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Systematic Review

Percutaneous Adhesiolysis in the Management of Chronic Low Back Pain in Post Lumbar Surgery Syndrome and Spinal Stenosis: A Systematic Review

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Background: Low back pain after either post lumbar surgery syndrome or spinal stenosis in the absence of surgery is a vexing problem. Post lumbar surgery syndrome can occur in any age group, while low back and radicular pain from spinal stenosis is a disease of aging. As the population ages, the incidence of symptomatic spinal stenosis will increase. There are currently limited treatment options for either group. Further surgery is not uniformly effective in relieving pain after previous surgery. While therapies are being developed to treat pain due to spinal stenosis, no therapy other than adhesiolysis will treat pain due to scarring.

Adhesiolysis was developed as a means of removing epidural scarring leading directly or indirectly to compression, inflammation, swelling, or a decreased nutritional supply of nerve roots. Adhesiolysis utilizes a number of modalities in the effort to break up epidural scarring, including the use of a wire-bound catheter for mechanical adhesiolysis, placement of the catheter in the ventro-lateral aspect of the epidural space at the site of the exiting nerve root, and the use of high volumes of injectate, including local anesthetics and saline, either hypertonic or isotonic, along with steroids.

Study Design: A systematic review of percutaneous adhesiolysis in the treatment of refractory low back and leg pain due to post lumbar surgery syndrome or spinal stenosis.

Objective: To evaluate the effectiveness of percutaneous adhesiolysis in the treatment of refractory low back and leg pain due to post lumbar surgery syndrome or spinal stenosis. The severity of risks and adverse events associated with percutaneous adhesiolysis were also evaluated.

Methods: The available literature on percutaneous adhesiolysis for the treatment of refractory low back and leg pain due to post lumbar surgery syndrome or spinal stenosis 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 June 2012, and manual searches of the bibliographies of known primary and review articles.

Outcome Measures:
The primary outcome measure was pain relief of at least 6 months. Secondary outcome measures were improvement in functional status, change in psychological status, return to work, and reduction in opioid use or interventions.

Results: For this systematic review, 15 studies were identified and selected for review. Of these, 5 randomized controlled trials and 2 observational studies met the inclusion criteria.

Applying the USPSTF criteria, these studies indicate that there is fair evidence that percutaneous adhesiolysis is effective in relieving low back and/or leg pain caused by post lumbar surgery syndrome and that there is fair evidence that percutaneous adhesiolysis is effective in relieving low back and/or leg pain caused by spinal stenosis.

The incidence of complications from percutaneous adhesiolysis is low and the complications are generally minimal and self-limited. The procedure should be considered to be low risk for serious adverse events when performed by well-trained physicians.

Limitations: The limitations of this systematic review include the paucity of literature.

Conclusion: In summary, there is fair evidence that percutaneous adhesiolysis is effective in relieving low back and/or leg pain due to post lumbar surgery syndrome or spinal stenosis.

Key words: Spinal pain, chronic low back pain, leg pain, adhesiolysis, Racz procedure, post lumbar surgery syndrome, spinal stenosis

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Chronic pain is a source of enormous suffering and disability (1-3). The Institute of Medicine (IOM) estimates that 116 million American adults are burdened by pain, at a national economic cost of about $600 billion (4). Chronic pain causes functional limitation in about 5% of the general population (5,6). Low back pain occurs in about two-thirds of adults (7). The prevalence of low back pain is increasing, going from 3.9% in North Carolina in 1992 to 10.2% in 2006 (8). Low back pain is associated with significant societal costs (9). It is present in all age groups (10). Once thought to be transient, multiple studies have shown that back pain is chronic and persistent (11-15).

Persistent low back pain caused by intervertebral disc herniation, spinal stenosis, and spondylolisthesis is the most common reason for back surgery (16,17). Surgery itself can fail to relieve pain and can itself be the cause of persistent back and leg pain (18-40). There are many causes for persistent low back pain, including stenosis, pseudoarthrosis, painful disc, recurrent disc herniation, facet disease, sacroiliac disease, neuropathic pain, adjacent segment disease, ligamentous disease, epidural scarring, and undefined (18,30,32-34,38,41-53). Minimally invasive techniques can be used to treat pain after surgery (44,45,54-65). Epidural scarring has attracted interest as a cause of pain after spine surgery in that it is potentially treatable (34,66-74).

Epidural scarring, in addition to developing after surgery, can also occur after infection, leakage of nuclear material, or bleeding (75). The presumed origin of fibrosis seen in patients with spinal stenosis is recurrent, clinically insignificant venous microbleeds occurring as the extensive epidural venous plexus is disrupted by the alterations that occur in the discs, facet joints, and ligamentum flavum as a part of the aging process (76-79). The role of epidural venous engorgement in generating nerve root pain has been underestimated (77). The concept of epidural scarring causing pain had generated controversy because of a reported lack of correlation between peridural scarring and radicular pain. Current evidence; however, documents the relationship between peridural scarring and pain (33,34,44,46,67,80-85). Fibrosis with neural compression can lead to increased neural sensitivity (65,86-88). Animal models support the clinical and imaging findings with evidence of pain behaviors in the presence of epidural scarring and adherence of the nerve to the adjacent disc and pedicle (81,89-92). Furthermore, scarring may generate pain arising from the peridural membrane (93).

With the increasing complexity of spine surgery and with the aging of the American population, the incidence of low back pain due to epidural fibrosis can be expected to increase (94). In addition, the aging process itself, with stenosis caused by ligamentum flavum hypertrophy, degenerative disc bulges, and facet hypertrophy can, with the presence of hypothesized intermittent and individually insignificant bleeding along with the presence of inflammatory material from the nucleus, lead to scarring (95-97).

Spinal stenosis and post lumbar surgery syndrome can lead to both low back pain with or without lower extremity pain and neurogenic claudication (18,25,95,98). Percutaneous adhesiolysis, also known as the Racz procedure, has been developed as a technique to relieve low back and radicular pain caused by epidural scarring (99-104). Originally developed as a 3-day procedure, the protocol has been modified so that it can also be done as a one-day procedure (101).

Adhesiolysis has been the subject of several systematic reviews (46,105-115). The most recent systematic review, published by Epter et al (46) in 2009, showed strong (Level I or II-1 using the United States Preventive Services Task Force (USPSTF) criteria (116) for the use of adhesiolysis for post lumbar laminectomy syndrome. The 2007 American College of Occupational and Environmental Medicine (ACOEM) guidelines found that

adhesiolysis was not recommended for the treatment of low back pain because of insufficient evidence. Manchikanti et al have criticized the ACOEM guidelines for methodological shortcomings (112). Chou and Huffman (109), in the 2007 American Pain Society (APS) guidelines, in discussing therapies for post lumbar surgery syndrome, commingle adhesiolysis with "forceful epidural injections," which appear to be high volume caudal injections. Chou and Huffman's review does not present specific evaluations of a treatment, rather, the ratings of individual studies, along with editorial comments regarding the quality of the studies. The APS findings were clarified at a conference as meaning that there was insufficient evidence to support a recommendation (113). Belozer and Wang (114), writing a Health Technology Assessment in 2004 for the Washington State Department of Labor and Industries, reviewed the then-available literature, but did not make any policy recommendations. Racz et al (110) found that the procedure was effective, that it did provide relief in patients who had failed epidural injections, that hyaluronidase did not improve outcomes, that the role of hypertonic saline was unclear, and that it was a safe procedure. Van Boxem et al (117), in an article reviewing treatment of radicular pain, found that adhesiolysis was an investigational procedure. Tran et al (108), in a review of treatment for spinal stenosis, citing one article (118), noted that adhesiolysis provided lower pain and Oswestry Disability Index (ODI) scores and longer duration of relief than did fluoroscopically guided epidural injections.

This systematic review will reassess all the literature on adhesiolysis up to June 2012, including new literature since the last review. This review will focus on both post lumbar surgery syndrome and on spinal stenosis.

1.0 Methods

1.1 Research Protocol

A systematic review of randomized trials, observational studies, and reports of complications dealing with percutaneous adhesiolysis for the treatment of pain of at least 6 months duration caused by either post lumbar surgery syndrome or spinal stenosis will be performed. Attendant to this review will be an analysis of complications of these procedures.

1.2 Eligibility Criteria (Criteria for Including and Excluding Studies in the Systematic Review)

This review will cover adhesiolysis. The definition of adhesiolysis has changed over time. Originally, it was defined as a 3-day inpatient procedure, using a flexible wire catheter, designed to prevent shearing of the catheter as it was manipulated through an introducer needle in the epidural space. Local anesthetic, steroid, 10% hypertonic saline, and hyaluronidase were injected on each day (99). In 1999, Manchikanti et al (101) described a one-day procedure. Heavner et al (100), in 1999, found that hyaluronidase did not improve outcomes. Manchikanti et al (119), in 2004, found an improvement using hypertonic saline versus normal saline, but that improvement did not reach statistical significance. Currently, adhesiolysis is usually performed as a one-day procedure using a soft-tip, wire-bound flexible catheter, steroids, local anesthetic, and hypertonic saline. The use of hyaluronidase is at the interventionalist's discretion. Additionally, a filling defect on fluoroscopy may be documented at the target area and, ideally, that defect will be resolved upon completion of the procedure. Any studies meeting these criteria for the definition of adhesiolysis are included. Thus, forceful epidural injections, without targeted delivery or adhesiolysis, are excluded.

Inclusion criteria for patients were those suffering with chronic intractable low back pain due either to post lumbar laminectomy syndrome or spinal stenosis with or without radicular findings of at least 6 months duration. Only percutaneous adhesiolysis procedures were evaluated. All the studies providing appropriate management with outcome evaluations of 6 months or longer and statistical evaluations were reviewed. Reports without appropriate diagnosis, non-systematic reviews, book chapters, and case reports were excluded. The patients had to be at least 18 years old.

Articles dealing with forceful spinal injections were excluded as forceful spinal injection is a procedure distinct from, and unrelated to, percutaneous adhesiolysis in that percutaneous adhesiolysis demands placement of the medication at the site of the target pathology; forceful spinal injections do not involve targeted delivery of injectate (120,121).

The primary outcome was pain relief. Secondary measures were functional improvement, change in psychological status, return to work, and reduction in opioid use or interventions.

Previously, a 2 point improvement in the 11-point (0-10) visual analog scale (VAS) was felt to be clinically significant (122-126). Clinically meaningful improvement is currently defined as a 50% improvement in pain relief or a 40%-50% improvement in functional

status (43,58,67,118,127-134). We will use either a 3 point or a 50% improvement in pain ratings or a 40% improvement in functional status as the threshold for clinically meaningful improvement. Successful results in at least 40% of the patients are considered as positive.

1.3 Key Questions and Analytic Framework

1.3.1 Key Questions

The purpose of the current review is to perform a systematic survey of the literature regarding the effectiveness of percutaneous adhesiolysis in the treatment of chronic low back and/or lower extremity pain of at least 6 months duration in patients with either spinal stenosis or post lumbar surgery syndrome. The evidence will be assessed in light of the previous reviews. The specific questions to be answered are:

Is percutaneous adhesiolysis effective in the treatment of intractable (at least 6 months duration) low back and/or leg pain in post lumbar surgery syndrome?

Is percutaneous adhesiolysis effective in the treatment of intractable (at least 6 months duration) low back and leg pain due to spinal stenosis?

What is the severity of the risks and adverse events associated with percutaneous adhesiolysis?

1.3.2 Databases and Other Information Sources Used to Identify Relevant Studies

The review included English language randomized trials, observational studies, and reports of complications published from 1966 to June 2012. Databases included in the search are Medline, EMBASE, Cochrane Review Database, and Google Scholar. Other sources include Clinical Trial Registry, systematic reviews, narrative reviews, and cross-references to the reviews. Bibliographies of reviewed papers were also examined. In addition, authors known to be active in the field were contacted.

1.3.3 Search Strategy

The search strategy focused on chronic low back pain secondary to post surgery syndrome or spinal stenosis treated with percutaneous adhesiolysis. The search terminology included post lumbar surgery syndrome, stenosis, scar, failed back surgery syndrome, epidural fibrosis, chronic low back pain, adhesiolysis, epidural neuroplasty, epidural neurolysis, lysis of adhesions, percutaneous adhesiolysis, hypertonic and saline neurolysis, and Racz procedure.

1.3.4 Study Selection Process

Only studies of clinical relevance were assessed. Clinical relevance was assessed according to the Cochrane Back Review Group (135,136). Table 1 shows the questions used to assess clinical relevance. At least 3 clinical relevance questions had to be positive for a study to be considered clinically relevant.

