

Systematic Review



An Update of Evaluation of Therapeutic Thoracic Facet Joint Interventions

Kavita N. Manchikanti, MD¹, Sairam Atluri, MD², Vijay Singh, MD³, Stephanie Geffert, MLIS⁴, Nalini Sehgal, MD⁵, and Frank J.E. Falco, MD⁴

From: ¹University of Kentucky, Lexington, KY; ²Tri-State Spine Care Institute, Cincinnati, OH; ³Spine Pain Diagnostics Associates, Niagara, WI; ⁴Mid Atlantic Spine & Pain Physicians of Newark, Newark, DE; and Temple University Hospital, Philadelphia, PA; and ⁵University of Wisconsin School of Medicine and Public Health, Madison, WI.

Dr. Manchikanti is a second year resident in Physical Medicine and Rehabilitation at the University of Kentucky, Lexington, KY.

Dr. Atluri is Medical Director, Tri-State Spine Care Institute, Cincinnati, OH. Dr. Singh is Medical Director, Spine Pain Diagnostics Associates, Niagara, WI.

Ms. Geffert is Director of Research and Education and Administrative Assistant at Mid Atlantic Spine & Pain Physicians of Newark, DE and Fellowship Coordinator at Temple University Hospital, Philadelphia, PA. Dr. Sehgal is Medical Director, Interventional Pain Program, University of Wisconsin School of Medicine and Public Health and Associate Professor, Department of Orthopedics and Rehabilitation Medicine, Madison, WI.

Dr. Falco is Medical Director of the Mid Atlantic Spine & Pain Physicians of Newark, DE; Director, Pain Medicine Fellowship, Temple University Hospital, Philadelphia, PA and Associate Professor, Department of PM&R, Temple University Medical School, Philadelphia, PA.

Address correspondence:
Frank J.E. Falco, MD
139 East Chestnut Hill Road
Newark, DE 19713
E-mail: cssm01@aol.com;

Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: None.

Manuscript received: 05/12/2012
Accepted for publication: 06/22/2012

Free full manuscript:
www.painphysicianjournal.com

Background: Chronic mid back and upper back pain caused by thoracic facet joints has been reported in 34% to 48% of patients based on responses to controlled diagnostic blocks. Systematic reviews have established moderate evidence for controlled comparative local anesthetic blocks of thoracic facet joints in the diagnosis of mid back and upper back pain, moderate evidence for therapeutic thoracic medial branch blocks, and limited evidence for radiofrequency neurotomy of thoracic medial branches.

Study Design: Systematic review of therapeutic thoracic facet joint interventions.

Objective: To determine the clinical utility of therapeutic thoracic facet joint interventions in the therapeutic management of chronic upper back and mid back pain.

Methods: The available literature for the utility of facet joint interventions in the therapeutic management of thoracic facet joint pain was reviewed. The quality assessment and clinical relevance criteria utilized were the Cochrane Musculoskeletal Review Group criteria as utilized for interventional techniques for randomized trials and the criteria developed by the Newcastle-Ottawa Scale criteria for observational studies.

The level of evidence was classified as good, fair, and limited (or poor) based on the quality of evidence developed by the U.S. Preventive Services Task Force (USPSTF).

Data sources included relevant literature identified through searches of PubMed and EMBASE from 1966 to March 2012, and manual searches of the bibliographies of known primary and review articles.

Outcome Measures: The primary outcome measure was pain relief (short-term relief = up to 6 months and long-term > 6 months). Secondary outcome measures were improvement in functional status, psychological status, return to work, and reduction in opioid intake.

Results: For this systematic review, 13 studies were identified. Of these, 7 studies were excluded, and a total of 4 studies (after removal of duplicate publication) met inclusion criteria for methodological quality assessment with one randomized trial and 3 non-randomized studies.

The evidence is fair for therapeutic thoracic facet joint nerve blocks, limited for thoracic radiofrequency neurotomy, and not available for thoracic intraarticular injections.

Limitations: The limitation of this systematic review includes a paucity of literature. The only positive studies were of medial branch blocks performed by the same group of authors.

Conclusion: The evidence for therapeutic facet joint interventions is fair for medial branch blocks, whereas it is not available for intraarticular injections, and limited for radiofrequency neurotomy due to lack of literature.

Key words: Chronic thoracic pain, mid back or upper back pain, thoracic facet or zygapophysial joint pain, facet joint nerve blocks, medial branch blocks, therapeutic thoracic medial branch blocks, thoracic radiofrequency neurotomy, thoracic intraarticular facet joint injections

Pain Physician 2012; 15:E463-E481

While the lifetime prevalence of spinal pain has been reported as occurring in 54% to 80% of the general population, patients suffering from chronic upper or mid back pain secondary to thoracic disorders is relatively small, specifically in interventional pain management settings, where it ranges from a low of 3% to a high of 22% (1-13). Multiple authors have estimated thoracic pain to be less prevalent than low back or neck pain. In fact, Leboeuf-Yde et al (1) reported that low back pain in the past year was most frequent in 43% of patients, followed by neck pain in 32%, and mid back pain in 13%. Regardless of the area of the complaint; however, care seeking and reduced physical activities are common with thoracic pain, greatly affecting quality of life. The prevalence of mid back and upper back pain secondary to involvement of the facet joints has been reported in controlled studies in as many as 34% to 48% of patients (6,14-18). Since conventional clinical and radiologic techniques are unreliable in diagnosing facet or zygapophyseal joint pain (3,16-32), controlled local anesthetic blocks of thoracic facet joints or medial branch blocks are employed to diagnose facet joint pain, and are considered the most reliable means of diagnosis (3,10,16-18,32,33).

Medial branch blocks and radiofrequency neurotomy have been described in managing chronic mid back and upper back pain from thoracic facet joints (10,34-46). However, the evidence has been highly variable.

Previous systematic reviews have provided moderate evidence for therapeutic thoracic medial branch blocks (16-18), whereas evidence for radiofrequency neurotomy of thoracic facet joint nerves was indeterminate (16-18). Consequently, this systematic review has been undertaken in order to update and determine the effectiveness of thoracic facet joint interventions in the management of chronic mid back and upper back pain (16).

1.0 METHODS

The methodology utilized in this systematic review followed the review process derived from evidence-based systematic reviews and meta-analysis of randomized trials and observational studies (3,47-56), Cochrane guidelines (52,53,57), Consolidated Standards of Reporting Trials (CONSORT) guidelines for the conduct of randomized trials (58-61), Standards for Reporting Observational Studies (STROBE) (62), Chou and Huffman's guidelines (63,64), and quality of reporting of analysis (49).

1.1 Criteria for Considering Studies for This Review

1.1.1 Types of Studies

- Randomized controlled trials
- Non-randomized observational studies
- Case reports and reviews for adverse effects

1.1.2 Types of Participants

Participants of interest were adults aged at least 18 years with chronic upper and mid back pain of at least 3 months duration.

Participants must have failed previous pharmacotherapy, exercise therapy, etc., prior to starting interventional pain management techniques.

1.1.3 Types of Interventions

The interventions were therapeutic thoracic facet joint blocks appropriately performed with proper techniques under fluoroscopic or computed tomography (CT) guidance.

1.1.4 Types of Outcome Measures

- ◆ The primary outcome parameter was pain relief.
- ◆ The secondary outcome measures were functional improvement; change in psychological status; return to work; reduction or elimination of opioid use, other drugs.
- ◆ At least 2 of the review authors independently, in an unblinded standardized manner, assessed the outcomes measures. Any disagreements between reviewers were resolved by a third author and consensus.

1.2 Literature Search

Searches were performed from the following sources without language restrictions:

1. PubMed from 1966
www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed
2. EMBASE from 1980
www.embase.com/
3. Cochrane Library
www.thecochranelibrary.com/view/0/index.html
4. U.S. National Guideline Clearinghouse (NGC)
www.guideline.gov
5. Previous systematic reviews and cross references
6. Clinical Trials
www.clinicaltrials.gov

The search period was from 1966 through March 2012.

1.3 Search Strategy

The search strategy emphasized chronic thoracic pain of facet joint origin with a focus on all types of therapeutic interventions. Search terminology included thoracic facet joint, thoracic facet joint pain, thoracic facet joint intraarticular injections, medial branch blocks, and radiofrequency neurotomy.

At least 2 of the review authors independently, in an unblinded standardized manner, performed each search. Accuracy was confirmed by a statistician. All searches were combined to obtain a unified search strategy. Any disagreements between reviewers were resolved by a third author and consensus.

1.4 Data Collection and Analysis

The review focused on randomized trials, observational studies, and reports of complications. The population of interest was patients suffering from chronic upper and mid back pain for at least 3 months. Only thoracic facet joint interventions were evaluated. All of the studies providing appropriate management, statistical evaluations and with outcome evaluations of one month or longer were reviewed. Reports without appropriate diagnosis, non-systematic reviews, book chapters, and case reports were excluded.

1.4.1 Selection of Studies

- ◆ In an unblinded standardized manner, 2 review authors screened the abstracts of all identified studies against the inclusion criteria.
- ◆ All articles with possible relevance were then retrieved in full text for a comprehensive assessment of internal validity, quality, and adherence to inclusion criteria.

