas NP, Macaskill P, Irwing L, Bogduk N. The development of a quality appraisal tool for studies of diagnostic reliability (QAREL). J Clin Epidemiol 2010; 63:854-861 (19).

Table 3 (cont.). *Quality appraisal of the diagnostic accuracy of lumbar facet joint nerve block diagnostic studies.*

	Manchikanti et al (177)	Manchikanti et al (147)	Manchikanti et al (148)	Manchikanti et al (146)
1. Was the test evaluated in a spectrum of subjects representative of patients who would normally receive the test in clinical practice?	Y	Y	Y	Y
2. Was the test performed by examiners representative of those who would normally perform the test in practice?	Y	Y	Y	Y
3. Were raters blinded to the reference standard for the target disorder being evaluated?	N	N	N	N
4. Were raters blinded to the findings of other raters during the study?	Y	Y	Y	Y
5. Were raters blinded to their own prior outcomes of the test under evaluation?	N	N	N	N
6. Were raters blinded to clinical information that may have influenced the test outcome?	N	N	N	N
7. Were raters blinded to additional cues, not intended to form part of the diagnostic test procedure?	Y	Y	Y	Y
8. Was the order in which raters examined subjects varied?	Y	Y	Y	Y
9. Were appropriate statistical measures of agreement used?	Y	Y	Y	Y
10. Was the application and interpretation of the test appropriate?	Y	Y	Y	Y
11. Was the time interval between measurements suitable in relation to the stability of the variable being measured?	Y	Y	Y	Y
12. If there were dropouts from the study, was this less than 20% of the sample.	Y	Y	Y	Y
TOTAL	9/12	9/12	9/12	9/12

	Manchikanti et al (149)	Manchikanti et al (150)	Manchikanti et al (151)	Manchukonda et al (152)	Manchikanti et al (153)
1. Was the test evaluated in a spectrum of subjects representative of patients who would normally receive the test in clinical practice?	Y	Y	Y	Y	Y
2. Was the test performed by examiners representative of those who would normally perform the test in practice?	Y	Y	Y	Y	Y
3. Were raters blinded to the reference standard for the target disorder being evaluated?	N	N	N	N	N
4. Were raters blinded to the findings of other raters during the study?	Y	Y	Y	Y	Y
5. Were raters blinded to their own prior outcomes of the test under evaluation?	N	N	N	N	N
6. Were raters blinded to clinical information that may have influenced the test outcome?	N	N	N	N	N
7. Were raters blinded to additional cues, not intended to form part of the diagnostic test procedure?	Y	Y	Y	Y	Y
8. Was the order in which raters examined subjects varied?	Y	Y	Y	Y	Y
9. Were appropriate statistical measures of agreement used?	Y	Y	Y	Y	Y
10. Was the application and interpretation of the test appropriate?	Y	Y	Y	Y	Y
11. Was the time interval between measurements suitable in relation to the stability of the variable being measured?	Y	Y	Y	Y	Y
12. If there were dropouts from the study, was this less than 20% of the sample.	Y	Y	Y	Y	Y
TOTAL	9/12	9/12	9/12	9/12	9/12

Y=yes; N=no; U=unclear; N/A=not applicable
Source: Lucas NP, Macaskill P, Irwing L, Bogduk N. The development of a quality appraisal tool for studies of diagnostic reliability (QAREL). J Clin Epidemiol 2010; 63:854-861 (19).

Table 4. *Quality appraisal of diagnostic accuracy of cervical and thoracic facet joint nerve block diagnostic studies.*

	Aprill & Bogduk (160)	Manchikanti et al (157)	Manchukonda et al (152)	Manchikanti et al (152)	Manchikanti et al (150)	Barnsley et al (36)	Yin and Bogduk (155)	Speldewinde et al (158)	Barnsley et al (161)	Lord et al (162)	Barnsley et al (163)	Manchikanti et al (164)
1. Was the test evaluated in a spectrum of subjects representative of patients who would normally receive the test in clinical practice?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Was the test performed by examiners representative of those who would normally perform the test in practice?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
3. Were raters blinded to the reference standard for the target disorder being evaluated?	N	N	N	N	N	N	N	N	N	N	N	N
4. Were raters blinded to the findings of other raters during the study?	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5. Were raters blinded to their own prior outcomes of the test under evaluation?	N	N	N	N	N	N	N	N	N	N	N	N
6. Were raters blinded to clinical information that may have influenced the test outcome?	N	N	N	N	N	N	N	N	N	N	N	N
7. Were raters blinded to additional cues, not intended to form part of the diagnostic test procedure?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
8. Was the order in which raters examined subjects varied?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9. Were appropriate statistical measures of agreement used?	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
10. Was the application and interpretation of the test appropriate?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
11. Was the time interval between measurements suitable in relation to the stability of the variable being measured?	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
12. If there were dropouts from the study, was this less than 20% of the sample.	NA	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
TOTAL	5/12	9/12	9/12	9/12	9/12	9/12	9/12	9/12	9/12	9/12	9/12	9/12

Y=yes; N=no; U=unclear; N/A=not applicable

Source: Lucas NP, Macaskill P, Irwing L, Bogduk N. The development of a quality appraisal tool for studies of diagnostic reliability (QAREL). J Clin Epidemiol 2010; 63:854-861 (19).

2.2 Characteristics of Diagnostic Accuracy Studies

Table 5 shows the characteristics of diagnostic accuracy studies of lumbar facet joint nerve blocks (42,43,54,55,57,58,146-154,176,177). Only one study utilized single blocks with ≥ 90% relief as the criterion standard (43). Four studies utilized controlled diagnostic blocks with ≥ 50% relief as the criterion standard

Table 5. *Characteristics of studies assessing the accuracy of diagnostic facet joint nerve blocks in lumbar spine with ≥ 50% pain relief.*

Study Study Characteristics Methodological Quality Scoring	Participants	Intervention(s) Injectate Volume	Outcome Measures	Results	Conclusion(s)
Pang et al, 1998 (43) Prospective, single block Quality Score: QAREL: 8/12	In a prospective evaluation, 100 consecutive adult patients with chronic low back pain with undetermined etiology were evaluated with spinal mapping.	Single block was performed by injecting 2% lidocaine into facet joints < 2 mL	Verbal analog scale Pain mapping 90% pain relief	Prevalence Only facet joint pain = 24% Lumbar nerve root and facet disease = 24% Total = 48%	This is the first study evaluating application of diagnostic blocks in the diagnosis of intractable low back pain of undetermined etiology with facet joint disease in potentially 48% of patients with a single block.
Schwarzer et al, 1994 (54,55) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	176 consecutive patients with chronic low back pain after some type of injury.	Zygapophysial joint nerve blocks or intraarticular injections were performed with either 2% lignocaine or 0.5% bupivacaine. 0.5 mL	At least 50% pain relief concordant with the duration of local anesthetic injected.	Prevalence = 15% False-positive rate = 38%	First study of evaluation of controlled prevalence and false-positive rates.
Schwarzer et al, 1995 (57) Randomized, impure placebo, controlled diagnostic blocks Quality Score: QAREL: 9/12	63 patients with low back pain lasting for longer than 3 months underwent computed tomography and blocks of the zygapophysial joints	A placebo injection followed by intraarticular zygapophysial joint injections with 1.5 mL of 0.5% bupivacaine. 1.5 mL	At least 50% reduction in pain maintained for minimum of 3 hours.	Prevalence = 40%	This study shows that computed tomography has no place in the diagnosis of lumbar zygapophysial joint pain, with an impure placebo design.
Manchikanti et al, 2010 (42) Retrospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	181 patients with at least 50% pain relief with concordant pain relief were evaluated with dual blocks. 491 patients with chronic low back pain undergoing evaluation for facet joint pain.	Controlled diagnostic blocks of lumbar facet joint nerves with 1% preservative-free lidocaine or 0.25% preservative-free bupivacaine. 0.5 mL	At least 50% or 80% pain relief and ability to perform previously painful movements.	≥ 50% pain relief Prevalence = 61% False-positive rate = 17% ≥ 80% pain relief Prevalence = 31% False-positive rate = 42%	An unusually high proportion of positive rate for facet joint prevalence with single blocks and ≥ 50% pain relief as the criterion standard.
Manchikanti et al, 2000 (58) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	200 consecutive patients with chronic low back pain were evaluated.	Controlled diagnostic blocks with 1% lidocaine or 0.25% bupivacaine. 0.5 mL	75% pain relief with ability to perform previously painful movements.	Prevalence = 42% False-positive rate = 37%	The study showed that the clinical picture failed to diagnose facet joint pain.
DePalma et al, 2011 (154) Retrospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	In a retrospective evaluation, a total of 156 patients with chronic low back pain were assessed for the source of chronic low back pain including discogenic pain, facet joint pain, and sacroiliac joint pain.	Controlled diagnostic blocks with 1% lidocaine or 0.5% bupivacaine. 0.5 mL	Concordant relief with 2 hours for lidocaine and 8 hours for bupivacaine with ≥ 75% pain relief as the criterion standard.	Prevalence = 31%	This is the third study evaluating various structures implicated in the cause of low back pain with controlled diagnostic blocks .

Table 5 (cont.). *Characteristics of studies assessing the accuracy of diagnostic facet joint nerve blocks in lumbar spine with ≥ 50% pain relief.*

Study Study Characteristics Methodological Quality Scoring	Participants	Intervention(s) Injectate Volume	Outcome Measures	Results	Conclusion(s)
Manchikanti et al, 2001 (176) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	Controlled comparative prevalence study in 100 patients with 50 patients below age of 65 and 50 patients aged 65 or over.	Controlled diagnostic blocks with 1% lidocaine or 0.25% bupivacaine. 0.4 mL to 0.6 mL	75% pain relief with ability to perform previously painful movements was utilized as the criterion standard.	Prevalence: < 65 years = 30% > 65 years = 52% False-positive rate: < 65 years = 26% > 65 years = 33%	This study showed higher prevalence of facet joint pain in the elderly compared to the younger age group in contrast to the latest study by Manchikanti et al which showed no differences (171).
Manchikanti et al, 2001 (177) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	Authors evaluated 100 patients with low back pain. Patients were divided into 2 groups, Group I was normal weight and Group II was obese.	Diagnostic blocks with lidocaine 1% or bupivacaine 0.25%. 0.4 mL to 0.6 mL	A definite response was defined as relief of at least 75% in the symptomatic area.	Prevalence: Non-obese individuals = 36% Obese individuals = 40% False-positive rate: Non-obese individuals = 44% Obese individuals = 33%	This study showed no significant difference between obese and non-obese individuals either with prevalence or false-positive rate of diagnostic blocks in chronic facet joint pain.
Manchikanti et al, 2001 (146) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	120 patients were evaluated with a chief complaint of chronic low back pain to evaluate relative contributions of various structures in chronic low back pain. All 120 patients underwent facet joint nerve blocks.	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine. 0.3 mL to 0.6 mL	80% pain relief with ability to perform previously painful movements	Prevalence = 40% False-positive rate = 47%	This study evaluated all the patients with low back pain, even with suspected discogenic pain.
Manchikanti et al, 1999 (147) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	120 patients with chronic low back pain after failure of conservative management were evaluated.	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine. 0.4 mL to 0.6 mL	Concordant pain relief with 75% or greater criterion standard with ability to perform previously painful movements.	Prevalence = 45% False-positive rate = 41%	This was the first study performed in the United States in the heterogenous population as previous studies were performed in only post-injury patients.
Manchikanti et al, 2000 (148) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	180 consecutive patients with chronic low back pain were evaluated after having failed conservative management	Controlled diagnostic blocks with lidocaine and 1% lidocaine and 0.25% bupivacaine with or without Sarapin and/or steroids 0.4 mL to 0.6 mL	75% pain relief with ability to perform previously painful movements	Prevalence = 36% False-positive rate = 25%	This study showed no significant difference if the steroids were used or not
Manchikanti et al, 2003 (149) Prospective, controlled diagnostic blocks QAREL: 9/12	At total of 300 patients with chronic low back pain were evaluated to assess the difference based on involvement of single or multiple spinal regions.	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine. 0.5 mL	80% pain relief with ability to perform previously painful movements.	Single region: Prevalence = 21% False-positive rate = 17% Multiple regions: Prevalence = 41% False-positive rate = 27%	This study shows a higher prevalence when multiple regions are involved.

Table 5 (cont.). *Characteristics of studies assessing the accuracy of diagnostic facet joint nerve blocks in lumbar spine with ≥ 50% pain relief.*

Study Study Characteristics Methodological Quality Scoring	Participants	Intervention(s) Injectate Volume	Outcome Measures	Results	Conclusion(s)
Manchikanti et al, 2002 (150) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	120 consecutive patients with chronic low back pain and neck pain were evaluated to assess involvement of facet joints as causative factors.	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine. 0.5 mL	80% pain relief with ability to perform previously painful movements.	Prevalence = 40% False-positive = 30%	The results are similar to involvement of multiple regions with a prevalence of 40% as illustrated in another study.
Manchikanti et al, 2004 (151) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	500 consecutive patients with chronic, non-specific spinal pain were evaluated of which 397 patients suffered with chronic low back pain.	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine. 0.5 mL	80% pain relief with ability to perform previously painful movements.	Prevalence = 31% False-positive rate = 27%	Largest study performed involving all regions of the spine.
Manchukonda et al, 2007 (152) Retrospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	500 consecutive patients with chronic spinal pain were evaluated of which 303 patients were evaluated for chronic low back pain.	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine. 0.5 mL	80% pain relief with ability to perform previously painful movements.	Prevalence = 27% False-positive rate = 45%	Second largest study performed involving all regions of the spine by the same group of authors (42).
Manchikanti et al, 2007 (153) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	A total of 117 consecutive patients with chronic non-specific low back pain were evaluated, after lumbar surgical interventions, with postsurgery syndrome and continued axial low back pain with controlled, comparative local anesthetic blocks.	Controlled, comparative, local anesthetic blocks with 1% lidocaine and 0.25% bupivacaine. 0.5 mL	80% relief as the criterion standard	Prevalence = 16% False-positive rate = 49%	Lower prevalence of facet joint pain in post surgery patients.

(42,54,55,57). Six studies utilized controlled diagnostic blocks with 75% relief as the criterion standard (58,147,148,154,176,177). In addition, 7 studies utilized 80% or greater pain relief as the criterion standard (42,146,149-153).

Table 6 shows the characteristics of the diagnostic accuracy of cervical and thoracic facet joint nerve blocks considered for inclusion (36,150-152,155,157,158,160-164).

In the cervical spine, only one study (160) utilized ≥ 50% relief as the criterion standard or cutoff threshold for a positive block. One study evaluated controlled diagnostic blocks with ≥ 75% relief as the criterion standard (157). Three studies utilized controlled diagnostic blocks with ≥ 80% as the criterion standard (150-152). Six studies utilized 100% pain relief as the criterion standard (36,155,158,161-163).

In the thoracic spine, there were no studies evaluating single blocks. Three studies utilized ≥ 80% relief as the criterion standard with controlled diagnostic blocks (151,152,164).

2.3 Characteristics of Studies of Factors Influencing Diagnosis

Table 7 shows the characteristics of studies of factors influencing the diagnosis of facet joint pain. The effect of age was considered in 3 studies (167,171,176), 2 studies assessed psychological variables (165,166), 6 studies assessed the clinical picture (44-46,58-60), one study with 2 publications (44,45), one study assessed the ability of computed tomography to identify painful facet joints (56), 2 studies assessed the influence of body mass index (167,177), 6 studies assessed the influence of surgery (153,168-170,172,174), 2 studies

Table 6. *Studies assessing the accuracy of diagnostic facet joint nerve blocks in cervical and thoracic spine with 50% pain relief.*

Study **Study Characteristics** **Methodological Quality Scoring**	**Participants**	**Intervention(s)** **Injectate Volume**	**Outcome Measures**	**Results**	**Conclusion(s)**
CERVICAL SPINE					
Aprill & Bogduk, 1992 (160) Prospective, single block Quality Score: QAREL: 5/12	The records were reviewed of 318 patients with chronic neck pain of at least 6 months without myelopathy from January 1989 to April 1990 in a radiology practice in New Orleans.	Intraarticular lidocaine injection after contrast injection with provocation with assessment of provocation and pain relief. 0.2 mL to 0.3 mL iohexol 0.5 mL betamethasone	Provocation and pain relief ≥ 50%)	Approximate prevalence = 63%. A 25% positive rate with the possibility that an additional 38% suffered with zygapophysial joint pain.	The study was performed in a radiology setting and only with patients who were involved in a motor vehicle injury. Only a single block was performed.
Barnsley et al, 1993 (36) Randomized, double-blind, controlled diagnostic blocks Quality Score: QAREL: 9/12	47 consecutive patients with chronic neck pain following motor vehicle accidents.	Cervical medial branch blocks utilizing comparative local anesthetics with 2% lidocaine or 0.5% bupivacaine. 0.5 mL	Definite or complete relief of pain (100%) following the medial branch blocks.	Prevalence=60%	Comparative local anesthetic medial branch blocks were used in the diagnosis of cervical zygapophysial joint pain.
Yin and Bogduk, 2008 (155) Retrospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	143 patients with chronic neck pain of various origins of at least 3 months duration were included. A total of 84 patients underwent cervical medial branch blocks.	Cervical controlled, comparative local anesthetic medial branch blocks with either 4% lignocaine or 0.75% bupivacaine. 0.5 mL	Complete pain relief (100%)	Prevalence = 55% Positive responses were determined with duration of relief based on the local anesthetic with concordant response (i.e., patients were required to have long-lasting relief when 0.75% bupivacaine was administered and short-lasting relief when 4% lignocaine was administered).	In this evaluation a large proportion of patients (36%) did not pursue investigations, which diluted the crude prevalence of various conditions. A diagnosis remained elusive in 32% of those patients who completed investigations.
Manchukonda et al, 2007 (152) Retrospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	A total of 251 consecutive patients receiving controlled, comparative local anesthetic blocks with chronic neck pain were included. Patients had pain for at least 6 months, which was nonspecific without a radicular component.	Controlled diagnostic medial branch blocks using 1% lidocaine or 0.25% bupivacaine. 0.5 mL	A positive response was considered at least 80% pain relief with the ability to perform previously painful movements. There were no withdrawals.	Prevalence = 39% False-positive rate = 45%	This is the second largest study following the previous one (151) with inclusion of the heterogenous population and 251 patients with neck pain yielding a moderate prevalence of 39% with a false-positive rate of 45%.
Manchikanti et al, 2004 (151) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	The study evaluated 255 consecutive patients presenting with chronic neck pain. Patients suffered with chronic neck pain without disc-related pain with radicular symptoms.	Controlled diagnostic medial branch blocks using 1% lidocaine or 0.25% bupivacaine. 0.5 mL	A positive response was considered at least 80% pain relief with the ability to perform previously painful movements. There were no withdrawals.	Prevalence = 55% False-positive rate = 63%	This is the largest study until 2004 with patients with neck pain, yielding a 55% prevalence rate in the cervical spine, with a false-positive rate of 63%.