The quality of each individual article used in this analysis was assessed by modified Cochrane review criteria (Table 2) (137) for randomized trials and the Newcastle-Ottawa Scale for observational studies (Tables 3 and 4) (138,139). The case series format for the Newcastle-Ottawa Scale was used for all studies with more than one group; otherwise, the cohort format was used. Non-randomized observational studies were included only if at least 50 subjects were enrolled or at least 25 in each group if there were comparison groups.

1.3.5 Data Extraction Process

Each study will be evaluated by at least 2 authors for stated criteria and any disagreements will be dis-

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 in a clinical 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 (136).

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 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: or 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" or 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 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 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" 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 re: 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 outcome assessment timing 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 (137).

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 (138).

cussed by a third reviewer. If there is a conflict of interest with the reviewed manuscript with authorship or any other type of conflict, the involved authors will not review the manuscript for quality assessment, clinical relevance, evidence synthesis, or grading of evidence.

Randomized trials meeting the inclusion criteria

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 (138).

utilizing the Cochrane review criteria, as shown in Table 2, with at least 9 of 12 criteria were considered high quality. Studies with Cochrane scores of 6 to 8 were considered moderate quality and studies with Cochrane scores less than 6 were excluded.

Observational studies had to meet a minimum of 7 out of 13 criteria for cohort studies and 5 of 10 for case-controlled studies.

Weighted scoring of the criteria was not utilized here; the latest Cochrane review recommendations do not include weighted scoring, even though they have utilized them repeatedly and we have utilized them in the past in systematic reviews on this subject.

If the literature search provided at least 5 randomized trials meeting the inclusion criteria for each condition evaluated, no observational studies were utilized.

1.3.6 Methods for Handling Missing Information

Missing information will be evaluated on a case by case basis. If the available data is insufficient to evaluate the study or if it does not meet the endpoint criteria, the study will be excluded. The authors of manuscripts with missing, incomplete, or unclear data will be contacted.

1.3.7 Information to be Extracted from Included Studies

The primary outcome parameter is pain relief. The secondary outcome measures are functional improvement, change in psychological status, return to work, continued opioid use, other drugs or other interventions, and complications.

1.4 Analysis of Evidence

The analysis of the strength of evidence was conducted using 3 levels of evidence: good, fair, and limited (or poor), as adapted from the U.S. Preventative Services Task Force (Table 5) (140).

2.0 Results

The literature search found 1,474 articles potentially relating to key questions concerning whether percutaneous adhesiolysis is effective in the treatment of intractable low back and/or leg pain due to either post lumbar surgery syndrome or spinal stenosis. Figure 1 shows a flow diagram of study selection. Of these, 15 were considered for inclusion,, of which 6 were randomized controlled trials (43,100,118,119,141,148) and 9 were observational studies (84,104,142-147, 149).

One of the randomized controlled trials did not meet the current criteria for inclusion (148). Six of the observational studies did not meet the current criteria for inclusion (104,142-144,147,149). One of the observational studies (144) merits mention as the title indicates that it is a randomized controlled trial. As patients were assigned to the control group based upon failure of the insurance company to cover the procedure rather than according to a true randomization process, it is not a randomized controlled trial. The author has acknowledged this fact, indicating that the study should be considered a prospective observational study (107,144). Table 6 lists the 1 randomized controlled trial (148) as well as the 6 observational studies excluded and the reason for exclusion (104,142-144,147,149).

Five randomized controlled trials (43,100,

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 (140).

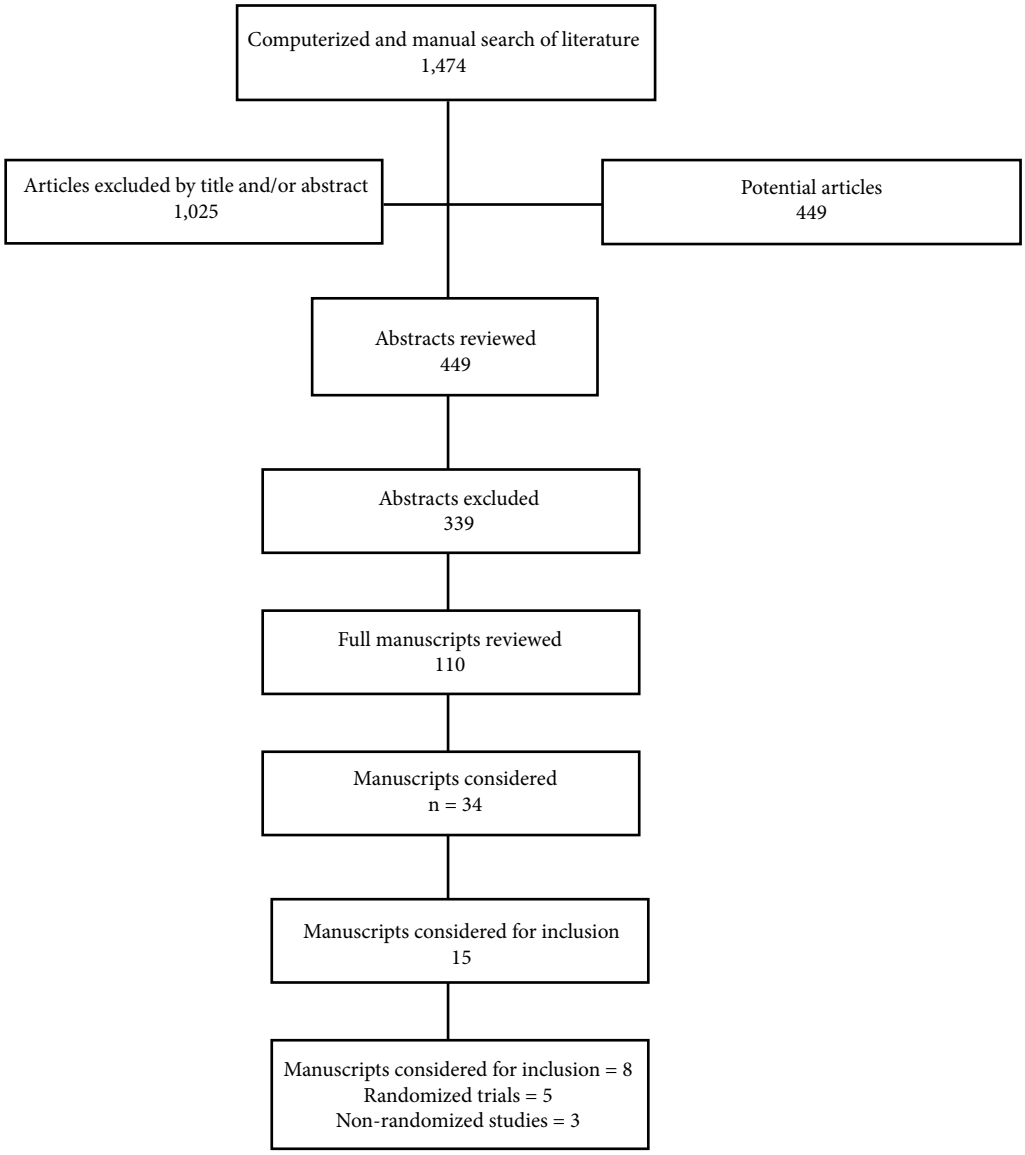

Fig. 1. *The flow diagram illustrating purcutaneous adhesiolysis in post lumbar surgery syndrome and spinal stenosis.*

118,119,141) and 3 observational studies (101,145,146) met the current criteria for inclusion. Table 7 shows the included studies and their characteristics. Two of the studies initially included for review reported on the same patient cohort (100,102). Three observational studies were evaluated (101,145,146).

2.1 Clinical Relevance

Of the 5 randomized controlled trials and 3 observational studies which met the inclusion criteria, all 8 passed the screening for clinical relevance, with a score of at least 3 out of 5. The clinical relevance findings are shown in Table 8.

Table 6. *List of excluded randomized trials and non-randomized studies.*

Manuscript Author(s)	Number of Patients	Treated vs Control	Reason for Exclusion	
			Follow-up Period	Other Reason(s)
RANDOMIZED CONTROLLED TRIAL				
Yousef et al (148)	38	Caudal epidural steroid with local anesthetic and hypertonic saline versus caudal epidural with hypertonic saline, local anesthetic, and hyaluronidase.	52 weeks	The authors studied caudal epidural steroid with local anesthetic and hypertonic saline versus caudal epidural with hypertonic saline, local anesthetic, and hyaluronidase; however, there was no adhesiolysis performed with catheter or by other means except potentially with hypertonic saline and hyaluronidase.
OBSERVATIONAL STUDIES				
Gerdesmeyer et al (104)	25	3-day adhesiolysis	12 weeks	Failure to meet requirement of at least 50 patients
Devulder et al (142)	34	Caudal epidural steroid injection with non-wire reinforced catheter No control	12 months	Failure to meet requirement of at least 50 patients; procedure was done without wire reinforced catheter; catheter not placed at site of pathology
Manchikanti et al (143)	120	60 in each group	12 months	Both groups (percutaneous adhesiolysis and endoscopic adhesiolysis) included patients who have already failed adhesiolysis, essentially acting as control.
Manchikanti et al (144)	45	1-day adhesiolysis v physical therapy	12 months	Failure to meet requirement of at least 50 patients
Manchikanti et al (147)	23	1-day adhesiolysis No control	2 years	Failure to meet requirement of at least 50 patients
Lee & Lee (149)	86	Percutaneous adhesiolysis with Navicath	One year	The authors studied clinical effectiveness of percutaneous adhesiolysis using Navicath for the management of chronic pain due to lumbosacral disc herniation.

Table 7. *Assessment of randomized trials and non-randomized studies for inclusion criteria.*

Manuscript Authors	Number of patients	Treatment vs. Comparator	Length of Follow up	Outcome Parameters	Comments
RANDOMIZED					
Manchikanti et al 2009 (43) Randomized, active-control	120 Post lumbar surgery syndrome	60 patients receiving 1-day adhesiolysis 60 patients with caudal epidural. Repeat procedures allowed at 3 months based upon initial improvement then deterioration of pain relief to below 50%.	12 months Crossover allowed at 3 months. Of caudal group, 10 were unblinded at 6 months and 33 at 12 months; of the adhesiolysis group, 2 were unblinded prematurely.	NRS ODI Opioid intake Employment/ work status	90% of adhesiolysis group had >50% relief at 3 months and 73% did at 12 months. 35% of caudal group had >50 relief at 3 months and 12% did at 12 months. 77% of adhesiolysis group had >40% improvement in ODI at 12 months compared to 13% of caudal group. Average of 3.5 adhesiolysis procedures/year with an average relief/year of 4½ weeks.
Heavner et al 1999 (100) Randomized, active-control	59 Epidural fibrosis with radicular pain	3 day adhesiolysis protocol 4 groups: Group I: hypertonic saline plus hyaluronidase Group II: hypertonic saline Group III: isotonic saline (0.9% NaCl) Group IV: isotonic saline plus hyaluronidase	12 months	MPQ VAS for back, right leg, and left leg pain	Purpose of study was to determine if hyaluronidase or hypertonic saline improved the outcome. 29% drop out rate Low back rather than leg pain was the greatest problem. Hyaluronidase did not provide benefit. Hypertonic saline patients required fewer additional treatments than patients treated with normal saline. Maximum VAS scores were improved in between 25% and 60% of patients at 12 months.

