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Health Policy Review

A Critical Review of the American Pain Society Clinical Practice Guidelines For Interventional Techniques: Part 2. Therapeutic Interventions

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Background: Clinical guidelines are a constructive response to the reality that practicing physicians require assistance in assimilating and applying the exponentially expanding, often contradictory, body of medical knowledge. They attempt to define practices that meet the needs of most patients under most circumstances. Ideally, specific clinical recommendations contained within practice guidelines are systematically developed by expert panels who have access to all the available evidence, have an understanding of the clinical problem, and have clinical experience with the procedure being assessed, as well as knowledge of relevant research methods. The recent development of American Pain Society (APS) guidelines has created substantial controversy because of their perceived lack of objective analysis and recommendations perceived to be biased due to conflicts of interest.

Objectives: To formally and carefully assess the APS guidelines' evidence synthesis for low back pain for therapeutic interventions using the same methodology utilized by the APS authors. The interventions examined were therapeutic interventions for managing low back pain, including epidural injections, adhesiolysis, facet joint interventions, and spinal cord stimulation.

Methods: A literature search by 2 authors was carried out utilizing appropriate databases from 1966 through July 2008. Articles in which conflicts arose were reviewed and mediated by a third author to arrive at a consensus. Selections of manuscripts and methodologic quality assessment was also performed by at least 2 authors utilizing the same criteria applied in the APS guidelines. The guideline reassessment process included the evaluation of individual studies and systematic reviews and their translation into practice recommendations.

Results: The conclusions of APS and our critical assessment based on grading of good, fair, and poor, agreed that there is fair evidence for spinal cord stimulation in post lumbar surgery syndrome, and poor evidence for lumbar intraarticular facet joint injections, lumbar interlaminar epidural injections, caudal epidural steroids for conditions other than disc herniation or radiculitis, sacroiliac joint injections, intradiscal electrothermal therapy, endoscopic adhesiolysis, and intrathecal therapy. However, our assessment of APS guidelines for other interventional techniques, utilizing their own criteria, showed fair evidence for therapeutic lumbar facet joint nerve blocks, caudal epidural injections in disc herniation or radiculitis, percutaneous adhesiolysis in post lumbar surgery syndrome, radiofrequency neurotomy, and transforaminal epidural injections in radiculitis. Also it is illustrated that inclusion of latest literature will change the conclusions, with improved grading – caudal epidural, adhesiolysis, and lumbar facet joint nerve blocks from fair to good or poor to fair.

The present critical assessment review illustrates that APS guidelines have utilized multiple studies inappropriately and have excluded appropriate studies. Our integrity assessment shows deep concerns that the APS guidelines illustrating significant methodologic failures which raise concerns about transparency, accountability, consistency, and independence.

Conclusion: The current reassessment, using appropriate methodology, shows evidence similar to APS guidelines for several procedures, but differs extensively from published APS guidelines for multiple other procedures including caudal epidural injections, lumbar facet joint nerve blocks, lumbar radiofrequency neurotomy, and percutaneous adhesiolysis.

Key words: Guidelines, evidence-based medicine, systematic reviews, American Pain Society, interventional pain management, interventional techniques

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Clinical guidelines have been defined by the Institute of Medicine (IOM), "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" (1). Thus, clinical guidelines are considered a constructive response to the reality that practicing physicians require assistance for assimilating and applying the exponentially expanding, often contradictory, body of medical knowledge (2). Clinical guidelines should not attempt to supplant the independent judgment of clinicians in responding to particular clinical situations, but rather they attempt to define practices that meet the needs of most patients under most circumstances (3). Guidelines enable the implementation of evidence-based medicine (EBM) and comparative effectiveness research (CER) in medical decision-making with the goal of encouraging effective care (4-9). Consequently, it is expected that the specific clinical recommendations that are contained within practice guidelines have been systematically developed by panels of experts who have access to the available evidence, have an understanding of the clinical problem, and have clinical experience with the procedure being assessed as well as relevant research methods in order to make considered judgments. Above all, these panels are expected to be objective and to produce recommendations that are not only up-to-date, but also must be unbiased and free from all conflicts of interest.

In Part 1 of our critical review of the American Pain Society Clinical Practice Guidelines for interventional techniques, diagnostic interventional techniques were assessed (10). Part 2 of this critical review provides an assessment of therapeutic interventional techniques.

The pace of innovation in health care has been rapid, constantly adding knowledge to broad and complex areas of health care interventions and systems (5,6). In addition, the demonstration of pervasive and persistent unexplained variability in clinical practice and high rates of perceived inappropriate care, combined with rising expenditures, have fueled a steady increase in demand for the appropriate application of modalities that have clinical effectiveness (4-29). A formal set of rules must complement medical training and common sense for clinicians so they may interpret the results of clinical research effectively (4-17,30-32). Thus, knowing the tools of evidence-based practice is necessary, but not completely sufficient, for delivering the highest quality patient care. Clinical guidelines must incorporate not only the work of methodologists, but also the clinicians who actually practice medicine and are experts in the technique being reviewed.

There are subtle differences between EBM and CER, as there also are between placebo-controlled and active-controlled trials. EBM is essentially focused upon the use of the right type and extent of knowledge to guide the right and good intentions and actions of medical practice, which is fundamental to prudent clinical decision-making (7,8). In contrast, CER is to assist consumers, clinicians, purchasers, and policy-makers to make informed decisions that will improve health care at the level of both the individual as well as the general population.

Many controversies exist in the United States relating to the development and implementation of clinical guidelines. In fact, Congress eliminated the Agency for Health Care Policy and Research (AHCPR) in 1995 soon after the development of acute low back pain guidelines. Over the years AHCPR issued 19 guidelines at a cost of $750 million (nearly $40 million per guideline). Those guidelines were not demonstrated to have saved health care dollars and were not widely utilized, thus questioning the cost-effectiveness of governmentally developed guidelines (33,34). However, smaller professional organizations are considered to lack the internal resources, including staff capacity and expertise, required to produce guidelines (3). At the same time, even larger professional organizations can face resource constraints in this area. However, the lack of utilization of governmental agency produced guidelines in the United States due to the private health care system, their expense, and the bureaucracy of larger organizations (similar to the government) raises numerous questions about the process, outcomes, and conclusions of any particular set of guidelines. Further, in clinical areas without extensive literature, the role of methodologists may be an exercise in futility.

Conflicts of interest in guideline development and inappropriate methodologies have come under careful scrutiny. Impropriety is suspect when guidelines are based on pharmaceutical and medical device company sponsorships, when members of the guidelines committee have a substantial financial association with an industry, when there is a relationship between the developing organization and industry, or, finally, when there is no relevant clinical relationship or expertise on the part of the developers of the guidelines. However, conflicts of interest do not involve just industry involvement; they also extend to numerous other conflicts of interest either in the

synthesis of EBM, CER, or in the preparation of clinical guidelines themselves.

Sniderman and Furberg (2) described the conflicts, controversies, and limitations of the guideline process. Limitations of the guideline preparation process include governance and composition of the guideline committee, unanimity in guidelines, lack of independent review, and conflict of interest.

Recently, the American Pain Society (APS) developed and published guidelines for managing low back pain resulting in multiple publications (35-42). Similarly, the American College of Occupational and Environmental Medicine (ACOEM) (43) American Society of Anesthesiologists (44) have published guidelines. Official Disability Guidelines (ODG) (45) have also beenpublished. There are numerous other guidelines available including the ones from the American Society of Interventional Pain Physicians (ASIPP), which were updated in 2009 (4,46-51). ASIPP guidelines were developed with an extensive search and review of the literature with systematic reviews including literature search, quality assessment of individual articles, and creation of new systematic reviews (52-73). In contrast, ACOEM guidelines for low back pain and chronic pain have been extensively criticized (74-76).

However, the issues surrounding practice guidelines' development and the evidence used in them are not limited to interventional pain management alone (77-79). The joint cardiovascular practice guidelines of the American College of Cardiology (ACC) and American Heart Association (AHA) have become important documents for guiding cardiology practice and establishing benchmarks for quality of care (79,80). However, an evaluation of the scientific evidence underlying these clinical practice guidelines showed that the recommendations issued were largely developed from lower levels of evidence or expert opinion. It was noted that these findings highlight the need to improve the process of writing guidelines and to expand the evidence base from which clinical practice guidelines are derived (79).

Methods

The guideline development process includes evidence assessment, peer systematic reviews, and developing clinical practice guidelines with recommendations (4,46). In the sequential process of grading recommendations, assessing the level of evidence is essential.

Translating systematic reviews into practice recommendations is not straightforward; the same information can be interpreted in different ways by different analysts, resulting in different guidance (81,82). Conclusions about clinical effectiveness can vary widely as a result of conflicting viewpoints, such as which outcomes are the most important and which course of action is appropriate recognizing that evidence is often imperfect.

1.0 Types of Interventions Included

Common types of interventional techniques in managing low back pain including facet joint interventions, epidural injections, percutaneous adhesiolysis, sacroiliac joint interventions, disc interventions, and spinal cord stimulation were included in this analysis.

2.0 Key Questions

Chou and Huffman (35) utilized the key question format. Those key questions were evaluated, answered, and compared in this analysis.

2.1 Key Questions 8 & 11

How effective are injections and different injection interventions and other interventional therapies for non-radicular low back pain, radicular low back pain, or spinal stenosis, and under what circumstances?

- Epidural steroid injection
- Intradiscal steroid injection (not included in this analysis)
- Chemonucleolysis (not included in this analysis)
- Radiofrequency denervation
- Intradiscal electrothermal therapy
- Spinal cord stimulation
- Percutaneous adhesiolysis
- Lumbar epidural adhesiolysis
- Facet joint injection, therapeutic medial branch block, and radiofrequency neurolysis
- Therapeutic sacroiliac joint interventions
- Intrathecal therapy

3.0 Literature Search

A comprehensive literature search was conducted. The search included entries in databases including PubMed and EMBASE for articles published from 1966 through July 2008. In addition, a search of the Cochrane database, Clinical Trial Registry, systematic reviews, narrative reviews, and cross-references to reviews published in the English language were performed.

The search was performed by at least 2 authors, emphasizing chronic low back pain with a focus on interventional techniques. Search strategy and MeSH terms utilized by Chou and Huffman (35) were utilized in this critical review.

4.0 Selection Criteria

This critical review focused on systematic reviews and randomized trials. Selection of manuscripts was performed by 2 authors for stated inclusion criteria. If there was a conflict of interest with the reviewed manuscripts with authorship or any other conflict, the involved authors did not review the manuscript for selection The population of interest was patients suffering with chronic low back pain. All the studies utilized by Chou and Huffman (35) that had appropriate management and outcome evaluations were analyzed along with the addition of studies that they did not include.

5.0 Outcome Measures

ASIPP evaluations (46) utilized pain relief and functional status improvement with at least 6 to 12 months follow-up for therapeutic interventions; with 6 months or less was considered short-term and longer than 6 months, long-term. For interventions such as discectomy and implantables, greater than one-year relief was considered as long-term.

Pain relief was the primary outcome measure for all interventions. Secondary outcomes were functional or psychological improvement, improvement in work status, and complications.