Table 6 (cont.). *Studies assessing the accuracy of diagnostic facet joint nerve blocks in cervical and thoracic spine with 50% pain relief.*

Study **Study Characteristics** **Methodological Quality Scoring**	**Participants**	**Intervention(s)** **Injectate Volume**	**Outcome Measures**	**Results**	**Conclusion(s)**
Manchikanti et al, 2002 (150) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	120 consecutive patients presenting with complaints of chronic low back pain and neck pain, in a non-university setting, in one private comprehensive interventional pain management practice were evaluated.	Controlled diagnostic medial branch blocks using 1% lidocaine or 0.25% bupivacaine. 0.5 mL	A positive response was considered at least 80% pain relief with the ability to perform previously painful movements. There were no withdrawals.	Prevalence = 67% False-positive rate = 63%	Prevalence may have been higher due to the nature of the selection criteria. Authors utilized controlled, comparative local anesthetic blocks yielding high false-positive rates.
Manchikanti et al, 2002 (157) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	106 consecutive patients with chronic neck pain of various origins were included. Patients must have had pain for at least 6 months and also have failed conservative management without any evidence of radiculitis or disc herniation.	Controlled diagnostic medial branch blocks using 1% lidocaine or 0.25% bupivacaine. 0.5 mL	A positive response was considered at least 75% reduction of pain with the ability to perform previously painful movements. There were no withdrawals.	Prevalence = 60% False-positive rate = 40%	This is the only study outside the group of Australians evaluating the prevalence of cervical facet joint pain in chronic neck pain of heterogenous origin yielding a prevalence of 60% with controlled diagnostic blocks and a false-positive rate of 40%.
Speldewinde et al, 2001 (158) Retrospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	97 patients with chronic neck pain undergoing diagnostic cervical medial branch blocks from 1994 to 1997 were evaluated by 3 independent rehabilitation physicians.	Controlled, comparative local anesthetic blocks, 2% lignocaine or 0.5% bupivacaine. 0.5 mL	Complete pain relief (100%) was the criterion standard.	Prevalence = 36%	The authors utilized 100% pain relief as the criterion standard with controlled diagnostic blocks utilizing strict selection criteria in a heterogenous population in a private practice setting in a retrospective evaluation.
Barnsley et al, 1995 (161) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	50 consecutive patients referred to the cervical spine research unit, a tertiary referral unit, in Australia were evaluated. The criteria for inclusion were neck pain of more than 3 months duration following and attributed to a motor vehicle accident, previous assessment.	Medial branch blocks with 2% lidocaine or 0.5% bupivacaine. 0.5 mL	Patients were classified as having a painful cervical zygapophysial joint only if they achieved definite or complete relief of pain (100%) with both anesthetics and a longer duration of pain relief after the use of bupivacaine.	Prevalence = 54%	The study was performed in a highly specialized academic research unit in Australia in patients after whiplash injury.
Lord et al, 1996 (162) Randomized, double-blind, controlled diagnostic blocks Quality Score: QAREL: 9/12	68 consecutive patients referred for chronic neck pain after whiplash were studied in a cervical spine research unit in Australia. The criteria for inclusion were 3 months duration of neck pain after a motor vehicle accident and evaluation by a consultant specialist before referral, and over 18 years of age.	Diagnostic blocks with 2% lidocaine or 0.5% bupivacaine. 0.5 mL	100% pain relief was the criterion standard.	Prevalence = 60%	The study was performed in a highly specialized academic research unit in Australia in patients after whiplash injury.

Table 6 (cont.). *Studies assessing the accuracy of diagnostic facet joint nerve blocks in cervical and thoracic spine with 50% pain relief.*

Study **Study Characteristics** **Methodological Quality Scoring**	**Participants**	**Intervention(s)** **Injectate Volume**	**Outcome Measures**	**Results**	**Conclusion(s)**
Barnsley et al, 1993 (163) Randomized, double-blind, controlled diagnostic blocks Quality Score: QAREL: 9/12	The study evaluated 55 consecutive patients with neck pain of greater than 3 months attributed to a motor vehicle accident, with random allocation.	Medial branch blocks with either 2% lignocaine or 0.5% bupivacaine. 0.5 mL	100% pain relief	False-positive rate = 27%	A well-performed study in a highly research oriented center in patients after whiplash.
THORACIC SPINE					
Manchikanti et al, 2004 (151) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	500 consecutive patients with chronic, non-specific spine pain 72 patients with thoracic pain were evaluated.	Controlled comparative local anesthetic blocks with 1% lidocaine or 0.25% bupivacaine. 0.5 mL	80% pain relief with the ability to perform previously painful movements. The relief with bupivacaine to last longer than lidocaine.	The prevalence of facet joint pain in patients with chronic thoracic spine pain was 42% (95% CI, 30% – 53%). The false-positive rate with single blocks with lidocaine was 55% (95% CI, 39% – 78%) in the thoracic spine.	Facet joints are clinically important spinal pain generators in a significant (42%) proportion of patients with chronic spinal pain, with a false-positive rate of 55%.
Manchikanti et al, 2002 (164) Prospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	46 consecutive patients with chronic midback and upper back pain	Diagnostic facet joint nerve blocks with lidocaine 1% or bupivacaine 0.25%. 0.5 mL	80% pain relief with the ability to perform previously painful movements. The relief with bupivacaine to last longer than lidocaine.	Prevalence = 48% False-positive rate = 58%	Comparative local anesthetic blocks showed the prevalence of facet joint pain to be 48%, with single blocks carrying a false-positive rate of 58%.
Manchukonda et al 2007 (152) Retrospective, controlled diagnostic blocks Quality Score: QAREL: 9/12	500 consecutive patients with chronic facet or zygapophysial joint pain. 65 patients with thoracic pain were evaluated.	Diagnostic blocks with 1% lidocaine or 0.25% bupivacaine. 0.5 mL	80% pain relief with the ability to perform previously painful movements. The relief with bupivacaine to last longer than lidocaine.	Prevalence of facet joint pain was 34% (95% CI, 22% - 47%) in the thoracic pain. The false-positive rate with a single block in the thoracic region was 42%.	Significant prevalence of facet joint pain in chronic spinal pain, with 34% prevalence and 42% false-positive rate.

assessed gender/smoking-related factors (167,173), 5 studies assessed the influence of sedation and opioid exposure (159,175,178-180), 4 studies assessed the influence of diagnostic blocks on therapeutic outcomes (41,42,130,181), and one study assessed the accuracy of cervical facet joint nerve blocks using different injectate volumes (182).

2.4 Analysis of Evidence

An analysis of evidence included prevalence and false-positive rates. However, factors influencing the diagnosis were not analyzed for level of evidence. The studies of prevalence and false-positive rates underwent methodological quality assessment, whereas other studies assessing the factors influencing the diagnosis were not feasible for methodological quality assessments due to significant differences in the quality, even though some were randomized controlled trials of high quality. The evidence was assessed separately based on the region: lumbar, cervical, or thoracic. Table 8 shows the data of prevalence and false-positive rate of facet joint pain in the lumbar spine; Table 9 shows the data of prevalence and false-positive rates of facet joint pain by diagnostic blocks in the cervical spine; and Table 10

Table 7. *Assessment of factors influencing prevalence and false-positive rates of facet joint pain in lumbar, cervical, and thoracic regions.*

Study	Methods and Assessment Criteria	Results	Comments
Influence of Age			
Manchikanti et al, 2008 (171) Lumbar and cervical Age-related prevalence of facet joint involvement in chronic low back and neck pain was evaluated in a retrospective assessment	A total of 424 patients were divided into 6 groups based upon age with Group I aged 18 - 30 years, Group II aged 31-40 years, Group III aged 41-50 years, Group IV aged 51-60 years, Group V aged 61-70 years, and Group VI greater than 70 years of age.	The prevalence of cervical facet joint-related pain was the lowest (33%) in Group VI and highest (42%) in Group I with overall prevalence of 39%. False-positive rates for cervical facet joint blocks ranged from 39% (Group III) to 58% (Group V) with an overall false-positive rate of 45%. The prevalence of facet joint involvement in lumbar spinal pain ranged from 18% (in Group II) to 44% (in Group IV), with significant differences noted when Group II and Group III were compared to other groups and with higher rates in Group V with overall prevalence of 27%. False-positive rates were highest in patients aged 61 to 70 years (64%) and lowest in patients aged 51 to 60 years (30%) with overall false-positive rate of 45%.	The first age-related prevalence study with controlled comparative local anesthetic blocks in a heterogenous population in a private practice setting assessing in a large proportion of patients, both cervical and lumbar spine facet joint pain.
DePalma et al, 2012 (167) Lumbar Assessment of relationships between age, gender, and body mass index and source of chronic low back pain	153 patients with chronic low back pain were evaluated in a retrospective evaluation with dual diagnostic blocks with 1% lidocaine and 0.5% bupivacaine with concordant relief of 75% of the criterion standard.	Age, gender, and body mass index were each significantly associated with the source of chronic low back pain. Facet joint pain was the most likely source of chronic low back pain for male patients who were approximately 54 years of age (30% - 54%) whereas, for female patients who were 65 years facet joint pain was most likely (46% - 57%).	This multivariate analysis of the relationships between age, gender, and body mass index and the source of chronic low back pain shows all factors are significantly associated with the source of chronic low back pain with findings suggesting a significant relationship among these factors. However, facet joint pain was more prevalent in females with increased BMI.
Manchikanti et al, 2001 (176) Lumbar Assessment of the role of facet joints in chronic low back pain in the elderly	Controlled comparative prevalence study in 100 patients, in which 50 patients below age of 65 and 50 patients aged 65 or over were assessed. Controlled diagnostic blocks were performed with 75% pain relief with ability to perform previously painful movements utilized as the criterion standard.	The prevalence of facet joint pain was determined as 30% in the adults below the age of 65 and 52% in the elderly above the age of 65 with false-positive rates of 26% and 33%, respectively.	This study showed higher prevalence of facet joint pain in the elderly compared to the younger age group in contrast to the latest study by Manchikanti et al which showed no differences (147).
Influence of Clinical Assessment			
Revel et al, 1992, 1998 (44,45) Lumbar Randomized controlled trials to identify facet joint blocks for low back pain to identify predictors of a good response for facet joint pain for low back pain and capacity of the clinical picture to characterize low back pain relieved by facet joint anesthesia.	In the preliminary study, they included 51 patients with identification of multiple variables such as older age, absence of exacerbation by coughing, relief when recumbent, absence of exacerbation by forward flexion, and when raising from this flexion, absence of worsening by hyperextension, and extension-rotation. In the second study, they tested these criteria to identify patients with painful facet joints in 80 patients utilizing diagnostic facet joint injections with injection of either 2% lidocaine or 1mL of sodium chloride solution with intraarticular of 1 mL of 2% lidocaine or 1 mL of sodium chloride solution in a randomized fashion with 75% pain relief as the criterion standard.	Following the first study, they identified what they called Revel et al's (44,45) criteria. In the second study, they tested these results. They showed that a set of 5 clinical characteristics may be utilized to select low back pain patients based on the response to local anesthetic injections. They showed that there was a significant interaction between clinical group and injection effect in patients with back pain. The presence of 5 among 7 variables, namely, age greater than 65 years and pain that was not exacerbated by coughing, not worsened by hyperextension, not worsened by forward flexion, not worsened when rising from flexion, not worsened by extension-rotation, and well relieved by recumbency with inclusion of the last item always, distinguished 92% of the patients responding to local anesthetic injections with a positive diagnosis, whereas 80% of those not responding when they had no such signs.	This study attempted to identify certain clinical features as predictors of facet joint pain which can be confirmed by local anesthetic blocks. While they show the importance of local anesthetic blocks, there is only a single study discussing Revel et al's (44,45) criteria. These criteria have been shown to be unreliable in other studies (58,60).

Table 7 (cont.). *Assessment of factors influencing prevalence and false-positive rates of facet joint pain in lumbar, cervical, and thoracic regions.*

Study	Methods and Assessment Criteria	Results	Comments
Laslett et al, 2004 (60) Lumbar Lumbar facet joint nerve blocks to test Revel et al's (44,45) model as a screening test in a prospective, blinded, concurrent reference standard related validity design.	In this study, the authors utilized controlled diagnostic blocks with a 75% or more reduction in pain as the criterion standard utilizing either 2% lidocaine or 0.75% bupivacaine, either into the target joint or the facet joint nerves. Patients were selected based on the clinical criteria described by Revel e tal (44,45). 151 chronic low back pain patients were evaluated.	The results of this study were in stark contrast to those of Revel et al (44,45) with low sensitivity and high specificity. The authors showed that 2 items, no pain with cough and sneezing and no exacerbation of pain rising from flexion approached statistical significance in a relation to reduction in pain after facet joint blocks. The authors concluded that neither strategy utilizing Revel et al's (44,45) criteria is suitable as a clinical device for screening of facet joint pain. The authors also concluded that these criteria cannot be considered diagnostic of painful lumbar facet joints. They also concluded that only placebo-controlled or dual controlled diagnostic blocks will be able to diagnose the source of low back pain from facet joints.	This study disproved the hypothesis by Revel et al's (44,45) criteria of 5 salient identifying predictors. Further, this study also emphasized the value of dual diagnostic blocks utilizing either placebo or 2 separate local anesthetics.
Manchikanti et al , 2000 (58) Lumbar, cervical and thoracic A prospective evaluation of the ability of clinical picture to characterize pain from facet joints.	In this study, the authors evaluated 200 patients with chronic low back pain utilizing controlled comparative local anesthetic blocks with 1% lidocaine or 0.25% bupivacaine. They compared the results of the blocks with Revel et al's (44,45) criteria with age, pain well relieved in supine position, absence of pain exacerbation by coughing, absence of pain exacerbation by forward flexion, absence of pain exacerbation by deflexion, absence of pain exacerbation by hyperextension, and absence of pain exacerbation by extension-rotation, and traumatic onset of pain.	In assessment of 200 patients, this study showed lack of correlation between Revel et al's (44,45) criteria and positive diagnosis by controlled diagnostic blocks. The authors concluded that the history, clinical features, and radiological features are of no significance or assistance in making the diagnosis of facet joint pain with certainty.	This study shows the value of controlled diagnostic value and lack of correlation with Revel et al's (44,45) criteria with similar results presented in the study by Laslett et al (60).
Schwarzer et al, 1995 (56) Lumbar A prospective cross-sectional analytic study to assess whether the presence or absence of pain originating from the lumbar facet joint correlates with changes seen on computed tomography.	The authors evaluated 57 patients with placebo injections or intraarticular injections. The patients also underwent computed tomography. The facet joints of all images were scored by multiple independent masked radiologists.	The results of this study showed there was poor interobserver agreement using total joint scores for all 3 assessments. There was no correlation between the positive diagnostic blocks and computed tomographic findings. The authors concluded that computed tomography has no place in the diagnosis of lumbar facet joint pain.	This study clearly shows lack of correlation between radiologic assessment and facet joint pain.
Young et al, 2003 (46) Lumbar In a prospective, criterion-related concurrent validity study performed at a private radiology practice specializing in spinal diagnostics in the United States, the authors attempted to identify significant components of a clinical examination that are associated with symptomatic facet joints, along with discs and sacroiliac joints.	The authors studied 120 patients with chronic lumbar or lumbopelvic pain in a private radiology practice with clinical examination by a physical therapist and injection procedures including lumbar discography, lumbar facet joint injections, or sacroiliac joint injections as requested by the referring physician or if deemed indicated by the radiologist. A single diagnostic block was performed with 80% pain relief as the criterion standard.	They failed to identify a significant relationship with clinical characteristics for lumbar facet joint pain, even though they were able to identify centralization for discogenic pain and 3 or more positive pain provocation tests for sacroiliac joint pain. The authors identified that absence of pain when rising from sitting as an indicator for lumbar facet joint pain. T	The authors identified absence of pain when rising from sitting as indicator of lumbar facet joint pain.