Table 7 (cont.). *Assessment of randomized trials and non-randomized studies for inclusion criteria.*

Manuscript Authors	Number of patients	Treatment vs. Comparator	Length of Follow up	Outcome Parameters	Comments
Manchikanti et al 2009 (118) Randomized, active-control	50 Spinal stenosis with radicular pain	25 patients receiving 1-day adhesiolysis. 25 patients with caudal epidural. Repeat procedures allowed at 3 months based upon initial improvement then deterioration of pain relief to below 50%.	12 months Crossover allowed at 3 months. Of caudal group, 18 prematurely; of the adhesiolysis group, 0 were unblinded prematurely.	NRS ODI Opioid intake, employment, work status	76% of adhesiolysis group had >50% pain relief at 12 months; 4% of caudal group did. 80% of adhesiolysis group had >40% improvement in ODI at 12 months; 0% of caudal group did. Average of 3.5 adhesiolysis procedures/year. Average pain relief was 12.3 weeks in adhesiolysis group and 3.2 weeks in caudal.
Manchikanti et al 2004 (119) Randomized, active-control	75 Low back pain without response to epidural injection and no facet disease Between 64% and 72% patients had prior lumbar surgery; between 4% and 20% had spinal stenosis	25 caudal epidural steroid injection 25 1-day adhesiolysis with normal saline 25 1-day adhesiolysis with hypertonic saline Patients averaged 2.1 to 2.7 procedures	12 months Unblinding at 3 or 6 months	VAS ODI Work status Opioid intake Range of motion Psychological evaluation by P3	72% of hypertonic saline and 60% of normal saline patients had >50% relief at 12 months, versus 0% of caudal injections. 18 of the caudal group were unblinded by 6 months.
Veihelmann et al 2006 (141) Randomized, active control	99 Low back pain with sciatica due to disc protrusion or failed back surgery (13 patients had discectomy)	47 1-day adhesiolysis 52 physical therapy	12 months Crossover from PT to adhesiolysis allowed at 3 months. 12 patients crossed over.	VAS for back and leg pain ODI Gerbershagen score Opioid use	Leg VAS in adhesiolysis group went from 7.2 to 2.4 at 3 months and 2.8 at 12 months. Physical therapy group showed no significant change. Because of drop out in the physical therapy group, no statistical comparison was done between the groups at 6 or 12 months.
OBSERVATIONAL					
Manchikanti et al 1999 (101) Retrospective	300 Chronic resistant low back and lower extremity pain	103 in 2-day adhesiolysis group 129 in 1-day adhesiolysis group 68 excluded Repeat procedures were provided	12 months	Significant (>50%) pain relief	41% of 2-day procedure and 33% of 1-day procedure had >50% relief at 3 months after 2 procedures. No difference between 1-day or 2-day procedures versus reported outcomes of 3-day procedure.
Gerdesmeyer et al 2005 (145) Prospective	61 Radiculopathy. Etiology not specified	3 day adhesiolysis protocol	6 months	ODI McNab score	ODI improved from 67 to 19 at 3 months and 28 at 6 months. Prior to intervention, 61 patients rated their pain moderate or bad; at 6 months, 33 were excellent or good while 22 were moderate or bad.
Park et al 2011 (146) Prospective	66 Symptomatic lumbar spinal stenosis	1 day adhesiolysis protocol	6 months	5 point satisfaction scale	51% of patients reported no pain or much improved pain at 6 months Relief did not correlate with dural sac cross sectional area.

VAS = Visual analog scale
ODI = Oswestry Disability Index
NRS = Numeric rating scale
MPQ = McGill Pain Questionnaire

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
RANDOMIZED CONTROLLED TRIALS						
Manchikanti et al (43)	+	+	+	+	+	5/5
Heavner et al (100)	+	+	+	+	+	5/5
Manchikanti et al (118)	+	+	+	+	+	5/5
Manchikanti et al (119)	+	+	+	+	+	5/5
Veihelmann et al (141)	+	+	+	+	+	5/5
OBSERVATIONAL STUDIES						
Manchikanti et al (101)	+	+	+	+	+	5/5
Gerdesmeyer et al (145)	-	+	+	+	+	4/5
Park et al (146)	+	+	+	+	+	5/5

+ = positive, - = negative, ? = unclear
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 (136).

Table 9. *Assessment of methodological quality of randomized trials.*

	Manchikanti et al (43)	Heavner et al (100)	Manchikanti et al (118)	Manchikanti et al (119)	Veihelmann et al (141)
Randomization adequate	Y	Y	Y	Y	Y
Concealed treatment allocation	Y	Y	Y	Y	N
Patient blinded	Y	Y	Y	Y	N
Care provider blinded	N	N	N	N	N
Outcome assessor blinded	N	Y	N	N	Y
Drop-out rate described	Y	N	Y	Y	Y
All randomized participants analyzed in the group	Y	Y	Y	Y	Y
Reports of the study free of suggestion of selective outcome reporting	Y	Y	Y	Y	Y
Groups similar at baseline regarding most important prognostic indicators	Y	Y	Y	Y	U
Co-interventions avoided or similar	Y	Y	Y	Y	Y
Compliance acceptable in all groups	Y	Y	Y	Y	N
Time of outcome assessment in all groups similar	Y	Y	Y	Y	Y
Score	10/12	10/12	10/12	10/12	7/12

Y=yes; N=no; U=unsure

2.2 Methodological Quality Assessment

A methodological quality assessment of the randomized controlled trials meeting the inclusion criteria was carried out using the Cochrane review criteria as shown in Table 9. Studies achieving Cochrane scores of 9 or higher were considered high quality, 6 to 8 were considered moderate quality, and studies scoring less than 6 were excluded. Of the 5 randomized controlled trials evaluated (43,100,118,119,141), 4 were high quality (43,100,118,119), and one study was moderate (141).

Of the accepted randomized controlled trials, one

study examined spinal stenosis (118), one study examined post lumbar surgery syndrome (43) and 3 studies evaluated low back and leg pain due to fibrosis from a variety of causes (100,119,141).

A methodological quality assessment of the 3 observational studies meeting the inclusion criteria was carried out utilizing the Newcastle-Ottawa Scales as illustrated in Table 10. All 3 studies were cohort studies.

Table 10. *Assessment of cohort studies.*

	Manchikanti et al (101)	Gerdesmeyer et al (145)	Park et al (146)
Selection			
1) Representativeness of the exposed cohort			
a) truly representative of the average pt with discogenic pain in the community *	X	X	
b) somewhat representative of the average pain patients in the community *			X
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 *	X		
b) drawn from a different source		X	X
c) no description of the derivation of the non exposed cohort			
3) Ascertainment of exposure			
a) secure record (eg surgical records) *	X	X	X
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 *	X	X	X
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 *			X
b) record linkage *	X	X	
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) *	X	X	X
b) no			
3) Adequacy of follow up of cohorts			
a) complete follow up - all subjects accounted for *		X	X
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	**6/13**	**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

Cohort studies achieving scores of 10 or higher were considered high quality; 7 to 9 were moderate quality; studies scoring less than 7 were considered low quality and were excluded. Two of the 3 studies were of moderate quality.

2.3 Study Characteristics

Table 11 illustrates the study characteristics of the 5 randomized controlled trials and the 2 observational studies of percutaneous adhesiolysis accepted for inclusion. One low quality observational study (101) was excluded from evidence synthesis.

2.4 Analysis of Evidence

The results of the analysis of evidence as to whether percutaneous adhesiolysis provides relief from low back and leg pain due to post lumbar surgery syndrome are shown in Table 12.

The results of the analysis of evidence as to whether percutaneous adhesiolysis provides relief from low back and leg pain due to spinal stenosis are shown in Table 13.

2.5 Effectiveness of Adhesiolysis

Based upon the 3 high quality randomized controlled trials (43,100,119) with positive results and one moderate quality randomized trial (141) with indeterminate results, using the USPSTF criteria, the evidence is fair that adhesiolysis is effective in the treatment of chronic low back and leg pain due to post lumbar surgery syndrome.

Based upon one high quality randomized controlled trial (118) and one moderate quality observational study (146), using the USPSTF criteria, the evidence is fair that adhesiolysis is effective in the treatment of chronic low back and leg pain due to spinal stenosis.

2.6 Meta-Analysis

No meta-analysis was performed due to lack of homogenous trials.

3.0 Complications

Complications of percutaneous epidural adhesiolysis have been extensively reviewed (105,106,150-192). The most commonly noted complication was dural puncture, which in and of itself can lead to post lumbar puncture headache and possibly the need for a blood patch. Veihelmann et al (141) noted 2 instances of dural puncture out of 47 patients, necessitating that the procedure be completed after waiting 4 weeks. Manchikanti et al (128) noted dural puncture in 4 of 60 patients. No treatment was required for the dural puncture. In subsequent studies (43,118) involving a total of 170 patients, Manchikanti et al noted one dural tear not requiring treatment. No other complications were noted in this series of studies.

A secondary consequence of lumbar puncture is the possibility of local anesthetic spinal blockade and, if hypertonic saline is injected into the subarachnoid space, neural damage (157). It is to prevent the occurrence of neural damage that Racz's protocol for adhesiolysis includes monitoring the patient for 30 minutes prior to the injection of hypertonic saline to ensure that there is no evidence of subarachnoid or subdural injection of local anesthetic. Given that it is not clear that hypertonic saline enhances outcomes, the procedure is commonly performed with normal saline, thereby systematically removing the risk of neural injury from hypertonic saline.

Transient neurologic deficits have been reported. Veihelmann et al (141) reported 15 cases of transient sensory deficit out of 47 patients. His higher incidence of sensory deficit may be related to his focus on placement of the catheter at the ventral aspect of the epidural space. Ho and Manghnani (158) reported a case of transient (less than 5 weeks) monoplegia involving L4, L5, and S1 in a patient with pre-existing neurologic deficits in the same area. The patient was given 5 mL of normal saline and 5 ml of 0.1% bupivacaine, indicating that the authors' suggestion that the injection of a large volume of fluid led to the deficit seems unlikely. The accompanying fluoroscopic images suggest that injection into an area of scarring (a loculation) leading to a localized area of compression of the nerve root with attendant deficits also seems unlikely. One is left to hypothesize that there was an unrecognized subarachnoid injection with persistent local anesthetic blockade of the damaged nerve roots, while sparring the lower sacral roots, but this explanation of the observed deficit is speculative.

Aldrete et al (161) attributed incidences of arachnoiditis following epidural adhesiolysis with hypertonic saline to subarachnoid leakage of hypertonic saline. However, the technique utilized in these cases was criticized (162-164).

Catheter shearing has also been reported. Usually, the catheter is left in situ as the risks of removing it are greater than the risks of leaving it. Veihelmann et al (141) reported one case of catheter shearing, which was

Table 11. *Study characteristics of randomized and observational studies of percutaneous adhesiolysis in post lumbar surgery syndrome and spinal stenosis.*

Reference, Year	Diagnosis	Number of Patients/ Selection Criteria	Control/ Comparator	Outcome Measures	Time of Measurements	Results	Strengths/ Weakness	Methodological Quality Assessment
RANDOMIZED								
Manchikanti et al 2009 (43)	Post lumbar surgery syndrome 45% of the caudal group and 38% of the adhesiolysis group had a prior fusion.	Inclusion: History of lumbar spine surgery at least 6 months prior to enrollment; >18 years of age; history of low back and/or leg pain after surgery; no facet pain; failure to respond to conservative therapy, including epidurals. Exclusion: >400 mg/day morphine equivalent use; uncontrolled psychiatric disorders	60 patients had a caudal epidural steroid injection with local anesthetic, steroid, and normal saline 60 patients had a 1 day adhesiolysis procedure with hypertonic saline. Repeat injection was done after at least 3 months based upon results of prior injection.	NRS, ODI, Employment status, opioid intake. A significant reduction was 50% for NRS and 40% for ODI.	3, 6, and 12 months	73% of adhesiolysis patients had >50% relief at 12 months; 12% of the epidural group did. 77% of the adhesiolysis patients had >40% reduction in ODI at 12 months; 13% of the epidural group did. The duration of relief was 11-13 weeks for adhesiolysis and 5-9 weeks for epidural. No difference between relief of back or leg pain. Adhesiolysis group received 3-4 injections per year.	Strengths: High quality RCT with active comparator group showing that adhesiolysis is effective in treating low back and leg pain from post lumbar surgery syndrome. Effectiveness rather than efficacy study. Weaknesses: Preliminary report with 50 patients; high number of epidural patients who were unblinded.	10/12
Heavner et al 1999 (100)	Low back and leg pain	59 patients Low back and unilateral pain below the knee unresponsive to conservative treatment and with a filling defect on epidurogram. 24 patients withdrew before the injection series was completed.	Adhesiolysis with hypertonic saline and hyaluronidase (17 patients); normal saline with hyaluronidase (15 patients); hypertonic saline without hyaluronidase (17 patients); and normal saline without hyaluronidase (10 patients).	VAS, MPQ VAS rated mild (0-29), moderate (30-54) or severe (55-100) Improvement was a 10 point change in VAS.	1, 3, 6, 12 months	No difference in outcomes regardless of whether hypertonic or normal saline was used or whether or not hyaluronidase was used. Between 33% and 100% of patients had improvement at each follow up period. ~2/3 of patients required more than one treatment in 12 months. Mean time to repeat treatment was 70 days.	Moderate quality study showing that neither the use of hypertonic saline nor hyaluronidase influenced the outcome of adhesiolysis. Weakness: Improvement was 10 points on 1-100 VAS, not the current 30 points. ~30% of patients withdrew. Facet disease was not ruled out	10/12
Manchikanti et al 2009 (118)	Spinal stenosis	50 patients Inclusion: lumbar spinal stenosis with radicular pain > 6 months' duration; Age >50; failure to respond to conservative therapy or epidural steroid injections. Exclusion: Previous lumbar surgery; foraminal stenosis; opioid abuse; uncontrolled psychiatric disorders	25 patients had a caudal epidural steroid injection with local anesthetic, steroid, and normal saline 25 patients had a 1 day adhesiolysis procedure with hypertonic saline.	NRS, ODI, Employment status, opioid intake. A significant reduction was 50% for NRS and 40% for ODI.	3, 6, and 12 months	76% of adhesiolysis patients had >50% relief at 12 months; 4% of the epidural group did. 80% of the adhesiolysis patients had >40% reduction in ODI at 12 months; 0% of the epidural group did. The duration of relief was 12.3 weeks for adhesiolysis and 3.2 weeks for epidural. Adhesiolysis group received 3-4 injections per year.	Strengths: High quality RCT with active comparator group showing that adhesiolysis is effective in treating refractory leg pain from central spinal stenosis. Effectiveness rather than efficacy study. Weaknesses: Preliminary report with 50 patients; high number of epidural patients who were unblinded.	10/12