6.0 Methodologic Quality Assessment

The methodologic quality assessment of various individual articles was based on the type of manuscript: systematic reviews or randomized trials.

Each study was evaluated by 2 physicians for stated criteria and disagreements were resolved by a third physician. If there was a conflict of interest with the reviewed manuscripts with authorship or any other conflict, the involved authors did not review the manuscripts for quality assessment or evidence synthesis.

6.1 Assessment of Systematic Reviews

Methodologic quality assessment of systematic reviews has been described by the Agency for Healthcare Research and Quality (AHRQ) (81) and Oxman and Guyatt (82) which was adapted by Furlan et al (83). Table 1 illustrates the AHRQ criteria for systematic reviews. Chou et al (35-37) utilized the criteria developed by Oxman and Guyatt (82) and adapted by Furlan et al (83) as illustrated in Table 2. While both appear to be similar, there are significant differences between these tools; however, the basic assumptions of quality assessment criteria remain the same for both. Thus, to satisfy the requirements used by Chou and Huffman (35), Oxman criteria were used.

6.2 Assessment of Randomized Trials

The quality assessment of randomized trials is generally carried out by Cochrane review criteria with or without weighted scores (77,78,84) (Table 3). The criteria with weighted scores has been extensively utilized in interventional pain management settings (52-78,85). In contrast, Chou and Huffman (35) utilized the criteria developed by the Cochrane review with some modifications, but without weighted scoring as shown in Table 4 (84), which therefore did not provide greater emphasis to higher quality individual randomized controlled trial. Even though both methods developed by Cochrane review for methodologic quality assessment are synonymous, there are subtle differences resulting in the possibility for the reviewer to provide a biased assessment. For the sake of simplicity, it was decided that in this critical review we would apply criteria as utilized by Chou et al (35,84).

Chou and Huffman (35) considered a maximum score to be 10, 9, or 8. They considered trials that received more than half of the total possible score to be "higher-quality" and those that received less than or equal to half "lower-quality."

6.3 Assessment of Observational Studies

Chou and Huffman (35) stated that to assess the internal validity of observational studies, they evaluated whether they used non-biased selection methods; whether rates of loss-to-follow-up were acceptable; whether predefined outcomes were specified; whether they used appropriate methods for ascertaining exposures, potential confounders, and outcomes; and whether they performed appropriate statistical analysis of potential confounders. They chose not to utilize quality assessment of non-randomized trials, based on the philosophy that there is no consensus on optimal quality rating methods (86). However, with careful scrutiny, AHRQ has provided quality rating assessment systems for observational studies (81). This system has been utilized with weighted scoring in multiple systematic reviews in the past (52-73,85). However, to follow the assessment done by Chou and Huffman (35), we did not assess observational studies.

7.0 Analysis of Evidence

Chou and Huffman (35) utilized the United States Preventive Services Task Force's (USPSTF) (87) method for grading an intervention's overall strength of evidence as illustrated in Table 5. USPSTF also developed the grading system for research design as shown in Table 6.

Table 1. *Domains in the Agency for Healthcare Research and Quality (AHRQ) criteria for evaluating systematic reviews.*

DOMAIN	ELEMENTS*
Study question	• **Question clearly specified and appropriate**
Search strategy	• ***Sufficiently comprehensive and rigorous with attention to possible publication biases*** • *Search restrictions justified (e.g., language or country of origin)* • Documentation of search terms and databases used • Sufficiently detailed to reproduce study
Inclusion and exclusion criteria	• **Selection methods specified and appropriate, with a priori criteria specified if possible**
Interventions	• **Intervention(s) clearly detailed for all study groups**
Outcomes	• **All potentially important harms and benefits considered**
Data extraction †	• Rigor and consistency of process • Number and types of reviewers • Blinding of reviewers • Measure of agreement or reproducibility • Extraction of clearly defined interventions/exposures and outcomes for all relevant subjects and subgroups
Study quality and validity	• ***Assessment method specified and appropriate*** • Method of incorporation specified and appropriate
Data synthesis and analysis	• *Appropriate use of qualitative and/or quantitative synthesis, with consideration of the robustness of results and heterogeneity issues* • Presentation of key primary study elements sufficient for critical appraisal and replication
Results	• **Narrative summary and/or quantitative summary statistic and measure of precision, as appropriate**
Discussion	• **Conclusions supported by results with possible biases and limitations taken into consideration**
Funding or sponsorship	• ***Type and sources of support for study***

* Elements appearing in italics are those with an empirical basis. Elements appearing in bold are those considered essential to give a system a Yes rating for the domain.
† Domain for which a Yes rating required that a majority of elements be considered.

Adapted from West S et al. Systems to Rate the Strength of Scientific Evidence, Evidence Report, Technology Assessment No. 47. AHRQ Publication No. 02-E016. Rockville, MD: Agency for Healthcare Research and Quality, 2002. www.thecre.com/pdf/ahrq-system-strength.pdf (81).

ASIPP used this system when developing its guidelines and multiple systematic reviews. ASIPP's guidelines and reviews continue to be quoted by numerous authorities. However, this approach has been criticized because it limits evaluation of internal validity (88).

To avoid confusion in this analysis, the criteria utilized by Chou and Huffman (35) was adopted, as illustrated in Table 5.

7.1 Outcome of the Studies

For systematic reviews, outcomes were based on the conclusions of the authors and reevaluation.

For randomized trials, a study was judged to be positive if the interventional therapy was effective, either with a placebo control or active control. This indicates that the difference in the effect for the primary outcome measure was statistically significant at the

Table 2. *Systematic reviews quality rating system.*

Criteria for Assessing Scientific Quality of Research Reviews*	
CRITERIA	**OPERATIONALIZATION OF CRITERIA**
1. Were the search methods reported? Were the search methods used to find evidence (original research) on the primary questions stated? "Yes" if the review states the databases used, date of most recent searches, and some mention of search terms.	The purpose of this index is to evaluate the scientific quality (i.e., adherence to scientific principles) of research overviews (review articles) published in the medical literature. It is not intended to measure literary quality, importance, relevance, originality, or other attributes of overviews. The index is for assessing overviews of primary ("original") research on pragmatic questions regarding causation, diagnosis, prognosis, therapy, or prevention. A research overview is a survey of research. The same principles that apply to epidemiological surveys apply to overviews: a question must be clearly specified, a target population identified and accessed, appropriate information obtained from that population in an unbiased fashion, and conclusions derived, sometimes with the help of formal statistical analysis, as is done in "meta-analyses." The fundamental difference between overviews and epidemiological studies is the unit of analysis, not the scientific issues that the questions in this index address. Since most published overviews do not include a methods section, it is difficult to answer some of the questions in the index. Base your answers, as much as possible, on information provided in the overview. If the methods that were used are reported incompletely relative to a specific question, score it as "can't tell," unless there is information in the overview to suggest either the criterion was or was not met.
2. Was the search comprehensive? Was the search for evidence reasonably comprehensive? "Yes" if the review searches at least 2 databases and looks at other sources (such as reference lists, hand searches, queries experts).	
3. Were the inclusion criteria reported? Were the criteria used for deciding which studies to include in the overview reported?	
4. Was selection bias avoided? Was bias in the selection of studies avoided? "Yes" if the review reports how many studies were identified by searches, numbers excluded, and gives appropriate reasons for excluding them (usually because of pre-defined inclusion/exclusion criteria).	
5. Were the validity criteria reported? Were the criteria used for assessing the validity of the included studies reported?	
6. Was validity assessed appropriately? Was the validity of all the studies referred to in the text assessed using appropriate criteria (either in selecting studies for inclusion or in analyzing the studies that are cited)? "Yes" if the review reports validity assessment and did some type of analysis with it (e.g. sensitivity analysis of results according to quality ratings, excluded low quality studies, etc.).	
7. Were the methods used to combine studies reported? Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported? "Yes" for studies that did qualitative analysis if there is some mention that quantitative analysis was not possible and reasons that it could not be done, or if 'best evidence' or some other grading of evidence scheme used.	
8. Were the findings combined appropriately? Were the findings of the relevant studies combined appropriately relative to the primary question the overview addresses? "Yes" if the review performs a test for heterogeneity before pooling, does appropriate subgroup testing, appropriate sensitivity analysis, or other such analysis.	For Question 8, if no attempt has been made to combine findings, and no statement is made regarding the inappropriateness of combining findings, check "No". If a summary (general) estimate is given anywhere in the abstract, the discussion, or the summary section of the paper, and it is not reported how that estimate was derived, mark "No" even if there is a statement regarding the limitations of combining the findings of the studies reviewed. If in doubt, mark "Can't tell."
9. Were the conclusions supported by the reported data? Were the conclusions made by the author(s) supported by the data and/or analysis reported in the overview?	For an overview to be scored as "Yes" in Question 9, data (not just citations) must be reported that support the main conclusions regarding the primary question(s) that the overview addresses.
10. What was the overall scientific quality of the overview? How would you rate the scientific quality of this overview?	The score for Question 10, the overall scientific quality, should be based on your answers to the first nine questions. The following guidelines can be used to assist with deriving a summary score: If the "Can't tell" option is used one or more times on the preceding questions, a review is likely to have minor flaws at best and it is difficult to rule out major flaws (i.e. a score of 4 or lower). If the "No" option is used on Question 2, 4, 6, or 8, the review is likely to have major flaws (i.e. a score of 3 or less, depending on the number and degree of the flaws).
Scoring:	Each Question is scored as Yes, Partially/Can't tell or No
Extensive Flaws Major Flaws Minor Flaws Minimal Flaws 1 2 3 4 5 6 7	

* Operationalization of Oxman AD, Guyatt GH. Validation of an index of the quality of review articles. J Clin Epidemiol 1991; 44:1271-1278 (82); Adapted from Furlan AD, Clarke J, Esmail R, Sinclair S, Irvin E, Bombardier C. A critical review of reviews on the treatment of chronic low back pain. Spine 2001; 26:E155-E162 (83).
Source: Chou R, Huffman L. Evaluation and Management of Low Back Pain: Evidence Review. American Pain Society; Glenview, IL: 2009 (35).

Table 3. *Modified and weighted Cochrane methodologic quality assessment criteria.*

CRITERION		Weighted Score (points)
1. Study population		35
A	Homogeneity	2
B	Comparability of relevant baseline characteristics	5
C	Randomization procedure adequate	4
D	Drop-outs described for each study group separately	3
E	< 20% loss for follow-up	2
	< 10% loss for follow-up	2
F	> 50 subjects in the smallest group	8
	> 100 subjects in the smallest group	9
2. Interventions		25
G	Interventions included in protocol and described	10
H	Pragmatic study	5
I	Co-interventions avoided or similar	5
J	Placebo-controlled	5
3. Effect		30
K	Patients blinded	5
L	Outcome measures relevant	10
M	Blinded outcome assessments	10
N	Follow-up period adequate	5
4. Data-presentation and analysis		10
O	Intention-to-treat analysis	5
P	Frequencies of most important outcomes presented for each treatment group	5
TOTAL SCORE		100

Adapted from Koes BW et al. Efficacy of epidural steroid injections for low-back pain and sciatica: An updated systematic review of randomized clinical trials. Pain Digest 1999; 9:241-247 (78).

conventional 5% level. In a negative study, there was no difference between the study treatments or no improvement from baseline.