1.4.2 Inclusion and Exclusion Criteria

Inclusion criteria were studies which documented the existence of thoracic spinal pain of facet joint ori-

gin using controlled diagnostic facet joint injections or medial branches. Three types of facet joint interventions were included in this review: intraarticular facet joint injections, medial branch blocks, and medial branch radiofrequency neurotomy. All studies must provide appropriate management with outcome evaluations of at least 6 months and appropriate statistical analysis.

Reports without appropriate diagnosis and elimination of false-positive responses, abstracts beyond 2 years, non-systematic reviews, book chapters, and case reports were excluded.

1.4.3 Clinical Relevance

The clinical relevance of the included studies were evaluated according to 5 questions recommended by the Cochrane Back Review Group (Table 1) (65). Each question was scored as positive (+) if the clinical relevance item was met, negative (-) if the item was not met, and unclear (?) if data were not available to answer the question.

1.4.4 Methodological Quality or Validity Assessment

The quality of each individual article used in this analysis was assessed by Cochrane review criteria (Table 2) (52) for randomized trials or the Newcastle-Ottawa Scale for observational studies (Tables 3 and 4) (66).

Each study was evaluated by at least 2 authors for stated criteria and any disagreements were discussed with a third reviewer. Authors with a perceived conflict of interest for any manuscript were recused from reviewing the manuscript.

For adverse effects, confounding factors, etc., it was not possible to use quality assessment criteria. Thus, these were considered based on interpretation of the reports published and critical analysis of the literature.

Table 1. *Clinical relevance questions.*

	P (+)	N (-)	U (unclear)
A) Are the patients described in detail so that one can decide whether they are comparable to those who are treated practice?			
B) Are the interventions and treatment settings described in sufficient detail to apply its use in clinical practice?			
C) Were clinically relevant outcomes measured and reported?			
D) Is the size of the effect clinically meaningful?			
E) Do the likely treatment benefits outweigh the potential harms?			

Scoring adapted and modified from Staal JB, et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (65).

Table 2. *Randomized controlled trials quality rating system.*

A	1. Was the method of randomization adequate?	A random (unpredictable) assignment sequence. Examples of adequate methods are coin toss (for studies with 2 groups), rolling a die (for studies with 2 or more groups), drawing of balls of different colors, drawing of ballots with the study group labels from a dark bag, computer-generated random sequence, pre-ordered sealed envelopes, sequentially ordered vials, telephone call to a central office, and pre-ordered list of treatment assignments. Examples of inadequate methods are alternation, birth date, social insurance/security number, date in which they are invited to participate in the study, and hospital registration number.	Yes/No/Unsure
B	2. Was the treatment allocation concealed?	Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.	Yes/No/Unsure
C	Was knowledge of the allocated interventions adequately prevented during the study?		
	3. Was the patient blinded to the intervention?	This item should be scored "yes" if the index and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful.	Yes/No/Unsure
	4. Was the care provider blinded to the intervention?	This item should be scored "yes" if the index and control groups are indistinguishable for the care providers or if the success of blinding was tested among the care providers and it was successful.	Yes/No/Unsure
	5. Was the outcome assessor blinded to the intervention?	Adequacy of blinding should be assessed for the primary outcomes. This item should be scored "yes" if the success of blinding was tested among the outcome assessors and it was successful or: –for patient-reported outcomes in which the patient is the outcome assessor (e.g., pain, disability): the blinding procedure is adequate for outcome assessors if participant blinding is scored "yes" –for outcome criteria assessed during scheduled visit and that supposes a contact between participants and outcome assessors (e.g., clinical examination): the blinding procedure is adequate if patients are blinded, and the treatment or adverse effects of the treatment cannot be noticed during clinical examination –for outcome criteria that do not suppose a contact with participants (e.g., radiography, magnetic resonance imaging): the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed when assessing the main outcome –for outcome criteria that are clinical or therapeutic events that will be determined by the interaction between patients and care providers (e.g., co-interventions, hospitalization length, treatment failure), in which the care provider is the outcome assessor: the blinding procedure is adequate for outcome assessors if item "4" (caregivers) is scored "yes" –for outcome criteria that are assessed from data of the medical forms: the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed on the extracted data.	Yes/No/Unsure
D	Were incomplete outcome data adequately addressed?		
	6. Was the drop-out rate described and acceptable?	The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias a "yes" is scored. (N.B. these percentages are arbitrary, not supported by literature).	Yes/No/Unsure
	7. Were all randomized participants analyzed in the group to which they were allocated?	All randomized patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of non-compliance and co-interventions.	Yes/No/Unsure
E	8. Are reports of the study free of suggestion of selective outcome reporting?	In order to receive a "yes," the review author determines if all the results from all pre-specified outcomes have been adequately reported in the published report of the trial. This information is either obtained by comparing the protocol and the report, or in the absence of the protocol, assessing that the published report includes enough information to make this judgment.	Yes/No/Unsure
F	Other sources of potential bias:		
	9. Were the groups similar at baseline regarding the most important prognostic indicators?	In order to receive a "yes," groups have to be similar at baseline regarding demographic factors, duration and severity of complaints, percentage of patients with neurological symptoms, and value of main outcome measure(s).	Yes/No/Unsure
	10. Were co-interventions avoided or similar?	This item should be scored "yes" if there were no co-interventions or they were similar between the index and control groups.	Yes/No/Unsure
	11. Was the compliance acceptable in all groups?	The reviewer determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s). For example, physiotherapy treatment is usually administered over several sessions; therefore, it is necessary to assess how many sessions each patient attended. For single-session interventions (e.g., surgery), this item is irrelevant.	Yes/No/Unsure
	12. Was the timing of the outcome assessment similar in all groups?	Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.	Yes/No/Unsure

Adapted and modified from Furlan AD, et al; Editorial Board, Cochrane Back Review Group. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine* (Phila Pa 1976) 2009; 34:1929-1941 (52).

Table 3. *Newcastle-Ottawa quality assessment scale for case control studies.*

Selection
1) Is the case definition adequate?
a) yes, with independent validation *
b) yes, e.g. record linkage or based on self reports
c) no description
2) Representativeness of the cases
a) consecutive or obviously representative series of cases *
b) potential for selection biases or not stated
3) Selection of controls
a) community controls *
b) hospital controls
c) no description
4) Definition of controls
a) no history of disease (endpoint) *
b) no description of source
Comparability
1) Comparability of cases and controls on the basis of the design or analysis
a) study controls for _____ (Select the most important factor.) *
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)
Exposure
1) Ascertainment of exposure
a) secure record (eg surgical records) *
b) structured interview where blind to case/control status *
c) interview not blinded to case/control status
d) written self report or medical record only
e) no description
2) Same method of ascertainment for cases and controls
a) yes *
b) no
3) Non-response rate
a) same rate for both groups *
b) non respondents described
c) rate different and no designation

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Wells GA, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (66).

Only the randomized trials meeting the inclusion criteria with at least 6 of 12 criteria were utilized for analysis. However, studies scoring lower were described and provided with an opinion and critical analysis.

Observational studies had to meet a minimum of 50% of the utilized criteria for cohort and case-control studies. Studies scoring less were also described and provided with an opinion and a critical analysis.

Table 4. *Newcastle-Ottawa quality assessment scale for cohort studies.*

Selection
1) Representativeness of the exposed cohort
a) truly representative of the average _____ (describe) in the community *
b) somewhat representative of the average _____ in the community *
c) selected group of users, e.g. nurses, volunteers
d) no description of the derivation of the cohort
2) Selection of the non exposed cohort
a) drawn from the same community as the exposed cohort *
b) drawn from a different source
c) no description of the derivation of the non exposed cohort
3) Ascertainment of exposure
a) secure record (e.g. surgical records) *
b) structured interview *
c) written self report
d) no description
4) Demonstration that outcome of interest was not present at start of study
a) yes *
b) no
Comparability
1) Comparability of cohorts on the basis of the design or analysis
a) study controls for _____ (select the most important factor) *
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)
Outcome
1) Assessment of outcome
a) independent blind assessment *
b) record linkage *
c) self report
d) no description
2) Was follow-up long enough for outcomes to occur
a) yes (select an adequate follow-up period for outcome of interest) *
b) no
3) Adequacy of follow-up of cohorts
a) complete follow-up - all subjects accounted for *
b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow-up, or description provided of those lost) *
c) follow-up rate < ____% (select an adequate %) and no description of those lost
d) no statement

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Wells GA, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (66).

If the literature search provided at least 5 randomized trials meeting the inclusion criteria and if they were homogenous for each modality (intraarticular injections, medial branch blocks, and radiofrequency neurotomy) evaluated, a meta-analysis was performed.

1.4.5 Data Extraction and Management

Two review authors independently, in an unblinded standardized manner, extracted the data from the included studies. Disagreements were resolved by discussion between the 2 reviewers; if no consensus could be reached, a third author was called in to break the impasse.

1.4.6 Assessment of Heterogeneity

Whenever meta-analyses were conducted, the I-squared (I²) statistic was used to identify heterogeneity (67). Combined results with I² > 50% were considered substantially heterogenous.

Analysis of the evidence was based on the modality of treatment provided (i.e., intraarticular injections, medial branch blocks, and radiofrequency neurotomy).

1.4.7 Measurement of Treatment Effect in Data Synthesis (Meta-Analysis)

Data was summarized using meta-analysis when at least 5 studies per type of treatment were available that met the inclusion criteria.