Table 11 (cont.). *Study characteristics of randomized and observational studies of percutaneous adhesiolysis in post lumbar surgery syndrome and spinal stenosis.*

Reference, Year	Diagnosis	Number of Patients/ Selection Criteria	Control/ Comparator	Outcome Measures	Time of Measurements	Results	Strengths/ Weakness	Methodological Quality Assessment
Manchikanti et al 2004 (119)	Low back and leg pain Approximately 70% of participants had previous lumbar surgery.	75 patients Inclusion 18-65 years with >2 year history of low back pain and minimum VAS of 6. No facet disease. Failure to respond to epidural injections. Exclusion: large disc herniation, cauda equine syndrome, lumbar surgery in the last 6 months, drug addiction, uncontrolled psychological disorders	25 patients with caudal epidural; 25 patients with adhesiolysis procedure using normal saline; 25 patients with adhesiolysis procedure using 10% hypertonic saline. Co-interventions included analgesics and exercise. Unblinding occurred after 3 months.	VAS, ODI, work status, opioid intake, ROM, and psychological evaluation using P-3. Significant pain relief was >50% relief.	3, 6, 12 months	Mean reduction of VAS at 12 months was 1.2 for epidural group, 3.6 for normal saline, and 4.2 for hypertonic saline. Average duration of >50% relief with one procedure was 0% for epidural group, 3.6 months for normal saline group, and 5.4 months for hypertonic group. 0% of epidural group had >50% relief at 12 months, 60% and 72% of normal saline, and hypertonic groups had >50% relief at 12 months.	Strengths: High quality RCT showing that adhesiolysis provides significant relief regardless of whether normal saline or hypertonic saline is used. Weaknesses: Repeat procedures allowed based upon response to previous procedures, rather than examining one injection only.	10/12
Veihelmann et al 2006 (141)	Low back and leg pain, specifically excluding stenosis	99 patients with chronic low back pain and sciatica. Location of pain corresponded to imaging findings. Patients had failed PT, injections, and medication. Exclusion: spinal stenosis, rheumatological disease, and malignancy. 5 PT and 8 adhesiolysis patients had discectomy.	1-day adhesiolysis (47 patients) versus physical therapy (52 patients) Patients could cross over at 3 months; 12 switched from PT to adhesiolysis	VAS for back and leg pain. ODI, Gerbershagen score	3, 6, and 12 months	Significant pain relief at 12 months in adhesiolysis group, with >4 points and >60% improvement in VAS and with a 50% decrease in ODI. Reduction in VAS and ODI at 3 months statistically significant between PT and adhesiolysis. 12 patients in PT group switched to adhesiolysis at 6 months. 13 were lost to follow up or had surgery; only 27 PT patients were followed up at 6, 12 months.	Strengths: Moderate quality RCT showing that adhesiolysis is more effective in treating refractory low back and leg pain from fibrosis than conservative treatment. Active comparator group; careful attention to catheter location; prospective RCT. Weakness: high dropout rate from PT group.	7/12
OBSERVATIONAL								
Gerdesmeyer et al 2005 (145)	Radiculopathy Etiology not specified	61 patients Chronic radiculopathy	3 day adhesiolysis protocol	ODI McNab score	6 months	ODI improved from 67 to 19 at 3 months and 28 at 6 months. Prior to intervention, 61 patients rated their pain moderate or bad; at 6 months, 33 were excellent or good while 22 were moderate or bad.	Strengths: Prospective evaluation Outcome parameter Weakness: Mixture of multiple etiologies No control group	7/13

Table 11 (cont.). *Study characteristics of randomized and observational studies of percutaneous adhesiolysis in post lumbar surgery syndrome and spinal stenosis.*

Reference, Year	Diagnosis	Number of Patients/ Selection Criteria	Control/ Comparator	Outcome Measures	Time of Measurements	Results	Strengths/ Weakness	Methodological Quality Assessment
Park et al 2011 (146)	Spinal Stenosis	66 patients with central spinal stenosis as determined by dural sac cross sectional area. Exclusion criteria were foraminal stenosis, spondylolisthesis, previous surgery, or multilevel stenosis.	1 day adhesiolysis procedure with hypertonic saline; no comparator. Concurrent therapies after the procedure included NSAIDs. Opioids were provided as necessary after 2 weeks. Non responsive patients received epidural steroid injections.	5 point patient satisfaction scale. Patients divided into responder (no pain, much pain, slightly improved) versus non-responders (no change, worse pain).	2 weeks, 6 months	66% of patients had improvement at 6 months. 2 patients had surgery. Response did not depend upon severity of spinal stenosis. 17 patients had no pain relief despite no filling defect after the procedure.	Strengths: Moderate quality observational study showing effectiveness of adhesiolysis in treating refractory pain due to central spinal stenosis. Patients limited to localized central stenosis. Rigorous observational study design. Weakness: Response based upon patient report of improvement, with no measure of amount of improvement. No comparator group.	7/13

VAS = visual analog scale. MPQ = McGill Pain Questionnaire. NRS = Numeric Rating Scale. ODI = Oswestry Disability Index. ROM = range of motion . RCT = randomized controlled trial . P-3 = Pain Patient Profile. PT = physical therapy. SI = sacroiliac. NSAIDs = Non-Steroidal Anti-Inflammatory Drugs

easily removed via an incision at the sacrum under local anesthetic. Perkins et al (153) reports a case in which an MRI was successfully obtained with a retained sheared Racz catheter being present. In this case, the MRI had a metallic artifact and a CT myelogram was necessary to identify a filling defect by the S1 nerve root. A laminectomy found the retained catheter in the epidural space by the S1 root; removal of the catheter resolved the radiculopathy which had occurred since the shearing of the catheter.

Manchikanti and Bakhit (160) reported a torn Racz catheter in the lumbar epidural space. This case report illustrated a difficult situation with a sheared and retained epidural catheter which could not be removed utilizing standard techniques, but was successfully removed without any residual problems using arthroscopy forceps.

The most widespread cause of catheter shearing is advancing an RK needle without the stylet being fully inserted, allowing the long lip of the needle to be bent up and catch the catheter causing it to shear. One commentator stated that sheared catheters seemed "to occur every time we have a new group of pain fellows" (159), suggesting that the complication is related to user experience. The current recommendation to use a Coude needle rather than an RK® needle minimizes the risk of this complication.

As with any procedure, there is a risk of infection or hematoma. Wagner et al (152) reported a case of meningitis. Gerdesmeyer et al (145), in his series of 61 cases, did report one case of epidural infection successfully treated with antibiotics and refers to 2 additional cases reported in the literature. Manchikanti (101) reported one case of infection out of 232 patients. This infection did require drainage but was not an epidural abscess. Talu and Erdine (150) reported 3 cases of epidural abscess in a study of 250 patients.

No cases of epidural hematoma have been reported.

There are no reported cases of serious neurologic deficits after adhesiolysis, including arachnoiditis, paralysis, weakness, or bowel or bladder dysfunction.

The incidence of complications from percutaneous adhesiolysis is low and the complications are generally minimal and self-limited. The procedure should be considered to be low risk for serious adverse events when performed by well-trained physicians.

4.0 Discussion

For this systematic review, 17 studies were identi-

Table 12. *Results of randomized studies on the efficacy of percutaneous adhesiolysis in post lumbar surgery syndrome.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief and Function	Results at 12 months	Comments
Manchikanti et al (43)	RA, AC	10/12	120 60 adhesiolysis 60 caudal epidural steroid	73% of adhesiolysis group had >50% relief at 12 months; 12% of caudal group did. 3-4 adhesiolysis procedures/year	P	High quality study showing good evidence of effectiveness.
Heavner et al (100)	RA, AC	10/12	59	83% of the patients showed significant improvement compared to 49% at 3 months, 43% at 6 months, and 49% at 12 months.	P	High quality study with positive results.
Manchikanti et al (119)	RA, AC	10/12	75 25 caudal epidural steroid injection 25 1-day adhesiolysis with normal saline 25 1-day adhesiolysis with hypertonic saline	72% of hypertonic saline and 60% of normal saline patients had >50% relief at 12 months, versus 0% of caudal injections.	P	High quality study with positive results.
Veihelmann et al (141)	RA, AC	7/12	47 1 –day adhesiolysis 52 physical therapy	There was a significant decrease in VAS and Oswestry scores at 1, 3, 6, and 12 months. 28 adhesiolysis patients were able to decrease Gerbershagen grade compared to 2 PT patients.	p	Results undetermined.

RA = randomized; AC = active-control; NR = non-randomized; PR = prospective; RE = retrospective; P = positive; N = negative

Table 13. *Results of randomized and observational studies on the effectiveness of percutaneous adhesiolysis in lumbar spinal stenosis.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain relief and Function	Results at 12 months	Comments.
Manchikanti et al (118)	R, AC	10/12	25 adhesiolysis; 25 caudal epidural steroid	76% of adhesiolysis patients had >50% relief at 12 months; 4% of the epidural group did. Average of 3-4 adhesiolysis procedures per year.	P	High quality study with positive results.
Park et al (146)	PR	7/13	66, all had adhesiolysis	66% had improvement at 6 months	NA	Moderate quality study with positive results.

R = randomized; AC = active-control; PR = prospective; P = positive; N = negative

fied and selected for review. Of these, 5 randomized controlled trials (43,100,118,119,141) and 2 observational studies (145,146) met the inclusion criteria. Of the 5 randomized controlled trials, one high quality study dealt with post lumbar surgery syndrome (43) and one high quality study dealt with spinal stenosis (118). The 3 remaining randomized controlled trials dealt with low back and leg pain due to fibrosis from a variety of causes including post surgery syndrome (100,119,141).

Applying the USPSTF criteria, these studies indicate that there is fair evidence that percutaneous adhesiolysis is effective in relieving low back and/or leg pain caused by post lumbar surgery syndrome and that there is fair evidence that percutaneous adhesiolysis is effective in relieving low back and/or leg pain caused by spinal stenosis.

The incidence of complications from percutaneous adhesiolysis is low and the complications are generally minimal and self-limited. The procedure should be considered to be low risk for serious adverse events when performed by well-trained physicians.

Percutaneous adhesiolysis is a procedure designed to lyse epidural scarring in patients with persistent low back and leg pain due to post lumbar surgery syndrome or spinal stenosis. Epidural scarring can arise from a number of causes, most obviously surgery, infection, or hematoma, but also because of disc herniation or simply the cumulative effect of recurrent subclinical bleeding as the rich plexus of veins in the epidural space suffer small tears during the slow process of degeneration that occurs with aging. At this point, it is accepted that scarring can cause pain, whether by tethering nerve roots so that they are placed under tension with movement or by decreasing nutrition to the roots either by direct compression or compression of adjacent veins. Furthermore, compression, degeneration, or leakage of nuclear material can lead to an inflammatory response, with pain.

There were 4 high quality randomized controlled trials (43,100,118,119) and 2 moderate quality observational studies (145,146) showing that adhesiolysis provides significant (greater than 50%) pain relief. The procedure does not provide permanent relief, but, repeated up to 3 to 4 times year, provides relief in patients who have no other option to find relief other than implantable devices or the unlikely benefit of further surgery.

The definition of percutaneous adhesiolysis has changed over time and it is important to consider what differentiates an adhesiolysis from an epidural injection. Adhesiolysis was originally described as a 3-day procedure using hypertonic saline, local anesthetic, steroid, and hyaluronidase administered using a shear-resistant steerable catheter. Heavner et al (100) showed that neither hypertonic saline nor hyaluronidase was critical for a successful outcome. Manchikanti et al (101) showed that the procedure could be done in one day, not 3 days. Manchikanti et al (119) also showed that hypertonic saline was not critical to the procedure. The common factor which differentiates percutaneous adhesiolysis from an epidural steroid injection, whether done through a needle or using a non-wire bound catheter, is the use of a wire-bound, steerable catheter to deliver appropriate volumes of saline, steroid, and local anesthetic into the target area. Veihelmann et al (141) noted the importance of placing the catheter at the ventrolateral aspect of the epidural space and the desirability of replicating the patient's pain complaints. Thus, there is a variety of factors which clearly differentiate adhesiolysis from other injections, including catheter placement, volumes injected and, most clearly, the use of a wire-bound catheter.