8.0 Assessment of Integrity

USPSTF defined evidence-based recommendation development with a description of aims and processes to ensure integrity (89,90). The goals include transparency, accountability, consistency, and independence.

8.1 Transparency

Transparency is provided by standardized methodology described in the methods section.

8.2 Accountability

A conflict of interest policy, the process for prioritizing the literature, peer review of evidence synthesis, and recommendations and updating of the recommendations consistent with current literature constitute accountability.

8.3 Consistency

Systematic reviews of the literature on effectiveness and harms utilize outcome tables to assess the balance of benefits and harms with a defining evidence grid and descriptions in a standardized language.

8.4 Independence

Finally, the evidence review process, voting process for members only, meeting attendance by invitation, and formalized communication among the stakeholders must be independent.

Table 4. *Randomized controlled trials quality rating system.*

Criteria List for Methodological Quality Assessment		
CRITERIA	**OPERATIONALIZATION OF CRITERIA**	**SCORE**
A. Was the method of randomization adequate?	A random (unpredictable) assignment sequence. An example of adequate methods is a computer generated random number table and use of sealed opaque envelopes. Methods of allocation using DOB, date of admission, hospital numbers, or alternation should not be regarded as appropriate.	Yes/No/Don't Know
B. 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/Don't Know
C. Were the groups similar at baseline regarding the most important prognostic factors? "Yes," if similar: • Age & gender • Description of type of pain • Intensity, duration, or severity of pain	In order to receive a "yes," groups have to be similar in baseline regarding demographic factors, duration or severity of complaints, percentage of patients with neurologic symptoms, and value of main outcome measure(s).	Yes/No/Don't Know
D. Was the patient blinded to the intervention?	The reviewer determines if enough information about the blinding is given in order to score a "yes": Use the author's statement on blinding, unless there is a differing statement/reason not to (no need for explicit information on blinding).	Yes/No/Don't Know
E. Was the care provider blinded to the intervention?		Yes/No/Don't Know
F. Was the outcome assessor blinded to the intervention?		Yes/No/Don't Know
G. Were cointerventions avoided or similar?	Cointerventions should either be avoided in the trial design or similar between the index and control groups.	Yes/No/Don't Know
H. Was the compliance acceptable in all groups?	The reviewer determines if the compliance to the interventions is acceptable, based on the reported intensity, duration, number, and frequency of sessions for both the index intervention and control intervention(s).	Yes/No/Don't Know
I. Was the drop-out rate described and acceptable? ≤ 15% drop out rate is acceptable.	The number of participants who are 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 15% and does not lead to substantial bias, a "yes" is scored.	Yes/No/Don't Know
J. Was the timing of the outcome assessment in all groups similar?	Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.	Yes/No/Don't Know
K. Did the analysis include an intention-to-treat analysis? "Yes" if less than 5% of randomized patients excluded.	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 noncompliance and cointerventions.	Yes/No/Don't Know
This list includes only the internal validity criteria (n=11) that refer to characteristics of the study that might be related to selection bias (criteria A and B), performance bias (criteria D, E, G, and H), attrition bias (criteria I and K), and detection bias (criteria F and J). The internal validity criteria should be used to define methodologic quality in the meta-analysis.		

Source: Chou R, Huffman L. Evaluation and Management of Low Back Pain: Evidence Review. American Pain Society; Glenview, IL: 2009 (35); adapted from methods developed by van Tulder M, Furlan AD, Bombardier C, Bouter L, the 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 (84).

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 two 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; two or more higher-quality trials or studies of diagnostic test accuracy with some inconsistency; at least two consistent, lower-quality trials or studies of diagnostic test accuracy, or multiple consistent observational studies with no significant methodological flaws).
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.

Source: Chou R, Huffman L. Evaluation and Management of Low Back Pain: Evidence Review. American Pain Society; Glenview, IL: 2009 (35). Adapted from methods developed by U.S. Preventive Services Task Force (87).

Table 6. *Quality of evidence developed by USPSTF.*

I:	Evidence obtained from at least one properly randomized controlled trial
II-1:	Evidence obtained from well-designed controlled trials without randomization
II-2:	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group
II-3:	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III:	Opinions of respected authorities, based on clinical experience descriptive studies and case reports or reports of expert committees

Adapted from the U.S. Preventive Services Task Force (USPSTF) (87).

Results

The methodology utilized followed the sequence as described in APS guidelines (35). The literature search extended through July 2008. The critical analysis in this document (Part 2) included therapeutic interventions. Diagnostic interventions are described in Part 1 (10).

1.0 Epidural Steroid Injections

Access to the epidural space is available by the caudal approach apart from interlaminar and transforaminal approaches. Substantial differences with the technique and outcomes have been described between these 3 approaches. Thus, due to the inherent variations, differences, advantages, and disadvantages applicable to each technique, including effectiveness and outcomes, caudal epidural injections, interlaminar epidural injections, and transforaminal epidural injections must be considered as separate entities. In addition, the response to epidural injections for various pathological conditions – disc herniation and/or radiculitis, discogenic pain without disc herniation, spinal stenosis, and lumbar post surgery syndrome – is variable.

Chou and Huffman (35) performed extensive searches of systematic reviews and original manuscripts. They identified 4 higher-quality (77,91-93) and 5 lower-quality (94-98) systematic reviews after excluding 11 outdated or already updated systematic reviews (78,99-108) and 3 reviews that were not clearly systematic (109-111).

They identified 40 randomized trials (reported in 39 articles) of epidural steroid injections for low back pain (112-150) and stated that 33 trials were included in at least 1 of the 9 systematic reviews (77,91-98) and they identified 7 additional trials (112-117,139). They concluded that 21 trials (with 2 trials reported in one article [128], were placebo-controlled (114,118-136), rating 11 placebo-controlled trials as higher quality (114,116,118,121,122,124,126,130,132,135,140).

Chou and Huffman (35) and multiple other systematic reviews (77,78,92,102,107,111) have evalu-

ated the effectiveness of epidural injections by combining lumbar interlaminar and caudal epidural injections.

1.1 Caudal Epidural Injections

Conn et al (59), Abdi et al (94,99), Boswell et al (100), and Bogduk et al (151) evaluated caudal epidural steroid injections as separate procedures, reaching favorable conclusions with moderate effectiveness in managing lumbar radiculopathy. In contrast, multiple systematic reviews, including the ones by Chou et al (35,37,77,78,92,102,107,111) combined interlaminar or translaminar epidural injections and caudal epidural injections into one category, and therefore reached erroneous conclusions that these treatments were only effective for short-term relief in radiculopathy.

1.1.1 Literature Search

A comprehensive literature search yielded over 3,000 manuscripts with inclusion of 42 manuscripts for this evaluation.

1.1.2 Methodologic Quality Assessment

Methodologic quality assessment of the randomized clinical trials evaluating the effectiveness of caudal epidural injections is illustrated in Table 7.

1.1.2.1 Assessment of Randomized Clinical Trials

Of the 33 trials which were included in at least one of the 9 systematic reviews, and 7 additional trials identified by Chou et al (114,118-136), they concluded that 21 trials (with 2 trials reported in one article (128) were placebo control (114,118-136) and further, that 11 placebo control trials were of higher quality (114,116,118,121,122,124,126,130,132,135,140). Of these trials, they conducted methodologic quality assessment of criteria for 26 trials. Of these, one trial (117) described percutaneous adhesiolysis; thus, it is not an epidural study as it was conducted in patients who had already failed to respond to caudal epidural steroid injections. Of the remaining 25, 7 studies were caudal (112,119-121,129,136,140), 13 were interlaminar (112,114,118,122-125,127,128,133-135,139), and 5 were transforaminal (112,116,126,130,132).

In the present critical assessment, methodologic quality assessment was carried out on all the caudal studies included by Chou and Huffman (35). Of the 10 studies considered as caudal (after elimination of the one adhesiolysis study), Chou and Huffman (35) excluded 3 studies in their quality assessment. Further, they considered among these studies only 2 as being high quality and placebo controlled (121,140). However, Dashfield et al (140), was described as a high quality placebo-controlled trial, even though it utilized an active control design.

Thus in this reassessment, 16 studies were evaluated for methodologic quality assessment. Seven of them (112,119-121,129,136,140) were from Chou and Huffman (35), 3 studies (142,144,147) were randomized trials not assessed by APS-AAPM evidence synthesis, and 6 studies (152-157) were published after the APS guidelines were published (35).

Of the 19 randomized trials (112,119-121,129,136, 140,142,144,147,152-160), 16 were included for methodologic quality assessment (112,119-121,129,136,140, 142,144,147,152-157). Three studies (112,119,136) were included in this methodologic quality assessment even though they were excluded by Conn et al (59).

Of the studies meeting the inclusion criteria for methodologic quality assessment, 6 were published in the latter part of 2008 or 2009 (152-157) beyond the inclusion criteria of Chou and Huffman (35). However, these were included in the present analysis of methodologic quality assessment so that judgment may be made including the most current evidence.

It appears that while most of the assessment was appropriate for the studies which were included by others in their systematic reviews, Chou and Huffman (35) included studies which did not meet inclusion criteria. This illustration shows that even though quality criteria is met, the study can be very poorly performed, and therefore not clinically relevant. Béliveau (119) had no data at 3 months. Justifiably, Chou and Huffman (35) rated this study as extremely low due to the lack of data at 3 months, along with many other deficiencies. Zahaar (136) utilized very high volumes of sterile saline with local anesthetic with or without steroid, 30 mL, injecting blindly without fluoroscopic guidance. The study was not placebo-controlled and so had low methodologic quality. Ackerman and Ahmad (112) provided inadequate descriptions and the study was poorly performed, even though it was rated by Chou and Huffman (35) as high quality; our assessment also showed high methodologic quality. However, this study was excluded from assessment and was not included by others due to the short-term follow-up of 24 weeks, along with other multiple deficiencies (59). Ackerman and Ahmad (112) was a low quality study. It also showed that there is no difference among the 3 types of treatments; but, did not show that caudal epidurals were ineffective.