1.5 Analysis of Evidence

An analysis of the evidence was performed based on USPSTF criteria as illustrated in Table 5, criteria which has been utilized by multiple authors (68).

The analysis was conducted using 3 levels of evidence: good, fair, and limited (or poor).

At least 2 of the review authors independently, in an unblinded standardized manner, analyzed the evi-

dence. 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.

1.6 Outcome of the Studies

In the randomized trials, a study was judged to be positive if the therapeutic thoracic facet joint intervention was clinically relevant and effective, either with a placebo control or active control. This indicates that the difference in effect for primary outcome measure is statistically significant at the conventional 5% level. In a negative study, no difference between the study treatments or no improvement from baseline is identified. Furthermore, the outcomes were judged at the reference point with positive or negative results reported at one month, 3 months, 6 months, and one year.

For observational studies, a study was judged to be positive if the intervention was effective, with outcomes reported at the reference point with positive or negative results at one month, 3 months, 6 months, and one year.

The minimum amount of change in a pain score in order to be clinically meaningful has been described as a 2-point change on a scale of 0 to 10 (or 20 percentage points), based on findings in commonly utilized trials studying general chronic pain (69), chronic musculoskeletal pain (70), and chronic low back pain (47,49,51,52,71,72). However, later descriptions of clinically meaningful improvement showed either pain relief or functional status as 50% (73-86). Consequently, for this analysis, we consider clinically meaningful pain relief of at least a 3-point change on an 11-point scale of 0 to 10, or 50% pain relief from the baseline, or a functional status improvement of 40% as being clinically significant.

Table 5. Method for grading the overall strength of the evidence for an intervention.

Grade	Definition
Good	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (at least 2 consistent, higher-quality RCTs or studies of diagnostic test accuracy).
Fair	Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (at least one higher-quality trial or study of diagnostic test accuracy of sufficient sample size; 2 or more higher-quality trials or studies of diagnostic test accuracy with some inconsistency; at least 2 consistent, lower-quality trials or studies of diagnostic test accuracy, or multiple consistent observational studies with no significant methodological flaws).
Limited or poor	Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality trials, important flaws in trial design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

Adapted and modified from methods developed by U.S. Preventive Services Task Force (63,64,68).

2.0 RESULTS

Figure 1 shows a flow diagram of study selection as recommended by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (50). There were 13 studies considered for inclusion (10,35-43,45,46,87).

Of the 13 studies (10,35-43,45,46,87) identified, 7 were excluded (35,40,41,43,45,46,87). Table 6 shows the reasons for exclusion. Among the included stud-

ies, there were 3 publications of one randomized trial (36,38,39), and 3 non-randomized studies (10,37,42).

Table 7 illustrates characteristics of studies considered for inclusion. There was one randomized trial evaluating long-term follow-up (39) with 2 duplicate publications (36,38), one non-randomized study for long-term follow-up (37) of therapeutic medial branch blocks, and 2 studies of thoracic radiofrequency neurotomy (10,42).

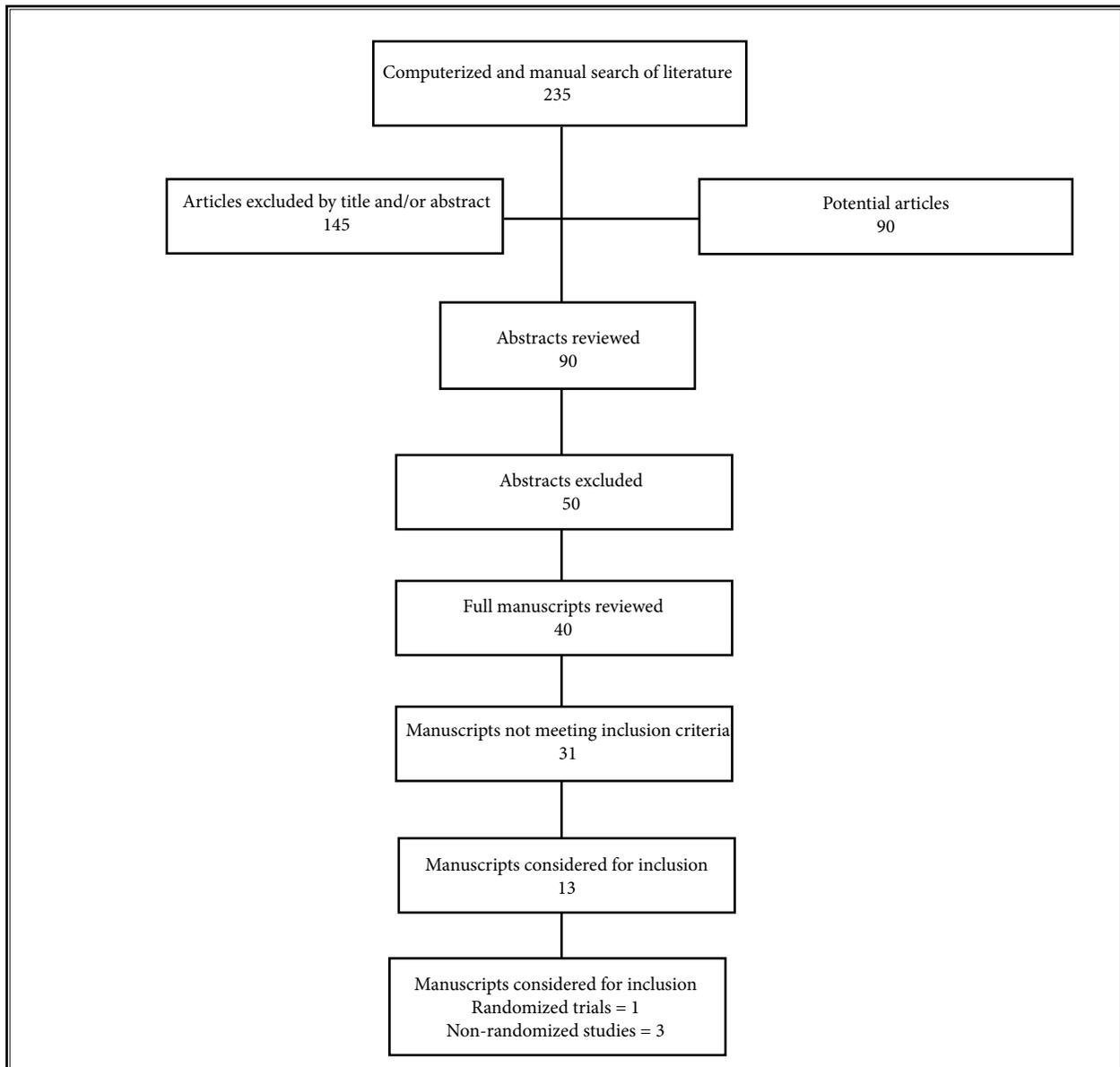


Fig. 1. The flow diagram illustrating published literature evaluating therapeutic thoracic facet joint interventions.

Table 6. List of excluded studies.

Manuscript Author(s)	Reason for Exclusion
Tzaan & Tasker (35)	This study showed results of percutaneous radiofrequency, facet rhizotomy, an experience with 118 procedures; however, the study included only 90 patients for cervical, lumbar, and thoracic regions. Thus, the number of patients treated in the thoracic region was only 17.
Stolker et al (40)	This was an anatomical study to verify if needle placement for thoracic percutaneous facet denervation, based on bony landmarks, and under fluoroscopic guidance would lead to constant anatomical positioning and adequate placement at the assumed target. The procedures were carried out in 2 cadavers at all 12 levels.
Stolker et al (41)	This study was undertaken to clarify if needle positioning in percutaneous partial rhizotomy in the thoracic area based on bony landmarks and guided by fluoroscopic control led to adequate placement in or at the target area of dorsal root ganglion in cadavers.
Chua et al (43)	This manuscript described mechanisms and potential indications of pulsed radiofrequency.
Golovac (45)	Review of radiofrequency neurolysis.
Mitra et al (46)	Describes thoracic compression fractures.
Haufe & Mork (87)	Authors described endoscopic facet debridement of facet arthritic pain.

2.1 Clinical Relevance

Four studies were assessed for clinical relevance (Table 8). All studies met criteria with a score of 5 (10,37,39,42).

2.2 Methodological Quality Assessment

A methodological quality assessment of the randomized controlled trials meeting inclusion criteria was carried out utilizing Cochrane review criteria as shown in Table 9. Studies achieving Cochrane scores of 9 or higher were considered as high quality, scores of 6 to 8 were considered as moderate quality, and studies scoring less than 6 were excluded.

There was only one randomized trial (after combining duplicates) evaluating a long-term response of 6 months or longer (36,38,39) that was considered high quality.

A methodological quality assessment of observational studies meeting inclusion criteria was carried out utilizing Newcastle-Ottawa Scales as illustrated in Table 10. For cohort studies, studies achieving scores of 75% or higher were considered high quality; scores of 50% were considered as moderate quality; and studies scoring less than 50% were considered as low quality and were excluded.

There was only one non-randomized or observational study evaluating the long-term effectiveness of thoracic facet joint medial branch blocks with follow-up of 6 months or longer (37). This study was considered as being of moderate quality. There were 2 observational studies evaluating thoracic radiofrequency (10,42).