Table 7 (cont.). *Assessment of factors influencing prevalence and false-positive rates of facet joint pain in lumbar, cervical, and thoracic regions.*

Study	Methods and Assessment Criteria	Results	Comments
Laslett et al , 2006 (59) Lumbar A prospective blinded study with a secondary analysis to seek evidence of variables potentially valuable as predictors of screening for zygapophysial joint block outcomes.	In this subgroup analysis, 151 chronic low back pain patients were assessed with controlled diagnostic blocks utilizing either lidocaine 2% or bupivacaine 0.75% with 75% to 95% or more pain reduction as the criterion standard. The authors correlated various factors including pain drawings, questionnaires, and a clinical examination before screening lumbar facet joint nerve blocks.	The results showed that at the 75% pain reduction standard, 24.5% responded to screening facet joint nerve blocks and 10.8% responded at the 95% standard. They also showed that there were no variables which were useful predictors of facet joint pain with 90% pain reduction of less than 90%. They also showed that 7 clinical findings were associated with 95% pain reduction after blocks. They showed 5 useful clinical predictor rules for ruling out a 95% pain reduction with 100% sensitivity and one clinical prediction rule had a likelihood ratio of 9.7, which produced a 5-fold improvement in post test probability. They concluded that a negative extension rotation test, the centralization phenomenon, and 4 clinical predictor rules effectively rule out pain ablation after screening zygapophysial joint block.	The results are inapplicable clinically as it demands 95% pain reduction after diagnostic blocks. However, for those utilizing 95% or higher pain relief for diagnostic purposes, the results are useful.
Influence of Psychological Factors			
Manchikanti et al, 2008 (165) Cervical, thoracic, and lumbar Assessment of influence of psychological variables on the diagnosis of facet joint involvement in spinal pain of chronic neck, low back, and thoracic pain	A total of 438 patients undergoing controlled comparative local anesthetic blocks were included in the study. Patients were allocated based on the psychological profile. Primary groups consisted of patients with major depression, generalized anxiety disorder, and somatization disorder.	The prevalence of facet joint pain in chronic spinal pain ranged from 25% to 40% in patients without psychopathology, whereas it ranged from 28% to 43% in patients with a positive diagnosis of major depression, generalized anxiety disorder, and somatization disorder, compared to 23% to 39% in patients with a negative diagnosis. Regional facet joint pain prevalence and false-positive rates were higher in the cervical region in patients with major depression. In the lumbar and thoracic regions, no significant differences were noted.	The study included a large proportion of patients with controlled comparative local anesthetic blocks in a private practice setting. A significant proportion of patients suffered with either a single or multiple psychological disorders. Surprisingly, the only differences observed were in the cervical region with no significant differences observed in thoracic and lumbar regions based on the psychological diagnosis or multiple diagnoses, or a combination of multiple diagnoses.
Wasan et al, 2009 (166) Lumbar and cervical Evaluation of influence of psychopathology to predict the outcome of medial branch blocks with corticosteroid injection for chronic axial low back or neck pain	86 patients for chronic axial low back or cervical pain in a prospective cohort study were classified into low psychopathology group, moderate psychopathology group, or high psychopathology group. Diagnostic blocks were performed utilizing facet joint nerve blocks with methylprednisolone 20 to 30 mg and 0.25% bupivacaine with a total volume of 1 to 1.25 mL injection per level.	The low psychopathology group reported a mean 23% improvement in pain at one month while the high psychopathology group reported a mean worsening of -5.8% of pain. 45% of low group had a least 30% improvement in pain versus 10% in the high group.	This is poorly performed flawed evaluation with inappropriate methodology.
Influence of Body Mass Index			
Manchikanti et al, 2001 (177) Lumbar Assessment of the role of obesity in chronic low back pain.	Authors evaluated 100 patients with low back pain. Patients were divided into 2 groups, Group I was normal weight and Group II was obese. Facet joints were investigated with diagnostic blocks using lidocaine 1% initially followed by bupivacaine 0.25%, at least 2 weeks apart. A definite response was defined as relief of at least 75% in the symptomatic area.	The results showed that the prevalence rate of facet joint pain in chronic low back pain in Group I or non-obese patients was 36%, in contrast to 40% in Group II, or the obese patient group, with no significant differences among the 2 groups. The study also showed a false-positive rate of 39% in the total sample, or 44% in Group I non-obese patients and 33% in Group II, or obese patients.	This study showed the prevalence of lumbar facet joint pain of 40% in obese patients and 36% in patients of normal weight with a false-positive rate of 33% in obese patients and 44% in non-obese patients is similar to the results of multiple previous studies concluding that facet joint pain is a common occurrence in obese patients; however, the incidence of facet joint mediated pain is similar in obese patients and non-obese patients.

Table 7 (cont.). *Assessment of factors influencing prevalence and false-positive rates of facet joint pain in lumbar, cervical, and thoracic regions.*

Study	Methods and Assessment Criteria	Results	Comments
DePalma et al, 2012 (167) Lumbar Assessment of relationships between age, gender, and body mass index and source of chronic low back pain	153 patients with chronic low back pain were evaluated in a retrospective evaluation with dual diagnostic blocks with 1% lidocaine and 0.5% bupivacaine with concordant relief of 75% of the criterion standard.	Body mass index was associated with significant increases in the prevalence of facet joint pain in female patients. Facet joint pain was the most likely source of chronic low back pain for men who were approximately 54 years of age (30% - 54%) , regardless of BMI, whereas, for women patients who were 65 years old, facet joint pain was most likely 46% - 57%.	Based on this study it appears that obese women may have a higher prevalence of facet joint pain.
Influence of Surgery			
Manchikanti et al, 2007 (153) Lumbar Assessment of facet joint pain in post lumbar surgery syndrome	A total of 117 consecutive patients with chronic, nonspecific low back pain, after lumbar surgical intervention(s) were evaluated with controlled, comparative local anesthetic blocks.	The prevalence of lumbar facet joint pain in patients with recurrent pain after various surgical intervention(s) was 16% (95% confidence interval, 9% - 23%). The false-positive rate with a single block with lidocaine was 49%.	This study showed prevalence of lumbar facet joint pain in patients after surgical interventions of 16% with a false-positive rate of 49% with a single block.
DePalma et al, 2011 (168) Lumbar Evaluation of etiology of chronic low back pain in patients having undergone lumbar fusion	A total of 28 fusion cases identified from 170 low back pain patients undergoing diagnostic procedures were assessed. Controlled diagnostic blocks were performed.	After 28 fusion cases, 5 patients were identified with zygapophysial pain with a prevalence of facet joint pain of approximately 18%.	The results showed that patients even after lumbar fusion have persistent low back pain secondary to facet joint involvement in approximately 18% of the patients. This is similar to other reports (59).
DePalma et al, 2012 (169) Lumbar Evaluation of the source of chronic low back pain based on the history of surgical discectomy.	158 patients underwent dual diagnostic blocks with 1% lidocaine and 0.5% bupivacaine with concordant relief of 75% of the criterion standard. A total of 158 patients were evaluated.	The study showed facet joint pain in 18.2% of the patients whereas it was 32.6% of the patients in patients without surgical intervention. However, there were only 2 patients positive in patients with surgical discectomy.	Results show lower prevalence in patients with surgical discectomy; however, the sample size was extremely small.
Manchikanti et al, 2001 (170) Lumbar Assessment of the role of facet joint pain in post-surgery syndrome	This prospective, randomized, controlled comparative evaluation was performed to determine the prevalence of facet joint pain in persistent low back pain in postlumbar laminectomy patients with a comparative non-surgical group. 100 patients with 50 patients in each group were randomly assigned with group I consisting of 50 patients without history of previous surgery and group II consisting of 50 patients with history of previous surgery.	Results showed that the prevalence of facet joint mediated pain in non-surgical patients was 44% compared to 32% in post-surgical patients determined by comparative controlled local anesthetic blocks utilizing lidocaine and bupivacaine. This study also showed a false-positive rate of 36% in the non-surgical group and 24% in the post-surgical group. In conclusion, this study shows that facet joint mediated symptomatology in chronic low back pain is prevalent, both in non-surgical as well as post-surgical patients even though the prevalence was somewhat higher in the non-surgical group compared to post-surgical group.	There was a lower prevalence of facet joint pain in patients after surgical interventions.
Manchikanti et al, 2008 (174) Cervical Retrospective evaluation in post cervical surgery syndrome	251 consecutive patients with persistent neck pain requiring diagnostic facet joint nerve blocks were evaluated. There were 45 patients post surgery and 206 patients without surgery with chronic persistent neck pain of at least 3 months duration after failure of conservative management	Without surgery: Prevalence = 39% False-positive rate = 43% Postsurgery: Prevalence = 36% False-positive rate = 50%	This is the only study evaluating the differences in prevalence following surgical intervention. Even though this is a retrospective evaluation, it utilized controlled, comparative local anesthetic blocks in a practical setting.

Table 7 (cont.). *Assessment of factors influencing prevalence and false-positive rates of facet joint pain in lumbar, cervical, and thoracic regions.*

Study	Methods and Assessment Criteria	Results	Comments
Klessinger, 2013 (172) Lumbar Retrospective practice audit	Medial branch blocks were performed using local anesthetic and bupivacaine for the first injection in 120 patients. They also tested in patients with positive response, but recurrence of pain with second diagnostic block utilizing bupivacaine 0.25%. Patients with persistent back pain after surgery were tested with repeated medial branch blocks. Those patients who consistently report at least 80% pain relief underwent radiofrequency neurotomy. A successful outcome was defined as at least 50% pain reduction enduring for 6 months.	479 patients who underwent microsurgical lumbar disc operations, persistent axial back pain occurred in 120, of whom 34 had positive responses to diagnostic blocks and were treated with radiofrequency neurotomy. Twenty patients (58.8%) achieved at least 50% reduction in pain for a minimum of 6 months.	This study shows prevalence of zygapophysial joint pain in post-lumbar surgery syndrome as 7%. They also treated the procedure with approximately 60% improvement with radiofrequency neurotomy which also confirms the diagnosis. The disadvantages include this is a retrospective assessment. Demographic features did not show the type of surgery these patients have had, including the type of fusion and the issues related to the access to the medial branches, specifically with radiofrequency neurotomy
Influence of Gender/Smoking			
DePalma et al, 2012 (167) Lumbar Assessment of relationships between age, gender, and body mass index and source of chronic low back pain	153 patients with chronic low back pain were evaluated in a retrospective evaluation with dual diagnostic blocks with 1% lidocaine and 0.5% bupivacaine with concordant relief of 75% of the criterion standard.	These findings suggest a significant relationship among gender and chronic low back pain. Facet joint pain is more prevalent in females with increased body mass index.	Based on this study it appears that women with higher body mass index may have higher prevalence of facet joint pain.
Manchikanti et al, 2002 (173) Lumbar Evaluation of the influence of gender, occupational injury, and smoking on prevalence of facet joint pain	320 patients were evaluated with controlled diagnostic blocks performed with 75% pain relief with the ability to perform previously painful movements utilized as the criterion standard.	Facet joint pain was present in 38% of men compared to 43% of women. Smokers had prevalence of 43% compared to nonsmokers of 41% in heavy smokers. Patients with occupational injury reported 28% of prevalence of facet joint pain compared to 44% with patients with gradual onset without injury. False-positive rates varied from 28% to 46%.	The study showed the prevalence of facet joint pain to be less in men. There were no differences based on smoking.
Influence of Sedation and Opioid Exposure			
Manchikanti et al, 2004 (178) Lumbar Assessment of the effect of sedation as a confounding factor in the diagnostic validity of lumbar facet joint pain	180 patients with confirmed diagnosis of facet joint pain following controlled comparative local anesthetic blocks were injected intravenously with sodium chloride solution, midazolam, or fentanyl.	Pain relief of 80% was noted in 2% of the patients in sodium chloride group, 5% of the patients in midazolam group, and 7% of the patients receiving fentanyl. However, pain relief of 50% or greater was noted in 7% of the patients in sodium chloride group, 5% of the patients in midazolam group, and 13% of the patients receiving fentanyl.	Overall there was no significant difference with placebo response with either sodium chloride solution, midazolam, or fentanyl intravenous injections. The administration of sedation with midazolam or fentanyl may be a confounding factor, specifically if 50% relief is used as a criterion standard.
Manchikanti et al, 2006 (179) Lumbar and cervical Assessment of placebo and nocebo effects of perioperative administration of sedatives and opioids in patients with facet joint pain. Randomized, double-blind, placebo control	A total of 360 patients were evaluated in this randomized, controlled trial on validity of facet joint nerve blocks in patients suffering a combination of lumbar and cervical facet joint pain.	Overall 50% of the patients in the placebo group and 100% of the patients in the midazolam and fentanyl groups were relaxed or sedated. Greater than 80% relief was observed in 5% of the patients in the placebo group, 10% in the midazolam group, and 10% in the fentanyl group. Greater than 50% relief was observed in 5% in the placebo group, 15% in the midazolam group, and 15% in the fentanyl group	This study is unique in that it evaluated both cervical and lumbar facet joint pain with no significant difference noted in the diagnostic validity whether midazolam or fentanyl is utilized with 80% as the criterion standard. With 50% pain relief as the criterion standard, 15% of the patients in the cervical region reported pain relief.

Table 7 (cont.). *Assessment of factors influencing prevalence and false-positive rates of facet joint pain in lumbar, cervical, and thoracic regions.*

Study	Methods and Assessment Criteria	Results	Comments
Manchikanti et al, 2005 (180) Lumbar and cervical Effect of placebo and nocebo	This study evaluated the role of placebo and nocebo effects of perioperative administration of sedatives and opioids in interventional pain management in 360 patients, 180 patients with chronic low back pain, in a placebo controlled randomized, double-blind evaluation.	Between 13% and 30% of all patients across all 3 groups of the study, rated their pain relief following injection as better than their previous experience. A small proportion, 3% to 8% of patients in all 3 groups rated their experience following injection as worse than their previous experience.	This study shows it is not only placebo effect that influences the patients experience, but also the nocebo effect even when opioid and benzodiazepine are used.
Manchikanti et al, 2004 (175) Cervical Randomized, double-blind, placebo control	The study was undertaken in an interventional pain management practice with inclusion of 180 patients randomized into 3 groups. All patients suffered with neck pain and have undergone diagnostic and therapeutic facet joint nerve blocks.	≥ 80% pain relief Placebo = 5% Midazolam = 8% Fentanyl = 8% Pain relief of 50% to 79% Sodium chloride solution = 8% Midazolam = 13% Fentanyl = 27%	This study showed that when higher relief (80%) is utilized, the false-positive rate of diagnostic cervical facet joint nerve blocks is extremely low with 8% in midazolam and fentanyl groups compared to 5% in the placebo group At 50% to 79% pain relief there was a higher proportion with 8%, 13%, and 27% with positive response. The advantages of this study are practical setting in patients already have been diagnosed with facet joint pain.
Manchikanti et al, 2008 (159) Cervical, thoracic, and lumbar Retrospective	Data were evaluated from 438 patients with chronic spinal pain who underwent diagnostic facet joint nerve blocks based on the level of opioid use with no opioid use, low opioid use, moderate opioid use, and high opioid use.	No opioid use: Prevalence = 33% False-positive rate = 53% Heavy opioid use: Prevalence = 37% to 53% False-positive rate =38%	This study evaluated the influence of prior opioid exposure on diagnostic facet joint nerve blocks. This appears to be the first study performed in a large proportion of patients in a private practice setting with controlled, comparative local anesthetic blocks
Influence of Diagnostic Blocks on Therapeutic Outcomes			
Pampati et al, 2009 (41) Lumbar Diagnostic validity study	Authors evaluated 152 patients diagnosed with lumbar facet joint pain utilizing controlled comparative local anesthetic blocks, with lidocaine 1% or bupivacaine 0.25% with concordant relief with criterion standard of 80%, the accuracy of diagnostic lumbar facet joint nerve blocks. Assessment was carried out at a 2 year follow-up.	At the end one year, 93% of the patients and at the end of 2 years 89.5% of the patients were considered to have lumbar facet joint pain.	Controlled comparative local anesthetic blocks with 80% pain relief showed validity.
Cohen et al, 2010 (130) Lumbar Evaluation of the role of diagnostic blocks without any diagnostic blocks, with a single diagnostic block, or dual diagnostic block	Authors evaluated 151 patients with suspected lumbar facet joint pain for radiofrequency neurotomy. Group I was treated with radiofrequency denervation without diagnostic blocks, Group II with a positive response for a single diagnostic block with 50% relief, and Group III underwent radiofrequency neurotomy in patients who were positive with controlled comparative local anesthetic blocks with a 50% relief of criterion standard.	In "0"group, 17 patients (33%) obtained a successful outcome at 3 months versus 8 patients (16%) in "1" and "2" group (22%) patients in group "2". Denervation success rates in groups 0, 1, and 2 were 33, 39, and 64%, respectively.	This study showed clearly that dual diagnostic blocks were superior to either no diagnostic block or a single diagnostic block, despite miscalculation of cost effectiveness.