Table 7. *Methodological assessment of randomized clinical trials evaluating the effectiveness of caudal epidural injections.*

	Bush and Hillier 1991 (121)*		Dashfield et al 2005 (140)#*		Mathews et al 1987 (129)*		Hesla and Breivik 1979 (142)•		Breivik et al 1976 (120)*		Revel et al 1996 (147)•	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Randomization	No	Don't know	Yes	Don't know	Yes	Don't know	Yes	NS	Yes	Yes	Yes	NS
Concealed treatment allocation	Don't know	Don't know	Yes	Yes	Don't know	Don't know	Yes	NS	Don't know	Don't know	No	NS
Baseline group similarity	No	Don't know	Yes	Yes	No	No data	No	NS	No	Don't know	Yes	NS
Patient blinded	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NS	Yes	Yes	No	NS
Care provider blinded	Yes	Don't know	No	No	No	Don't know	Yes	NS	No	No	No	NS
Outcome assessor blinded	Yes	Yes	No	Don't know	Yes	Yes	No	NS	Yes	Yes	Yes	NS
Cointerventions avoided or similar	Yes	Yes	No	Don't know	Yes	Yes	No	NS	No	Don't know	Yes	NS
Compliance acceptable in all groups	Yes	Yes	Yes	Yes	Yes	Yes	No	NS	No	Yes	No	NS
Drop-out rate described and acceptable	No	No	Yes	Yes	Yes	No	Yes	NS	Yes	No	No	NS
Timing of outcome assessment in all groups similar	Yes	Yes	Yes	Yes	Yes	Don't know	Yes	NS	Yes	Don't know	Yes	NS
Intention to treat analysis	Yes	Yes	Yes	Yes	Yes	Don't know	Yes	NS	Yes	Yes	No	NS
Score	7/11	6/11	8/11	7/11	8/11	4/11	7/11	NS	6/11	5/11	5/11	NS

*Included by Chou and Huffman (35) and Conn et al (59)
+Included by Conn et al (59), but not Chou and Huffman (35)
•Included by Chou and Huffman (35), but not Conn (59)
§Included in present review, but not Chou and Huffman (35)
ΔNot available at the time of Chou's search
#Fluoroscopy used in performing caudal epidural injections

NS = Not scored by APS-AAPM review

Among high quality studies reporting positive results, 5 were performed under fluoroscopy (140,152-155), and one was performed without fluoroscopy (156). However, none of them were placebo-controlled. All the fluoroscopic studies were performed on chronic low back pain patients who had disc herniation; discogenic pain with or without disc herniation or radiculitis, post lumbar laminectomy syndrome; or spinal stenosis (140,152-155). The non-fluoroscopic study was performed with local anesthetic injection with or without steroid (156) in patients with disc herniation and pain duration of one month. The results were positive in this study.

1.1.2.2 Assessment of Systematic Reviews

We identified multiple systematic reviews evaluating the effectiveness of caudal epidural injections (59, 76,77,92,98,102,107,111,161). As shown in Table 8, all

Table 7 (cont). *Methodological assessment of randomized clinical trials evaluating the effectiveness of caudal epidural injections.*

	Manchikanti et al 2008 (152)# ✚Δ		Manchikanti et al 2008 (153)#✚Δ		Manchikanti et al 2008 (154)# ✚Δ		Manchikanti et al 2008 (155)#✚ Δ		Ackerman and Ahmad 2007 (112)•	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Randomization	Yes	NS	Yes	NS	Yes	NS	Yes	NS	Yes	Yes
Concealed treatment allocation	Yes	NS	Yes	NS	Yes	NS	Yes	NS	No	Don't know
Baseline group similarity	Yes	NS	Yes	NS	Yes	NS	Yes	NS	Yes	Yes
Patient blinded	Yes	NS	Yes	NS	Yes	NS	Yes	NS	No	Yes
Care provider blinded	Yes	NS	Yes	NS	Yes	NS	Yes	NS	No	No
Outcome assessor blinded	No	NS	No	NS	No	NS	No	NS	Can't tell	Yes
Cointerventions avoided or similar	Yes	NS	Yes	NS	Yes	NS	Yes	NS	Yes	Yes
Compliance acceptable in all groups	Yes	NS	Yes	NS	Yes	NS	Yes	NS	Yes	Yes
Drop-out rate described and acceptable	No	NS	No	NS	Yes	NS	Yes	NS	Yes	Yes
Timing of outcome assessment in all groups similar	Yes	NS	Yes	NS	No	NS	No	NS	Yes	Yes (for pain relief)
Intention to treat analysis	Yes	NS	Yes	NS	Yes	NS	Yes	NS	Yes	Yes
Score	9/11	NS	9/11	NS	9/11	NS	9/11	NS	7/11	9/11

*Included by Chou and Huffman (35) and Conn et al (59)
+Included by Conn et al (59), but not Chou and Huffman (35)
•Included by Chou and Huffman (35), but not Conn (59)
§Included in present review, but not Chou and Huffman (35)
ΔNot available at the time of Chou's search
#Fluoroscopy used in performing caudal epidural injections

NS = Not scored by APS-AAPM review

the systematic reviews included by Chou and Huffman (35) were included with another systematic review (76), which was not considered by Chou and Huffman (35). Conn et al (59) and Staal et al (161), which were published in 2009, were included for evaluation purposes.

Quality assessment results of systematic reviews are illustrated in Table 8. The rating was judged to be inappropriate in some studies as resulting in favorable or unfavorable opinions. The overall quality score was a maximum of 9; however, Chou and Huffman (35) utilized a maximum score of 7. We were unable to understand the rationale related to the modified score and analysis. Manchikanti et al (76) was not evaluated, even though it met 7 of 9 criteria. Luijsterburg et al (91) in this assessment met only 5 of 9 criteria, but APS-AAPM scored it 7/7 or (9/9 corrected) meaning it met all criteria. Abdi et al (94) was described as low quality and that it met 3 of 7 criteria. However, looking at the 9 items, even by their own (35) determination, this study met 6 of 9 criteria, with one item meeting partial criteria; our assessment showed 7 of 9 criteria were met. Vroomen et al (93) were evaluated as meeting 5 of 7 criteria, even though it should have been 8 of 9 by their own assessment; our reassessment showed only 6 of

Table 7 (cont). *Methodological assessment of randomized clinical trials evaluating the effectiveness of caudal epidural injections.*

	Beliveau 1971 (119)♦		Zahaar 1991 (136)♦		Sayegh et al 2009 (156)§Δ		Laiq et al 2009 (157)§Δ		McGregor et al 2001 (144) ♦	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Randomization	No	No	Don't know	Don't know	Yes	NS	Yes	NS	No	NS
Concealed treatment allocation	No	No	No	Don't know	Yes	NS	No	NS	No	NS
Baseline group similarity	No	Don't know	Yes	Don't know	Yes	NS	Yes	NS	No	NS
Patient blinded	No	Don't know	Yes	Yes	Yes	NS	No	NS	No	NS
Care provider blinded	No	Don't know	No	No	Yes	NS	No	NS	No	NS
Outcome assessor blinded	No	Don't know	No	Don't know	Yes	NS	No	NS	Yes	NS
Cointerventions avoided or similar	No	Don't know	No	Don't know	Yes	NS	No	NS	Yes	NS
Compliance acceptable in all groups	Yes	Yes	Yes	Yes	Yes	NS	Yes	NS	Yes	NS
Drop-out rate described and acceptable	No	Don't know	No	No	Yes	NS	Don't know	NS	No	NS
Timing of outcome assessment in all groups similar	No	No	No	No (for long term f/u)	Yes	NS	Yes	NS	Yes	NS
Intention to treat analysis	No	Don't know	Yes	Yes	Yes	NS	No	NS	Yes	NS
Score	1/11	1/11	4/11	3/11	11/11	NS	4/11	NS	5/11	NS

*Included by Chou and Huffman (35) and Conn et al (59)
+Included by Conn et al (59), but not Chou and Huffman (35)
♦Included by Chou and Huffman (35), but not Conn (59)
§Included in present review, but not Chou and Huffman (35)
ΔNot available at the time of Chou's search
#Fluoroscopy used in performing caudal epidural injections

NS = Not scored by APS-AAPM review

9. Most systematic reviews except by Conn et al (59), Manchikanti et al (76), and Abdi et al (94) separated the 3 techniques, whereas DePalma et al (96) evaluated selective nerve root blocks. Luijsterburg et al (91) also utilized highly inconsistent criteria with the evaluation that findings must be consistent 80% of the time to be judged positive. Armon et al (95) received a score of 4/7 (5/9 corrected), which is higher than the reassessment score of 3/9.

It was surprising that since Chou and Huffman (35) were not able to identify the type of injections, they grouped everything into interlaminar if the procedure was not specified. DePalma et al (96) appraised the evidence for selective nerve root injection in the treatment of lumbosacral radiculopathy, yet Chou and Huffman (35) concluded that they included 3 interlaminar studies, one caudal study, and 5 transforaminal studies. However, there were no caudal studies. Thus, it appears that the evaluators were either unable to identify the type of injection or were not interested in finding accurate information.

1.1.3 Disc Herniation and Radiculitis

Eight randomized trials met criteria for inclusion for evidence synthesis (112,120,121,129,140,142,153,156). Ackerman and Ahmad (112) was not included in

Table 8. *Quality rating of systematic reviews of caudal epidural injections.*

	Conn et al 2009 (59)Δ♦		Manchikanti et al 2008 (76)♦		Nelmans et al 2001 (77)*		Luijsterburg et al 2007 (91)*	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Search Method	Yes	NS	Yes	NS	Yes	Yes	Yes	Yes
Comprehensive	Yes	NS	Yes	NS	Yes	Yes	Yes	Yes
Inclusion Criteria	Yes	NS	Yes	NS	Yes	Yes	Yes	Yes
Bias Avoided	Yes	NS	Yes	NS	Yes	Yes	No	Yes
Validity Criteria	Yes	NS	Yes	NS	Yes	Yes	No	Yes
Validity Assessed	Yes	NS	Yes	NS	Yes	Yes	Yes	Yes
Methods for Combining Studies	No	NS	No	NS	Yes	Yes	Yes	Yes
Appropriately Combined	No	NS	No	NS	No	Yes	No	Yes
Conclusions Supported	Yes	NS	Yes	NS	No	Yes	No	Yes
Overall Quality	7/9	NS	7/9	NS	7/9	7/7	5/9	7/7
Corrected Score	7/9	NS	7/9	NS	7/9	9/9	5/9	9/9

	Staal et al 2008, 2009 (92*,161Δ♦)		Abdi et al 2007 (94)*		Armon et al 2007 (95)♦		Resnick et al 2005 (97)♦		Tonkovich-Quaranta and Winkler 2000 (98)♦		Vroomen et al 2000 (93)*	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Search Method	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Comprehensive	Yes	Yes	Yes	Yes	No	Partial	No	Partial	No	No	Yes	Yes
Inclusion Criteria	Yes	Yes	Yes	Yes	Yes	Yes	No	Partial	No	No	No	Can't tell
Bias Avoided	Yes	Yes	Yes	Yes	Yes	Yes	No	Can't tell	No	No	Yes	Yes
Validity Criteria	Yes	Yes	Yes	Partial	No	Partial	No	No	No	No	Yes	Yes
Validity Assessed	Yes	Yes	Yes	Yes	No	Partial	No	No	No	Partial	Yes	Yes
Methods for Combining Studies	Yes	Yes	No	No	No	Partial	No	Partial	No	Can't tell	Yes	Yes
Appropriately Combined	No	Yes	No	No	No	Partial	No	Can't tell	No	Can't tell	No	Yes
Conclusions Supported	No	Yes	Yes	Yes	No	Partial	No	Can't tell	No	No	No	Yes
Overall Quality	7/9	7/7	7/9	3/7	3/9	4/7	1/9	2/7	0/9	1/7	6/9	5/7
Corrected Score	7/9	9/9	7/9	6/9	3/9	5/9	1/9	1/9	1/9	1/9	6/9	8/9

*Included by Chou and Huffman (35) and Conn et al (59)
+Included by Chou and Huffman (35), but not the present reviews
♦Included by Chou and Huffman (35), but not Conn (59)
§Included in present review, but not Chou and Huffman (35)
ΔNot available at the time of Chou's search
#Fluoroscopy used in performing caudal epidural injections

other reviews. Based on Chou and Huffman's (35) criteria, it met the inclusion criteria. However, Zahaar (136) was not added since the methodologic criteria was low and it was not placebo-controlled, a feature misunderstood by APS guidelines. Béliveau (119) also had low methodologic quality assessment criteria. Sayegh et al (156), published in 2009, was included by us. The study, which was randomized and double-blinded, did not utilize fluoroscopy. Of the 9 studies, 3 included fluoroscopy (112,140,153).