2.3 Meta-Analysis

There was only one trial for medial branch blocks, with none for intraarticular injections or radiofrequency neurotomy. Consequently, no meta-analysis was feasible.

2.4 Analysis of Evidence

The evidence was synthesized based on the specific condition for which the thoracic facet joint interventions were provided. Table 11 illustrates the results of thoracic facet joint interventions.

2.5 Summary of Evidence

In summary, the evidence is fair for medial branch blocks, whereas it is not available for intraarticular injections, and limited for radiofrequency neurotomy.

3.0 DISCUSSION

This systematic review evaluating the effectiveness of therapeutic facet joint interventions with the inclusion of one double-blind randomized trial (36,38,39), 2 duplicate publications (36,38), and one observational report (37) of medial branch blocks provides fair evidence for medial branch blocks in managing chronic mid back or upper back pain. Two observational studies of radiofrequency neurotomy (10,42) provide limited evidence for radiofrequency neurotomy. There was no evidence to be reviewed for intraarticular injections. In addition, due to a paucity of evidence, non-randomized studies were also included with only 25 patients and without comparative groups. Even then, we were un-

Table 7. Study characteristics of published reports of therapeutic thoracic medial branch blocks and radiofrequency neurotomy.

Study/ Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief ≤ 6 mos Long-term relief > 6 mos
Stolker et al, 1993 (10) Prospective outcome study	40 patients with thoracic pain were evaluated	Radiofrequency neurotomy	Pain relief with numeric rating scale	Forty patients underwent 51 percutaneous facet denervation sessions. Nine patients underwent more than one session, 7 patients 2 sessions, and 2 patients 3 sessions. The results per treatment based on a numeric rating scale were 84% of the patients reporting greater than 50% pain reduction, 36 patients were followed on a long-term basis. Of these, 23 patients responded with good or excellent results (64%).	Effectiveness of radiofrequency was demonstrated in this early study with positive short-term and long-term relief.
Manchikanti, et al, 2008, 2010,2012 (36,38,39) Randomized, double-blind, controlled trial	100 patients were included with 50 patients in each of the local anesthetic and steroid groups	Group I patients received thoracic medial branch blocks with bupivacaine. Group II patients received thoracic medial branch blocks with bupivacaine and non-particulate betamethasone.	Numeric pain scores, Oswestry Disability Index, opioid intake, and return to work status. All outcomes were assessed at baseline, 6 months, 12 months, and 24 mos. Significant pain relief was defined as > 50% relief. Significant functional improvement was > 40% reduction of Oswestry Disability Index.	In Group I, 80% of patients showed significant pain relief and functional improvement at 12 and 24 months. In Group II, 84% of patients showed significant pain relief and functional improvement at 12 months and 24 mos. The majority of patients experienced significant pain relief for 46 to 47 weeks, requiring approximately 3 to 4 treatments with an average relief of 14 to 16 weeks per episode of a treatment.	The majority of patients in both groups experienced significant pain relief and improvement in functional status. Therapeutic thoracic medial branch blocks, with or without steroid, may provide a management option for chronic function-limiting mid back or upper back pain of facet joint origin. Positive short-term and long-term relief.
Manchikanti et al, 2006 (37) Prospective outcome study	55 consecutive patients, all meeting diagnostic criteria for thoracic facet joint pain	Thoracic facet joint nerve blocks performed using bupivacaine with or without Sarapin and deponethylprednisolone prednisolone	Measured numeric pain scores, Oswestry Disability Index, employment status, and Pain Patient Profile at 3, 6, 12, 24, and 36 months.	Significant (≥ 50%), was observed in 71% of the patients at 3 months and 6 months, 76% at 12 months, 71% at 24 months, and 69% at 36 months.	Therapeutic thoracic medial branch blocks were an effective modality of treatment in managing chronic thoracic pain secondary to facet joint involvement confirmed by controlled, comparative local anesthetic blocks. Positive short-term and long-term relief.
Speldewinde, 2011 (42) Prospective outcome evaluation	28 patients with thoracic pain as part of outcomes of percutaneous zygapophysial and sacroiliac joint neurotomy in a community setting with total of 379 patients included	Radiofrequency neurotomy	Numeric rating scale, functional rating index, activities of daily living scale, general health questionnaire, depression and anxiety scale, duration of pain relief.	Successful outcome defined as at least 50% reduction of pain, for at least 2 months, in the region relevant to the joint or joints treated was present in 68% of the patients in the thoracic region with radiofrequency neurotomy.	The results also showed 85% pain relief for 9 months in 18 of 28 patients (64%). Radiofrequency neurotomy of thoracic facet joint nerve may provide positive short-term and long-term relief.

Table 8. Clinical relevance of included studies.

Manuscript Author(s)	A) Patient description	B) Description of interventions and treatment settings	C) Clinically relevant outcomes	D) Clinical importance	E) Benefits versus potential harms	Total Criteria Met
Stolker et al (10)	+	+	+	+	+	5/5
Manchikanti, et al (36,38,39)	+	+	+	+	+	5/5
Manchikanti, et al (37)	+	+	+	+	+	5/5
Speldewinde (42)	+	+	+	+	+	5/5

+ = positive; - = negative ; U = unclear

Scoring adapted from Staal JB, et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (65).

able to assess any evidence for intraarticular injections. However, with medial branch blocks, both the studies (36-39), with 2 duplicate publications (36,38), meeting the inclusion criteria were performed by the same group of authors.

In this evaluation, a total of 4 studies meeting inclusion criteria were included (10,36,37,38,39,42), with 2 duplicate publications (36,38). Only one randomized trial was available which was of high quality (36,38,39), whereas the observational studies included for medial branch nerve blocks (37) and for radiofrequency neurotomy were of moderate quality (10,42). Consequently, the paucity of published reports describing the effectiveness of thoracic facet joint interventions for the treatment of chronic thoracic pain is the obvious shortcoming of this review. Even though thoracic facet joint pain is lower in incidence and prevalence than lumbar and cervical pain, the disability may be similar. The only one randomized trial to date (36,38,39) of medial branch blocks showed effectiveness for patients with chronic pain secondary to thoracic facet joint arthropathy. The results were also supported by an observational study which was published prior to the randomized trial. In reference to radiofrequency neurotomy there were multiple studies. Although, there have not been any randomized trials. Among the observational studies only 2 studies met inclusion criteria.

Multiple complications are similar to those of the cervical or lumbar region (88-99), these include bleeding, infection, and neural trauma. In the United States, facet joint interventions are one of the most commonly utilized modalities of treatments in managing chronic thoracic pain, similar to neck and low back pain (3,100-108). The facet joint interventions are administered by 3 approaches utilizing either intraarticular injection, medial branch block, or by performing radiofrequency

Table 9. Methodological quality assessment of randomized trials.

	Manchikanti et al (36,38,39)
Randomization adequate	+
Concealed treatment allocation	+
Patient blinded	+
Care provider blinded	+
Outcome assessor blinded	-
Drop-out rate described	+
All randomized participants analyzed in the group	+
Reports of the study free of suggestion of selective outcome reporting	+
Groups similar at baseline regarding most important prognostic indicators	-
Co-interventions avoided or similar	+
Compliance acceptable in all groups	+
Time of outcome assessment in all groups similar	+
Score	10/12

+ = positive; - = negative ; U = unclear

neurotomy. Radiofrequency neurotomy may be performed with conventional heat radiofrequency, pulsed radiofrequency, or cooled radiofrequency.

Atluri et al (16) in a systematic review of the effectiveness of thoracic facet joint interventions discussed the effectiveness as well as complications arising from interventions, along with a paucity of the literature. They concluded that there was fair evidence supporting therapeutic medial branch nerve blocks. However, there was no significant evidence for radiofrequency

Table 10. *Methodologic quality assessment of cohort studies utilizing Newcastle-Ottawa quality assessment scale.*

	Stolker et al (10)	Manchikanti et al (37)	Speldewinde (42)
Selection			
1) Representativeness of the exposed cohort			
a) truly representative of the average _____ (describe) in the community *	+	+	+
b) somewhat representative of the average pain patients in the community *			
c) selected group of users (e.g. nurses, volunteers)			
d) no description of the derivation of the cohort			
2) Selection of the non exposed cohort			
a) drawn from the same community as the exposed cohort *	+	+	+
b) drawn from a different source			
c) no description of the derivation of the non exposed cohort			
3) Ascertainment of exposure			
a) secure record (e.g. surgical records) *			
b) structured interview *	+	+	+
c) written self report			
d) no description			
4) Demonstration that outcome of interest was not present at start of study			
a) yes *	+		
b) no			
Comparability			
1) Comparability of cohorts on the basis of the design or analysis			
a) study controls for _____ (select the most important factor) *			
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)			
Outcome (Exposure)			
1) Assessment of outcome			
a) independent blind assessment *			
b) record linkage *	+	+	+
c) self report			
d) no description			
2) Was follow-up long enough for outcomes to occur			
a) yes (select an adequate follow-up period for outcome of interest) *	+	+	+
b) no			
3) Adequacy of follow up of cohorts			
a) complete follow-up - all subjects accounted for *	+	+	+
b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow-up, or description provided of those lost) *	+	+	+
c) follow-up rate < ____% (select an adequate %) and no description of those lost			
d) no statement			
SCORE	8/13	7/13	7/13

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Wells GA, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (66).