This review provides formal analysis of the quality of literature relating to the use of percutaneous adhesiolysis in persistent low back and leg pain due to post lumbar surgery syndrome or lumbar spinal stenosis.

This review does reach differing conclusions than some previous reviews and guidelines; whereas conclusions are similar to some others. The reason for this different conclusion is the availability of new high or moderate quality literature since the previous reviews were performed and methodological rigor applied.

The major issues related to the conduct of research pertaining to adhesiolysis revolves around the control group or placebo. Placebo-control neural blockade is not realistic even though it has been misinterpreted and inaccurately promoted (44,109,111,193-206). It continues to be a major issue. Some have mistakenly reported that any local anesthetic injection yielding similar results as steroids is considered placebo. Methodologists tend to focus on the differences between the 2 groups, ignoring the equivalency trials and non-inferiority trials, as well as the basis of comparative effectiveness research, which essentially evaluates the differences between 2 treatments or similarities (193-205). Consequently, this does not imply that the treatments do not work. The experimental and clinical findings from a multitude of investigations of electrophysiological effects, injections into the disc, facet joint, or paraspinal muscles have illustrated numerous vari-

ables with therapeutic or active effects, even though an inactive solution was injected into an active structure (207-215). In addition, for the placebo effect to be evident, it has to be non-existent with prior treatments and present repeatedly. The design of a placebo is an extremely difficult venture in interventional pain management, specifically with percutaneous adhesiolysis (216-219). Highly acclaimed authors Chou and Huffman have considered that the use of a control group for percutaneous adhesiolysis is a failure for caudal epidural injections (109,111,119). However, they also ignored positive results when it was derived by a less traumatic procedure in non-surgical patients instead of fluoroscopy, categorizing the study as a negative study for those purposes (219). It may be ideal to use the design by Manchikanti et al (43,68,118,119) for controlled purposes in evaluating the role of adhesiolysis. However, methodologists with substantial bias enjoy their role in criticizing this aspect.

Percutaneous adhesiolysis involves multiple components of treatment with adhesiolysis, injection of local anesthetic, steroid, and hypertonic sodium chloride solution. There has been varying evidence for all the drugs utilized despite its targeted delivery (119). Furthermore, all the drugs have varying mechanisms and results in managing chronic, persistent, recalcitrant pain secondary to either spinal stenosis or post surgery syndrome. Consequently, the underlying mechanism of action of epidurally administered steroids, local anesthetics, and hypertonic sodium chloride solution is still not well understood. It is believed that the achieved neural blockade alters or interrupts nociceptive input. This reflects the mechanicians of the afferent fibers, self-sustaining activity of the neurons, and the pattern of central neuronal activities (44,220). In addition to this, corticosteroids always have been shown to be anti-inflammatory agents by inhibition of either the synthesis or release of the number of pro-inflammatory mediators and by causing a reversible local anesthetic effect (220-225). Similarly, local anesthetics have also been described to provide short- to long-term symptomatic relief based on alteration of various mechanisms including excess nociceptive process, excess release of neurotransmitters, nociceptive sensitization of the nervous system, and phenotype changes (226-233). There also has been experimental evidence illustrating the effectiveness of local anesthetics similar to steroids (226,233).

The hypertonic saline commonly administered with adhesiolysis has been shown that osmolar depletion of water content within peripheral axons resulted in decreased nerve conduction (234). It was later demonstrated; however, that the attenuation of transmitter release was from the neuromuscular junction exposed to hypertonic solution (235). While Hitchcock provided that evidence for the effectiveness of an intrathecal injection of cold saline (236), it was subsequently shown that the efficacy of hypertonic saline was due to the hypertonicity of the solution rather than to any thermal effect (237). Multiple other studies have shown various mechanisms including selective C-fiber blockade in cat dorsal rootlets with an increased concentration of chloride ion (238); decrease of the spinal cord water content and depressed lateral column-evoked ventral root response (174); change in the volume due to outflow of water across the membrane and ionic concentration changes (239); reduction in swelling or by osmotically induced fluid shifts, reducing pressure on the nerve, and producing a local anesthetic effect of the hypertonic solution (240); whereas some have illustrated an actual increase in tissue mass in the case of intravertebral tissue incubated in 10% sodium chloride solution (241). In contrast, Racz and colleagues (242) showed that the study of dural permeability in dogs demonstrated transdural calibration of hypertonic saline to occur very slowly, but resulted in the doubling of the cerebral spinal sodium concentration 20 minutes after extradural placement of 10% sodium chloride solution. Consequently, the anesthetic effects of epidural hypertonic saline not only remain controversial and lack definition, but also cast doubt on the hypothesis that it achieves its therapeutic effect by shrinking the mass.

In addition, there have also been multiple discussions in reference to the type of local anesthetic, steroids, hypertonic sodium chloride solution, as well as the dosage and time of administration. These have been discussed in various studies and in previous reviews (102,103,110,155,167,242).

The results of this systematic review may be applied in interventional pain management practices utilizing appropriate evaluations (43,111,112,118,,132-134,203,243,244). Future implications for research should include a clear case definition with consistent inclusion and exclusion criteria; technical consideration; frequency, type, and volume of injectate; outcome measures; appropriate design; and reporting of randomized trials (245-249).

Ongoing controversies exist, as do methodological flaws in evaluation. For clinical purposes and in order to implement comparative effectiveness research, there

must be substantial alterations in the thinking of the methodologists and in the evaluation of the literature so as to provide appropriate clinical guidance rather than negative opinions based on bias.

In conclusion, this systematic review provides practical evidence for the management of an extremely difficult problem with recalcitrant low back and lower extremity pain either secondary to post surgery syndrome or spinal stenosis with a modality which is considered as safe with moderate results.

5.0 Conclusion

A systematic review of the literature regarding percutaneous adhesiolysis shows fair evidence for the effectiveness of the procedure in both spinal stenosis and in post lumbar surgery syndrome.

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References

1. Salovey P, Sieber WJ, Smith AF, Turk DC, Jobe JB, Willis GB. *Reporting chronic pain episodes on health surveys.* National Center for Health Statistics Vital Health Stat 6, 1992, pp 92-1081.
2. Schizas C, Kulik G, Kosmopoulos V. Disc degeneration: Current surgical options. *Eur Cell Mater* 2010; 20:306-315.
3. 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.
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.
   www.iom.edu/~/media/Files/Report%20Files/2011/Relieving-Pain-in-America-A-Blueprint-for-Transforming-Prevention-Care-Education-Research/Pain%20Research%202011%20Report%20Brief.pdf
5. Ramage-Morin PL, Gilmour H. Chronic pain at ages 12 to 44. *Health Rep* 2010; 21:53-61.
6. Currow DC, Agar M, Plummer JL, Blyth FM, Abernethy AP. Chronic pain in South Australia - population levels that interfere extremely with activities of daily living. *Aust N Z J Public Health* 2010; 34:232-239.
7. Knox J, Orchowski J, Scher DL, Owens BD, Burks R, Belmont PJ. The incidence of low back pain in active duty United States military service members. *Spine (Phila Pa 1976)* 2011; 36:1492-1500.
8. 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.
9. Wenig CM, Schmidt CO, Kohlmann T, Schweikert B. Costs of back pain in Germany. *Eur J Pain* 2009; 13:280-286.
10. Pellisé F, Balagué F, Rajmil L, Cedraschi C, Aguirre M, Fontecha CG, Pasarín M, Ferrer M. Prevalence of low back pain and its effect on health-related quality of life in adolescents. *Arch Pediatr Adolesc Med* 2009; 163:65-71.
11. Elliott AM, Smith BH, Hannaford PC, Smith WC, Chambers WA. The course of chronic pain in the community: Results of a 4-year follow-up study. *Pain* 2002; 99:299-307.
12. Croft PR, Macfarlane GJ, Papageorgiou AC, Thomas E, Silman AJ. Outcome of low back pain in general practice: A prospective study. *BMJ* 1998; 316:1356-1359.
13. Enthoven P, Skargren E, Oberg B. Clinical course in patients seeking primary care for back or neck pain: A prospective 5-year follow-up of outcome and health care consumption with subgroup analysis. *Spine (Phila Pa 1976)* 2004; 29:2458-2465.
14. Miedema HS, Chorus AM, Wevers CW, van der Linden S. Chronicity of back problems during working life. *Spine (Phila Pa 1976)* 1998; 23:2021-2028.
15. Shiri R, Solovieva S, Husgafvel-Pursiainen K, Viikari J, Raitakari OT, Viikari-Juntura E. Incidence of nonspecific and radiating low back pain: Follow-up of 24-39-year-old adults of the Young Finns Study. *Arthritis Care Res (Hoboken)* 2010; 62:455-459.
16. Cummins J, Lurie JD, Tosteson TD, Hanscom B, Abdu WA, Birkmeyer NJ, Herkowitz H, Weinstein J. Descriptive epidemiology and prior healthcare utilization of patients in the Spine Patient Outcomes Research Trial's (SPORT) three observational cohorts: Disc herniation, spinal stenosis, and degenerative spondylolisthesis. *Spine (Phila Pa 1976)* 2006; 31:806-814.
17. Cherkin DC, Deyo RA, Loeser JD, Bush T, Waddell G. An international comparison

of back surgery rates. *Spine (Phila Pa 1976)* 1994; 19:1201-1206.