In the 8 studies examined, illustrated in Table 9, 7 were positive for short-term relief (less than 6 months) and 4 of 5 were positive for long-term relief (more than 6 months). Even with elimination of the 2 studies which were not available at the time the APS guidelines were published (153,156), the results still continue to be positive, with 5 of the 6 studies positive for short-term relief (112,120,121,140,142) and 2 of the 3 studies positive for long-term relief (129,142).

1.1.3.1 Effectiveness

The present critical assessment showed positive results for short-term relief in 7 of 8 studies (112,120, 121,140,142,153,156). Of 5 trials reporting long-term follow-up of more than 6 months, 4 reported positive results (129,142,153,156). The results in 3 studies utilizing fluoroscopy (112,140,153) were superior to blind epidural injections (Table 9).

The 2008 study by Manchikanti et al (153) and the 2009 study by Sayegh et al (156) were published after the APS guidelines were published. Even so, of the studies examined by Chou and Huffman (35) the results were positive in 5 of 6 for short-term relief (less than 6 months) (112,120,121,140,142), and 2 of 3 showed positive results for long-term relief (more than 6 months) (129,142).

Based on the present evidence, utilizing Chou and Huffman's criteria with grading of good, fair, and poor, it appears that there is fair evidence for the therapeutic

Table 9. *Results of randomized trials of effectiveness of caudal epidural steroid injections in managing the pain from lumbar disc herniation/radiculitis.*

Study	Study Characteristics	Methodological Quality Scoring		Participants	Pain Relief			Results	
		ASIPP	APS-AAPM		3 mos.	6 mos.	12 mos.	Short-term relief ≤ 6 mos.	Long-term relief > 6 mos.
Manchikanti et al 2008 (153)*Δ	RA, DB	9/11	NS	LA with steroids = 42 LA only = 42	81%	86%	79% to 81%	P	P
Dashfield et al 2005 (140)*	RA, DB	8/11	7/11	Caudal = 30 Endoscopy = 30	SI	SI	NA	P	NA
Bush and Hillier 1991 (121)	RA, DB	7/11	6/11	23	SI	NSI	NSI	P	N
Mathews et al 1987 (129)	RA, DB	8/11	4/11	C = 34 T = 23	SI	SI	SI	N	P
Hesla and Breivik 1979 (142)	RA, DB	7/11	NS	69 patients: crossover design	29% versus 77%	25% versus 59%	25% versus 59%	P	P
Breivik et al 1976 (120)	RA, DB	6/11	5/11	C = 19 T = 16	20% vs 50%	20% vs 50%	NA	P	NA
Ackerman and Ahmad 2007 (112)*	RA, DB	8/11	9/11	Caudal = 30 Interlaminar = 30 Transforaminal = 30	Caudal = 17 of 30 (57%)	NA	NA	P	NA
Sayegh et al 2009 (156)Δ	RA,DB	11/11	NS	Steroid with LA = 93 LA only = 90	SI	SI	SI	P	P

*Indicates use of fluoroscopy
ΔNot available at the time of Chou's search
RA = randomized; DB = double blind; NS = Not scored by APS-AAPM review; C = control; T = treatment; LA = local anesthetic; NA = not available; SI = significant improvement; NSI = no significant improvement; vs = versus; P = positive; N = negative

effectiveness of caudal epidural injections, in patients with disc herniation or radiculitis with or without steroids, for short-term and long-term relief. However, with addition of new studies the evidence is good for therapeutic effectiveness of caudal epidural injections in disc herniation or radiculitis.

Supporting these findings is a recent evidence-based radiology evaluation of therapeutic injections conducted by Peterson and Hodler (162). They concluded, based on multiple systematic reviews (59-61), that a caudal approach is the most effective for epidural injections of corticosteroids into the lumbar region.

1.1.4 Post Surgery Syndrome

Three studies evaluating the effectiveness of caudal epidural injections used for post surgery syndrome pain met inclusion criteria (142,147,154). Only one study (154) was performed under fluoroscopy. Of these, 2 studies (142,154) provided outcomes of longer than 6 months. Of note is that Manchikanti et al's study (154) had not been published by the time Chou and Huffman (35) completed their search.

The study by Meadeb et al (145), not included in the evidence synthesis, evaluated forceful caudal epidural injections in the treatment of post laminectomy syndrome. They forcefully injected 20 mL of sodium chloride solution, with or without prednisolone acetate 120 mg, whereas in the second group, they injected 125 mg of epidural prednisolone without any mixture. They showed positive results in the forceful injection group for short-term relief. Surprisingly, in this study by Meadeb et al (145), patients receiving a forceful sodium chloride injection of 20 mL showed better results than those receiving steroids.

1.1.4.1 Effectiveness

All 3 randomized trials (142,147,154) studying the effectiveness of caudal epidural steroid injections for post-surgery syndrome were shown to be positive for short-term relief (142,147,154). Two studies that conducted long-term follow-up also showed positive results (142,154). Based on Chou and Huffman's (35) criteria of 6 weeks of relief, all of them showed positive results for short-term relief; in addition, all 3s (142,147,154) showed long-term improvement. If the study published after the selection criteria of APS guidelines is excluded (154), the results were positive in one study (142) with the results that are available (Table 10).

Among the systematic reviews, only Conn et al (59) focused on post lumbar surgery syndrome. They showed moderate evidence based on 3 trials, one of which had not been published prior to the evaluation by Chou and Huffman (35).

Based on the present evidence, utilizing Chou and Huffman's criteria with grading good, fair, and poor, it appears that there is poor evidence for short-term and long-term relief. However, addition of new studies may change the level of evidence to fair.

1.1.5 Spinal Stenosis

There were no randomized trials meeting the inclusion criteria based on Chou and Huffman's (35) search

Table 10. *Results of randomized trials in managing low back pain of post-surgery syndrome with caudal epidural injections.*

Study	Study Characteristics	Methodological Quality Scoring		Participants	Pain Relief			Results	
		ASIPP	APS-AAPM		3 mos.	6 mos.	12 mos.	Short-term relief ≤ 6 mos.	Long-term relief > 6 mos.
Manchikanti et al 2008 (154)*	RA, DB	9/11	NS	40	65% to. 70%	60%	60% to 65%	P	P
Revel et al 1996 (147)	RA	5/11	NS	Forceful injection = 29 Regular = 31	NA	49% vs 19%	NA	P	NA
Hesla and Breivik 1979 (142)	RA, DB	7/11	NS	69 patients: crossover design	77% vs 29%	59% vs 25%	59% vs 25%	P	P

*Indicates use of fluoroscopy
RA = randomized; DB = double blind; NS = Not scored by APS-AAPM review; NA = not available; vs = versus; P = positive; N = negative

criteria. However, one randomized trial (155) evaluating the role of caudal epidural injections in spinal stenosis was published in 2008 and was not included in their search.

1.1.5.1 Effectiveness

The one randomized trial evaluating spinal stenosis with or without steroids with local anesthetic (155) showed positive results for short- and long-term relief.

The only systematic review discussing the effectiveness of spinal stenosis was by Conn et al (59) showing moderate evidence based on one randomized trial performed under fluoroscopy. However, this study was published after the search conducted by Chou and Huffman (35). With the exclusion of Manchikanti et al (155), the evidence is based on only 2 observational studies though positive, will be poor. Further, Chou and Huffman (35) did not utilize any of these studies in their evidence synthesis.

1.1.6 Discogenic Pain

The literature is sparse for using epidural injections in the management of discogenic pain without radiculitis. In a systematic review, Conn et al (59) analyzed the evidence of caudal epidural injections for patients with discogenic pain utilizing one randomized double-blind trial (152).

1.1.6.1 Effectiveness

One randomized trial (152) showed positive long-term results. A recent evidence-based review (162) indicated caudal epidural injections are effective in managing discogenic pain without herniation or nerve root compression based on the results of the above randomized trial and systematic reviews (59,152).

Based on Chou and Huffman's criteria with grading of good, fair, and poor, the evidence is poor. However, addition of new studies may change the level of evidence to fair.

1.2 Lumbar Interlaminar Epidural Injections

Chou and Huffman (35) evaluated and published the results of interlaminar and caudal epidural steroid injections as one category for low back pain related to sciatica or radiculopathy and spinal stenosis. They concluded that for epidural steroid injections, there is fair evidence of moderate benefit compared with placebo injection for short-term pain relief in patients with radiculopathy. However, there was no evidence for long-term benefits because few trials have evaluated long-term outcomes. They also concluded that there was inconsistency because of the type of control used. Specifically, trials that evaluated a soft-tissue placebo injection more consistently reported short-term benefits, and trials that evaluated epidural placebo injection mostly reported no short-term benefits. They postulated that this observation suggests that effects could be mediated more by the non-specific physical effects of increased pressure within the epidural space than by specific corticosteroid anti-inflammatory effects. They showed a lack of effectiveness for spinal stenosis and also low back pain without radiculopathy (35).

Multiple guidelines and systematic reviews have been conducted separately evaluating interlaminar, caudal, and transforaminal epidural injections, along with evaluating them independently for disc herniation and radiculitis, discogenic pain without disc herniation or radiculitis, lumbar post surgery syndrome, and lumbar spinal stenosis. The guidelines (46) showed that multiple systematic reviews provided negative opinions for lumbar interlaminar epidural injections (60,78,91-108,152). Similar to APS guidelines (35), ASIPP guidelines provided Level II-2 evidence for short-term relief of pain of disc herniation or radiculitis utilizing blind interlaminar epidural steroid injections; there is a lack of evidence for long-term relief (60). Staal et al (92,161) updated Nelemans et al's (77,103) study concluding that there was insufficient evidence to support the use of injection therapy in subacute and chronic low back pain. In a recent systematic review (60), the effectiveness of lumbar interlaminar epidural injections was assessed for disc herniation and radiculitis, spinal stenosis, and discogenic pain.

1.2.1 Literature Search

Our literature search yielded over 1,600 manuscripts, leading to 60 manuscripts considered for inclusion. There were 20 randomized trials and multiple systematic reviews (60,77,78,91-108,114,118,122-125,127,128,131,133-135,137-139,144,146-149,160,161). The deficiencies of randomized interlaminar epidural studies has been described by Parr et al (60) and others (49) regarding design flaws, placebo injection into the epidural space, lack of fluoroscopy, and other limitations.

1.2.2 Methodologic Quality Assessment

Chou and Huffman (35), along with a multitude of other reviewers, have focused on interlaminar epidurals and combined caudal epidural injections with them. The majority of the systematic reviews that exclude cau-

dal and transforaminal epidural injections and the present guidelines will arrive at the same conclusions for lumbar interlaminar epidural injections, with the available literature. Hence, no separate methodologic quality assessment of individual studies was carried out.