Table 7 (cont.). *Assessment of factors influencing prevalence and false-positive rates of facet joint pain in lumbar, cervical, and thoracic regions.*

Study	Methods and Assessment Criteria	Results	Comments
Manchikanti et al, 2010 (42) Lumbar Assessment of the accuracy of diagnostic lumbar facet joint nerve blocks with either 50% relief or 80% relief as the criterion standard with controlled comparative local anesthetic blocks	Controlled comparative local anesthetic blocks were performed with lidocaine, bupivacaine, with either 50% to 79% relief or over 80% relief as the criterion standard with ability to perform previously painful movements.	At the end of one year, the diagnosis was confirmed in 75% of the group with 50% relief, whereas it was 93% in the group with 80% relief. At the end of 2-year follow-up, the diagnosis of lumbar facet joint pain was sustained in 51% of the patients in the group with 50% relief, whereas it was sustained in 89.5% of the patients with 80% relief.	Application of 80% relief with controlled comparative local anesthetic blocks provides a robust diagnostic criteria.
Manchikanti et al, 2003 (181) Lumbar Evaluation of the accuracy of diagnostic facet joint nerve blocks with a long-term follow-up	The diagnosis was established with dual blocks with 80% pain relief with ability to perform previously painful movements.	85% of the patients available for follow-up withstood the diagnosis of facet joint pain at the end of 2 years, whereas this proportion decreased to 75% if all the patients in the study were included in the intent-to-treat analysis.	The study shows that diagnostic lumbar medial branch blocks are valid and the diagnosis of facet joint pain is sustainable after 2 years.
Miscellaneous (Volume of Local Anesthetic)			
Cohen et al, 2010 (182) Cervical Randomized	24 patients with chronic neck pain were allocated to receive cervical medial branch blocks. Patients were selected with predominance of axial cervical pain for more than 3 months, with failure to respond to conservative therapy, and asymmetry in laterality.	Prevalence = 55% with low volume and 25% with high volume.	A very small proportion of patients were included with 12 patients in each group. The results are perplexing in that volume spread and the specificity of the blocks had no relevance to positive response.

shows the data of prevalence and false-positive rates of facet joint pain by diagnostic blocks in the thoracic spine.

2.4.1 Lumbar Facet Joint Pain

Table 8 shows the data of prevalence and false-positive rate of facet joint pain in the lumbar spine. There were a total of 17 studies assessing the prevalence of lumbar facet joint pain, with single blocks in one study (43) and dual blocks in 16 studies (42,54,55,57,58,141-154,176,177). Only one study (43) utilizing 90% pain relief as the criterion standard showed 48% prevalence with a single block in 100 patients studied.

Controlled diagnostic blocks utilized 50% relief, 75% relief, or 80% relief or greater as the criterion standard. The 3 studies of prevalence utilizing 50% pain relief as the criterion standard were of high quality, including over 400 patients and showing variable results (42,54,57). The first 2 studies performed by Schwarzer et al (54,57) showed variable prevalence rates based on the country and the population studied with 15% (54) and 40% with Australian study performed with intraarticular injection of saline (57), with a false-positive rate of 38% (55) in a third study in the population in the United States. Consequently, the evidence for 50% pain relief as the criterion standard when performed in certain populations appears to be high; however, another study following these pioneering studies with a large number of patients showed a high prevalence of 61% with a false-positive rate of 17% (42). Thus, the evidence for 50% pain relief with controlled diagnostic blocks is Level II, due to variable evidence despite 3 high quality studies due to internal inconsistency.

Six studies were performed utilizing ≥ 75% pain relief as the criterion standard (58,147,148,154,176,177) with 856 patients in a heterogenous population with prevalence ranging from 30% to 45%, and a false-positive rate of 25% to 44%. These results are also similar to 80% pain relief as the criterion standard studied in 7 studies (42,146,149-153) in 1,848 patients that showed a prevalence ranging from 16% to 41% in a heterogenous population. However, utilizing controlled diagnostic blocks, the prevalence was shown to be somewhat

Table 8. *Data of prevalence and false-positive rate of facet joint pain by diagnostic blocks in the lumbar spine.*

Study	Methodological Criteria Score	Number of Patients	Criterion Standard of Percent Relief	Prevalence Estimates with 95% Confidence Intervals	False-Positive Rate with 95% Confidence Intervals
Single Blocks					
Pang et al (43)	8/12	100	90%	48%	NA
Controlled Blocks					
Schwarzer et al (54,55)	9/12	176	≥ 50%	15% (10% - 20%)	38% (95% CI, 30%-46%)
Schwarzer et al (57)	9/12	57 of 63	≥ 50%	40% (27% - 53%)	NA
Manchikanti et al (42)	9/12	181 491	≥ 50% ≥ 80%	61% (53% - 81%) 31% (26% - 35%)	17% (95% CI, 10%-24%) 42% (95% CI, 35%-50%)
Manchikanti et al (58)	9/12	200	≥ 75%	42% (35% - 42%)	37% (95% CI, 32%-42%)
DePalma et al (154)	9/12	156	≥ 75%	31% (24% - 38%)	NA
Manchikanti et al (176)	9/12	100 I: (<65 years) = 50 II:(>65 years) = 50	≥ 75%	I: 30% (17% - 43%) II: 52% (38% - 66%)	I: 26% (95% CI, 11%-40%) II: 33% (95% CI, 14%-35%)
Manchikanti et al (177)	9/12	100 I: (BMI<30) = 50 II: (BMI >30) = 50	≥ 75%	I: 36% (22%, 50%) II: 40% (26%, 54%)	I: 44% (95% CI, 26%-61%) II: 33% (95% CI, 16%-51%)
Manchikanti et al (147)	9/12	120	≥ 75%	45% (36% - 54%)	41% (95% CI, 29%-53%)
Manchikanti et al (148)	9/12	180	≥ 75%	36% (29% - 43%)	25% (95% CI, 21%-39%)
Manchikanti et al (146)	9/12	120	≥ 80%	40% (31%–49%)	47% (95% CI, 35%-59%)
Manchikanti et al (149)	9/12	300 I: Single region II: Multiple regions	≥80%	I: 21% (14%-27%) II: 41% (33%-49%)	I: 17% (95% CI, 10%-24%) II: 27% (95% CI, 18%-36%)
Manchikanti et al (150)	9/12	120	≥ 80%	40% (31% - 49%)	30% (95% CI, 20%-40%)
Manchikanti et al (151)	9/12	397	≥ 80%	31% (27% - 36%)	27% (95% CI, 22%-32%)
Manchukonda et al (152)	9/12	303	≥ 80%	27% (22% - 33%)	45% (95% CI, 36%-53%)
Manchikanti et al (153)	9/12	117	≥ 80%	16% (9% – 23%)	49% (95% CI, 39%–59%)

NA = not applicable; CI = confidence interval

different in specific populations with 30% in patients below the age of 65 years and 52% in elderly patients over the age of 65 (176), 36% in nonobese patients and 40% in obese patients (177), and 16% in postsurgery patients (153). Thus, based on 7 controlled diagnostic studies with 80% or more pain relief and 6 studies with 75% or more pain relief as the criterion standard, the evidence is Level I for the diagnosis of lumbar facet joint pain with controlled diagnostic blocks.

2.4.2 Cervical Facet Joint Pain

Table 9 shows the false-positive rates of cervical facet joint nerve blocks in the assessment of facet joint pain in the neck for a total of 11 studies (36,150-152,155,157,158,160-163) with one of them being a single block study (160). Consequently, a total of 10 studies assessed prevalence and/or false-positive rates of facet joint pain with controlled diagnostic blocks in almost 1,200 patients with one study utilizing 75% pain

Table 9. *Data of prevalence and false-positive rate of facet joint pain by diagnostic blocks in the cervical spine.*

Study	Methodological Criteria Score	Number of Patients	Criterion Standard of Percent Relief	Prevalence Estimates with 95% Confidence Intervals	False-Positive Rate with 95% Confidence Intervals
Single Blocks					
Aprill & Bogduk (160)	5/12	318	≥ 50%	25%-63%	NA
Controlled Blocks					
Manchikanti et al (157)	9/12	106	≥ 75%	60% % (95% CI, 50%, 70%)	40% % (95% CI, 34%-46%)
Manchukonda et al (152)	9/12	251 of 500	≥ 80%	39% (95% CI, 32%, 45%)	45% (95% CI, 37%-52%)
Manchikanti et al (151)	9/12	255 of 500	≥ 80%	55% (95% CI, 49%, 61%)	63% (95% CI, 54%-72%)
Manchikanti et al (150)	9/12	120	≥ 80%	67% (95% CI 58% , 75%)	63% (95% CI, 48%-78%)
Barnsley et al (36)	9/12	47	100%	60%	NA
Yin and Bogduk (155)	9/12	143	100%	55% (95% CI, 38%, 62%)	NA
Speldewinde et al (158)	9/12	97	100%	36% (95% CI, 27%, 45%)	NA
Barnsley et al (161)	9/12	50	100%	54% (95% CI, 40%, 68%)	NA
Lord et al (162)	9/12	68	100%	60% (95% CI, 46%, 73%)	NA
Barnsley et al (163)	9/12	55	100%	NA	27% (95% CI, 15%-38%)

NA = not applicable; CI = confidence interval

relief as the criterion standard (157), 3 studies utilizing 80% pain relief as the criterion standard (150-152), and the remaining 6 studies utilizing 100% pain relief as the criterion standard (36,155,158,161-163). The sole single block study (161) was of moderate quality with a prevalence estimate of 25% to 63% in 318 patients.

In reference to controlled diagnostic blocks, only one study (157) assessed the prevalence of cervical facet joint pain in 106 patients utilizing ≥ 75% pain relief as the criterion standard with a prevalence of 60% and false-positive rate of 40% in a heterogenous population in the United States. There were 3 studies utilizing 80% pain relief as the criterion standard (150-152) involving over 626 patients, all of them performed by one group of authors showing a prevalence ranging from 39% to 67% with false-positive rates ranging from 45% to 63%. Among the 6 studies utilizing 100% pain relief as the criterion standard (36,155,158,161-163), only one study was in a heterogenous population in the United States (155), which yielded a prevalence rate of 55%. All other studies with 100% pain relief as the criterion standard were from Australia, with 4 of them from one group of authors (36,161-163) and only one study by other authors (158). One of them was a study on only false-positive rates (163). The prevalence shown by these authors ranged from 55% in the United States to 36% to 60% in Australia. Many of the studies were in patients with whiplash. Thus, the most relevant and recent study was with 251 patients (152) showed a prevalence of 39% with a false-positive rate of 45%. This was also echoed by one Australian study with 97 patients (158) with prevalence of 36%.

Consequently, the evidence for dual blocks with controlled diagnostic blocks of cervical facet joint pain is Level II with multiple studies showing variable prevalence with internal inconsistency ranging from 36% to 67% and false-positive rates ranging from 27% to 63%.

2.4.3 Thoracic Facet Joint Pain

Table 10 shows the data of prevalence and false-positive rates of thoracic facet joint pain by diagnostic blocks from 3 studies by the same group of clinicians (151,152,164) in high quality studies with inclusion of 183 patients with 80% pain relief as the criterion standard with prevalence ranging from 34% to 48% and a false-positive rate of 42% to 58%.

The evidence for the accuracy of thoracic facet joint nerve blocks is Level II based on 3 high quality studies.

3.0 Discussion

This systematic review of the diagnostic accuracy of spinal facet joint nerve blocks in the evaluation of chronic spinal pain without evidence of disc herniation, radiculitis, or sacroiliac joint arthritis after failure of

Table 10. *Data of prevalence and false-positive rate of facet joint pain by diagnostic blocks in the thoracic spine.*

Study	Methodological Criteria Score	Number of Patients	Criterion Standard of Percent Relief	Prevalence Estimates with 95% Confidence Intervals	False-Positive Rate with 95% Confidence Intervals
Controlled Blocks					
Manchikanti et al (164)	9/12	46	≥ 80%	48% (95% CI; 34%-62%)	58% (95% CI, 38%-78%)
Manchikanti et al (151)	9/12	72	≥ 80%	42% (95% CI; 30%-53%)	55% (95% CI, 38%-78%)
Manchukonda et al (152)	9/12	65	≥ 80%	34% (95% CI; 22%-47%)	42% (95% CI, 36%-53%)

NA = Not Available or Not Applicable; CI = Confidence Interval

conservative management utilizing various criteria for diagnosis of facet joint pain with single blocks, as well as controlled diagnostic blocks, shows varying results. The evidence is stronger for lumbar facet joint nerve blocks (Level I), compared to cervical and thoracic facet joint nerve blocks (Level II), in the diagnosis of chronic pain with the use of controlled diagnostic blocks with placebo or comparative local anesthetic blocks and a criterion standard of at least 75% pain relief in the lumbar spine and 80% in the cervical and thoracic spines with the ability to perform previously painful maneuvers. Overall, there were 13 studies utilizing controlled blocks with at least 75% pain relief as the criterion standard in the lumbar spine (42,58,146-154,176,177), 10 studies in the cervical spine with one study with ≥ 75% pain relief as the criterion standard (157) and 9 studies with ≥ 80% pain relief (36,150-152,155,157,158,161-163), and 3 studies in the thoracic spine with 80% pain relief as the criterion standard (151,152,164) with the ability to perform previously painful movements. Significant homogeneity of prevalence in a heterogenous population was evident in the lumbar spine. In contrast, in the cervical spine, even though there were high quality studies with controlled diagnostic blocks and placebo control and many of them were pioneering studies establishing standards, there was a lack of significant homogeneity in the prevalence patterns in a heterogenous population with internal inconsistency, even though significant homogeneity was observed in patients with whiplash. In the thoracic spine, there was significant homogeneity among the studies. However, a disadvantage in the thoracic spine studies is that all the studies were performed by one group of clinicians.

The prevalence of lumbar facet joint pain is 16% to 41% based on a majority of the evidence with a false-positive rate of 25% to 44% with single blocks. In the cervical spine, the prevalence is 36% to 67% with a false-positive rate of 27% to 63%. In the thoracic spine, the prevalence is 34% to 48% with a false-positive rate of 42% to 48%. Overall, the evidence appears to be superior with controlled diagnostic blocks utilizing at least 75% pain relief as the criterion standard. Further, in the lumbar spine, a lower prevalence was demonstrated in post surgery patients with a 16% prevalence rate (153).

The evidence presented here with strict inclusion criteria and methodological quality assessment is similar to some previous assessments (7,22-24), whereas it varies from others (38,48).

In the cervical spine, there were 2 randomized controlled trials (161,162) with one of them utilizing placebo-controlled diagnostic blocks (162) with a prevalence of 54% (161) and 60% (162) in patients after whiplash. In a detailed study, the false-positive rate was also assessed, which was shown to be 27% by the same group of authors (163). These studies utilized samples ranging from 50 to 68 patients. Manchikanti et al (151), in a large study with 255 patients, showed a prevalence of 55%. In a later study which included 251 patients, Manchukonda et al (152) showed a prevalence of 39%. Overall, Manchikanti et al's group performed 2 studies with the largest population involved (150-152,157). In these studies, they showed prevalence to range from 39% to 67% with false-positive rates ranging from 40% to 63%. The study by Yin and Bogduk (155) of 143 patients had a prevalence of 55%. Similarly, in another study, Speldewinde et al (158) showed a 36% prevalence rate in 97 patients.

In the lumbar spine, of 13 high quality studies with a criterion standard of pain relief of 75% or more, 11 studies were performed by the same group of authors (42,146-153,176,177). These authors utilized large populations with over 300 patients in 3 studies. In other studies, the number of patients utilized was 100 or more. Manchikanti et al (151) in 397 patients, Manchukonda et al (152) in 303 patients, and Manchikanti

et al (42) in 491 patients showed an overall prevalence of 27% to 31% in a heterogenous population with a false-positive rate of 27%, 42%, and 45% respectively, whereas in specific populations of post lumbar surgery syndrome, prevalence was shown to be 16% with a false-positive rate of 49%. In a comprehensive assessment, DePalma et al (154) studied 156 patients showing a prevalence of 31% in a heterogenous population in the United States. There was one placebo-controlled and randomized trial in assessing the accuracy of facet joint injections in the lumbar spine. Schwarzer et al (57) injected sodium chloride into the joints, which might not be considered as a pure placebo.

In the thoracic spine, there were 3 high quality studies, all of them performed by one group of authors (151,152,164) showing prevalence ranging from 34% to 48% and a false-positive rate ranging from 42% to 58%. There were no randomized studies in the thoracic spine.

As described above, over the years, multiple manuscripts have been published supporting and opposing the accuracy of diagnostic facet joint nerve blocks (7,36-38,41,115-125,127,130). In contrast to multiple diagnostic tests in medicine, which can be validated using conventional means, with comparison of the results of the test with the results of a criterion standard, either a blood test, a biopsy, or a surgical observation, or at least a feature on imaging (20), diagnostic facet joint nerve blocks and essentially anything related to pain might not be based on a physical standard, biopsy, or an imaging modality. Engel et al (25) described that while diagnostic blocks cannot be validated by conventional means, the opposition is similar to multiple other concepts, such as germ theory, facing philosophical objections which were overcome by multiple postulates established and satisfied. Similar problems have been experienced in the occupational determination of cause and effect such as scrotal or pulmonary malignancy which were regularly rejected on the basis that they were not proven. However, proposal of multiple viewpoints of association should be considered before causation might be claimed based on the criteria proposed by Bradford Hill (183) and Howick et al (184).