18. Schofferman J, Reynolds J, Herzog R, Covington E, Dreyfuss P, O'Neill C. Failed back surgery: Etiology and diagnostic evaluation. *Spine J* 2003; 3:400-403.
19. Parks PD, Pransky GS, Kales SN. Iatrogenic disability and narcotics addiction after lumbar fusion in a worker's compensation claimant. *Spine (Phila Pa 1976)* 2010; 35:E549-E552.
20. Esmer G, Blum J, Rulf J, Pier J. Mindfulness-based stress reduction for failed back surgery syndrome: A randomized controlled trial. *J Am Osteopath Assoc* 2010; 110:646-652.
21. Thomson S, Jacques L. Demographic characteristics of patients with severe neuropathic pain secondary to failed back surgery syndrome. *Pain Pract* 2009; 9:206-215.
22. Tomycz ND, Ortiz V, Moossy JJ. Simultaneous intrathecal opioid pump and spinal cord stimulation for pain management: Analysis of 11 patients with failed back surgery syndrome. *J Pain Palliat Care Pharmacother* 2010; 24:374-383.
23. Eldabe S, Kumar K, Buchser E, Taylor RS. An analysis of the components of pain, function, and health-related quality of life in patients with failed back surgery syndrome treated with spinal cord stimulation or conventional medical management. *Neuromodulation* 2010; 13:201-209.
24. Chan CW, Peng P. Failed back surgery syndrome. *Pain Med* 2011; 12:577-606.
25. Waguespack A, Schofferman J, Slosar P, Reynolds J. Etiology of long-term failures of lumbar spine surgery. *Pain Med* 2002; 3:18-22.
26. Mirza SK, Deyo RA. Systematic review of randomized trials comparing lumbar fusion surgery to nonoperative care for treatment of chronic back pain. *Spine (Phila Pa 1976)* 2007; 32:816-823.
27. Deyo RA, Mirza SK, Turner JA, Martin BI. Overtreating chronic back pain: Time to back off? *J Am Board Fam Med* 2009; 22:62-68.
28. Nguyen TH, Randolph DC, Talmage J, Succop P, Travis R. Long-term outcomes of lumbar fusion among worker's compensation subjects: A historical cohort study. *Spine (Phila Pa 1976)* 2011; 36:320-331.
29. White AP, Brothers JG, Vaccaro AR. Review of the medical evidence regarding the surgical treatment of low back pain. In: Szpalski M, Gunzburg R, Rydevik BL, Le Huec JC, Mayer MH (eds). *Surgery for Low Back Pain.* Springer Berlin Heidelberg, 2010, pp 267-277.
30. Law JD, Lehman RA, Kirsch WM. Reoperation after lumbar intervertebral disc surgery. *J Neurosurg* 1978; 48:259-263.
31. Bono CM, Lee CK. Critical analysis of trends in fusion for degenerative disc disease over the past 20 years: Influence of technique on fusion rate and clinical outcome. *Spine (Phila Pa 1976)* 2004; 29:455-463.
32. Osterman H, Sund R, Seitsalo S, Keskimäki I. Risk of multiple reoperations after lumbar discectomy: A population-based study. *Spine (Phila Pa 1976)* 2003; 28:621-627.
33. Fritsch EW, Heisel J, Rupp S. The failed back surgery syndrome: Reasons, intraoperative findings, and long-term results: A report of 182 operative treatments. *Spine (Phila Pa 1976)* 1996; 21:626-633.
34. Ross JS, Robertson JT, Frederickson RC, Petrie JL, Obuchowski N, Modic MT, deTribolet N. Association between peridural scar and recurrent radicular pain after lumbar discectomy: Magnetic resonance evaluation. ADCON-L European Study Group. *Neurosurgery* 1996; 38:855-861.
35. Deyo RA, Gray DT, Kreuter W, Mirza S, Martin BI. United States trends in lumbar fusion surgery for degenerative conditions. *Spine (Phila Pa 1976)* 2005; 30:1441-1445.
36. Deyo RA, Ciol MA, Cherkin DC, Loeser JD, Bigos SJ. Lumbar spinal fusion. A cohort study of complications, reoperations, and resource use in the Medicare population. *Spine (Phila Pa 1976)* 1993; 18:1463-1470.
37. Weinstein JN, Tosteson TD, Lurie JD, Tosteson AN, Blood E, Hanscom B, Herkowitz H, Cammisa F, Albert T, Boden SD, Hilibrand A, Goldberg H, Berven S, An H; SPORT Investigators. Surgical versus nonsurgical therapy for lumbar spinal stenosis. *N Engl J Med* 2008; 358:794-810.
38. Waddell G, Kummel EG, Lotto WN, Graham JD, Hall H, McCulloch JA. Failed lumbar disc surgery and repeat surgery following industrial injuries. *J Bone Joint Surg Am* 1979; 61:201-207.
39. Bosscher HA, Heavner JE. Incidence and severity of epidural fibrosis after back surgery: An endoscopic study. *Pain Pract* 2010; 10:18-24.
40. Lee YS, Choi ES, Song CJ. Symptomatic nerve root changes on contrast-enhanced MR imaging after surgery for lumbar disk herniation. *AJNR Am J Neuroradiol* 2009; 30:1062-1067.
41. Siepe CJ, Korge A, Grochulla F, Mehren C, Mayer HM. Analysis of post-operative pain patterns following total lumbar disc replacement: Results from fluoroscopically guided spine infiltrations. *Eur Spine J* 2008; 17:44-56.
42. Hayek SM, Helm S, Benyamin RM, Singh V, Bryce DA, Smith HS. Effectiveness of spinal endoscopic adhesiolysis in post lumbar surgery syndrome: A systematic review. *Pain Physician* 2009; 12:419-435.
43. Manchikanti L, Singh V, Cash KA, Pampati V, Datta S. A comparative effectiveness evaluation of percutaneous adhesiolysis and epidural steroid injections in managing lumbar post surgery syndrome: A randomized, equivalence controlled trial. *Pain Physician* 2009; 12:E355-E368.
44. Manchikanti L, Boswell MV, Singh V, Benyamin RM, Fellows B, Abdi S, Buenaventura RM, Conn A, Datta S, Derby R, Falco FJ, 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.
45. Diwan S, Benyamin RM, Bryce D, Falco FJE, Geffert S, Hameed H, Sharma M, Abdi S. Effectiveness of cervical epidurals in the management of chronic neck and upper extremity pain. *Pain Physician* 2012; 15:E405-E444.
46. Epter RS, Helm S 2nd, Hayek SM, Benyamin RM, Smith HS, Abdi S. Systematic review of percutaneous adhesiolysis and management of chronic low back pain in post lumbar surgery syndrome. *Pain Physician* 2009; 12:361-378.
47. Manchikanti L, Boswell MV, Singh V, Derby R, Fellows B, Falco FJ, 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.
48. 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.
49. Conn A, Buenaventura RM, Datta S, Abdi S, Diwan S. Systematic review of caudal epidural injections in the management of chronic low back pain. *Pain Physician*

2009; 12:109-135.

50. Saal JS. The role of inflammation in lumbar pain. *Spine (Phila Pa 1976)* 1995; 20:1821-1827.
51. Kayama S, Konno S, Olmarker K, Yabuki S, Kikuchi S. Incision of the anulus fibrosus induces nerve root morphologic, vascular, and functional changes. An experimental study. *Spine (Phila Pa 1976)* 1996; 21:2539-2543.
52. Ohtori S, Suzuki M, Koshi T, Takaso M, Yamashita M, Inoue G, Yamauchi K, Orita S, Eguchi Y, Kuniyoshi K, Ochiai N, Kishida S, Nakamura J, Aoki Y, Ishikawa T, Arai G, Miyagi M, Kamoda H, Suzuki M, Toyone T, Takahashi K. Proinflammatory cytokines in the cerebrospinal fluid of patients with lumbar radiculopathy. *Eur Spine J* 2011; 20:942-746.
53. Kuslich SD, Ulstrom CL, Michael CJ. The tissue origin of low back pain and sciatica: A report of pain response to tissue stimulation during operations on the lumbar spine using local anesthesia. *Orthop Clin North Am* 1991; 22:181-187.
54. Huntoon MA. Imaging in interventional pain management. In: Narouze SN (ed). *Atlas of Ultrasound-Guided Procedures in Interventional Pain Management*. Springer, New York, 2011, pp 3-12.
55. Collighan N, Gupta S. Epidural steroids. Continuing education in anaesthesia. *Critical Care & Pain* 2010; 10:1-5.
56. 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.
57. Manchikanti L, Cash KA, McManus CD, Pampati V, Smith HS. One year results of a randomized, double-blind, active controlled trial of fluoroscopic caudal epidural injections with or without steroids in managing chronic discogenic low back pain without disc herniation or radiculitis. *Pain Physician* 2011; 14:25-36.
58. 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.
59. Yi X, McPherson B. Application of X STOP device in the treatment of lumbar spinal stenosis. *Pain Physician* 2010; 13:E327-E336.
60. Parr AT, Manchikanti L, Hameed H, Conn A, Manchikanti KN, Benyamin RM, Diwan S, Singh V, Abdi S. Caudal epidural injections in the management of chronic low back pain: A systematic appraisal of the literature. *Pain Physician* 2012; 15:E159-E198.
61. Manchikanti L, Buenaventura RM, Manchikanti KN, Ruan X, Gupta S, Smith HS, Christo PJ, Ward SP. Effectiveness of therapeutic lumbar transforaminal epidural steroid injections in managing lumbar spinal pain. *Pain Physician* 2012; 15:E199-E245.
62. Datta S, Lee M, Falco FJ, Bryce DA, Hayek SM. Systematic assessment of diagnostic accuracy and therapeutic utility of lumbar facet joint interventions. *Pain Physician* 2009; 12:437-460.
63. Simopoulos TT, Manchikanti L, Singh V, Gupta S, Hameed H, Diwan S, Cohen SP. A systematic evaluation of prevalence and diagnostic accuracy of sacroiliac joint interventions. *Pain Physician* 2012; 15:E305-E344.
64. Hansen H, Manchikanti L, Simopoulous TT, Christo PJ, Gupta S, Smith HS, Hameed H, Cohen SP. A systematic evaluation of the therapeutic effectiveness of sacroiliac joint interventions. *Pain Physician* 2012; 15:E247-E278.
65. Songer MN, Ghosh L, Spencer DL. Effects of sodium hyaluronate on peridural fibrosis after lumbar laminotomy and discectomy. *Spine (Phila Pa 1976)* 1990; 15:550-554.
66. Masopust V, Häckel M, Netuka D, Bradác O, Rokyta R, Vrabec M. Postoperative epidural fibrosis. *Clin J Pain* 2009; 25:600-606.
67. 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.
68. Manchikanti L, Pampati V, Cash KA. Protocol for evaluation of the comparative effectiveness of percutaneous adhesiolysis and caudal epidural steroid injections in low back and/or lower extremity pain without post surgery syndrome or spinal stenosis. *Pain Physician* 2010; 13:E91-E110.
69. Preul MC, Campbell PK, Garlick DS, Spetzler RF. Application of a new hydrogel dural sealant that reduces epidural adhesion formation: Evaluation in a large animal laminectomy model. *J Neurosurg Spine* 2010; 12:381-390.
70. Medley J. *Targeted Polymeric Biomaterials for the Prevention of Post Surgical Adhesions*.

https://archive.uky.edu/handle/10225/1118.

71. Denaro V, Di Martino A, Longo UG, Costa V, Papalia R, Forriol F, Denaro L. Effectiveness of a mucolythic agent as a local adjuvant in revision lumbar spine surgery. *Eur Spine J* 2008; 17:1752-1756.
72. Fransen P. Reduction of postoperative pain after lumbar microdiscectomy with DuraSeal Xact Adhesion Barrier and Sealant System. *Spine J* 2010; 10:751-761.
73. Richards PJ, Turner AS, Gisler SM, Kraft S, Nuss K, Mark S, Seim HB 3rd, Schense J. Reduction in postlaminectomy epidural adhesions in sheep using a fibrin sealant-based medicated adhesion barrier. *J Biomed Mater Res B Appl Biomater* 2010; 92:439-446.
74. Petrie JL, Ross JS. Use of ADCON-L to inhibit postoperative peridural fibrosis and related symptoms following lumbar disc surgery: A preliminary report. *Eur Spine J* 1996; 1:S10-S17.
75. McCarron RF, Wimpee MW, Hudkins PG, Laros GS. The inflammatory effect of nucleus pulposus. A possible element in the pathogenesis of low-back pain. *Spine (Phila Pa 1976)* 1987; 12:760-764.
76. Hoyland JA, Freemont AJ, Jayson MI. Intervertebral foramen venous obstruction. A cause of periradicular fibrosis? *Spine (Phila Pa 1976)* 1989; 14:558-568.
77. Berthelot JM, Le Goff B, Maugars Y. The role for radicular veins in nerve root pain is underestimated: Limitations of imaging studies. *Joint Bone Spine* 2011; 78:115-117.
78. LaRocca H, MacNab I. The laminectomy membrane. Studies in its evolution, characteristics, effects and prophylaxis in dogs. *J Bone Joint Surg Br* 1974; 56B:545-550.
79. Cooper RG, Freemont AJ, Hoyland JA, Jenkins JP, West CG, Illingworth KJ, Jayson MI. Herniated intervertebral disc-associated periradicular fibrosis and vascular abnormalities occur without inflammatory cell infiltration. *Spine (Phila Pa 1976)* 1995; 20:591-598.
80. North RB, Campbell JN, James CS, Conover-Walker MK, Wang H, Piantadosi S, Rybock JD, Long DM. Failed back surgery syndrome: 5-year follow-up in 102 patients undergoing repeated operation. *Neurosurgery* 1991; 28:685-690; discussion 690-691.
81. Massie JB, Huang B, Malkmus S, Yaksh TL, Kim CW, Garfin SR, Akeson WH. A

preclinical post laminectomy rat model mimics the human post laminectomy syndrome. *J Neurosci Methods* 2004; 137:283-289.