1.3 Transforaminal Epidural Injections

Chou and Huffman (35) separated transforaminal epidural steroid injections from caudal and interlaminar and evaluated their role. They also made the statement that most placebo-controlled trials evaluated either the interlaminar or caudal approach. They concluded that 3 higher quality, placebo-controlled trials evaluating the transforaminal approach reported mixed results (126,130,132), and concluded that for low back pain with sciatica, evidence for the efficacy of epidural steroid injection by the transforaminal approach was mixed, with 2 of 3 higher quality trials showing no benefit compared to controlled injections.

1.3.1 Literature Search

Our literature search yielded over 2,000 manuscripts with multiple studies considered for inclusion (62,96,99,112,113,115,116,126,128,130,132,139,141,143,150,163,164).

1.3.2 Methodologic Quality Assessment

1.3.2.1 Randomized Trials

Chou and Huffman (35) utilized 4 studies meeting the quality assessment criteria (116,126,130,132). We utilized these studies and Ackerman and Ahmad's study (112) for this analysis, as it was rated as high quality by Chou and Huffman (35). Vad et al (165) and Devulder et al (141) were not included in the methodologic quality assessment. Gallucci et al (115) was excluded because that it was not included by Chou and Huffman (35); also because intradiscal injections were combined with transforaminal epidurals, thus negating the individual effects to be evaluated.

The methodologic quality assessment of the criteria of randomized trials of transforaminal epidural injections are illustrated in Table 11 for 5 studies (112,116,126,130,132). There were 2 studies with dupli-

Table 11. *Quality rating of randomized trials of lumbar transforaminal epidural injections.*

	Riew et al 2000, 2006 (132*,163✚)		Karppinen et al 2001, 2001 (126*,164✚)		Ackerman and Ahmad 2007 (112) §		Jeong et al 2007 (116)*		Ng et al 2005 (130)#	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Randomization	Yes	Don't know	Yes	Yes	Yes	Yes	Yes	Don't know	Yes	Yes
Concealed treatment allocation	Yes	Yes	Yes	Yes	No	Don't know	Yes	Don't know	Yes	Yes
Baseline group similarity	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Don't know	Yes	Yes
Patient blinded	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Care provider blinded	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes
Outcome assessor blinded	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Cointerventions avoided or similar	Yes	Don't know	Yes	No	Yes	Yes	Yes	Don't know	Yes	Yes
Compliance acceptable in all groups	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drop-out rate described and acceptable	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Timing of outcome assessment in all groups similar	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Intention to treat analysis	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Score	11/11	9/11	11/11	10/11	8/11	9/11	9/11	4/11	11/11	11/11

*Included by Chou and Huffman (35) and Buenaventura et al (62)
#Included by Chou and Huffman (35) and present review
✚Included by Buenaventura et al (62), but not Chou and Huffman (35)
§Included in present review, but not Chou and Huffman (35) for transforaminal, but was included for caudal and interlaminar

cate presentations: Riew et al (132,163) and Karppinen et al (126,164).

The quality rating for randomized trials of transforaminal epidural injections was inappropriate although Chou and Huffman (35) followed methodology, with weak clinical relevance. The study by Jeong et al (116) met criteria in 9 of 11 assessments, instead of 4 of 11 as shown by Chou and Huffman (35). The influence of placebo injection over the nerve root has not been delineated even though Karppinen et al's study is considered as high quality (126). The deficiencies of this study (126,164) in reference to terminology, technique, randomization, and outcomes were described (166). Surprisingly, the Ackerman and Ahmad study (112) was rated as high quality and was utilized for caudal and interlaminar approaches, but not for a transforaminal approach; it was rated 9 of 11 by Chou and Huffman (35). Ackerman and Ahmad (112) also showed superior results with an 83% success rate using a transforaminal approach, due to a ventral filling pattern.

1.3.2.2 Assessment of Systematic Reviews

Multiple systematic reviews were performed evaluating the effectiveness of lumbar transforaminal epidural steroid injections (62,76,91,94-96) with conflicting results. The methodologic quality assessment is shown in Table 12.

One systematic review (94) showed the evidence of lumbar transforaminal epidural steroid injections for lumbar nerve root pain was strong for short-term and moderate for long-term improvement. The recent systematic review by Buenaventura et al (62) indicated the evidence is Level II-1 for short-term relief and Level II-2 for long-term relief in managing chronic low back and lower extremity pain. They evaluated methodologic quality assessment, relief of longer than 6 months as long-term relief, and appropriate outcomes. Thus, this systematic review met all the criteria for inclusion in the guideline synthesis. Manchikanti et al (76) showed strong evidence for lumbar transforaminal epidural injections for short-term and long-term relief of 6 months

Table 12. *Quality rating of systematic reviews of lumbar transforaminal epidural injections.*

	Buenaventura et al 2009 (62) ♦Δ		Manchikanti et al 2008 (76) ♦		Luijsterburg et al 2007 (91)✚		Abdi et al 2007 (94)*		Armon et al 2007 (95)✚		DePalma et al 2005 (96)✚	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Search Method	Yes	NS	Yes	NS	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Comprehensive	Yes	NS	Yes	NS	Yes	Yes	Yes	Yes	No	Partial	Yes	Yes
Inclusion Criteria	Yes	NS	Yes	NS	Yes	Yes	Yes	Yes	Yes	Yes	No	Can't tell
Bias Avoided	Yes	NS	Yes	NS	No	Yes	Yes	Yes	Yes	Yes	No	Yes
Validity Criteria	Yes	NS	Yes	NS	No	Yes	Yes	Partial	No	Partial	No	Partial
Validity Assessed	Yes	NS	Yes	NS	Yes	Yes	Yes	Yes	No	Partial	No	Yes
Methods for Combining Studies	No	NS	No	NS	Yes	Yes	No	No	No	Partial	No	No
Appropriately Combined	No	NS	No	NS	No	Yes	No	No	No	Partial	No	Can't tell
Conclusions Supported	Yes	NS	Yes	NS	No	Yes	Yes	Yes	No	Partial	No	Yes
Overall Quality	7/9	NS	7/9	NS	5/9	7/7	7/9	3/7	3/9	4/7	2/9	4/7
Corrected Score	7/9	NS	7/9	NS	5/9	9/9	7/9	6/9	3/9	5/9	2/9	5/9

*Included by Chou and Huffman (35) and the present review
✚ Included by Chou and Huffman (35), but not present review
♦ Included in the present review, but not by Chou and Huffman (35)
ΔNot available at the time of Chou's search
NS = Not scored by APS-AAPM review

or longer. This systematic review was not included by Chou and Huffman (35). The systematic review by Buenaventura et al (62) was published after the search by Chou and Huffman (35).

DePalma et al (96) performed a critical appraisal of the evidence for selective nerve root injection in treating lumbosacral radiculopathy. The methodologic quality assessment of DePalma et al (96) was illustrated as 4 of 7; however, the corrected score appears to be 5 of 9. This critical assessment showed a score of 2 of 9. Further, Chou and Huffman (35) misinterpreted the systematic review and stated that this also included 3 interlaminar studies, one caudal study, and 5 transforaminal studies. DePalma et al (96) included 2 studies comparing interlaminar with transforaminal corticosteroid injections. There were no caudal studies. Despite the poorly conducted systematic review, they (96) concluded that there was moderate evidence, Level III, for transforaminal epidural injections for painful lumbar radicular symptoms.

Armon et al (95), which was included in the systematic review, was classified as a low-quality systematic review with a score 4 of 7 or 5 of 9 with corrected scoring. Our reassessment score was 3 of 9.

Luijsterburg et al (91) included 2 transforaminal epidural injections in their analysis. However, they utilized highly inconsistent criteria by evaluating that findings must be consistent 80% of the time to be judged positive. The scoring by Chou and Huffman (35) for this systematic review was 7 of 7 or 9 of 9 corrected, whereas, it was 5 of 9 with our reassessment. Further, Luijsterburg et al (91) combined caudal, interlaminar, and transforaminal epidurals as one category in their evaluation, thereby inevitably leading to negative conclusions.

The quality assessment criteria was biased against Abdi et al (94). The reassessment showed a score of 7 of 9, instead of 3 of 7. By Chou and Huffman's (35) own criteria, the score for the systematic review of Abdi et al (94) should be 6 of 9 or higher because they rated some validity criteria as partial, which essentially was positive, which would have yielded the same score as our reassessment score of 7 of 9.

1.3.2.3 Effectiveness

The results of randomized trials of the effectiveness of lumbar transforaminal epidural injections incorporated by Chou and Huffman (35) are illustrated in Table 13.

Even though the study by Ng et al (130) measured only a 3 month follow-up and was an active control trial, it was utilized by Chou and Huffman (35); thus, we also utilized it in our evidence synthesis. This study

Table 13. *Results of randomized trials of the effectiveness of lumbar transforaminal epidural injections.*

Study	Methodological Quality Scoring		Study Characteristics	Participants	Pain Relief			Results	
	ASIPP	APS-AAPM			3 mos.	6 mos.	12 mos.	Short-term relief ≤ 6 mos.	Long-term relief > 6 mos.
Karppinen et al 2001, 2001 (126,164)	11/11	10/11	RA, DB	C = 80 T = 80	SICH	NSI	NSI	P	N
Riew et al 2000, 2006 (132,163)	11/11	9/11	P, RA, DB	55	NA	NA	33% vs. 71% (avoided surgery)	P	P
Jeong et al 2007 (116)	9/11	4/11	RA, DB	239	PG 99 of 112 G 90 of 127	PG 64 of 106 G 78 of 116	NA	P	NA
Ng et al 2005 (130)	11/11	11/11	RA, DB	C = 43 T = 43	NSD	NA	NA	NA	NA
Ackerman and Ahmad 2007 (112)	8/11	9/11	RA, DB	Transforaminal = 30 Caudal = 30 Interlaminar = 30	Transforaminal = 25 of 30 (83%) Caudal = 17 of 30 (57%) Interlaminar = 18 of 30 (60%)	NA	NA	P	NA

RA = randomized; DB = double blind; P = prospective; C = control; T = treatment; PG = pre-ganglionic; G = ganglionic; SICH = significant improvement in contained disc herniation; NSD = no significant difference; vs. = versus; NA = not available; P = positive; N = negative; NSI = no significant improvement.

showed improvement in both groups without differences between bupivacaine and bupivacaine with steroid. This is a study that even though it had a short-term follow-up, it scored high on methodologic quality. The study also included a rather high volume (4 mL) injection of 2 mL of bupivacaine and 2 mL of injectate into the transforaminal epidural space. Karppinen et al (126,164) showed short-term relief, Riew et al (132,163) showed short-term and long-term improvement, Jeong et al (116) showed short-term improvement. Ackerman and Ahmad (112), at the 24-week follow-up, reported significant pain relief in 25 of 30 patients (83%).