Table 11. Results of randomized and observational studies of thoracic facet joint interventions.

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief			Results	
				3 mos.	6 mos.	12 mos.	Short-term relief ≤ 6 months	Long-term relief > 6 months
MEDIAL BRANCH BLOCKS								
Manchikanti et al (36,38,39)	RA, DB	10/12	Group I - no steroid = 50 Group II- steroid = 50	79% vs 83%	79% vs 81%	80% vs 83%	P	P
Manchikanti et al (37)	P	7/13	55 consecutive patients, all meeting diagnostic criteria for thoracic facet joint pain	71%	71%	71%	P	P
CONVENTIONAL RADIOFREQUENCY NEUROTOMY								
Stolker et al (10)	P	8/13	40 patients with thoracic pain were evaluated	N/A	N/A	64%	N/A	P
Speldewinde (42)	P	7/13	28 patients with thoracic pain as part of outcomes of percutaneous zygapophysial and sacroiliac joint neurotomy in a community setting with total of 379 patients included	N/A	N/A	64%	P	P

RA = randomized; DB = double-blind; P = prospective; O = observational; vs = versus; P = positive

neurotomy, as in past reviews, and there was no literature available for intraarticular injections. In reference to therapeutic medial branch blocks, there was no difference noted between local anesthetic alone compared to local anesthetic with steroids.

The present systematic review shows that therapeutic medial branch blocks, when appropriately performed, should result in significant improvement with or without steroids. There is also emerging evidence for conventional radiofrequency neurotomy of medial branches. With the majority of interventional techniques, as with thoracic facet joint interventions, a common problem encountered is the lack of studies with placebo control. However, placebo controlled neural blockade is not realistic and has been misinterpreted (109). As a result, many authors have reported that any local anesthetic injection that yields a result simi-

lar to that of steroids is considered a placebo, though inappropriately and inaccurately. The experimental and clinical findings from investigations of the electrophysiological effects of 0.9% sodium chloride and dextrose 5% in water solution have illustrated a potential inaccuracy created by 0.9% sodium chloride solution versus 5% dextrose (110,111). In addition to this, the evidence also shows that sodium chloride solution when injected into either the disc, the facet joint, or paraspinal muscles, exerts differing effects with interactions between the porcine lumbar intervertebral disc, zygapophyseal joints, and paraspinal muscles (112,113). They also showed that the introduction of lidocaine or physiologic saline into the zygapophysial joint reduces the stimulation pathway from the intervertebral disc or paraspinal musculature (112,113). Consequently, they hypothesized that the paraspinal muscle activation

caused by nerve stimulation in the annulus fibrosis of a lumbar intervertebral disc could be altered by saline injections into the zygapophysial joints. In addition, intraarticular facet joint sodium chloride injections along with epidural sodium chloride injections have exerted active and therapeutic effects (114-117). Furthermore, for the placebo effect to be evident, it has to be non-existent with prior treatments and present progressively with repeat treatments. It also has been illustrated that there was no significant difference in therapeutic effect whether or not steroids were utilized (118-120). Finally, the placebo effects, along with various considerations of placebo and nocebo effects, have not been appropriately evaluated in performing interventional techniques (121-128). However, in a manuscript by Ghahreman et al (129), they describe how appropriate results were obtained utilizing a proper placebo-sodium chloride solution by injection into the inactive tissue.

The underlying mechanism of action of steroid and local anesthetic injections is still not well understood. It is believed that the achieved neural blockade alters or interrupts nociceptive input, the reflex mechanism of the afferent fibers, self-sustaining activity of the neurons, and the pattern of central neuronal activities (3,130). Corticosteroids have been shown to reduce inflammation by inhibiting either the synthesis or release of a number of proinflammatory mediators and by causing a reversible local anesthetic effect (130-135). Similarly, local anesthetics also have been described to provide short- to long-term symptomatic relief based on the alteration of various mechanisms including excess nociceptive process, excess release of neurotransmitters, nociceptive sensitization of the nervous system, and phenotype changes (120,130,136-141). The prolonged effect of local anesthetics in facet joint nerve blocks and epidural injections has been demonstrated in multiple studies (3,6,14,15,25,29,31,34,36-39,73,75-86). Sato et al (120) evaluated the prolonged analgesic effect of epidural bupivacaine in a rat model of neuropathic pain with repeated administration, possibly by inducing a plastic change in nociceptive input. Furthermore, Tachihara et al (118) demonstrated that nerve root infiltration in a rat prevented mechanical allodynia, even though no additional benefit from using corticosteroids was observed.

In recent years, multiple manuscripts have been published in reference to evidence, preferences, and recommendations with the intent of finding the right

balance in patient care (142-144). The literature has been replete with manuscripts in reference to randomization, evidence-based medicine requiring medicine-based evidence, and the necessity of integrating clinical research with medical practice. These evaluations and the recent flurry of criticism of evidence-based guidelines (145,146) illustrate the difficulties associated with providing practical recommendations based on evidence dependent only on randomized trials. Thus this systematic review incorporates not only the observational studies, but also emerging evidence derived from these observational studies apart from randomized trials. Furthermore, even among the randomized trials only active-control trials have been available due to the extreme difficulty in designing an appropriate randomized trial with proper sample size and utilizing appropriate outcome parameters.

The results of this systematic review may be applied in interventional pain management practices. For this systematic review, only placebo-active control trials and observational studies in practical settings were included. Active-control or practical clinical trials measure effectiveness, and may better reflect how a treatment will fair in clinical practice than placebo-control studies evaluating efficacy, which frequently have poor generalizability (73-86,147-151). The differences between placebo-control trials and active-control trials include the fact that whereas placebo-control trials measure an absolute effect size, active-control trials compare different therapies (152).

Even though the study is limited by the inclusion of only one randomized trial and 3 clinically relevant observational studies meeting inclusion criteria, radiofrequency observational studies add to the small sample sizes with perceived variations in methodology, selection criteria, outcome measures, and technique. Even then, the results of this systematic review suggest that significant improvements in pain scores and functional status can be obtained with medial branch blocks with or without steroids with fair evidence and with the radiofrequency neurotomy illustrating only limited evidence.

4.0 CONCLUSION

Based on the results of this systematic review, there is fair evidence for therapeutic medial branch blocks, with a lack of available evidence for intraarticular injections, and limited evidence for radiofrequency neurotomy.

ACKNOWLEDGMENTS

The authors wish to thank *Pain Physician* for permission to reproduce Atluri et al's manuscript from 2008 and the editorial board of *Pain Physician* for review and criticism in improving the manuscript. The authors also wish to thank Vidyasagar Pampati, MSc, for statistical

assistance; Sekar Edem for assistance in the search of the literature; Alvaro F. Gómez, MA, Bert Fellows, MA, and Laurie Swick, BS, for manuscript review; and Tonie M. Hatton and Diane E. Neihoff, transcriptionists, for their assistance in preparation of this manuscript.