Engel et al (25) proposed a set of axiomatic criteria that provided a philosophical basis for the validation of diagnostic blocks. These 8 criteria included plausibility, experiment, target-specificity, effect of the diagnostic blocks, duration of pain relief, consistency, establishment of controls, and finally, replication. They further classified that essential criteria included target-specificity and duration, critical criteria included controls, relative criteria included effect and consistency, and finally, academic criteria included plausibility, experiment, and replication. They also provided scoring for each criteria with a total scoring for each criteria. Even then, some of the theories provided by Engel et al (25) could be problematic, specifically in relation to duration of relief which they mandate must not last any longer than the duration of the action of local anesthetic and placebo controls with randomization.

A true placebo control for nerve blocks has been extremely difficult to achieve and thus far, true placebo-controlled trials of diagnostic accuracy have not been established. The role of placebo and nocebo effects has not been appropriately assessed in interventional pain management settings in general and for diagnostic accuracy studies in particular (180). Placebo and nocebo effects may exert significant effect on diagnostic accuracy. Further, all the studies which have been described utilized flawed designs; they injected sodium chloride solution intraarticularly, which is not amenable to true placebo effect. However, appropriate placebo designs have been developed to assess therapeutic interventions.

Further issues have been observed from those who oppose diagnostic interventions in general, as well as those who oppose any positive clinical trials such as the DARE (132-134,177) often without appropriate analysis and interpretation. Multiple other reviewers also have utilized inappropriate methodology, which led to inappropriate conclusions (38). However, criticism of these inappropriate methodologies (39) has been met with significant resistance with continued inappropriate analysis (38-40,48). Bogduk et al and Carragee et al extensively discussed cervical facet joint nerve blocks' validity (47,49). Cohen et al (185), while not directly assessing the accuracy of diagnostic blocks, improperly evaluated sedation's effect on treatment and the accuracy of outcomes for diagnostic injections in a randomized controlled crossover study. However, they included sacroiliac joint and sympathetic blocks. The flawed design of this trial and inaccurate conclusions and the inability of the authors to correct misimpressions were highlighted in a letter to the editor (186).

Recently, multiple physical diagnostic measures have been proposed (29-33,187). Mainka et al (187) concluded that only true positive findings, were concurrent effusion and/or edema, and positive provocation test results in the same facet joint were discriminate enough between controlled patients and patients with current

low back pain. However, neither effusion and/or edema nor facet joint provocation tests alone are suitable to detect suspected facet joint arthropathy (187). While facet joints with effusion and/or edema and painful facet joints were present significantly more frequently in patients with low back pain, these conditions were also common in control patients (27% vs. 21% and 50% vs. 12%, respectively). However, effusion and/or edema were present in 87% of the patients with low back pain and 75% without low back pain. Hybrid imaging SPECT (single-photon emission computed tomography)/CT was also assessed (29). Hybrid SPECT/CT imaging identified potential pain generators in 92% of cervical spine scans and in 86% of lumbar spine scans. The scan precisely localized SPECT/CT positive facet joint targets in 65% of the referral population and a clinical decision to inject was made in 60% of these cases. However, this type of evaluation with SPECT/CT is expensive, hard to imagine in routine clinical practice, and has not been validated with replication of these findings.

The diagnosis of facet joint pain in the cervical spine has been studied rather extensively recently (29-32). Schneider et al, in multiple manuscripts (30-32), assessed the role of physical examination and clinical tests in patients with cervical facet joint pain. In assessing the screening of patients suitable for diagnostic cervical facet joint blocks and the role of physiotherapists (30), they utilized a combination of findings: physical, manual and psychological assessments called the clinical prediction guide (CPG) and concluded that the results of the patient history, self-report measures, and a physical examination may be helpful toward optimal diagnostic and therapeutic decisions. In the second manuscript, Schneider et al (31), utilizing CPG, as well as diagnostic blocks, showed that a CPG involving the findings of the manual spine examination (MSE), palpation for segmental tenderness (PST), and extension-rotation (ER) test demonstrated a specificity of 84% and a positive likelihood ratio of 4.94. They showed that the sensitivity of the PST and MSE were 94% and 92% respectively. They also showed that negative findings on the PST were associated with a negative likelihood ratio of 0.08. They concluded that MSE, PST, and ER may be useful tests in identifying patients suitable for diagnostic facet joint blocks. In the third manuscript, Schneider et al (32) looked at selected clinical tests that patients referred for diagnostic cervical facet joint blocks underwent to determine intrarater and interrater reliability. In this study, 56 patients were included. They concluded that the standardized clinical test exhibited moderate to substantial reliability in patients with axial neck pain referred for diagnostic facet joint blocks. Further, they indicate that their data justify using these tests as part of a clinical prediction model for screening patients before referring them for diagnostic facet blocks.

In another manuscript, Watson and Drummond (33) assessed head pain referral during examination of the neck in migraine and tension-type headache. They concluded that the data supported the continuum concept of the headache, whereby noxious cervical afferent information is often miscalculated. In this assessment, they mainly stressed atlanto-occipital segments and C2/3 zygapophysial joints. The descriptions by Schneider et al were similar to their descriptions in the past (28). In addition, these techniques are already utilized in selecting patients for diagnostic cervical facet joint nerve blocks. Further, substantial confusion also has been created by some authors not understanding appropriate cost effectiveness assessment, leading to the unfounded conclusion that diagnostic blocks may not be necessary (130,179,180,182) even though the necessity of diagnostic blocks was proven repeatedly to avoid unnecessary facet joint nerve blocks and also significant response for patients who were shown to be negative for facet joint pain to be managed with epidural injections.

Understanding the multiple factors affecting diagnostic accuracy is crucial. Multiple manuscripts have been published assessing multiple factors affecting diagnostic accuracy and also outcomes based on diagnostic accuracy. It is generally conceptualized that facet joint nerve blocks are inherently nonspecific, even when performed precisely with fluoroscopic guidance utilizing low volumes. Multiple confounding factors have been assessed in the literature in reference to spinal pain (41,42,130,153,159,165-182). The influence of age was assessed in 3 studies (167,171,176) with only one of them utilizing patients suffering from cervical facet joint pain (171). Manchikanti et al (171), in assessing 424 patients suffering from either cervical or lumbar facet joint pain, showed the lowest prevalence (33%) to be in patients over 70 years old and the highest in patients aged 18 to 30 years. In contrast, they also showed false-positive rates for cervical facet joint nerve blocks were 39% in the group of patients aged 41 to 50 and 58% in the group of patients aged 61 to 70 with an overall false-positive rate of 45%. However, the results were different in the lumbar spine with the lowest prevalence (18%) in patients aged 31 to 40 years and 44% in patients aged 51 to 60 years.

Two other studies also described age-related influence (167,176). In one study by DePalma et al (167), of 153 patients with controlled diagnostic blocks, the results showed that lumbar facet joint pain was the most likely source of chronic low back pain for men who were approximately 54 years of age, regardless of body mass index. However, for women who were 65 years old, facet joint pain was most likely. Manchikanti et al (176), in an earlier study of 100 patients, showed a significantly higher prevalence of facet joint pain in those over 65 years old. The influence of psychological factors was assessed in 2 studies (165,166). Manchikanti et al (165) assessed 438 patients undergoing controlled comparative local anesthetic blocks for cervical, thoracic, and lumbar facet joint pain. They showed the prevalence of facet joint pain to range from 25% to 40% in those who had no psychopathology; from 28% to 43% in those diagnosed with either major depression, generalized anxiety disorder, or somatization disorder, compared to 23% to 39% in patients with a negative diagnosis. Regional facet joint pain prevalence and false positive rates were higher in the cervical region in patients with major depression. However, no differences were identified in the lumbar and thoracic regions. Wasan et al (166) also assessed the influence of psychological factors in lumbar and cervical facet joint pain; however, the sample size of patients was only 86. The results showed that the low psychopathology group reported a mean 23% improvement in pain at one month, while the high psychopathology group reported worsening of pain. Further, 45% of the low group had at least 30% improvement in pain versus 10% in the high psychopathology group. In this poorly performed assessment with inappropriate methodology, the authors concluded that psychopathology does influence the outcome of medial branch blocks.

The influence of body mass index was assessed in 2 studies (167,177). DePalma et al (167), in studying 153 patients with chronic low back pain, showed that There was a correlation between significant increases in facet joint pain's prevalence and body mass index. However, Manchikanti et al (177) showed a similar prevalence of 36% versus 40% in both groups.

The influence of surgery was assessed in 6 studies in the lumbar spine (153,168-170,172,174), one study on the cervical spine (174), and none on the thoracic spine. Overall, the prevalence of facet joint pain was shown to be lower in patients after surgical interventions in the lumbar spine, a uniform finding in all the studies in the cervical spine. The prevalence in patients without surgery and post surgery was similar as shown by Manchikanti et al (174).

An assessment of the influence of gender and smoking (167,173) showed that women patients may have a higher prevalence of facet joint pain in the lumbar spine. No studies were conducted in the other regions. However, there were no significant differences observed based on a history of smoking (167).

An assessment of the influence of sedation and opioid exposure also yielded different results in the cervical and lumbar spine. All the studies were performed by Manchikanti et al (159,175,178-180). Overall, there was no significant difference in patients who were exposed to opioids prior to undergoing facet joint nerve blocks with a prevalence of 33% and a false-positive rate of 53% in patients without opioid exposure and in those with heavy opioid use, prevalence ranged from 37% to 53% with a false-positive rate of 38% (159). There was no significant influence of benzodiazepines such as midazolam or opioids with 80% pain relief as the criterion standard. However, when 50% relief was used as the criterion standard, fentanyl was a confounding factor in both the lumbar and cervical spines (175,178,179). Manchikanti et al (180) also showed placebo and nocebo effects with not only sodium chloride solution, but also with midazolam, and fentanyl. Finally, the influence of diagnostic blocks on therapeutic outcomes (41,42,130,181,188-196) showed variable results with Pampati et al (41) and Manchikanti et al (42,181) demonstrating the importance of controlled diagnostic blocks with 80% pain relief as the criterion standard with superior outcomes in the lumbar spine, whereas Cohen et al (130) provided contradictory results that we believe were based on flawed assessments. Even though in their study (130) patients receiving dual blocks showed superior outcomes, they concluded that there was no significant difference. Finally, the volume of injectate was studied in the cervical spine by Cohen et al (182) in a small number of patients; however, the results were contradictory to the hypothesis showing a higher prevalence of 55% of facet joint pain when low volume was utilized in contrast to a prevalence of 25% when a high volume was utilized.

Even though the exact source of pain in the facet joints continues to be ambiguous, it has been suggested for decades that arthrosis causes spinal pain, specifically low back pain. It has been postulated that facet joint degeneration with alteration of the motion

associated with disc degeneration and arthritis, may be responsible for facet joint pain (111,112). Proposed pain mechanisms such as capsular stretch, entrapment of synovial villa between the articular surfaces, nerve impingement by osteophytes, and release of multiple inflammatory chemicals, have been postulated to be causes of facet joint pain (114,115-124). With abundant innervation of the facet joints, with presence of free and encapsulated nerve endings and nerves containing substance *P* and calcitonin gene-related peptide (29,36,37,120,121,127,132-143,176), facet joint pain appears to be based on neuroanatomic, neurophysiologic, and biochemical processes. However, studies also have repeatedly shown that facet joint arthritis was not a requirement to experience facet joint pain (7,22-24,34). Further, there also has been evidence linking heavy work and occupational exposure to facet arthritis (51,68,197). As described by Kuslich et al (27), discs, facet joints, and sacroiliac joints amenable to diagnostic blocks have been responsible for low back and lower extremity pain. Manchikanti et al (146) have evaluated the relative contributions of various structures in chronic low back pain of 120 patients with a diagnosis of discogenic pain in 26%, facet joint pain in 40%, and sacroiliac joint pain in 2%. Further, DePalma et al (154), in assessing the relative contributions of various sources, also showed similar results to Manchikanti et al (146) in 156 patients with prevalence of internal disc disruption in 42%, facet joint pain in 31%, and sacroiliac joint pain in 18%. In a similar study, Pang et al (43) assessed 104 consecutive adult patients with what they described as spinal pain mapping with diagnostic blocks including provocation discography and other assessments. They showed internal disc disruption in 7% of patients, sacroiliac joint pain in 6%, lumbar nerve root pain in 20%, and facet joint pain in 24%, with a combined lumbar nerve root and facet disease in 24%, combined facet and sacroiliac joint disease in 4%, with lumbar sympathetic dystrophy in 2% of the patients. However, Pang et al (43) utilized a single block rather than dual blocks. Despite these relative contribution studies, there is always a proportion of patients to which a diagnosis can be provided. With 19% of the patients in the study, if one considers selective nerve root blocks as valid and without selective nerve root blocks, they were unable to identify the diagnosis in 32% of the patients by Manchikanti et al (146), in 13% of the patients in the study by Pang et al (43), whereas DePalma et al (154) identified a diagnosis in all patients.

In the cervical spine, relative contributions were assessed by Yin and Bogduk (155) in the United States in 143 patients showing a prevalence of zygapophysial joint pain in 55%, discogenic pain in 16%, and lateral atlanto-axial joint pain in 9%. Similar to the lumbar spine, a diagnosis remained elusive in 32% of those patients who completed investigations. To confirm the validity of diagnostic blocks, in interventional pain management, there is no tissue diagnosis (biopsy autoscopy is available). Consequently, indirect measures are applied to assess the accuracy of diagnostic blocks with long-term follow-up as the criterion standard, which has been accepted across multiple medical disciplines (181,198). Consequently, the validity of controlled diagnostic facet joint nerve blocks has been implicated as a reference or gold standard in the diagnosis of facet joint pain (7,18,22-24,34,41,42,45,46,59,60). Consequently, based on the criterion standard of controlled diagnostic facet joint nerve blocks, performed under fluoroscopy with utilization of local anesthetic of 0.5 mL or less per nerve with 75% or greater relief in the lumbar spine and 80% or greater relief in the cervical and thoracic spines with the ability to perform previously painful movements, with demonstrated efficacy in long-term follow-ups. With pain relief for one to 2 years with either radiofrequency neurotomy or therapeutic facet joint nerve blocks, the criterion standard of long-term follow-up appears to be appropriate (7,22-24,34,41,183-193). A study conducted on the lumbar spine (41) also has demonstrated sustained relief in only 51% of the patients with 50% relief considered as the criterion standard for diagnostic accuracy at the end of 2 years. In addition, the flawed conclusions of Cohen et al (130) also have been highlighted. Cohen et al (130) performed a randomized, multicenter study in 151 patients with suspected lumbar facet joint pain with comparison of 3 treatment regimens which included radiofrequency denervation in 3 groups, either with no diagnostic blocks, or with one or 2 diagnostic blocks. The success rate they reported was 33% when no diagnostic blocks were performed, whereas it was 39% with a single diagnostic block and 64% with dual diagnostic blocks. Consequently, the study essentially shows that dual diagnostic blocks were more effective; however, they erroneously showed the cost effectiveness to be in favor of no diagnostic blocks. In assessing cost effectiveness, they failed to take into consideration the amount of relief the patients received with diagnostic blocks; instead, they utilized only the total cost without the outcomes.

The rationale and validity of diagnostic facet joint nerve blocks have been well established. The anatomic characteristics of spinal facet joints are that they can be anesthetized either with an intraarticular injection of local anesthetic or by anesthetizing the medial branches of the dorsal rami that innervate the target joint (7,18,22-24,26,33,35-37,43-46,59,60,114). Controlled diagnostic blocks are performed either by placebo injections or by comparative local anesthetic blocks. It is crucial to follow the required steps to eliminate false-positive responses. The joint may be considered to be the source of pain if the pain is relieved by joint blockade. True-positive responses may be obtained only by performing controlled blocks.

The rationale of facet joints as a pain source is established by their abundant innervation (7,22-24,35,82-105). The facet joints have been shown to be capable of causing axial spinal pain and referred pain in the extremities and chest wall (105,116-127). There has been a demonstrated lack of correlation of facet joint pain with demographic features, pain characteristics, physical findings, and specific signs or symptoms (7,22-24). In addition, referral patterns for joints are variable (7,116-119,198). A pattern of pain similar to that of facet joint pain is produced by many other structures in the spine.

Further, most maneuvers used in a physical examination are likely to stress several structures simultaneously, including discs, muscles, and facet joints. The use of controlled local anesthetic facet joint blocks for diagnosing chronic axial spinal pain has been reviewed and validated (7,18,22-24,26,33,35-37,43-46,59,60,114). Thus, placebo-controlled blocks or comparative local anesthetic blocks using 2 different local anesthetics of differing duration of action on 2 separate occasions are the only means of confirming the diagnosis of facet joint pain.

The face validity of intraarticular facet injections and medial branch blocks has been established by injecting small volumes of local anesthetic into the joint or onto the sensory nerves of the joint. The construct validity of facet joint blocks also has been established (7,18,22-24,26,33,35-37,43-46,59,60,114). The placebo effect of facet joint injections may be controlled by using strict criteria for determining a positive response to controlled anesthetic blocks. It has been proven that a way to test for placebo response is to first administer lidocaine and subsequently administer bupivacaine. Pain provocation response of facet joint injections has been shown to be unreliable (199). Further, false-positive rates for facet joint blockade have been reported to range from 17% to 49% (7,22-24,114). Finally, the false-negative rate for diagnostic facet joint blocks has been shown to be approximately 8% due to unrecognized intravascular injection of local anesthetic (200,201).