Karppinen et al (164) in a subgroup analysis looked at the cost effectiveness of transforaminal epidural injections. They showed that in cases of contained herniations, the steroid injection produced significant treatment effects and short-term efficacy in leg pain for symptomatic lesions at L3-L4-L5; and that steroid was superior to saline for leg pain, disability, and straight leg raising in the short-term. By one-year, steroids seemed to have prevented the need for operations for contained herniations, costing $12,666 less per responder in the steroid group. For extrusions, the steroid seemed to increase the operation rate, and the steroid infiltration was more expensive, costing $4,445 per responder. However, in their initial cost estimations (126) after an adjustment for baseline differences, the total cost during the one-year follow-up period did not differ between the 2 treatment groups. Analysis showed there was no significant difference in outcomes with sodium chloride solution compared to bupivacaine with steroids. Leg pain had decreased on the average by 65% in both groups.

Overall results were positive in 4 of 5 studies for short-term (112,116,126,132), whereas they were positive in one of the 2 studies (126,132) for long-term follow-up of > 6 months. Based on the available evidence and utilizing Chou and Huffman's (35) criteria, the evidence appears to be fair, based on grading of good, fair, and poor in managing lumbar nerve root pain with transforaminal epidural injections.

2.0 Lumbar Epidural Adhesiolysis

Chou and Huffman (35) evaluated the efficacy of epidural steroid injections versus other interventions for adhesiolysis. The purpose of percutaneous epidural adhesiolysis is to minimize the deleterious effects of epidural scarring, which can physically prevent direct application of drugs to nerves and other spinal tissues; it is also used to treat chronic back pain (117,167-176). Epidural lysis of adhesions and direct deposition of corticosteroids in the spinal canal can also be achieved with a 3-dimensional view provided by epiduroscopy or spinal endoscopy (177-179).

Chou and Huffman (35) described adhesiolysis as a treatment modality for failed back surgery. They also included forceful epidural injections along with adhesiolysis with large volumes of sodium chloride solution, with or without a corticosteroid. In their search, they identified the systematic review by Trescot et al (170) which they considered as lower quality and they excluded an earlier version of this review (169). They also included one lower quality systematic review of endoscopic division of epidural adhesions (180). They identified 6 randomized trials (117,140,175,176,178,181).

Chou and Huffman (35) excluded one study (181) which was quasi-randomized; however, they stated that the authors of the systematic review (170) did not report quality ratings for included trials even though they were reported. Of the remaining studies, they rated one study as higher quality (117). The study by Manchikanti et al (117) compared adhesiolysis to caudal epidural steroid injection without adhesiolysis. They considered the study by Veihelmann et al (175) as a trial comparing adhesiolysis to a poorly defined physical therapy intervention. The third trial they considered was by Heavner et al (176) comparing different adhesiolysis methods.

Chou and Huffman (35) also identified Dashfield et al (140) as a higher-quality trial regarding the efficacy of targeted steroid placement using epidural endoscopy with adhesiolysis if adhesions were observed at the target nerve, versus caudal epidural steroid without endoscopy. They included this study even though it was performed on patients who had not undergone any other interventions; thus, percutaneous endoscopic adhesiolysis is meaningless as there are not expected to be any significant adhesions.

Chou and Huffman (35) were unable to identify a systematic review (76) and a double-blind randomized trial of spinal endoscopic adhesiolysis with one-year follow-up published in 2005 (177). Instead they utilized a preliminary report with 6-month follow-up published in 2003 (178).

Multiple systematic reviews and health technology assessments have evaluated the clinical effectiveness of percutaneous endoscopic adhesiolysis (58,66,69,167,169-171). Epter et al (66) concluded that the indicated level of evidence is I or II-1 for short- and long-term relief for percutaneous adhesiolysis in post

lumbar surgery syndrome. Hayek et al (69) concluded that the indicated evidence is II-1 or II-2 for short- and long-term relief with endoscopic adhesiolysis.

2.1 Literature Search

Our literature search yielded overall approximately 400 manuscripts. There were multiple systematic reviews (169-171), along with 7 randomized trials with 9 reports (117,140,172-178).

2.2 Methodologic Quality Assessment

2.2.1 Assessment of Randomized Trials

Nine randomized trials were identified for percutaneous and endoscopic adhesiolysis (117,140,172-178). Of these, 7 met inclusion criteria (117,140,173-177) after exclusion of duplicates and non-randomized studies.

Table 14 illustrates the quality ratings of randomized trials of percutaneous and endoscopic adhesiolysis

Table 14. *Quality ratings of randomized trials of percutaneous and endoscopic adhesiolysis studies.*

	Manchikanti et al 2005 (177)*		Manchikanti et al 2009 (173)*Δ		Manchikanti et al 2009 (174) *Δ		Heavner et al 1999 (176)*		Manchikanti et al 2004 (117)*		Veihelmann et al 2006 (175)*		Dashfield et al 2005 (140)*	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Randomization	Yes	NS	Yes	NS	Yes	NS	Yes	Don't know	Yes	Yes	Yes	No	Yes	Don't know
Concealed treatment allocation	Yes	NS	Yes	NS	Yes	NS	Yes	Don't know	Yes	Don't know	Yes	Don't know	Yes	Yes
Baseline group similarity	Yes	NS	Yes	NS	Yes	NS	Yes	Don't know	Yes	Yes	Yes	Don't know	Yes	Yes
Patient blinded	Yes	NS	Yes	NS	Yes	NS	Yes	Don't know	Yes	Yes	No	No	Yes	Yes
Care provider blinded	No	NS	No	NS	No	NS	No	Don't know	No	No	No	No	No	No
Outcome assessor blinded	No	NS	No	NS	No	NS	Yes	Don't know	Yes	Yes	No	Yes	Yes	Don't know
Cointerventions avoided or similar	Yes	NS	Yes	NS	Yes	NS	Yes	Don't know	Yes	Don't know	No	Don't know	No	Don't know
Compliance acceptable in all groups	Yes	NS	Yes	NS	Yes	NS	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Drop-out rate described and acceptable	Yes	NS	Yes	NS	Yes	NS	No	No	Yes	Yes	No	No	Yes	Yes
Timing of outcome assessment in all groups similar	Yes	NS	Yes	NS	Yes	NS	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Intention to treat analysis	Yes	NS	Yes	NS	Yes	NS	No	No	Yes	Yes	No	No	Yes	Yes
Score	9/11	NS	9/11	NS	9/11	NS	8/11	2/11	10/11	8/11	4/11	2/11	9/11	7/11

ΔNot available at the time of Chou's search
+Included in present review, but not Chou and Huffman (35)
*Included by Chou and Huffman (35) and present review
♦Included by Chou and Huffman (35), but not present review
NS = Not scored by APS-AAPM review
Manchikanti et al 2005 (177) was not rated by Chou and Huffman (35), instead they utilized a preliminary report

studies. We included all 7 studies due to inclusion by Chou and Huffman (35). Further, 2 studies were published after the search (173,174) by Chou and Huffman (35). We also used an article by Manchikanti et al (177) whose full results were published prior to the search. Our analysis of the quality ratings showed significant changes on Heavner et al's (176) publication from 2 of 11 to 8 of 11 and Veihelmann et al's (175) publication from 2 of 11 to 4 of 11. It also increased the score on one of the other publications (117); however, this was already rated as higher quality by Chou and Huffman (35).

2.2.2 Assessment of Systematic Reviews

Multiple systematic reviews have evaluated the effectiveness of adhesiolysis both percutaneous and endoscopic (66,69,76,169-171). Four of them (66,69,76,170) met inclusion criteria after exclusion of updates.

Of these, Chou and Huffman (35) utilized only one systematic review by Trescot et al (170). They missed one systematic review (76); 2 systematic reviews (66,69) were published after the search by Chou and Huffman (35). They mistakenly rated Trescot et al (170) giving it a score of 3 of 7; however, our analysis of their own numbers shows it should be 7 of 9, which is identical to our reassessment score. Similarly, for all other systematic reviews which either were not included (76) or were not published at the time of their publication, our score was 7 of 9.

The methodologic quality assessment of the criteria of systematic reviews of percutaneous and endoscopic adhesiolysis is illustrated in Table 15.

2.3 Effectiveness

Chou and Huffman (35) utilized only one appropriate study pertaining to adhesiolysis by Manchikanti et al (117), which was rated as higher quality, but was not considered of any value by them because of their inaccurate assumption that the caudal epidural group, which they considered as a placebo group, failed to respond according to their expectations. However, the manuscript illustrated significant pain relief (≥ 50%) in 33% of the patients in Group I with less than 3 months of relief. However, at 3 months and after, no significant relief was illustrated in the caudal epidural group. Further, they also included Dashfield et al (140) where spinal endoscopic adhesiolysis is not indicated. Essentially, Dashfield et al (140) is an excellent fluoroscopic caudal epidural injection study with positive results for caudal epidural injections.

Table 15. *Methodologic quality assessment of systematic reviews of percutaneous and endoscopic adhesiolysis.*

	Trescot et al 2007 (170)*		Manchikanti et al 2008 (76)§		Epter et al 2009 (66)Δ§		Hayek et al 2009 (69) Δ§	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Search Method	Yes	Yes	Yes	NS	Yes	NS	Yes	NS
Comprehensive	Yes	Yes	Yes	NS	Yes	NS	Yes	NS
Inclusion Criteria	Yes	Yes	Yes	NS	Yes	NS	Yes	NS
Bias Avoided	Yes	Yes	Yes	NS	Yes	NS	Yes	NS
Validity Criteria	Yes	Yes	Yes	NS	Yes	NS	Yes	NS
Validity Assessed	Yes	Partial	Yes	NS	Yes	NS	Yes	NS
Methods for Combining Studies	No	Yes	No	NS	No	NS	No	NS
Appropriately Combined	No	No	No	NS	No	NS	No	NS
Conclusions Supported	Yes	Partial	Yes	NS	Yes	NS	Yes	NS
Overall Quality	7/9	3/7	7/9	NS	7/9	NS	7/9	NS
Corrected Score	7/9	6/9	7/9	NS	7/9	NS	7/9	NS

ΔNot available at the time of Chou's search
§Included in present review, but not Chou and Huffman (35)
*Included by Chou and Huffman (35) and present review
+Included by Chou and Huffman (35), but not present review
NS = Not scored by APS-AAPM review

Table 16. *Results of published randomized trials of percutaneous lysis of lumbar epidural adhesions.*

Study	Study Characteristics	Methodological Quality Scoring		Participants	Pain Relief				Results	
		ASIPP	APS-AAPM		≤ 3 mos.	3 mos.	6 mos.	12 mos.	Short-term ≤ 6 mos.	Long-term > 6 mos.
Manchikanti et al 2004 (117)	RA, DB	10/11	8/11	G1 = 25 (C) G2 = 25 (T) G3 = 25 (T)	G1 = 33% G2 = 64% G2 = 72%	G1 = 0% G2 = 64% G3 = 72%	G1 = 0% G2 = 60% G3 = 72%	G1 = 0% G2 = 60% G3 = 72%	P	P
Heavner et al 1999 (176)	RA, DB	8/11	2/11	59	83%	49%	43%	49%	P	N
Veihelmann et al 2006 (175)	RA	4/11	2/11	99	SI	SI	SI	SI	P	P
Manchikanti et al 2009 (174)	RA, DB	9/11	NS	C = 60 T = 60	90% vs 35%	90% vs 35%	85% vs 18%	73% vs 12%	P	P
Manchikanti et al 2005 (177)	RA, DB	9/11	NS	C = 33 T = 50	80% vs 33%	80% vs 0%	56% vs 0%	48% vs 0%	P	N
Manchikanti et al 2009 (173)	RA, DB	9/11	NS	C = 25 T = 25	80% vs 28%	80% vs 28%	80% vs 12%	76% vs 4%	P	P

RA = randomized; DB = double blind; NS = not scored by APS-AAPM review; G = group; C = control; T = treatment; vs = versus; SI = significant improvement; P = positive; N = negative

The results of published studies of the effectiveness of percutaneous endoscopic lysis of lumbar epidural adhesions is illustrated in Table 16, with exclusion of, Dashfield et al (140). Thus, it appears that there is significant evidence for percutaneous epidural adhesiolysis even though for spinal endoscopic adhesiolysis it is based on only one study (177). It should be noted that 2 systematic reviews (66,69) and 2 randomized double-blind trials of percutaneous adhesiolysis (173,174) were published after the search criteria. However, Chou and Huffman (35) did not include one additional systematic review (76). Even then, based on Chou and Huffman's (35) grading of good, fair, and poor and the analysis of the included studies, it appears that there is at least fair evidence for percutaneous lumbar epidural adhesiolysis for short-term and long-term relief, whereas it may be considered poor for long-term improvement with spinal endoscopic adhesiolysis, and fair for short-term improvement of 6 months. However, with inclusion of more recent studies (173,174) and systematic reviews (66,76) the evidence is good for percutaneous adhesiolysis.