82. Nygaard OP, Kloster R, Dullerud R, Jacobsen EA, Mellgren SI. No association between peridural scar and outcome after lumbar microdiscectomy. *Acta Neurochir (Wien)* 1997; 139:1095-1100.
83. Kobayashi S, Takeno K, Yayama T, Awara K, Miyazaki T, Guerrero A, Baba H. Pathomechanisms of sciatica in lumbar disc herniation: Effect of periradicular adhesive tissue on electrophysiological values by an intraoperative straight leg raising test. *Spine (Phila Pa 1976)* 2010; 35:2004-2014.
84. Eseoğlu M, Akdemir H. Failed back surgery syndrome in lumber disc herniation: The retrospective analysis of success scorings of epidural fibrosis and recurrent cases in reoperations. *Eur J Gen Pract* 2010; 7:130-135.
85. Parke WW, Watanabe R Adhesions of the ventral lumbar dura. An adjunct source of discogenic pain? *Spine (Phila Pa 1976)* 1990; 15:300-303.
86. Huang WL, Robson D, Liu MC, King VR, Averill S, Shortland PJ, Priestley JV. Spinal cord compression and dorsal root injury cause up-regulation of activating transcription factor-3 in large-diameter dorsal root ganglion neurons. *Eur J Neurosci* 2006; 23:273-278.
87. Rydevik BL. The effects of compression on the physiology of nerve roots. *J Manipulative Physiol Ther* 1992; 15:62-66.
88. Huang WL, George KJ, Ibba V, Liu MC, Averill S, Quartu M, Hamlyn PJ, Priestley JV. The characteristics of neuronal injury in a static compression model of spinal cord injury in adult rats. *Eur J Neurosci* 2007; 25:362-372.
89. Haq I, Cruz-Almeida Y, Siqueira EB, Norenberg M, Green BA, Levi AD. Postoperative fibrosis after surgical treatment of the porcine spinal cord: A comparison of dural substitutes. Invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves, March 2004. *J Neurosurg Spine* 2005; 2:50-54.
90. Buvanendran A, Kroin JS, Kerns JM, Nagalla SN, Tuman KJ. Characterization of a new animal model for evaluation of persistent postthoracotomy pain. *Anesth Analg* 2004; 99:1453-1460.
91. Schimizzi AL, Massie JB, Murphy M, Perry A, Kim CW, Garfin SR, Akeson WH. High-molecular-weight hyaluronan inhibits macrophage proliferation and cytokine release in the early wound of a preclinical postlaminectomy rat model. *Spine J* 2006; 6:550-556.
92. Jenschke M. Aging confers an increase in sensitivity and sensitization to pain and results in shifts of spinal NR1 expression. In: *Graduate School of Biomedical Sciences*. University of North Texas, 2009.
93. Ansari S, Heavner JE, McConnell DJ, Azari H, Bosscher HA. The peridural membrane of the spinal canal: A critical review. *Pain Pract* 2012; 12:315-325.
94. Deyo RA, Mirza SK, Martin BI, Kreuter W, Goodman DC, Jarvik JG. Trends, major medical complications, and charges associated with surgery for lumbar spinal stenosis in older adults. *JAMA* 2010; 303:1259-1265.
95. Chopko B, Caraway DL. MiDAS I (mild Decompression Alternative to Open Surgery): A preliminary report of a prospective, multi-center clinical study. *Pain Physician* 2010; 13:369-378.
96. Postacchini F, Cinotti G, Postacchini R. Surgical decompression for spinal stenosis. In: Slipman C, Derby R, Simone F, Mayer T (eds). *Interventional Spine: An Algorithmic Approach*. Saunders, Philadelphia, 2008, pp 951-966.
97. Shamji MF, Allen KD, So S, Jing L, Adams SB Jr, Schuh R, Huebner J, Kraus VB, Friedman AH, Setton LA, Richardson WJ. Gait abnormalities and inflammatory cytokines in an autologous nucleus pulposus model of radiculopathy. *Spine (Phila Pa 1976)* 2009; 34:648-654.
98. Genevay S, Atlas SJ, Katz JN. Variation in eligibility criteria from studies of radiculopathy due to a herniated disc and of neurogenic claudication due to lumbar spinal stenosis: A structured literature review. *Spine (Phila Pa 1976)* 2010; 35:803-811.
99. Racz GB, Heavner JE, Raj PP. Epidural neuroplasty. *Seminars in Anesthesia* 1997; 16:302-312.
100. Heavner JE, Racz GB, Raj P. Percutaneous epidural neuroplasty: Prospective evaluation of 0.9% NaCl versus 10% NaCl with or without hyaluronidase. *Reg Anesth Pain Med* 1999; 24:202-207.
101. Manchikanti L, Pakanati RR, Bakhit CE, Pampati V. Role of adhesiolysis and hypertonic saline neurolysis in management of low back pain: Evaluation of modification of the Racz protocol. *Pain Digest* 1999; 9:91-96.
102. Racz GB, Heavner JE, Raj PP. Percutaneous epidural neuroplasty: Prospective one-year follow-up. *Pain Digest* 1999; 9:97-102.
103. Anderson SR, Racz GB, Heavner J. Evolution of epidural lysis of adhesions. *Pain Physician* 2000; 3:262-270.
104. Gerdesmeyer L, Rechl H, Wagenpfeil S, Ulmer M, Lampe R, Wagner K. Minimally invasive percutaneous epidural neurolysis in chronic radiculopathy. A prospective controlled pilot study to prove effectiveness. *Orthopade* 2003; 32:869-876.
105. Trescot AM, Chopra P, Abdi S, Datta S, Schultz DM. Systematic review of effectiveness and complications of adhesiolysis in the management of chronic spinal pain: An update. *Pain Physician* 2007; 10:129-146.
106. Chopra P, Smith HS, Deer TR, Bowman RC. Role of adhesiolysis in the management of chronic spinal pain: A systematic review of effectiveness and complications. *Pain Physician* 2005; 8:87-100.
107. American College of Occupational and Environmental Medicine (ACOEM) Low back Disorders. In: *Occupational Medicine Practice Guidelines: Evaluation and Management of Common Health Problems and Functional Recovery of Workers*. Second Edition. American College of Occupational and Environmental Medicine Press, Elk Grove Village, 2007.
108. Tran de QH, Duong S, Finlayson RJ. Lumbar spinal stenosis: A brief review of the nonsurgical management. *Can J Anaesth* 2010; 57:694-703.
109. 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

110. Racz GB, Heavner JE, Trescot A. Percutaneous lysis of epidural adhesions--evidence for safety and efficacy. *Pain Pract* 2008; 8:277-286.
111. 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.
112. Manchikanti L, Singh V, Derby R, Helm S, Trescot AM, Staats PS, Prager JP, Hirsch JA. Review of occupational medicine practice guidelines for interventional pain management and potential implications. *Pain Physician* 2008; 11:271-289.
113. Rosenquist RW. American Pain Society (APS) low back pain guidelines: A pro/

con debate. In: *American Academy of Pain Medicine's 27th Annual Meeting*. Washington DC, 2011.

114. Belozer M, Wang G. *Epidural Adhesiolysis for the Treatment of Back Pain. Health Technology Assessment*. Washington State Department of Labor and Industries, Office of the Medical Director, Olympia, WA, July 13, 2004.
115. American Society of Anesthesiologists Task Force on Chronic Pain Management; American Society of Regional Anesthesia and Pain Medicine. Practice guidelines for chronic pain management: An updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. *Anesthesiology* 2010; 112:810-833.
116. Berg AO, Allan JD. Introducing the third U.S. Preventive Services Task Force. *Am J Prev Med* 2001; 20:S3-S4.
117. Van Boxem K, Cheng J, Patijn J, van Kleef M, Lataster A, Mekhail N, Van Zundert J. 11. Lumbosacral radicular pain. *Pain Pract* 2010; 10:339-358.
118. Manchikanti L, Cash KA, McManus CD, Pampati V, Singh V, Benyamin R. The preliminary results of a comparative effectiveness evaluation of adhesiolysis and caudal epidural injections in managing chronic low back pain secondary to spinal stenosis: A randomized, equivalence controlled trial. *Pain Physician* 2009; 12:E341-E354.
119. Manchikanti L, Rivera JJ, Pampati V, Damron KS, McManus CD, Brandon DE, Wilson SR. One day lumbar epidural adhesiolysis and hypertonic saline neurolysis in treatment of chronic low back pain: A randomized, double-blind trial. *Pain Physician* 2004; 7:177-186.
120. Meadeb J, Rozenberg S, Duquesnoy B, Kuntz JL, Le Loët X, Sebert JL, Le Goff P, Fallut M, Marty M, Blévin S, Guggenbuhl P, Chalès G, Duvauferrier R. Forceful sacrococcygeal injections in the treatment of postdiscectomy sciatica. A controlled study versus glucocorticoid injections. *Joint Bone Spine* 2001; 68:43-49.
121. Revel M, Auleley GR, Alaoui S, Nguyen M, Duruoz T, Eck-Michaud S, Roux C, Amor B. Forceful epidural injections for the treatment of lumbosciatic pain with post-operative lumbar spinal fibrosis. *Rev Rhum Engl Ed* 1996; 63:270-277.
122. Farrar JT, Portenoy RK, Berlin JA, Kinman JL, Strom BL. Defining the clinically important difference in pain outcome measures. *Pain* 2000; 88:287-294.
123. Freeman BJ, Fraser RD, Cain CM, Hall DJ, Chapple DC. Letters RE: Freeman BJ et al. A randomized, double-blind, controlled trial: intradiscal electrothermal therapy versus placebo for the treatment of chronic discogenic low back pain. *Spine (Phila Pa 1976)* 2005; 30:2369-2377; *Spine (Phila Pa 1976)* 2006; 31:1638.
124. 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.
125. Bombardier C. Outcome assessments in the evaluation of treatment of spinal disorders: Summary and general recommendations. *Spine (Phila Pa 1976)* 2000; 25:3100-3103.
126. Hägg O, Fritzell P, Nordwall A; Swedish Lumbar Spine Study Group. The clinical importance of changes in outcome scores after treatment for chronic low back pain. *Eur Spine J* 2003; 12:12-20.
127. 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.
128. Manchikanti L, Singh V, Falco FJ, 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.
129. Manchikanti L, Singh V, Falco FJ, 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.
130. Manchikanti L, Singh V, Falco FJ, Cash KM, 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.
131. Manchikanti L, Singh V, Falco FJ, 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.
132. 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.
133. 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.
134. 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.
135. 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.
136. 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.
137. 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.
138. 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.
139. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; 327:557-560.
140. 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: A review of the process. *Am J Prev Med* 2001; 20:21-35.
141. Veihelmann A, Devens C, Trouillier H, Birkenmaier C, Gerdesmeyer L, Refior HJ. Epidural neuroplasty versus physiotherapy to relieve pain in patients with sciatica: A prospective randomized blinded clinical trial. *J Orthop Sci* 2006; 11:365-369.
142. Devulder J, Bogaert L, Castille F, Moer-

man A, Rolly G. Relevance of epidurography and epidural adhesiolysis in chronic failed back surgery patients. *Clin J Pain* 1995; 11:147-150.