Systematic reviews have been considered as occupying the highest level of hierarchy and are considered as providing the best evidence synthesis with or without meta-analysis (39,137,202-208). Systematic reviews apply scientific strategies that limit bias. These strategies include the systematic assembly, critical appraisal, and synthesis of all relevant studies on a specific topic and may or may not include a meta-analysis. Meta-analysis incorporates quantitative analysis following the qualitative analysis in a systematic review. However, homogeneity of the studies included is extremely important. In recent years, multiple authors have ignored appropriate assessment of homogeneity and included heterogenous studies in meta-analysis and obviously provided inaccurate conclusions (38,203-209). Many of these authors have significant conflicts of interest and may lack expertise in clinical aspects of the diagnostic tests or treatments being studied. This lack of clinical expertise in the area under study may lead to an inaccurate conclusion, in turn leading to an inappropriate application of the results (203-205). However, in contrast to multiple systematic reviews in the past, as well as opinions of experts with substantial conflicts of interest, this systematic review minimizes bias by comprehensiveness and reproducibility of the search and selection of articles for review and methodological quality assessment by reaching appropriate conclusions without a meta-analysis.

The major questions answered in this systematic review are related to the diagnostic accuracy and validity of facet joint nerve blocks and the level of evidence, which led to the recommendations. The factors influencing the diagnosis were also assessed as a secondary outcome. This systematic review met all the criteria established by Institute of Medicine (IOM) standards for systematic reviews (202), which included 4 major standards, with initiation of the systematic review, finding and assessing individual studies, synthesizing the body of evidence, and reporting of systematic reviews. Further, we also utilized expanded conflict of interest criteria, which we believe minimizes bias in this review (202). In fact, studies have shown that multiple US agencies such as the Centers for Medicare and Medicaid Services (CMS), the Food and Drug Administration (FDA), and the Agency for Healthcare Research and Quality (AHRQ) fail to follow established IOM standards (210).

4.0 Conclusion

This systematic review assessing the accuracy of diagnostic facet joint nerve blocks in chronic spinal pain showed Level I evidence for diagnosing chronic lumbar facet joint pain, and Level II for cervical and thoracic facet joint pain, based on multiple high quality studies of controlled diagnostic blocks.

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Conflict of interest:

Dr. Manchikanti has provided limited consulting services to Semnur Pharmaceuticals, Incorporated, which is developing nonparticulate steroids.

Dr. Kaye is a speaker for Depomed, Inc.

Dr. Gupta has been paid honorarium for presenting at meetings and teaching on the interventional pain medicine cadaver courses and by pharmaceutical companies for presenting to health care professionals. Pharmaceutical companies and companies that manufacture equipments used in pain medicine have supported meetings organized by Dr S Gupta

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References

1. US Burden of Disease Collaborators. The state of US health, 1999-2010: Burden of diseases, injuries, and risk factors. *JAMA* 2013; 310:591-608.
2. Hoy D, March L, Brooks P, Blyth F, Woolf A, Bain C, Williams G, Smith E, Vos T, Barendregt J, Murray C, Burstein R, Buchbinder R. The global burden of low back pain: Estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014; 73:968-974.
3. Hoy D, March L, Woolf A, Blyth F, Brooks P, Smith E, Vos T, Barendregt J, Blore J, Murray C, Burstein R, Buchbinder R. The global burden of neck pain: Estimates from the global burden of disease 2010 study. *Ann Rheum Dis* 2014; 73:1309-1315.
4. Institute of Medicine (IOM). *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. The National Academies Press, Washington, DC, June 29, 2011.
5. Martin BI, Turner JA, Mirza SK, Lee MJ, Comstock BA, Deyo RA. Trends in health care expenditures, utilization, and health status among US adults with spine problems, 1997-2006. *Spine (Phila Pa 1976)* 2009; 34:2077-2084.
6. Gaskin DJ, Richard P. The economic costs of pain in the United States. *J Pain* 2012; 13:715-724.
7. Manchikanti L, Abdi S, Atluri S, Benyamin RM, Boswell MV, Buenaventura RM, Bryce DA, Burks PA, Caraway DL, Calodney AK, Cash KA, Christo PJ, Cohen SP, Colson J, Conn A, Cordner HJ, Coubarous S, Datta S, Deer TR, Diwan SA, Falco FJE, Fellows B, Geffert SC, Grider JS, Gupta S, Hameed H, Hameed M, Hansen H, Helm II S, Janata JW, Justiz R, Kaye AD, Lee M, Manchikanti KN, McManus CD, Onyewu O, Parr AT, Patel VB, Racz GB, Sehgal N, Sharma M, Simopoulos TT, Singh V, Smith HS, Snook LT, Swicegood J, Vallejo R, Ward SP, Wargo BW, Zhu J, Hirsch JA. An update of comprehensive evidence-based guidelines for interventional techniques of chronic spinal pain: Part II: Guidance and recommendations. *Pain Physician* 2013; 16:S49-S283.
8. Manchikanti L, Pampati V, Falco FJE, Hirsch JA. Growth of spinal interventional pain management techniques:

Analysis of utilization trends and Medicare expenditures 2000 to 2008. *Spine (Phila Pa 1976)* 2013; 38:157-168.

9. Manchikanti L, Helm II S, Singh V, Hirsch JA. Accountable interventional pain management: A collaboration among practitioners, patients, payers, and government. *Pain Physician* 2013; 16:E635-E670.
10. Rajaee SS, Bae HW, Kanim LE, Delamarter RB. Spinal fusion in the United States: Analysis of trends from 1998 to 2008. *Spine (Phila Pa 1976)* 2012; 37:67-76.
11. Yoshihara H, Yoneoka D. National trends in the surgical treatment for lumbar degenerative disc disease: United States, 2000 to 2009. *Spine J* 2015; 15:265-271.
12. Freburger JK, Holmes GM, Agans RP, Jackman AM, Darter JD, Wallace AS, Castel LD, Kalsbeek WD, Carey TS. The rising prevalence of chronic low back pain. *Arch Intern Med* 2009; 169:251-258.
13. Atluri S, Sudarshan G, Manchikanti L. Assessment of the trends in medical use and misuse of opioid analgesics from 2004 to 2011. *Pain Physician* 2014; 17:E119-E128.
14. Manchikanti L, Hirsch JA. Lessons learned in the abuse of pain relief medication: A focus on health care costs. *Expert Rev Neurother* 2013; 13:527-544.
15. Dart RC, Surratt HL, Cicero TJ, Parrino MW, Severtson SG, Bucher-Bartelson B, Green JL. Trends in opioid analgesic abuse and mortality in the United States. *N Engl J Med* 2015; 372:241-248.
16. Manchikanti L, Falco FJE, Benyamin RM, Helm II S, Singh V, Hirsch JA. Value-based interventional pain management: A review of Medicare national and local coverage determination policies. *Pain Physician* 2013; 16:E145-E180.
17. Hancock MJ, Maher CG, Latimer J, Spindler MF, McAuley JH, Laslett M, Bogduk N. Systematic review of tests to identify the disc, SIJ or facet joint as the source of low back pain. *Eur Spine J* 2007; 16:1539-1550.
18. Bogduk N. On diagnostic blocks for lumbar zygapophysial joint pain. *F1000 Med Rep* 2010; 2:57.
19. Lucas NP, Macaskill P, Irwing L, Bogduk N. The development of a quality appraisal tool for studies of diagnostic reliability (QAREL). *J Clin Epidemiol* 2010; 63:854-861.
20. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, Lijmer JG, Moher D, Rennie D, de Vet HC; STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: The STARD Initiative. *Ann Intern Med* 2003; 138:40-44.
21. Whiting P, Rutjes AW, Reitsma JB, Bossuyt PM, Kleijnen J. The development of QUADAS: A tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol* 2003; 3:25.
22. Falco FJE, Manchikanti L, Datta S, Sehgal N, Geffert S, Onyewu O, Singh V, Bryce DA, Benyamin RM, Simopoulos TT, Vallejo R, Gupta S, Ward SP, Hirsch JA. An update of the systematic assessment of the diagnostic accuracy of lumbar facet joint nerve blocks. *Pain Physician* 2012; 15:E869-E907.
23. Falco FJE, Datta S, Manchikanti L, Sehgal N, Geffert S, Singh V, Smith HS, Boswell MV. An updated review of diagnostic utility of cervical facet joint injections. *Pain Physician* 2012; 15:E807-E838.
24. Atluri S, Singh V, Datta S, Geffert S, Sehgal N, Falco FJE. Diagnostic accuracy of thoracic facet joint nerve blocks: An update of the assessment of evidence. *Pain Physician* 2012; 15:E483-E496.
25. Engel A, MacVicar J, Bogduk N. A philosophical foundation for diagnostic blocks, with criteria for their validation. *Pain Med* 2014; 15:998-1006.
26. Rubinstein SM, van Tulder M. A best-evidence review of diagnostic procedures for neck and low-back pain. *Best Pract Res Clin Rheumatol* 2008; 22:471-482.
27. Kuslich SD, Ulstrom CL, Michael CJ. The tissue origin of low back pain and sciatica: A report of pain response to tissue stimulation during operation on the lumbar spine using local anesthesia. *Orthop Clin North Am* 1991; 22:181-187.
28. King W, Lau P, Lees R, Bogduk N. The validity of manual examination in assessing patients with neck pain. *Spine J* 2007; 7:22-26.
29. Matar HE, Navalkissoor S, Berovic M, Shetty R, Garlick N, Casey AT, Quigley AM. Is hybrid imaging (SPECT/CT) a useful adjunct in the management of suspected facet joints arthropathy? *Int Orthop* 2013; 37:865-870.
30. Schneider GM, Jull G, Thomas K, Salo P. Screening of patients suitable for diagnostic cervical facet joint blocks--a role for physiotherapists. *Man Ther* 2012; 17:180-183.
31. Schneider GM, Jull G, Thomas K, Smith A, Emery C, Faris P, Cook C, Frizzell B, Salo P. Derivation of a clinical decision guide in the diagnosis of cervical facet joint pain. *Arch Phys Med Rehabil* 2014; 95:1695-1701.
32. Schneider GM, Jull G, Thomas K, Smith A, Emery C, Faris P, Schneider K, Salo P. Intrarater and interrater reliability of select clinical tests in patients referred for diagnostic facet joint blocks in the cervical spine. *Arch Phys Med Rehabil* 2013; 94:1628-1634.
33. Watson DH, Drummond PD. Head pain referral during examination of the neck in migraine and tension-type headache. *Headache* 2012; 52:1226-1235.
34. Jull G, Bogduk N, Marsland A. The accuracy of manual diagnosis for cervical zygapophysial joint pain syndromes. *Med J Aust* 1988; 148:233-236.
35. Barnsley L, Bogduk N. Medial branch blocks are specific for the diagnosis of cervical zygapophyseal joint pain. *Reg Anesth* 1993; 18:343-350.
36. Barnsley L, Lord S, Bogduk N. Comparative local anesthetic blocks in the diagnosis of cervical zygapophysial joints pain. *Pain* 1993; 55:99-106.
37. Lord SM, Barnsley L, Bogduk N. The utility of comparative local anesthetic blocks versus placebo-controlled blocks for the diagnosis of cervical zygapophysial joint pain. *Clin J Pain* 1995; 11:208-213.
38. Chou R, Huffman L. *Guideline for the Evaluation and Management of Low Back Pain: Evidence Review*. American Pain Society, Glenview, IL, 2009.
39. Manchikanti L, Datta S, Derby R, Wolfer LR, Benyamin RM, Hirsch JA. A critical review of the American Pain Society clinical practice guidelines for interventional techniques: Part 1. Diagnostic interventions. *Pain Physician* 2010; 13:E141-E174.
40. Manchikanti L, Benyamin RM, Falco FJE, Caraway DL, Datta S, Hirsch JA. Guidelines warfare over interventional techniques: Is there a lack of discourse or straw man? *Pain Physician* 2012; 15:E1-E26.
41. Pampati S, Cash KA, Manchikanti L. Accuracy of diagnostic lumbar facet joint nerve blocks: A 2-year follow-up of 152 patients diagnosed with controlled diagnostic blocks. *Pain Physician* 2009; 12:855-866.
42. Manchikanti L, Pampati S, Cash KA. Making sense of the accuracy of diagnostic lumbar facet joint nerve blocks: An assessment of implications of 50% relief, 80% relief, single block or controlled diagnostic blocks. *Pain Physician* 2010; 13:133-143.
43. Pang WW, Mok MS, Lin ML, Chang DP,

Hwang MH. Application of spinal pain mapping in the diagnosis of low back pain--analysis of 104 cases. *Acta Anaesthesiol Sin* 1998; 36:71-74.

44. Revel ME, Listrat VM, Chevalier XJ, Dougados M, N'Guyen MP, Vallee C, Wybier M, Gires F, Amor B. Facet joint block for low back pain: Identifying predictors of a good response. *Arch Phys Med Rehabil* 1992; 73:824-828.
45. Revel ME, Poiraudeau S, Auleley GR, Payan C, Denke A, Nguyen M, Chevrot A, Fermanian J. Capacity of the clinical picture to characterize low back pain relieved by facet joint anesthesia. Proposed criteria to identify patients with painful facet joints. *Spine (Phila Pa 1976)* 1998; 23:1972-1976.
46. Young S, Aprill C, Laslett M. Correlation of clinical examination characteristics with three sources of chronic low back pain. *Spine J* 2003; 3:460-465.
47. Carragee EJ, Haldeman S, Hurwitz E. The pyrite standard: The Midas touch in the diagnosis of axial pain syndromes. *Spine J* 2006; 7:27-31.
48. Chou R, Atlas SJ, Loeser JD, Rosenquist RW, Stanos SP. Guideline warfare over interventional therapies for low back pain: Can we raise the level of discourse? *J Pain* 2011; 12:833-839.
49. Bogduk N. In defense of King et al: The validity of manual examination in assessing patients with neck pain. *Spine J* 2007; 7:749-752; author reply (Carragee EJ) 752-753.
50. Maataoui A, Vogl TJ, Middendorp M, Kafchitsas K, Khan MF. Association between facet joint osteoarthritis and the Oswestry Disability Index. *World J Radiol* 2014; 6:881-885.
51. Eubanks JD, Lee MJ, Cassinelli E, Ahn NU. Prevalence of lumbar facet arthrosis and its relationship to age, sex, and race: An anatomic study of cadaveric specimens. *Spine (Phila Pa 1976)* 2007; 32:2058-2062.
52. Harris RI, Macnab I. Structural changes in the lumbar intervertebral discs; their relationship to low back pain and sciatica. *J Bone Joint Surg Br* 1954; 36-B:304-322.
53. Kalichman L, Li L, Kim DH, Guermazi A, Berkin V, O'Donnell CJ, Hoffmann U, Cole R, Hunter DJ. Facet joint osteoarthritis and low back pain in the community-based population. *Spine (Phila Pa 1976)* 2008; 33:2560-2565.
54. Schwarzer AC, Aprill C, Derby R, Fortin J, Kine G, Bogduk N. Clinical features of patients with pain stemming from the lumbar zygapophyseal joints. Is the lumbar facet syndrome a clinical entity? *Spine (Phila Pa 1976)* 1994; 10:1132-1137.
55. Schwarzer AC, Aprill CN, Derby R, Fortin J, Kine G, Bogduk N. The false-positive rate of uncontrolled diagnostic blocks of the lumbar zygapophysial joints. *Pain* 1994; 58:195-200.
56. Schwarzer AC, Wang SC, O'Driscoll D, Harrington T, Bogduk N, Laurent R. The ability of computed tomography to identify a painful zygapophysial joint in patients with chronic low back pain. *Spine (Phila Pa 1976)* 1995; 20:907-912.
57. Schwarzer AC, Wang S, Bogduk N, McNaught PJ, Laurent R. Prevalence and clinical features of lumbar zygapophysial joint pain: A study in an Australian population with chronic low back pain. *Ann Rheum Dis* 1995; 54:100-106.
58. Manchikanti L, Pampati V, Fellows B, Baha GA. The inability of the clinical picture to characterize pain from facet joints. *Pain Physician* 2000; 3:158-166.
59. Laslett M, McDonald B, Aprill CN, Tropp H, Oberg B. Clinical predictors of screening lumbar zygapophyseal joint blocks: Development of clinical prediction rules. *Spine J* 2006; 6:370-379.
60. Laslett M, Oberg B, Aprill CN, McDonald B. Zygapophysial joint blocks in chronic low back pain: A test of Revel's model as a screening test. *BMC Musculoskeletal Disord* 2004; 5:43-48.
61. Bogduk N, Aprill C. On the nature of neck pain, discography and cervical zygapophysial joint blocks. *Pain* 1993; 54:213-217.
62. Henry JL, Yashpal K, Vernon H, Kim J, Im HJ. Lumbar facet joint compressive injury induces lasting changes in local structure, nociceptive scores and inflammatory mediators in a novel rat model. *Pain Res Treat* 2012; 2012:127636.
63. Bykowski JL, Wong WH. Role of facet joints in spine pain and image-guided treatment: A review. *AJNR Am J Neuroradiol* 2012; 33:1419-1426.
64. Kras JV, Dong L, Winkelstein BA. Increased interleukin-1α and prostaglandin E2 expression in the spinal cord at 1 day after painful facet joint injury: Evidence of early spinal inflammation. *Spine (Phila Pa 1976)* 2014; 39:207-212.
65. Anderst WJ, Donaldson WF 3rd, Lee JY, Kang JD. In vivo cervical facet joint capsule deformation during flexion-extension. *Spine (Phila Pa 1976)* 2014; 39:E514-E520.
66. Gellhorn AC, Katz JN, Suri P. Osteoarthritis of the spine: The facet joints. *Nat Rev Rheumatol* 2013; 9:216-224.
67. Oppenheimer A. Diseases of the apophyseal (intervertebral) articulations. *J Bone Joint Surg* 1938; 20:285-313.
68. Lewin T. Osteoarthritis in lumbar synovial joints. A morphologic study. *Acta Orthop Scand* 1964; 73:1-112.
69. Igarashi A, Kikuchi S, Konno S, Olmarker K. Inflammatory cytokines released from the facet joint tissue in degenerative lumbar spinal disorders. *Spine (Phila Pa 1976)* 2004; 29:2091-2095.
70. Schulte TL, Filler TJ, Struwe P, Liem D, Bullman V. Intra-articular meniscoid folds in thoracic zygapophysial joints. *Spine (Phila Pa 1976)* 2010; 35:E191-E197.
71. Kim JS, Kroin JS, Buvanendran A, Li X, van Wijnen AJ, Tuman KJ, Im HJ. Characterization of a new animal model for evaluation and treatment of back pain due to lumbar facet joint osteoarthritis. *Arthritis Rheum* 2011; 63:2966-2973.
72. Shuang F, Zhu J, Song K, Hou S, Liu Y, Zhang C, Tang J. Establishment of a rat model of adjuvant-induced osteoarthritis of the lumbar facet joint. *Cell Biochem Biophys* 2014; 70:1545-1551.
73. Ko S, Vaccaro AR, Lee S, Lee J, Chang H. The prevalence of lumbar spine facet joint osteoarthritis and its association with low back pain in selected Korean populations. *Clin Orthop Surg* 2014; 6:385-391.
74. Sagar DR, Ashraf S, Xu L, Burston JJ, Menhinick MR, Poulter CL, Bennett AJ, Walsh DA, Chapman V. Osteoprotegerin reduces the development of pain behaviour and joint pathology in a model of osteoarthritis. *Ann Rheum Dis* 2014; 73:1558-1565.
75. Bullock CM, Wookey P, Bennett A, Mobasheri A, Dickerson I, Kelly S. Peripheral calcitonin gene-related peptide receptor activation and mechanical sensitization of the joint in rat models of osteoarthritis pain. *Arthritis Rheumatol* 2014; 66:2188-2200.
76. Lee H, Park Y, Ahn CW, Park SH, Jung EY, Suh HJ. Deer bone extract suppresses articular cartilage damage induced by monosodium iodoacetate in osteoarthritic rats: An in vivo micro-computed tomography study. *J Med Food* 2014; 17:701-706.
77. Dong L, Crosby ND, Winkelstein BA. Gabapentin alleviates facet-mediated pain in the rat through reduced neuronal hyperexcitability and astrocytic activation in the spinal cord. *J Pain* 2013;