REFERENCES

1. Leboeuf-Yde C, Nielsen J, Kyvik KO, Fejer R, Hartvigsen J. Pain in the lumbar, thoracic or cervical regions: Do age and gender matter? A population-based study of 34,902 Danish twins 20-71 years of age. *BMC Musculoskelet Disord* 2009; 10:39.
2. Manchikanti L, Singh V, Datta S, Cohen SP, Hirsch JA. Comprehensive review of epidemiology, scope, and impact of spinal pain. *Pain Physician* 2009; 12:E35-E70.
3. Manchikanti L, Boswell MV, Singh V, Benyamin RM, Fellows B, Abdi S, Buenaventura RM, Conn A, Datta S, Derby R, Falco FJE, Erhart S, Diwan S, Hayek SM, Helm S, Parr AT, Schultz DM, Smith HS, Wolfer LR, Hirsch JA. Comprehensive evidence-based guidelines for interventional techniques in the management of chronic spinal pain. *Pain Physician* 2009; 12:699-802.
4. Manchikanti L, Pampati V, Fellows B, Beyer CD, Damron KS, Barnhill RC, Burks T. Characteristics of chronic low back pain in patients in an interventional pain management setting: A prospective evaluation. *Pain Physician* 2001; 4:131-142.
5. Manchikanti L, Pampati V. Research designs in interventional pain management: Is randomization superior, desirable or essential? *Pain Physician* 2002; 5:275-284.
6. Manchikanti L, Boswell MV, Singh V, Pampati VS, Damron KS, Beyer CD. Prevalence of facet joint pain in chronic spinal pain of cervical, thoracic, and lumbar regions. *BMC Musculoskelet Disord* 2004; 5:15.
7. Linton SJ, Hallden K. Can we screen for problematic back pain? A screening questionnaire for predicting outcome in acute and subacute back pain. *Clin J Pain* 1998; 14:209-215.
8. Anderson R, Meeker WC, Wirick BE, Mootz RD, Kirk DH, Adams A. A meta-analysis of clinical trials of spinal manipulation. *J Manipulative Physiol Ther* 1992; 15:181-194.
9. Occhipinti E, Colombini D, Grieco A. Study of distribution and characteristics of spinal disorders using a validated questionnaire in a group of male subjects not exposed to occupational spinal risk factors. *Spine (Phila Pa 1976)* 1993; 18:1150-1159.
10. Stolker RJ, Vervest AC, Groen GJ. Percutaneous facet denervation in chronic thoracic spinal pain. *Acta Neurochir* 1993; 122:82-90.
11. Linton SJ, Hellsing AL, Hallden K. A population based study of spinal pain among 35-45-year-old individuals. *Spine (Phila Pa 1976)* 1998; 23:1457-1463.
12. Wilson PR. Thoracic facet joint syndrome – a clinical entity? *Pain Suppl* 1987; 4:S87.
13. Leboeuf-Yde C, Fejer R, Nielsen J, Kyvik KO, Hartvigsen J. Consequences of spinal pain: Do age and gender matter? A Danish cross-sectional population-based study of 34,902 individuals 20-71 years of age. *BMC Musculoskelet Disord* 2011; 12:39.
14. 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.
15. 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.
16. Atluri S, Datta S, Falco FJE, Lee M. Systematic review of diagnostic utility and therapeutic effectiveness of thoracic facet joint interventions. *Pain Physician* 2008; 11:611-629.
17. Sehgal N, Dunbar EE, Shah RV, Colson JD. Systematic review of diagnostic utility of facet (zygapophysial) joint injections in chronic spinal pain: An update. *Pain Physician* 2007; 10:213-228.
18. Boswell MV, Singh V, Staats PS, Hirsch JA. Accuracy of precision diagnostic blocks in the diagnosis of chronic spinal pain of facet or zygapophysial joint origin. *Pain Physician* 2003; 6:449-456.
19. Dreyfuss P, Tibiletti C, Dreyer SJ. Thoracic zygapophysial joint pain patterns: A study in normal volunteers. *Spine (Phila Pa 1976)* 1994; 19:807-811.
20. Merskey H, Bogduk N. Thoracic zygapophysial joint pain. In: *Classification of Chronic Pain. Descriptions of Chronic Pain Syndromes and Definition of Pain Terms*. 2nd ed. International Association for the Study of Pain. IASP Press, Seattle, 1994, pp 116-117.
21. Bogduk N. International Spinal Injection Society guidelines for the performance of spinal injection procedures. Part 1: Zygapophysial joint blocks. *Clin J Pain* 1997; 13:285-302.
22. Bogduk N. On diagnostic blocks for lumbar zygapophysial joint pain. *F1000 Med Rep* 2010; 2:57.
23. Datta S, Lee M, Falco FJE, Bryce DA, Hayek SM. Systematic assessment of diagnostic accuracy and therapeutic utility of lumbar facet joint interventions. *Pain Physician* 2009; 12:437-460.
24. Falco FJE, Erhart S, Wargo BW, Bryce DA, Atluri S, Datta S, Hayek SM. Systematic review of diagnostic utility and therapeutic effectiveness of cervical facet joint interventions. *Pain Physician* 2009; 12:323-344.
25. Manchikanti L, Boswell MV, Singh V, Derby R, Fellows B, Falco FJE, Datta S, Smith HS, Hirsch JA. Comprehensive review of neurophysiologic basis and diagnostic interventions in managing chronic spinal pain. *Pain Physician* 2009; 12:E71-E120.
26. 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.
27. Hancock MJ, Maher CG, Latimer J, Spin-

28. dler 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.
29. Barnsley L, Lord S, Bogduk N. Comparative local anesthetic blocks in the diagnosis of cervical zygapophysial joints pain. *Pain* 1993; 55:99-106.
30. 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.
31. 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.
32. Manchikanti L, Datta S, Gupta S, Munglani R, Bryce DA, Ward SP, Benyamin RM, Sharma ML, Helm II S, Fellows B, Hirsch JA. A critical review of the American Pain Society clinical practice guidelines for interventional techniques: Part 2. Therapeutic interventions. *Pain Physician* 2010; 13:E215-E264.
33. 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.
34. 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:E483-496.
35. Manchikanti L, Singh V, Vilims BD, Hansen HC, Schultz DM, Kloth DS. Medial branch neurotomy in management of chronic spinal pain: Systematic review of the evidence. *Pain Physician* 2002; 5:405-418.
36. Tzaan W, Tasker R. Percutaneous radiofrequency facet rhizotomy—experience with 118 procedures and reappraisal of its value. *Can J Neurol Sci* 2000; 27:125-130.
37. Manchikanti L, Singh V, Falco FJ, Cash KM, Pampati V. Effectiveness of thoracic medial branch blocks in managing chronic pain: A preliminary report of a randomized, double-blind controlled trial: Clinical Trial NCT00355706. *Pain Physician* 2008; 11:491-504.
38. Manchikanti L, Singh V, Falco FJE, Cash KA, Pampati V, Fellows B. Comparative effectiveness of a one-year follow-up of thoracic medial branch blocks in management of chronic thoracic pain: A randomized, double-blind active controlled trial. *Pain Physician* 2010; 13:535-548.
39. 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; in submission.
40. Stolker RJ, Vervest AC, Groen GJ. Parameters in electrode positioning in thoracic percutaneous facet denervation: An anatomical study. *Acta Neurochir* 1994; 128:32-39.
41. Stolker RJ, Vervest AC, Groen GJ. The treatment of chronic thoracic segmental pain by radiofrequency percutaneous partial rhizotomy. *J Neurosurg* 1994; 80:986-992.
42. Speldewinde GC. Outcomes of percutaneous zygapophysial and sacroiliac joint neurotomy in a community setting. *Pain Med* 2011; 12:209-218.
43. Chua NH, Vissers KC, Sluijter ME. Pulsed radiofrequency treatment in interventional pain management: Mechanisms and potential indications—a review. *Acta Neurochir (Wien)* 2011; 153:763-771.
44. Stolker RJ, Vervest AC, Ramos LM, Groen GJ. Electrode positioning in thoracic percutaneous partial rhizotomy: An anatomical study. *Pain* 1994; 57:241-251.
45. Golovac S. Radiofrequency neurolysis. *Neuroimaging Clin N Am* 2010; 20:203-214.
46. Mitra R, Do H, Alamin T, Cheng I. Facet pain in thoracic compression fractures. *Pain Med* 2010; 11:1674-1677.
47. Manchikanti L, Hirsch JA, Smith HS. Evidence-based medicine, systematic reviews, and guidelines in interventional pain management: Part 2: Randomized controlled trials. *Pain Physician* 2008; 11:717-773.
48. Manchikanti L, Benyamin RM, Helm S, Hirsch JA. Evidence-based medicine, systematic reviews, and guidelines in interventional pain management: Part 3: Systematic reviews and meta-analysis of randomized trials. *Pain Physician* 2009; 12:35-72.
49. Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF. Improving the quality of reports of meta-analyses of randomised controlled trials: The QUOROM statement. Quality of reporting of meta-analyses. *Lancet* 1999; 354:1896-1900.
50. 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.
51. van Tulder M, Furlan A, Bombardier C, Bouter L; Editorial Board of the Cochrane Collaboration Back Review Group. Updated method guidelines for systematic reviews in the Cochrane Collaboration Back Review Group. *Spine (Phila Pa 1976)* 2003; 28:1290-1299.
52. Furlan AD, Pennick V, Bombardier C, van Tulder M; Editorial Board, Cochrane Back Review Group. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine (Phila Pa 1976)* 2009; 34:1929-1941.
53. van Tulder MW, Suttrop M, Morton S, Bouter LM, Shekelle P. Empirical evidence of an association between internal validity and effect size in randomized controlled trials of low-back pain. *Spine (Phila Pa 1976)* 2009; 34:1685-1692.
54. Manchikanti L, Datta S, Smith HS, Hirsch JA. Evidence-based medicine, systematic reviews, and guidelines in interventional pain management: Part 6. Systematic reviews and meta-analyses of observational studies. *Pain Physician* 2009; 12:819-850.
55. Manchikanti L, Singh V, Helm S, Schultz DM, Datta S, Hirsch J. An introduction to an evidence-based approach to interventional techniques in the management of chronic spinal pain. *Pain Physician* 2009; 12:E1-E33.
56. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: A proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; 283:2008-2012.
57. Staal JB, de Bie RA, de Vet HC, Hildebrandt J, Nelemans P. Injection therapy for subacute and chronic low back pain: An updated Cochrane review. *Spine (Phila Pa 1976)* 2009; 34:49-59.

58. Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, Gøtzsche PC, Lang T; CONSORT GROUP (Consolidated Standards of Reporting Trials). The revised CONSORT statement for reporting randomized trials: Explanation and elaboration. *Ann Intern Med* 2001; 134:663-694.
59. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, Elbourne D, Egger M, Altman DG. CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. *BMJ* 2010; 340:c869.
60. Moher D, Schulz KF, Altman DG; CONSORT Group (Consolidated Standards of Reporting Trials). The CONSORT statement: Revised recommendations for improving the quality of reports of parallel-group randomized trials. *J Am Podiatr Med Assoc* 2001; 91:437-442.
61. Moher D, Schulz KF, Altman DG; CONSORT. The CONSORT statement: Revised recommendations for improving the quality of reports of parallel group randomized trials. *BMC Med Res Methodol* 2001; 1:2.
62. Vandenberghe JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M; STROBE Initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): Explanation and elaboration. *Ann Intern Med* 2007; 147:W163-W194.
63. Chou R, Huffman L. *Guideline for the Evaluation and Management of Low Back Pain: Evidence Review*. American Pain Society, Glenview, IL, 2009. www.ampainsoc.org/pub/pdf/LBPEvidRev.pdf
64. Chou R, Huffman L. *Use of Chronic Opioid Therapy in Chronic Noncancer Pain: Evidence Review*. American Pain Society, Glenview, IL, 2009. www.ampainsoc.org/library/pdf/Opioid_Final_Evidence_Report.pdf
65. Staal JB, de Bie R, de Vet HC, Hildebrandt J, Nelemans P. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824.
66. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp
67. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; 327:557-560.
68. Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, Atkins D; Methods Work Group, Third US Preventive Services Task Force. Current methods of the US Preventive Services Task Force. *Am J Prevent Med* 2001; 20:21-35.
69. Farrar JT. What is clinically meaningful: Outcome measures in pain clinical trials. *Clin J Pain* 2000; 16:S106-S112.
70. Salaffi F, Stancati A, Silvestri CA, Ciapetti A, Grassi W. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain* 2004; 8:283-291.
71. Bombardier C. Outcome assessments in the evaluation of treatment of spinal disorders: Summary and general recommendations. *Spine (Phila Pa 1976)* 2000; 25:3100-3103.
72. Hagg O, Fritzell P, Nordwall A. The clinical importance of changes in outcome scores after treatment for chronic low back pain. *Eur Spine J* 2003; 12:12-20.
73. Manchikanti L, Singh V, Falco FJE, 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.
74. 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.
75. Manchikanti L, Singh V, Cash KA, Pampati V, Damron KS, Boswell MV. A randomized, controlled, double-blind trial of fluoroscopic caudal epidural injections in the treatment of lumbar disc herniation and radiculitis. *Spine (Phila Pa 1976)* 2011; 36:1897-1905.
76. Manchikanti L, Singh V, Cash KA, Pampati V, Datta S. Management of pain of post lumbar surgery syndrome: One-year results of a randomized, double-blind, active controlled trial of fluoroscopic caudal epidural injections. *Pain Physician* 2010; 13:509-521.
77. Manchikanti L, Cash RA, McManus CD, Pampati V, Fellows B. Fluoroscopic caudal epidural injections with or without steroids in managing pain of lumbar spinal stenosis: One year results of randomized, double-blind, active-controlled trial. *J Spinal Disord* 2012; 25:226-234.
78. Manchikanti L, Singh V, Falco FJE, Cash KA, Pampati V. Evaluation of the effectiveness of lumbar interlaminar epidural injections in managing chronic pain of lumbar disc herniation or radiculitis: A randomized, double-blind, controlled trial. *Pain Physician* 2010; 13:343-355.
79. Manchikanti L, Cash KA, McManus CD, Pampati V, Benyamin RM. Preliminary results of a randomized, double-blind, controlled trial of fluoroscopic lumbar interlaminar epidural injections in managing chronic lumbar discogenic pain without disc herniation or radiculitis. *Pain Physician* 2010; 13:E279-E292.
80. Manchikanti L, Cash KA, Pampati V, Wargo BW, Malla Y. Cervical epidural injections in chronic discogenic neck pain without disc herniation or radiculitis: Preliminary results of a randomized, double-blind, controlled trial. *Pain Physician* 2010; 13:E265-E278.
81. Manchikanti L, Cash KA, Pampati V, Wargo BW, Malla Y. The effectiveness of fluoroscopic cervical interlaminar epidural injections in managing chronic cervical disc herniation and radiculitis: Preliminary results of a randomized, double-blind, controlled trial. *Pain Physician* 2010; 13:223-236.
82. Manchikanti L, Cash KA, McManus CD, Pampati V, Benyamin RM. A preliminary report of a randomized double-blind, active controlled trial of fluoroscopic thoracic interlaminar epidural injections in managing chronic thoracic pain. *Pain Physician* 2010; 13:E357-E369.
83. Manchikanti L, Cash KA, McManus CD, Damron KS, Pampati V, Falco FJE. Lumbar interlaminar epidural injections in central spinal stenosis: Preliminary results of a randomized, double-blind, active control trial. *Pain Physician* 2012; 15:51-63.
84. Manchikanti L, Malla Y, Cash KA, McManus CD, Pampati V. Fluoroscopic cervical interlaminar epidural injections in managing chronic pain of cervical post-surgery syndrome: Preliminary results of a randomized, double-blind active control trial. *Pain Physician* 2012; 15:13-26.
85. Manchikanti L, Malla Y, Cash KA, McManus CD, Pampati V. Fluoroscopic epidural injections in cervical spinal stenosis: Preliminary results of a randomized, double-blind, active control trial. *Pain Physician* 2012; 15:E59-E70.
86. Manchikanti L, Cash KA, Pampati V, Malla Y. Fluoroscopic cervical epidural

- injections in chronic axial or disc-related neck pain without disc herniation, facet joint pain, or radiculitis. *J Pain Res* 2012; 227-236.
87. Haufe SM, Mork AR. Endoscopic facet debridement for the treatment of facet arthritic pain--A novel new technique. *Int J Med Sci* 2010; 7:120-123.
 88. Manchikanti L, Malla Y, Wargo BW, Cash KA, Pampati V, Fellows B. Complications of fluoroscopically directed facet joint nerve blocks: A prospective evaluation of 7,500 episodes with 43,000 nerve blocks. *Pain Physician* 2012; 15:E143-E150.
 89. Doita M, Nabeshima Y, Nishida K, Fujioka H, Kurosaka M. Septic arthritis of lumbar facet joints without predisposing infection. *J Spinal Disord Tech* 2007; 20:290-295.
 90. Magee M, Kannangara S, Dennien B, Lonergan R, Emmett L, Van der Wall H. Paraspinal abscess complicating facet joint injection. *Clin Nucl Med* 2000; 25:71-73.
 91. Marks RC, Semple AJ. Spinal anaesthesia after facet joint injection. *Anaesthesia* 1988; 43:65-66.
 92. Berrigan T. Chemical meningism after lumbar facet joint block. *Anaesthesia* 1992; 47:905-906.
 93. Thomson SJ, Lomax DM, Collett BJ. Chemical meningism after lumbar facet joint block with local anaesthetic and steroids. *Anaesthesia* 1993; 46:563-564.
 94. Sehgal A, Valentine JM. Lumbar radiculopathy after zygapophyseal joint injection. *Br J Anaesth* 2007; 99:412-414.
 95. Kim SY, Han SH, Jung MW, Hong JH. Generalized infection following facet joint injection -A case report. *Korean J Anesthesiol* 2010; 58:401-404.
 96. Ghosh PS, Loddenkemper T, Blanco MB, Marks M, Sabella C, Ghosh D. Holo-cord spinal epidural abscess. *J Child Neurol* 2009; 24:768-771.
 97. Yeh TT, Wen ZH, Lee HS, Lee CH, Yang Z, Jean YH, Wu SS, Nimni ME, Han B. Intra-articular injection of collagenase induced experimental osteoarthritis of the lumbar facet joint in rats. *Eur Spine J* 2008; 17:734-742.
 98. Hoelzer BC, Weingarten TN, Hooten WM, Wright RS, Wilson WR, Wilson PR. Paraspinal abscess complicated by endocarditis following a facet joint injection. *Eur J Pain* 2008; 12:261-265.
 99. Park MS, Moon SH, Hahn SB, Lee HM. Paraspinal abscess communicated with epidural abscess after extra-articular facet joint injection. *Yonsei Med J* 2007; 48:711-714.
 100. Abbott ZI, Nair KV, Allen RR, Akuthota VR. Utilization characteristics of spinal interventions. *Spine J* 2012; 1:35-43.
 101. Manchikanti L, Pampati V, Boswell MV, Smith HS, Hirsch JA. Analysis of the growth of epidural injections and costs in the Medicare population: A comparative evaluation of 1997, 2002, and 2006 data. *Pain Physician* 2010; 13:199-212.
 102. Manchikanti L, Singh V, Pampati V, Smith HS, Hirsch JA. Analysis of growth of interventional techniques in managing chronic pain in Medicare population: A 10-year evaluation from 1997 to 2006. *Pain Physician* 2009; 12:9-34.
 103. Manchikanti L, Singh V, Caraway DL, Benyamin RM, Hirsch JA. Medicare physician payment systems: Impact of 2011 schedule on interventional pain management. *Pain Physician* 2011; 14:E5-E33.
 104. Manchikanti L, Hirsch JA. Medicare physician payment rules for 2011: A primer for the neurointerventionalist. *J Neuro-intervent Surg* 2011; 3:399-402.
 105. Manchikanti L, Singh V, Hirsch JA. Saga of payment systems of ambulatory surgery centers for interventional techniques: An update. *Pain Physician* 2012; 15:109-130.
 106. Manchikanti L, Parr AT, Singh V, Fellows B. Ambulatory surgery centers and interventional techniques: A look at long-term survival. *Pain Physician* 2011; 14:E177-E215.
 107. Manchikanti L, Singh V, Caraway DL, Benyamin RM, Falco FJE, Hirsch JA. Physician payment outlook for 2012: Déjà Vu. *Pain Physician* 2012; 15:E27-E52.
 108. Medicare Part B Carrier Summary Data Files. Centers for Medicare and Medicaid Services. www.cms.gov/NonIdentifiableDataFiles/04_5_PartBCarrierSummaryDataFile.asp#TopOfPage
 109. Manchikanti L, Singh V, Falco FJE. In response to Smuck M, Levin JH. RE: Manchikanti L, Singh V, Falco FJE, Cash KA, Fellows B. Cervical medial branch blocks for chronic cervical facet joint pain: A randomized double-blind, controlled trial with one-year follow-up. *Spine (Phila PA 1976)* 2008; 33:1813-1820; author reply 2009; 34:1116-1117.
 110. Pham Dang C, Lelong A, Guilley J, Nguyen JM, Volteau C, Venet G, Perrier C, Lejus C, Blanloeil Y. Effect on neurostimulation of injectates used for perineural space expansion before placement of a stimulating catheter: Normal saline versus dextrose 5% in water. *Reg Anesth Pain Med* 2009; 34:398-403.
 111. Tsui BC, Kropelin B, Ganapathy S, Finucane B. Dextrose 5% in water: Fluid medium maintaining electrical stimulation of peripheral nerve during stimulating catheter placement. *Acta Anaesthesiol Scand* 2005; 49:1562-1565.
 112. Indahl A, Kaigle AM, Reikerås O, Holm SH. Interaction between the porcine lumbar intervertebral disc, zygapophysiological joints, and paraspinal muscles. *Spine (Phila Pa 1976)* 1997; 22:2834-2840.
 113. Indahl A, Kaigle A, Reikerås O, Holm S. Electromyographic response of the porcine multifidus musculature after nerve stimulation. *Spine (Phila Pa 1976)* 1995; 20:2652-2658.
 114. Bhatia MT, Parikh LCJ. Epidural saline therapy in lumbo-sciatic syndrome. *J Indian Med Assoc* 1966; 47:537-542.
 115. Gupta AK, Mital VK, Azmi RU. Observations of the management of lumbosciatic syndromes (sciatica) by epidural saline. *J Indian Med Assoc* 1970; 54:194-196.
 116. Carette S, Leclaire R, Marcoux S, Morin F, Blaise GA, St-Pierre A, Truchon R, Parent F, Levesque J, Bergeron V, Montminy P, Blanchette C. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. *N Engl J Med* 1997; 336:1634-1640.
 117. Carette S, Marcoux S, Truchon R, Grondin C, Gagnon J, Allard Y, Latulippe M. A controlled trial of corticosteroid injections into facet joints for chronic low back pain. *N Engl J Med* 1991; 325:1002-1007.
 118. Tachihara H, Sekiguchi M, Kikuchi S, Konno S. Do corticosteroids produce additional benefit in nerve root infiltration for lumbar disc herniation. *Spine (Phila Pa 1976)* 2008; 33:743-747.
 119. Karppinen J, Malmivaara A, Kurunlahti M, Kyllönen E, Pienimäki T, Nieminen P, Ohinmaa A, Tervonen O, Vanharanta H. Periradicular infiltration for sciatica: A randomized controlled trial. *Spine (Phila Pa 1976)* 2001; 26:1059-1067.
 120. Sato C, Sakai A, Ikeda Y, Suzuki H, Sakamoto A. The prolonged analgesic effect of epidural ropivacaine in a rat model of neuropathic pain. *Anesth Analg* 2008; 106:313-320.
 121. Blease C. The principle of parity: The "placebo effect" and physician communication. *J Med Ethics* 2012; 38:199-203.
 122. Holm I, Friis A, Brox JI, Gunderson R, Steen H. Minimal influence of facet joint anesthesia on isokinetic mus-