143. Manchikanti L, Pampati V, Bakhit CE, Pakanati RR. Non-endoscopic and endoscopic adhesiolysis in post-lumbar laminectomy syndrome: A one-year outcome study and cost effectiveness analysis. *Pain Physician* 1999; 2:52-58.
144. Manchikanti L, Pampati V, Fellows B, Rivera J, Beyer CD, Damron KS. Role of one day epidural adhesiolysis in management of chronic low back pain: A randomized clinical trial. *Pain Physician* 2001; 4:153-166.
145. Gerdesmeyer L, Lampe R, Veihelmann A, Burgkart R, Göbel M, Gollwitzer H, Wagner K. Chronic radiculopathy. Use of minimally invasive percutaneous epidural neurolysis according to Racz. *Schmerz* 2005; 19:285-295.
146. Park CH, Lee SH, Jung JY. Dural sac cross-sectional area does not correlate with efficacy of percutaneous adhesiolysis in single level lumbar spinal stenosis. *Pain Physician* 2011; 14:377-382.
147. Manchikanti L, Pampati V, Fellows B, Rivera JJ, Damron KS, Beyer C, Cash KA. Effectiveness of percutaneous adhesiolysis with hypertonic saline neurolysis in refractory spinal stenosis. *Pain Physician* 2001; 4:366-373.
148. Yousef AA, EL-Deen AS, Al-Deeb AE. The role of adding hyaluronidase to fluoroscopically guided caudal steroid and hypertonic saline injection in patients with failed back surgery syndrome: A prospective, double-blinded, randomized study. *Pain Pract* 2010; 10:548-553.
149. Lee JH, Lee SH. Clinical effectiveness of percutaneous adhesiolysis using navicath for the management of chronic pain due to lumbosacral disc herniation. *Pain Physician* 2012; 15:213-221.
150. Talu GK, Erdine S. Complications of epidural neuroplasty: A retrospective evaluation. *Neuromodulation* 2003; 6:237-247.
151. Richter H. Is the so-called epidural neuroplasty (Racz catheter) a harmless procedure? In: Rochirurgie DGF (ed). *Deutsche Gesellschaft fur Neurochirurgie*. Deutsche Gesellschaft fur Neurochirurgie, Strasburg, Germany, 2005.
152. Wagner KJ, Sprenger T, Pecho C, Kochs EF, Tölle TR, Berthele A, Gerdesmeyer L. Risks and complications of epidural neurolysis -- a review with case report. *Anasthesiol Intensivmed Notfallmed Schmerzther* 2006; 41:213-222.
153. Perkins WJ, Davis DH, Huntoon MA, Horlocker TT. A retained Racz catheter fragment after epidural neurolysis: Implications during magnetic resonance imaging. *Anesth Analg* 2003; 96:1717-1719.
154. Manchikanti L, Singh V. Epidural lysis of adhesions and myeloscopy. *Curr Pain Headache Rep* 2002; 6:427-435.
155. Manchikanti L, Bakhit CE. Percutaneous lysis of epidural adhesions. *Pain Physician* 2000; 3:46-64.
156. Manchikanti L, Saini B, Singh V. Spinal endoscopy and lysis of epidural adhesions in the management of chronic low back pain. *Pain Physician* 2001; 4:240-265.
157. Kim RC, Porter RW, Choi BH, Kim SW. Myelopathy after the intrathecal administration of hypertonic saline. *Neurosurgery* 1988; 22:942-945.
158. Ho KY, Manghnani P. Acute monoplegia after lysis of epidural adhesions: A case report. *Pain Pract* 2008; 8:404-407.
159. Lou L, Racz G, Heavner J. Percutaneous epidural neuroplast. In: *Interventional Pain Management*. Waldman S. (ed). W.B. Saunders, Philadelphia, 2001, pp 434-445.
160. Manchikanti L, Bakhit CE. Removal of a torn Racz® catheter from lumbar epidural space. *Reg Anesth* 1997; 22:579-581.
161. Aldrete JA, Zapata JC, Ghaly R. Arachnoiditis following epidural adhesiolysis with hypertonic saline report of two cases. *Pain Digest* 1996 6:368-370.
162. Heavner JE. Comments on arachnoiditis following epidural adhesiolysis. *Pain Digest* 1997; 7:157.
163. Manchikanti L. Comments on arachnoiditis following epidural adhesiolysis. *Pain Digest* 1997; 7:157-158.
164. Erdine S, Ozyalcin S. Comments on arachnoiditis following epidural adhesiolysis. *Pain Digest* 1997; 7:158-159.
165. Fibuch EE. Percutaneous epidural neuroplasty: Cutting edge or potentially harmful pain management? *Reg Anesth Pain Med* 1999; 24:198-201.
166. Kim CH, Issa MA, Vaglienti RM. Flushing following interlaminar lumbar epidural steroid injection with dexamethasone. *Pain Physician* 2010; 13:481-484.
167. Racz GB, Holubec JT. Lysis of adhesions in the epidural space. In: Racz GB (ed). *Techniques of Neurolysis*. Kluwer Academic, Boston, 1989, pp 57-72.
168. Racz GB, Sabonghy M, Gintautas J, Kline WM. Intractable pain therapy using a new epidural catheter. *JAMA* 1982; 248:579-581.
169. Lima RM, Navarro LH, Carness JM, Barros GA, Marques ME, Solanki D, Ganem EM. Clinical and histological effects of the intrathecal administration of methylprednisolone in dogs. *Pain Physician* 2010; 13:493-501.
170. Hitchcock ER, Prandini MN. Hypertonic saline in management of intractable pain. *Lancet* 1973; 1:310-312.
171. Lucas JS, Ducker TB, Perot PL. Adverse reactions to intrathecal saline injections for control of pain. *J Neurosurg* 1975; 42:57-61.
172. Dagi TF. Comments on myelopathy after the intrathecal administration of hypertonic saline. *Neurosurgery* 1988; 22:944-945.
173. Lundy JS, Essex HE, Kernohan JW. Experiments with anesthetics. IV. Lesions produced in the spinal cord of dogs by a dose of procaine hydrochloride sufficient to cause permanent and fatal paralysis. *JAMA* 1936; 101:1546-1550.
174. Rojiani AM, Cho ES, Sharer L, Prineas JW. Electrolyte-induced demyelination in rats. 2. Ultrastructural evolution. *Acta Neuropathol* 1994; 88:293-299.
175. Rojiani AM, Prineas JW, Cho ES. Protective effect of steroids in electrolyte-induced demyelination. *J Neuropathol Exp Neurol* 1987; 46:495-504.
176. Lake DA, Barnes CD. Effects of changes in osmolality on spinal cord activity. *Exp Neurol* 1980; 68:555-567.
177. Abram SE, O'Connor TC. Complications associated with epidural steroid injections. *Reg Anesth* 1996; 212:149-162.
178. Nelson DA. Intraspinal therapy using methylprednisolone acetate. Twenty-three years of clinical controversy. *Spine (Phila Pa 1976)* 1993; 18:278-286.
179. Kushner FH, Olson JC. Retinal hemorrhage as a consequence of epidural steroid injection. *Arch Ophthalmol* 1995; 113:309-313.
180. Ling C, Atkinson PL, Munton CG. Bilateral retinal hemorrhages following epidural injection. *Br J Ophthalmol* 1993; 77:316-317.
181. Purdy EP, Ajimal GS. Vision loss after lumbar epidural steroid injection. *Anesth Analg* 1998; 86:119-122.
182. Victory RA, Hassett P, Morrison G. Transient blindness following epidural analgesia. *Anaesthesia* 1991; 46:940-941.
183. Clark CJ, Whitwell J. Intraocular hemorrhage after epidural injection. *Brit Med J* 1961; 2:1612-1613.
184. Usubiaga JE, Wikinski JA, Usubiaga LE. Epidural pressure and its relation to

spread of anesthetic solutions in epidural space. *Anesth Analg* 1967; 46:440-446.

185. Sampath P, Rigamonti D. Spinal epidural abscess: A review of epidemiology, diagnosis, and treatment. *J Spinal Disord* 1999; 12:89-93.
186. Wang LP, Haverberg J, Schmidt JF. Incidence of spinal epidural abscess after epidural analgesia. *Anesthesiology* 1999; 91:1928-1936.
187. Bromage PR. Complications and contraindications. In: *Epidural Analgesia*. WB Saunders, Philadelphia, 1978, pp 469-471.
188. Bromage PR, Benumof JL. Paraplegia following intracord injection during attempted epidural anesthesia under general anesthesia. *Reg Anesth Pain Med* 1998; 23:104-107.
189. Kapoor R, Liu J, Devasenapathy A, Gordin V. Gadolinium encephalopathy after intrathecal gadolinium injection. *Pain Physician* 2010; 13:E321-E326.
190. Möller JC, Cron RQ, Young DW, Girschick HJ, Levy DM, Sherry DD, Kukita A, Saijo K, Pessler F. Corticosteroid-induced spinal epidural lipomatosis in the pediatric age group: Report of a new case and updated analysis of the literature. *Pediatr Rheumatol Online J* 2011; 9:5.
191. Weinstein RS. Glucocorticoid-induced bone disease. *New Engl J Med* 2011; 365:62-70.
192. Coumans JV, Walcott BP. Rapidly progressive lumbar subdural empyema following acromial bursal injection. *J Clin Neurosci* 2011; 18:1562-1563.
193. 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.
194. 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.
195. Louhiala P, Puustinen R. Rethinking the placebo effect. *J Med Ethics* 2008; 34:107-109.
196. Louhiala P. The ethics of the placebo in clinical practice revisited. *J Med Ethics* 2009; 35:407-409.
197. Blease C. The principle of parity: The "placebo effect" and physician communication. *J Med Ethics* 2012; 38:199-203.
198. 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.
199. Lyby PS, Forsberg JT, Asli O, Flaten MA. Induced fear reduces the effectiveness of a placebo intervention on pain. *Pain* 2012; 153:1114-1121.
200. 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.
201. 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.
202. Manchikanti L, Falco FJE, Boswell MV, Hirsch JA. Facts, fallacies, and politics of comparative effectiveness research: Part 1. Basic considerations. *Pain Physician* 2010; 13:E23-E54.
203. Manchikanti L, Falco FJE, Boswell MV, Hirsch JA. Facts, fallacies, and politics of comparative effectiveness research: Part 2. Implications for interventional pain management. *Pain Physician* 2010; 13:E55-E79.
204. Manchikanti L, Falco FJ, Benyamin RM, Helm S 2nd, Parr AT, Hirsch JA. The impact of comparative effectiveness research on interventional pain management: Evolution from Medicare Modernization Act to Patient Protection and Affordable Care Act and the Patient-Centered Outcomes Research Institute. *Pain Physician* 2011; 14:E249-E282.
205. Manchikanti L, Helm II S, Hirsch JA. The evolution of the Patient-Centered Outcome Research Institute. *J Neurointervent Surg* 2012; 4:157-162.
206. 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.
207. 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.
208. 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.
209. Indahl A, Kaigle AM, Reikeräs O, Holm SH. Interaction between the porcine lumbar intervertebral disc, zygapophysial joints, and paraspinal muscles. *Spine (Phila Pa 1976)* 1997; 22:2834-2840.
210. Indahl A, Kaigle A, Reikeräs O, Holm S. Electromyographic response of the porcine multifidus musculature after nerve stimulation. *Spine (Phila Pa 1976)* 1995; 20:2652-2658.
211. Bhatia MT, Parikh LCJ. Epidural saline therapy in lumbo-sciatic syndrome. *J Indian Med Assoc* 1966; 47:537-542.
212. 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.
213. 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.
214. 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.
215. Holm I, Friis A, Brox JI, Gunderson R, Steen H. Minimal influence of facet joint anesthesia on isokinetic muscle performance in patients with chronic degenerative low back disorders. *Spine (Phila Pa 1976)* 2000; 25:2091-2094.
216. 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.
217. 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.
218. Iversen T, Solberg TK, Romner B, Wilsgaard T, Twisk J, Anke A, Nygaard O, Hasvold T, Ingebrigtsen T. Effect of caudal epidural steroid or saline injection in chronic lumbar radiculopathy: Multicentre, blinded, randomised controlled trial. *BMJ* 2011; 343:d5278.
219. Dashfield AK, Taylor MB, Cleaver JS, Farrow D. Comparison of caudal steroid epidural with targeted steroid placement during spinal endoscopy for chronic sciatica: A prospective, randomized, double-

blind trial. *Br J Anaesth* 2005; 94:514-559.

220. 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.
221. Pasqualucci A, Varrassi G, Braschi A, Peduto VA, Brunelli A, Marinangeli F, Gori F, Colò F, Paladini 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.
222. Byrod 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.
223. 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.
224. 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.
225. 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 experimental study in the rabbit. *Spine (Phila Pa 1976)* 1998; 23:870-876.
226. 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.
227. Mao J, Chen LL. Systemic lidocaine for neuropathic pain relief. *Pain* 2000; 87:7-17.
228. Pasqualucci A. Experimental and clinical studies about the preemptive analgesia with local anesthetics. Possible reasons of the failure. *Minerva Anestesiol* 1998; 64:445-457.
229. 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.
230. Lavoie PA, Khazen T, Filion PR. Mechanisms of the inhibition of fast axonal transport by local anesthetics. *Neuropharmacology* 1989; 28:175-181.
231. 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.
232. 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.
233. 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.
234. Hodgkin AL, Katz B. The effect of sodium ions on the electrical activity of the giant axon of the squid. *J Physiol* 1949; 108:37-77.
235. Hubbard JL, Jones SF, Landau EM. An examination of the effects of osmotic pressure changes upon transmitter release from mammalian motor nerve terminals. *J Physiol* 1968; 197:639-657.
236. Hitchcock ER. Hypothermic subarachnoid irrigation for intractable pain. *Lancet* 1967; i:1133-1135.
237. Hitchcock ER. Osmolytic neurolysis for intractable facial pain. *Lancet* 1969; i:434-436.
238. King LS, Jewett DL, Sundberg HR. Differential blockade of cat dorsal root C-fibers by various chloride solutions. *J Neurosurg* 1972; 36:569-583.
239. Kukita F, Yamagishi H. Excitation of squid giant axons in hypotonic and hypertonic solutions. *J Physiol* 1979; 20:669-681.
240. Jewett DL, King JS. Conduction block of monkey dorsal rootlets by water and hypertonic saline solutions. *Exp Neurol* 1971; 33:225-237.
241. Wittenberg RH, Greskotter KR, Steffen R, Schoenfeld BL. Is epidural injection treatment with hypertonic saline solution in intervertebral disk replacement useful? *Z Orthop Ihre Grezgeb* 1990; 128:223-226.
242. Racz GB, Heaver JE, Singleton W, Carline M. Hypertonic saline and corticosteroid injected epidurally for pain control. In: Raj P (ed). *Techniques of Neurolysis.* Klumer Academic Publishers, Boston, 1989, 73-86.
243. 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.
244. Manchikanti L, Singh V, Derby R, Schultz DM, Benyamin RM, Prager JP, Hirsch JA. Reassessment of evidence synthesis of occupational medicine practice guidelines for interventional pain management. *Pain Physician* 2008; 11:393-482.
245. 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.
246. 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.
247. 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.
248. Piaggio G, Elbourne DR, Altman DG, Pocock SJ, Evans SJ; CONSORT Group. Reporting of noninferiority and equivalence randomized trials: An extension of the CONSORT statement. *JAMA* 2006; 295:1152-1160.
249. Zwarenstein M, Treweek S, Gagnier JJ, Altman DG, Tunis S, Haynes B, Oxman AD, Moher D; CONSORT Group, Pragmatic Trials in Healthcare (Practihc) Group. Improving the reporting of pragmatic trials: An extension of the CONSORT statement. *BMJ* 2008; 337:a2390.