14:1564-1572.

78. Masini M, Paiva WS, Araujo AS, Jr. Anatomical description of the facet joint innervation and its implication in the treatment of recurrent back pain. *J Neurosurg Sci* 2005; 49:143-146.
79. Suseki K, Takahashi Y, Takahashi K, Chiba T, Tanaka K, Morinaga T, Nakamura S, Moriya H. Innervation of the lumbar facet joints. Origins and functions. *Spine (Phila Pa 1976)* 1997; 22:477-485.
80. Cavanaugh JM, Lu Y, Chen C, Kallakuri S. Pain generation in lumbar and cervical facet joints. *J Bone Joint Surg Am* 2006; 88:63-67.
81. Cavanaugh JM, Ozaktay AC, Yamashita T, Avramov A, Getchell TV, King AI. Mechanisms of low back pain: A neurophysiologic and neuroanatomic study. *Clin Orthop Relat Res* 1997; 335:166-180.
82. Bogduk N, Wilson AS, Tynan W. The human lumbar dorsal rami. *J Anat* 1982; 134:383-397.
83. Bogduk N. The clinical anatomy of the cervical dorsal rami. *Spine (Phila Pa 1976)* 1982; 7:319-330.
84. Ohtori S, Takahashi K, Chiba T, Yamagata M, Sameda H, Moriya H. Sensory innervation of the cervical facet joints in rats. *Spine (Phila Pa 1976)* 2001; 26:147-150.
85. Zhang J, Tsuzuki N, Hirabayashi S, Saiki K, Fujita K. Surgical anatomy of the nerves and muscles in the posterior cervical spine. *Spine (Phila Pa 1976)* 2003; 28:1379-1384.
86. Kallakuri S, Li Y, Chen C, Cavanaugh JM. Innervation of cervical ventral facet joint capsule: Histological evidence. *World J Orthop* 2012; 3:10-14.
87. Ishikawa T, Miyagi M, Ohtori S, Aoki Y, Ozawa T, Doya H, Saito T, Moriya H, Takahashi K. Characteristics of sensory DRG neurons innervating the lumbar facet joints in rats. *Eur Spine J* 2005; 14:559-564.
88. Chua WH, Bogduk N. The surgical anatomy of thoracic facet denervation. *Acta Neurochir* 1995; 136:140-144.
89. Stilwell DL. The nerve supply of the vertebral column and its associated structures in the monkey. *Anat Rec* 1956; 125:139-169.
90. Sato T, Koizumi M, Kim JH, Kim JH, Wang BJ, Murakami G, Cho BH. Fetal development of deep back muscles in the human thoracic region with a focus on transversospinalis muscles and the medial branch of the spinal nerve posterior ramus. *J Anat* 2011; 219:756-765.
91. Lau P, Mercer S, Govind J, Bogduk N. The surgical anatomy of lumbar medial branch neurotomy (facet denervation). *Pain Med* 2004; 5:289-298.
92. Miyagi M, Ohtori S, Ishikawa T, Aoki Y, Ozawa T, Doya H, Saito T, Moriya H, Takahashi K. Up-regulation of TNFalpha in DRG satellite cells following lumbar facet joint injury in rats. *Eur Spine J* 2006; 15:953-958.
93. Dong L, Smith JR, Winkelstein BA. Ketorolac reduces spinal astrocytic activation and PAR1 expression associated with attenuation of pain after facet joint injury. *J Neurotrauma* 2013; 30:818-825.
94. Kras JV, Tanaka K, Gilliland TM, Winkelstein BA. An anatomical and immunohistochemical characterization of afferents innervating the C6-C7 facet joint after painful joint loading in the rat. *Spine (Phila Pa 1976)* 2013; 38:E325-E331.
95. Ohtori S, Takahashi K, Chiba T, Yamagata M, Sameda H, Moriya H. Substance P and calcitonin gene-related peptide immunoreactive sensory DRG neurons innervating the lumbar facet joints in rats. *Auton Neurosci* 2000; 86:13-17.
96. Suseki K, Takahashi Y, Takahashi K, Chiba T, Tanaka K, Moriya H. CGRP-immunoreactive nerve fibers projecting to lumbar facet joints through the paravertebral sympathetic trunk in rats. *Neurosci Lett* 1996; 221:41-44.
97. Ohtori S, Takahashi K, Chiba T, Yamagata M, Sameda H, Moriya H. Brain-derived neurotrophic factor and vanilloid receptor subtype 1 immunoreactive sensory DRG neurons innervating the lumbar facet joints in rats. *Auton Neurosci* 2001; 94:132-135.
98. Yamashita T, Cavanaugh J, el-Bohy AA, Getchell TV, King AI. Mechanosensitive afferent units in the lumbar facet joint. *J Bone Joint Surg Am* 1990; 72:865-870.
99. Yamashita T, Cavanaugh JM, Ozaktay AC, Avramov AI, Getchell TV, King AI. Effect of substance P on mechanosensitive units of tissues around and in the lumbar facet joint. *J Orthop Res* 1993; 11:205-214.
100. Beaman DN, Graziano GP, Glover RA, Wojtys EM, Chang V. Substance P innervation of lumbar spine facet joints. *Spine (Phila Pa 1976)* 1993; 18:1044-1049.
101. Lu Y, Chen C, Kallakuri S. Patwardhan A, Cavanaugh JM. Neurophysiological and biomechanical characterization of goat cervical facet joint capsules. *J Orthop Res* 2005; 30:779-787.
102. Inami S, Shiga T, Tsujino A, Yabuki T, Okado N, Ochiai N. Immunohistochemical demonstration of nerve fibers in the synovial fold of the human cervical facet joint. *J Orthop Res* 2001; 19:593-596.
103. Chen C, Lu Y, Kallakuri S, Patwardhan A, Cavanaugh JM. Distribution of A-delta and C-fiber receptors in the cervical facet joint capsule and their response to stretch. *J Bone Joint Surg Am* 2006; 88:1087-1816.
104. Kallakuri S, Singh A, Chen C, Cavanaugh JM. Demonstration of substance P, calcitonin gene-related peptide, and protein gene product 9.5 containing nerve fibers in human cervical facet joint capsules. *Spine (Phila Pa 1976)* 2004; 29:1182-1186.
105. McLain RF. Mechanoreceptors ending in human cervical facets joints. *Spine (Phila Pa 1976)* 1994; 5:495-501.
106. Winkelstein BA, Santos DG. An intact facet capsular ligament modulates behavioral sensitivity and spinal glial activation produced by cervical facet joint tension. *Spine (Phila Pa 1976)* 2008; 33:856-862.
107. Lee KE, Thinnes JH, Gokhin DS, Winkelstein BA. A novel rodent neck pain model of facet-mediated behavioral hypersensitivity: Implications for persistent pain and whiplash injury. *J Neurosci Methods* 2004; 137:151-159.
108. Schneider GM, Smith AD, Hooper A, Stratford P, Schneider KJ, Westaway MD, Frizzell B, Olson L. Minimizing the source of nociception and its concurrent effect on sensory hypersensitivity: An exploratory study in chronic whiplash patients. *BMC Musculoskelet Disord* 2010; 11:29.
109. Chua NH, van Suijlekom HA, Vissers KC, Arendt-Nielsen L, Wilder-Smith OH. Differences in sensory processing between chronic cervical zygapophyseal joint pain patients with and without Cervicogenic headache. *Cephalalgia* 2011; 31:953-963.
110. Quinn KP, Dong L, Golder FJ, Winkelstein BA. Neuronal hyperexcitability in the dorsal horn after painful facet joint injury. *Pain* 2010; 151:414-421.
111. Dong L, Odeleye AO, Jordan-Sciutto KL, Winkelstein BA. Painful facet joint injury induces neuronal stress activation in the DRG: implications for cellular mechanisms of pain. *Neurosci Lett* 2008; 443:90-94.
112. Dong L, Winkelstein BA. Simulated whiplash modulates expression of the glutamatergic system in the spinal cord suggesting spinal plasticity is associated with painful dynamic cervical facet load-

ing. *J Neurotrauma* 2010; 27:163-174.

113. Sakuma Y, Ohtori S, Miyagi M, Ishikawa T, Inoue G, Doya H, Koshi T, Ito T, Yamashita M, Yamauchi K, Suzuki M, Moriya H, Takahashi K. Up-regulation of p55 TNF alpha-receptor in dorsal root ganglia neurons following lumbar facet joint injury in rats. *Eur Spine J* 2007; 16:1273-1278.
114. Bogduk N. Low back pain. *Clinical Anatomy of Lumbar Spine and Sacrum,* 4th edition. Churchill Livingstone, New York, 2005, pp 183-216.
115. Jung JH, Kim HI, Shin DA, Shin DG, Lee JO, Kim HJ, Chung JH. Usefulness of pain distribution pattern assessment in decision-making for the patients with lumbar zygapophyseal and sacroiliac joint arthropathy. *J Korean Med Sci* 2007; 22:1048-1054.
116. Marks RC. Distribution of pain provoked from lumbar facet joints and related structures during diagnostic spinal infiltration. *Pain* 1989; 39:37-40.
117. Fukui S, Ohseto K, Shiotani M, Ohno K, Karasawa H, Naganuma Y. Distribution of referred pain from the lumbar zygapophyseal joints and dorsal rami. *Clin J Pain* 1997; 13:303-307.
118. Hirsch C, Ingelmark BE, Miller M. The anatomical basis for low back pain. Studies on the presence of sensory nerve endings in ligamentous, capsular and intervertebral disc structures in the human lumbar spine. *Acta Orthop Scand* 1963; 33:1-17.
119. Windsor RE, King FJ, Roman SJ, Tata NS, Cone-Sullivan LA, Thmapi S, Acebey M, Gilhool JJ, Rao R, Sugar R. Electrical stimulation induced lumbar medial branch referral patterns. *Pain Physician* 2002; 5:347-353.
120. Mooney V, Robertson J. The facet syndrome. *Clin Orthop Relat Res* 1976; 115:149-156.
121. McCall IW, Park WM, O'Brien JP. Induced pain referral from posterior lumbar elements in normal subjects. *Spine (Phila Pa 1976)* 1979; 4:441-446.
122. Dreyfuss P, Tibiletti C, Dreyer SJ. Thoracic zygapophyseal joint pain patterns: A study in normal volunteers. *Spine (Phila Pa 1976)* 1994; 19:807-811.
123. Fukui S, Ohseto K, Shiotani M. Patterns of pain induced by distending the thoracic zygapophyseal joints. *Reg Anesth* 1997; 22:332-336.
124. Dwyer A, Aprill C, Bogduk N. Cervical zygapophyseal joint pain patterns: A study in normal volunteers. *Spine (Phila Pa 1976)* 1990; 15:453-457.
125. Aprill C, Dwyer A, Bogduk N. The prevalence of cervical zygapophyseal joint pain patterns II: A clinical evaluation. *Spine (Phila Pa 1976)* 1990; 15:458-461.
126. Fukui S, Ohseto K, Shiotani M, Ohno K, Karasawa H, Naganuma Y, Yuda Y. Referred pain distribution of the cervical zygapophyseal joints and cervical dorsal rami. *Pain* 1996; 68:79-83.
127. Windsor RE, Nagula D, Storm S. Electrical stimulation induced cervical medial branch referral patterns. *Pain Physician* 2003; 6:411-418.
128. Linov L, Klindukhov A, Li L, Kalichman L. Lumbar facet joint orientation and osteoarthritis: A cross-sectional study. *J Back Musculoskelet Rehabil* 2013; 26:421-426.
129. Quinn KP, Winkelstein BA. Detection of altered collagen fiber alignment in the cervical facet capsule after whiplash-like joint retraction. *Ann Biomed Eng* 2011; 39:2163-2173.
130. Cohen SP, Williams KA, Kurihara C, Nguyen C, Shields C, Kim P, Griffith SR, Larkin TM, Crooks M, Williams N, Morlando B, Strassels SA: Multicenter, randomized, comparative cost-effectiveness study comparing 0, 1, and 2 diagnostic medial branch (facet joint nerve) block treatment paradigms before lumbar facet radiofrequency denervation. *Anesthesiology* 2010; 113:395-405.
131. Derby R, Melnik I, Lee JE, Lee SH. Correlation of lumbar medial branch neurotomy results with diagnostic medial branch block cutoff values to optimize therapeutic outcome. *Pain Med* 2012; 13:1533-1546.
132. Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews. York (UK): Centre for Reviews and Dissemination. Systematic review of diagnostic utility of facet (zygapophysial) joint injections in chronic spinal pain: An update; 2007; (cited 2008 Feb 29).
133. Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews. York (UK): Centre for Reviews and Dissemination. An update of the systematic assessment of the diagnostic accuracy of lumbar facet joint nerve blocks. 2012 (cited 2013 Feb 21).
134. Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews. York (UK): Centre for Reviews and Dissemination. Diagnostic accuracy of thoracic facet joint nerve blocks: an update of the assessment of evidence. 2012 (cited 2013 Jan 9).
135. Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews. York (UK): Centre for Reviews and Dissemination. Systematic review of diagnostic utility and therapeutic effectiveness of cervical facet joint interventions. 2009 (cited 2009 Dec 2).
136. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *Ann Intern Med* 2009; 151:W65-W94.
137. Manchikanti L, Falco FJE, Singh V, Benyamin RM, Racz GB, Helm II S, Caraway DL, Calodney AK, Snook LT, Smith HS, Gupta S, Ward SP, Grider JS, Hirsch JA. An update of comprehensive evidence-based guidelines for interventional techniques of chronic spinal pain. Part I: Introduction and general considerations. *Pain Physician* 2013; 16:S1-S48.
138. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MM, Sterne JA, Bossuyt PM; QUADAS-2 Group. QUADAS-2: A revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011; 155:529-536.
139. Lucas N, Macaskill P, Irwig L, Moran R, Rickards L, Turner R, Bogduk N. The reliability of a quality appraisal tool for studies of diagnostic reliability (QAREL). *BMC Med Res Methodol* 2013; 13:111.
140. Gemmell H, Miller P. Interexaminer reliability of multidimensional examination regimens used for detecting spinal manipulable lesions: A systematic review. *Clin Chiropractic* 2005; 8:199-204.
141. May S, Littlewook C, Bishop A. Reliability of procedures used in the physical examination of non-specific low back pain: A systematic review. *Aust J Physiother* 2006; 52:91-102.
142. Stochkendahl MJ, Christensen HW, Hartvigsen J, Vach W, Haas M, Hestbaek L, Adams A, Bronfort G. Manual examination of the spine: A systematic critical literature review of reproducibility. *J Manipulative Physiol Ther* 2006; 29:475-485, 485.e1-10.
143. Manchikanti L, Falco FJE, Benyamin RM, Kaye AD, Boswell MV, Hirsch JA. A modified approach to grading of evidence. *Pain Physician* 2014; 17:E319-E325.
144. Schütz U, Cakir B, Dreinhöfer K, Richter M, Koepp H. Diagnostic value of lumbar facet joint injection: A prospective

triple cross-over study. *PLoS One* 2011; 6:e27991.