- cle performance in patients with chronic degenerative low back disorders. *Spine (Phila Pa 1976)* 2000; 25:2091-2094.
123. Kang YM, Choi WS, Pickar JG. Electrophysiologic evidence for an intersegmental reflex pathway between lumbar paraspinal tissues. *Spine (Phila Pa 1976)* 2002; 27:E56-E63.
 124. Manchikanti L, Giordano J, Fellows B, Hirsch JA. Placebo and nocebo in interventional pain management: A friend or a foe – or simply foes? *Pain Physician* 2011; 14:E157-E175.
 125. Manchikanti L, Pampati V, Damron K. The role of placebo and nocebo effects of perioperative administration of sedatives and opioids in interventional pain management. *Pain Physician* 2005; 8:349-355.
 126. Häuser W, Bartram C, Bartram-Wunn E, Tölle T. Adverse events attributable to nocebo in randomized controlled drug trials in fibromyalgia syndrome and painful diabetic peripheral neuropathy: Systematic review. *Clin J Pain* 2012; 28:437-451.
 127. Lyby PS, Forsberg JT, Asli O, Flaten MA. Induced fear reduces the effectiveness of a placebo intervention on pain. *Pain* 2012; 153:1114-1121.
 128. Wells RE, Kaptchuk TJ. To tell the truth, the whole truth, may do patients harm: The problem of the nocebo effect for informed consent. *Am J Bioeth* 2012; 12:22-29.
 129. Ghahreman A, Ferch R, Bogduk N. The efficacy of transforaminal injection of steroids for the treatment of lumbar radicular pain. *Pain Med* 2010; 11:1149-1168.
 130. Manchikanti L, Singh V. Corticosteroids. In: Manchikanti L, Christo PJ, Trescot AM, Falco FJE (eds). *Foundations of Pain Medicine and Interventional Pain Management: A Comprehensive Review*. ASIPP Publishing, Paducah, KY, 2011, pp 589-606.
 131. Pasqualucci A, Varrassi G, Braschi A, Peduto VA, Brunelli A, Marinangeli F, Gori F, Colò F, Paladín A, Mojoli F. Epidural local anesthetic plus corticosteroid for the treatment of cervical brachial radicular pain: Single injection versus continuous infusion. *Clin J Pain* 2007; 23:551-557.
 132. Byröd G, Otani K, Brisby H, Rydevik B, Olmarker K. Methylprednisolone reduces the early vascular permeability increase in spinal nerve roots induced by epidural nucleus pulposus application. *J Orthop Res* 2000; 18:983-987.
 133. Hayashi N, Weinstein JN, Meller ST, Lee HM, Spratt KF, Gebhart GF. The effect of epidural injection of betamethasone or bupivacaine in a rat model of lumbar radiculopathy. *Spine (Phila Pa 1976)* 1998; 23:877-885.
 134. Lee HM, Weinstein JN, Meller ST, Hayashi N, Spratt KF, Gebhart GF. The role of steroids and their effects on phospholipase A2. An animal model of radiculopathy. *Spine (Phila Pa 1976)* 1998; 23:1191-1196.
 135. Minamide A, Tamaki T, Hashizume H, Yoshida M, Kawakami M, Hayashi N. Effects of steroids and lipopolysaccharide on spontaneous resorption of herniated intervertebral discs. An experience study in the rabbit. *Spine (Phila Pa 1976)* 1998; 23:870-876.
 136. Mao J, Chen LL. Systemic lidocaine for neuropathic pain relief. *Pain* 2000; 87:7-17.
 137. Pasqualucci A. Experimental and clinical studies about the preemptive analgesia with local anesthetics. Possible reasons of the failure. *Minerva Anestesiol* 1998; 64:445-457.
 138. Arner S, Lindblom U, Meyerson BA, Molander C. Prolonged relief of neuralgia after regional anesthetic block. A call for further experimental and systematic clinical studies. *Pain* 1990; 43:287-297.
 139. Lavoie PA, Khazen T, Filion PR. Mechanisms of the inhibition of fast axonal transport by local anesthetics. *Neuropharmacology* 1989; 28:175-181.
 140. Ji RR, Woolf CJ. Neuronal plasticity and signal transduction in nociceptive neurons: Implications for the initiation and maintenance of pathological pain. *Neurobiol Dis* 2001; 8:1-10.
 141. Cassuto J, Sinclair R, Bonderovic M. Anti-inflammatory properties of local anesthetics and their present and potential clinical implications. *Acta Anaesthesiol Scand* 2006; 50:265-282.
 142. Concato J. When to randomize, or “Evidence-based medicine needs medicine-based evidence.” *Pharmacoepidemiol Drug Saf* 2012; 21:6-12.
 143. Quill TE, Holloway RG. Evidence, preferences, recommendations--finding the right balance in patient care. *N Engl J Med* 2012; 366:1653-1655.
 144. Gelijns AC, Gabriel SE. Looking beyond translation--integrating clinical research with medical practice. *N Engl J Med* 2012; 366:1659-1661.
 145. 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.
 146. 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.
 147. Hotopf M. The pragmatic randomized controlled trial. *Adv Psychiatr Treat* 2002; 8:326-333.
 148. Hotopf M, Churchill R, Lewis G. Pragmatic randomized controlled trials in psychiatry. *Br J Psychiatry* 1999; 175:217-223.
 149. Tunis SR, Stryer DB, Clancy CM. Practical clinical trials. Increasing the value of clinical research for decision making in clinical and health policy. *JAMA* 2003; 290:1624-1632.
 150. Roland M, Torgerson DJ. What are pragmatic trials? *BMJ* 1998; 316:285.
 151. Alexander GC, Stafford RS. Does comparative effectiveness have a comparative edge? *JAMA* 2009; 301:2488-2490.
 152. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Tripartite Guideline. Choice of Control Group and Related Issues in Clinical Trials E10. July 20, 2000.