145. Bokov A, Perlmutter O, Aleynik A, Rasteryaeva M, Mlyavykh S. The potential impact of various diagnostic strategies in cases of chronic pain syndromes associated with lumbar spine degeneration. *J Pain Res* 2013; 6:289-296.
146. Manchikanti L, Singh V, Pampati V, Damron K, Barnhill R, Beyer C, Cash K. Evaluation of the relative contributions of various structures in chronic low back pain. *Pain Physician* 2001; 4:308-316.
147. Manchikanti L, Pampati V, Fellows B, Bakhit CE. Prevalence of lumbar facet joint pain in chronic low back pain. *Pain Physician* 1999; 2:59-64.
148. Manchikanti L, Pampati V, Fellows B, Bakhit CE. The diagnostic validity and therapeutic value of medial branch blocks with or without adjuvants. *Curr Rev Pain* 2000; 4:337-344.
149. Manchikanti L, Hirsch JA, Pampati V. Chronic low back pain of facet (zygapophysial) joint origin: Is there a difference based on involvement of single or multiple spinal regions? *Pain Physician* 2003; 6:399-405.
150. Manchikanti L, Singh V, Pampati V, Damron KS, Beyer CD, Barnhill RC. Is there correlation of facet joint pain in lumbar and cervical spine? An evaluation of prevalence in combined chronic low back and neck pain. *Pain Physician* 2002; 5:365-371.
151. Manchikanti L, Boswell MV, Singh V, Pampati V, Damron KS, Beyer CD. Prevalence of facet joint pain in chronic spinal pain of cervical, thoracic, and lumbar regions. *BMC Musuloskeletal Disord* 2004; 5:15.
152. Manchukonda R, Manchikanti KN, Cash KA, Pampati V, Manchikanti L. Facet joint pain in chronic spinal pain: An evaluation of prevalence and false-positive rate of diagnostic blocks. *J Spinal Disord Tech* 2007; 20:539-545.
153. Manchikanti L, Manchukonda R, Pampati V, Damron KS, McManus CD. Prevalence of facet joint pain in chronic low back pain in postsurgical patients by controlled comparative local anesthetic blocks. *Arch Phys Med Rehabil* 2007; 88:449-455.
154. DePalma MJ, Ketchum JM, Saullo T. What is the source of chronic low back pain and does age play a role? *Pain Med* 2011; 12:224-233.
155. Yin W, Bogduk N. The nature of neck pain in a private pain clinic in the United States. *Pain Med* 2008; 9:196-203.
156. Theodore BR, Olamikan S, Keith RV, Gofeld M. Validation of self-reported pain reduction after diagnostic blockade. *Pain Med* 2012; 13:1131-1136.
157. Manchikanti L, Singh V, Rivera J, Pampati V. Prevalence of cervical facet joint pain in chronic neck pain. *Pain Physician* 2002; 5:243-249.
158. Speldewinde G, Bashford G, Davidson I. Diagnostic cervical zygapophyseal joint blocks for chronic cervical pain. *Med J Aust* 2001; 174:174-176.
159. Manchikanti L, Boswell MV, Manchukonda R, Cash KA, Giordano J. Influence of prior opioid exposure on diagnostic facet joint nerve blocks. *J Opioid Manage* 2008; 4:351-360.
160. Aprill C, Bogduk N. The prevalence of cervical zygapophyseal joint pain. A first approximation. *Spine (Phila Pa 1976)* 1992; 17:744-747.
161. Barnsley L, Lord SM, Wallis BJ, Bogduk N. The prevalence of chronic cervical zygapophyseal joint pain after whiplash. *Spine (Phila Pa 1976)* 1995; 20:20-26.
162. Lord SM, Barnsley L, Wallis BJ, Bogduk N. Chronic cervical zygapophysial joint pain with whiplash: A placebo-controlled prevalence study. *Spine (Phila Pa 1976)* 1996; 21:1737-1744.
163. Barnsley L, Lord S, Wallis B, Bogduk N. False-positive rates of cervical zygapophysial joint blocks. *Clin J Pain* 1993; 9:124-130.
164. Manchikanti L, Singh V, Pampati VS, Beyer CD, Damron KS. Evaluation of the prevalence of facet joint pain in chronic thoracic pain. *Pain Physician* 2002; 5:354-359.
165. Manchikanti L, Cash KA, Pampati V, Fellows B. Influence of psychological variables on the diagnosis of facet joint involvement in chronic spinal pain. *Pain Physician* 2008; 11:145-160.
166. Wasan AD, Jamison RN, Pham L, Tipirneni N, Nedeljkovic SS, Katz JN. Psychopathology predicts the outcome of medial branch blocks with corticosteroid for chronic axial low back or cervical pain: A prospective cohort study. *BMC Musculoskelet Disord* 2009; 10:22.
167. DePalma MJ, Ketchum JM, Saullo TR. Multivariable analyses of the relationships between age, gender, and body mass index and the source of chronic low back pain. *Pain Med* 2012; 13:498-506.
168. DePalma MJ, Ketchum JM, Saullo TR. Etiology of chronic low back pain in patients having undergone lumbar fusion. *Pain Med* 2011; 12:732-739.
169. DePalma MJ, Ketchum JM, Saulio TR, Laplante BL. Is the history of a surgical discectomy related to the source of chronic low back pain? *Pain Physician* 2012; 15:E1-E6.
170. Manchikanti L, Pampati V, Baha A, Fellows B, Damron KS, Barnhill RC. Contribution of facet joints to chronic low back pain in postlumbar laminectomy syndrome: A controlled comparative prevalence evaluation. *Pain Physician* 2001; 4:175-180.
171. Manchikanti L, Manchikanti K, Cash KA, Singh V, Giordano J. Age-related prevalence of facet joint involvement in chronic neck and low back pain. *Pain Physician* 2008; 11:67-75.
172. Klessinger S. Zygapophysial joint pain in post lumbar surgery syndrome. The efficacy of medial branch blocks and radiofrequency neurotomy. *Pain Med* 2013; 14:374-377.
173. Manchikanti L, Singh V, Fellows B, Pampati V. Evaluation of influence of gender, occupational injury, and smoking on chronic low back pain of facet joint origin: A subgroup analysis. *Pain Physician* 2002; 5:30-35.
174. Manchikanti L, Manchikanti K, Pampati V, Brandon D, Giordano J. The prevalence of facet joint-related chronic neck pain in postsurgical and non-postsurgical patients: A comparative evaluation. *Pain Pract* 2008; 8:5-10.
175. Manchikanti L, Pampati V, Damron KS, McManus CD, Jackson SD, Barnhill RC, Martin JC. A randomized, prospective, double-blind, placebo-controlled evaluation of the effect of sedation on diagnostic validity of cervical facet joint pain. *Pain Physician* 2004; 7:301-309.
176. Manchikanti L, Pampati V, Rivera JJ, Fellows B, Beyer CD, Damron KS. Role of facet joints in chronic low back pain in the elderly: A controlled comparative prevalence study. *Pain Practice* 2001; 1:332-337.
177. Manchikanti L, Pampati V, Singh V, Beyer C, Damron K, Fellows B. Evaluation of role of facet joints in persistent low back pain in obesity: A controlled, prospective, comparative evaluation. *Pain Physician* 2001; 4:266-272.
178. Manchikanti L, Damron KS, Rivera J, McManus C, Jackson S, Barnhill R, Martin J. Evaluation of effect of sedation as a confounding factor in the diagnostic validity of lumbar facet joint pain: A prospective, randomized, double blind,

placebo-controlled evaluation. *Pain Physician* 2004; 7:411-417.

179. Manchikanti L, Pampati V, Damron KS, McManus CD, Jackson SD, Barnhill RC, Martin JC. The effect of sedation on diagnostic validity of facet joint nerve blocks: An evaluation to assess similarities in population with involvement in cervical and lumbar regions (ISRCTNo: 76376497). *Pain Physician* 2006; 9:47-52.
180. Manchikanti L, Pampati V, Damron KS. The role of placebo and nocebo effects of perioperative administration of sedatives and opioids in interventional pain management. *Pain Physician* 2005; 8:349-355.
181. Manchikanti L, Singh V, Pampati V. Are diagnostic lumbar medial branch blocks valid? Results of 2-year follow-up. *Pain Physician* 2003; 6:147-153.
182. Cohen SP, Strassels SA, Kurihara C, Forsythe A, Buckenmaier CC 3rd, McLean B, Riedy G, Seltzer S. Randomized study assessing the accuracy of cervical facet joint nerve (medial branch) blocks using different injectate volumes. *Anesthesiology* 2010; 112:144-152.
183. Bradford Hill A. The environment and disease: Association or causation? *Proc Roy Soc Med* 1965; 58:295-300.
184. Howick J, Glasziou P, Aronson JK. The evolution of evidence hierarchies: What can Bradford Hill's "guidelines for causation" contribute? *J R Soc Med* 2009; 102:186-194.
185. Cohen SP, Hameed H, Kurihara C, Pasquina PF, Patel AM, Babade M, Griffith SR, Erdek ME, Jamison DE, Hurley RW. The effect of sedation on the accuracy and treatment outcomes for diagnostic injections: A randomized, controlled, crossover study. *Pain Med* 2014; 15:588-602.
186. Manchikanti L, Benyamin RM, Candido KD, Hirsch JA. Cohen et al reach inappropriate conclusions on the effect of sedation on the accuracy and treatment outcomes for diagnostic injections Letter to the editor RE: Cohen SP, Hameed H, Kurihara C, et al. The effect of sedation on the accuracy and treatment outcomes for diagnostic injections: A randomized, controlled, crossover study. *Pain Med* 2014; 15:588-602. *Pain Med* 2014; 15:1978-1980.
187. Mainka T, Lemburg SP, Heyer CM, Altenscheidt J, Nicolas V, Maier C. Association between clinical signs assessed by manual segmental examination and findings of the lumbar facet joints on magnetic resonance scans in subjects with and without current low back pain: A prospective, single-blind study. *Pain* 2013; 154:1886-1895.
188. Manchikanti L, Singh V, Falco FJ, Cash KA, Pampati V. Evaluation of lumbar facet joint nerve blocks in managing chronic low back pain: A randomized, double-blind, controlled trial with a 2-year follow-up. *Int J Med Sci* 2010; 7:124-135.
189. Manchikanti L, Singh V, Falco FJE, Cash KA, Fellows B. Comparative outcomes of a 2-year follow-up of cervical medial branch blocks in management of chronic neck pain: A randomized, double-blind controlled trial. *Pain Physician* 2010; 13:437-450.
190. Manchikanti L, Singh V, Falco FJE, Cash KA, Pampati V, Fellows B. The role of thoracic medial branch blocks in managing chronic mid and upper back pain: A randomized, double-blind, active-control trial with a 2-year follow-up. *Anesthesiol Res Pract* 2012; 2012:585806.
191. Manchikanti L, Kaye AD, Boswell MV, Bakshi S, Gharibo CG, Grami V, Grider JS, Gupta S, Jha S, Mann DP, Nampiaparampil DE, Sharma ML, Shroyer LN, Singh V, Soin A, Vallejo R, Wargo BW, Hirsch JA. A systematic review of efficacy and best evidence synthesis of therapeutic facet joint interventions in managing chronic spinal pain. *Pain Physician* 2015; in press.
192. Leggett LE, Soril LJ, Lorenzetti DL, Noseworthy T, Steadman R, Tiwana S, Clement F. Radiofrequency ablation for chronic low back pain: A systematic review of randomized controlled trials. *Pain Res Manag* 2014; 19:e146-e153.
193. Poetscher AW, Gentil AF, Lenza M, Ferretti M. Radiofrequency denervation for facet joint low back pain: A systematic review. *Spine (Phila Pa 1976)* 2014; 39:E842-E849.
194. Lord SM, Barnsley L, Wallis BJ, McDonald GJ, Bogduk N. Percutaneous radiofrequency neurotomy for chronic cervical zygapophyseal-joint pain. *N Engl J Med* 1996; 335:1721-1726.
195. Civelek E, Cansever T, Kabatas S, Kircelli A, Yilmaz C, Musluman M, Ofluoglu D, Caner H. Comparison of effectiveness of facet joint injection and radiofrequency denervation in chronic low back pain. *Turk Neurosurg* 2012; 22:200-206.
196. Nath S, Nath CA, Pettersson K. Percutaneous lumbar zygapophysial (facet) joint neurotomy using radiofrequency current, in the management of chronic low back pain. A randomized double-blind trial. *Spine (Phila Pa 1976)* 2008; 33:1291-1297.
197. Fujiwara A, Tamai K, Yamato M, An HS, Yoshida H, Saotome K, Kurihashi A. The relationship between facet joint osteoarthritis and disc degeneration of the lumbar spine: An MRI study. *Eur Spine J* 1999; 8:396-401.
198. Saal JS. General principles of diagnostic testing as related to painful lumbar spine disorders: A critical appraisal of current diagnostic techniques. *Spine (Phila Pa 1976)* 2002; 27:2538-2545.
199. Schwarzer AC, Derby R, Aprill CN, Fortin J, Kine G, Bogduk N. The value of the provocation response in lumbar zygapophysial joint injections. *Clin J Pain* 1994; 10:309-313.
200. Kaplan M, Dreyfuss P, Halbrook B, Bogduk N. The ability of lumbar medial branch blocks to anesthetize the zygapophysial joint. *Spine (Phila Pa 1976)* 1998; 23:1847-1852.
201. Dreyfuss P, Schwarzer AC, Lau P, Bogduk N. Specificity of lumbar medial branch and L5 dorsal ramus blocks. A computed tomography study. *Spine (Phila Pa 1976)* 1997; 22:895-902.
202. Eden J, Levit L, Berg A, Morton S (eds); Committee on Standards for Systematic Reviews of Comparative Effectiveness Research; Institute of Medicine. *Finding What Works in Health Care. Standards for Systematic Reviews.* The National Academies Press, Washington, DC, 2011.
203. Pinto RZ, Maher CG, Ferreira ML, Hancock M, Oliveira VC, McLachlan AJ, Koes B, Ferreira PH. Epidural corticosteroid injections in the management of sciatica: A systematic review and meta-analysis. *Ann Intern Med* 2012; 157:865-877.
204. Chou R, Hashimoto R, Friedly J, Fu Rochelle, Dana T, Sullivan S, Bougatsos C, Jarvik J. Pain Management Injection Therapies for Low Back Pain. Technology Assessment Report ESIB0813. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. HHSA 290-2012-00014-I.) Rockville, MD: Agency for Healthcare Research and Quality; March 20, 2015.
www.cms.gov/Medicare/Coverage/DeterminationProcess/Downloads/id98TA.pdf
205. Health Technology Assessment, Washington State Health Care Authority. *Spinal Injections,* Updated Final Evidence Report. Spectrum Research, Inc., March 10, 2011.
www.hta.hca.wa.gov/documents/updated_final_report_spinal_injec-

tions_0310-1.pdf

206. Manchikanti L, Benyamin RM, Falco FJ, Kaye AD, Hirsch JA. Do epidural injections provide short- and long-term relief for lumbar disc herniation? A systematic review. *Clin Orthop Relat Res* 2015; 473:1940-1956.
207. Manchikanti L, Nampiaparampil DE, Candido KD, Bakshi S, Grider JS, Falco FJE, Sehgal N, Hirsch JA. Do cervical epidural injections provide long-term relief in neck and upper extremity pain? A systematic review. *Pain Physician* 2015; 18:39-60.
208. Manchikanti L, Kaye AD, Manchikanti KN, Boswell MV, Pampati V, Hirsch JA. Efficacy of epidural injections in the treatment of lumbar central spinal stenosis: A systematic review. *Anesthesiol Pain Med* 2015; 5:e23139.
209. Manchikanti L, Hirsch JA, Cohen SP, Heavner JE, Falco FJE, Diwan S, Boswell MV, Candido KD, Onyewu O, Zhu J, Sehgal N, Kaye AD, Benyamin RM, Helm II S, Singh V, Datta S, Abdi S, Christo PJ, Hameed H, Hameed M, Vallejo R, Pampati V, Racz GB, Raj PP. Assessment of methodologic quality of randomized trials of interventional techniques: Development of an interventional pain management specific instrument. *Pain Physician* 2014; 17:E263-E290.
210. Young BK, Greenberg PB. Are the Institute of Medicine's Trustworthiness Guidelines Trustworthy? *R I Med J* 2013; 96:13-14.