3.0 Facet Joint Injection, Therapeutic Medial Branch Block, and Radiofrequency Neurolysis

Chou and Huffman (35) described facet joint injection and medial branch blocks as one category, whereas they described radiofrequency denervation in another category along with intradiscal electrothermal therapy and related procedures. However, for this analysis we combined all lumbar facet joint interventions.

Facet joint pain can be managed by intraarticular injections, facet joint nerve blocks, and neurolysis of facet joint nerves. However, conflicting results have been reported for the value of the different treatment modalities in systematic reviews (54,76,92,161,182-186). In multiple systematic reviews (54,76,185), therapeutic facet joint interventions were shown to have limited to no evidence for lumbar intraarticular facet joint injections. Geurts et al (184) concluded that there was moderate evidence that radiofrequency lumbar facet denervation was more effective for chronic low back pain than placebo. However, Geurts et al (184) included both

medial branch neurotomy and intraarticular neurotomy in their evaluation, along with dorsal root denervation. Manchikanti et al (182) evaluated medial branch neurotomy for the management of chronic spinal pain utilizing randomized and observational reports, and concluded that there was strong evidence for short-term relief and moderate evidence for long-term relief of facet joint pain.

Chou and Huffman (35) utilized 15 randomized trials evaluating intraarticular facet joint injections, medial branch blocks, and radiofrequency neurotomy (187-201) with multiple placebo-controlled trials (189,190,191,196-201), and one study published as 2 reports (190,191). They also illustrated that 7 of the studies were included in at least one of 4 systematic reviews (92,97,185,202). They concluded that there was no evidence for the efficacy of facet joint injections or medial branch blocks of acute low back pain, no evidence for the efficacy of medial branch block versus placebo injection for chronic low back pain, no evidence for presumed chronic facet joint pain with facet joint injection and medial branch block with or without steroid for presumed facet joint pain; for presumed lumbar segmental rigidity, and any type of pain. For radiofrequency denervation, Chou and Huffman (35) concluded that the evidence was difficult to interpret. They also described that interpretation of the results was controversial because some trials used uncontrolled facet joint blocks to select patients and the radiofrequency denervation technique might have been suboptimal in some of the trials, leading to their conclusion that the level of evidence was poor.

3.1 Literature Search

The present literature search yielded over 1,400 manuscripts. This comprehensive literature search included lumbar intraarticular facet joint injections, lumbar facet joint nerve blocks, and lumbar facet joint radiofrequency neurotomy, with multiple manuscripts considered for inclusion (54,76,92,161,181-206).

3.2 Methodologic Quality Assessment

All 3 types of facet joint interventions were included in this review: intraarticular facet joint injections, facet joint nerve blocks, and medial branch radiofrequency neurotomy. Datta et al (54) established the criteria that studies must have provided appropriate management with outcome evaluations of at least 6 months and appropriate statistical analysis. Studies should also have met diagnostic criteria with controlled (placebo or dual diagnostic blocks) with at least 80% relief. Reports without appropriate diagnosis and elimination of false-positive responses were excluded in their analysis (54) as per the inclusion criteria. Even then, if studies were included by Chou and Huffman (35), they were also included for the analysis purposes herewith.

3.2.1 Assessment of Randomized Trials

Of the 5 randomized trials identified evaluating the effectiveness of lumbar intraarticular facet joint injections (189,190,191,194,195), all of them failed to meet inclusion criteria for methodologic quality assessment due to the lack of controlled diagnostic blocks by Datta et al (54). However, Chou and Huffman (35) utilized Carette et al (189), Lilius et al (190,191), Fuchs et al (192), Mayer et al (188), and Nash (195) in their analysis. Thus, these were included in the methodologic quality assessment of the criteria even though they did not meet the established criteria by others (54). The importance of strict inclusion criteria has been emphasized (207-210).

There were 4 studies published in 6 reports evaluating therapeutic lumbar facet joint nerve blocks (187,193-195,203,204). Two studies (194,195) only reported short-term evaluation without diagnostic blocks. Two studies (187,203) were a preliminary report and a one-year report of the 2-year follow-up (204). The 2-year report was published in 2010 (204). Consequently, 2 studies met inclusion criteria (193,203). However, Chou and Huffman (35) included Nash (195), which was excluded by all other studies. Consequently, this study was considered in the methodological quality assessment.

There were 7 studies evaluating radiofrequency neurotomy of lumbar facet joint nerves (196-201,206). Of these, only one study met the inclusion criteria (196) by Datta et al (54). van Wijk et al (198), Leclaire et al (201), Gallagher et al (197), van Kleef et al (199), and Tekin et al (200) failed to meet inclusion criteria, due to a lack of controlled diagnostic blocks. Samders and Zuurmond (206) failed to meet the inclusion criteria of Datta et al (54) since it evaluated intraarticular facet joint denervation, which is not medial branch neurotomy, without appropriate diagnostic criteria. However, Chou and Huffman (35) included Gallagher et al (197), Leclaire et al (201), Tekin et al (200), and van Kleef et al (199) for evidence consideration, along with Nath et al (196). Thus, all these were included in the methodologic quality assessment of the criteria.

Table 17 illustrates the methodologic quality assessment of randomized clinical trials evaluating the role of facet joint interventions.

Table 17. *Methodological quality assessment of randomized clinical trials of therapeutic lumbar facet joint interventions.*

	Manchikanti et al 2001 (193)*		Manchikanti et al 2008, 2010 (187,203✚,204§)		Carette et al 1991 (189)Δ		Fuchs et al 2005 (192)Δ		Lilius et al 1989,1989 (190,191)Δ		Nash 1989 (195)Δ	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Randomization	Yes	No	Yes	NS	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Concealed treatment allocation	Yes	No	Yes	NS	Yes	Don't know	No	Don't know	No	Don't know	No	No
Baseline group similarity	Yes	No	Yes	NS	Yes	Yes	Yes	Yes	Yes	No	No	Don't know
Patient blinded	Yes	No	Yes	NS	Yes	Yes	Yes	No	Can't tell	Yes	No	No
Care provider blinded	No	No	Yes	NS	Yes	Yes	No	No	No	Yes	No	No
Outcome assessor blinded	No	No	No	NS	Yes	Don't know	Yes	Yes	Can't tell	Yes	No	Don't know
Cointerventions avoided or similar	Yes	Don't know	Yes	NS	No	No	No	Don't know	Yes	Don't know	No	Don't know
Compliance acceptable in all groups	Yes	Yes	Yes	NS	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drop-out rate described and acceptable	Yes	Yes	Yes	NS	Yes	Yes	No	No	Yes	Yes	No	No
Timing of outcome assessment in all groups similar	Yes	No	Yes	NS	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Intention to treat analysis	No	Yes	Yes	NS	Yes	Yes	Yes	Yes	No	Yes	No	No
Score	8/11	3/11	10/11	NS	10/11	7/11	7/11	6/11	6/11	8/11	2/11	2/11
Corrected Score	8/11	3/11	10/11	NS	10/11	8/11	7/11	6/11	6/11	8/11	2/11	2/11

*Included by Chou and Huffman (35) and Datta et al (54)
✚Included by Datta et al (54), but not Chou and Huffman (35)
ΔIncluded by Chou and Huffman (35), but not Datta et al (54)
§Included in present review, but not Chou and Huffman (35)
NS = Not scored by APS-AAPM review

The 2 placebo controlled trials identified by Chou and Huffman (35), namely, Carette et al (189) and Lilius et al (190,191) were also classified as high quality by Staal et al (92,161). Lilius et al (190,191) utilized a broad selection criteria without diagnosis by controlled blocks and also utilized inordinately high volumes of solutions in blocking these structures. Carette et al (189), while utilizing only a single block for diagnosis, also injected sodium chloride solution into the joint. However, multiple interactions and clinical effects have been illustrated with the injection of either sodium chloride solution or lidocaine into the lumbar facet joint (211,212). They also utilized Mayer et al (188) in their conclusions even though quality assessment criteria was not employed, which was considered as flawed comparing facet joint injections in relation to segmental rigidity, with no relevance in managing chronic facet joint pain. Thus, even though we do agree that intraarticular facet joint injections are not effective, the methodological issues raise questions regarding the guidelines' preparation.

With reference to lumbar facet joint nerve blocks, our search strategy yielded 2 randomized trials of facet joint nerve blocks published in 4 reports (187,193,203,204) meeting the methodologic assessment of criteria (54). However, Chou and Huffman (35) concluded that there was no trial evaluating the efficacy of therapeutic medial branch blocks versus sham or placebo injection. They also included 2 trials which evaluated the short-term relief of medial branch blocks (194,195), but rated one of them (195) as low quality.

Table 17 (cont.) . *Methodological quality assessment of randomized clinical trials of therapeutic lumbar facet joint interventions.*

	Gallagher et al 1994 (197)Δ		Leclaire et al 2001 (201)Δ		Nath et al 2008 (196)✚		Tekin et al 2007 (200)Δ		van Kleef et al 1999 (199)Δ		Mayer et al 2004 (188)Δ		van Wijk et al 2005 (198)*	
	Yes	NS	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Randomization	No	NS	Yes	Don't know	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NS	Yes	Yes
Concealed treatment allocation	No	NS	Yes	Yes	Yes	Don't know	Don't know	Don't know	Yes	Don't know	No	NS	Yes	Yes
Baseline group similarity	No	NS	Yes	Yes	Yes	No	Yes	Yes	Yes	Don't know	No	NS	Yes	Yes
Patient blinded	No	NS	Yes	Yes	Yes	Yes	Yes	Don't know	Yes	Yes	No	NS	Yes	Yes
Care provider blinded	No	NS	Don't know	Don't know	Yes	Yes	Yes	Don't know	Yes	Yes	No	NS	Yes	Yes
Outcome assessor blinded	Yes	NS	Yes	Yes	Yes	Yes	No	Don't know	Yes	Yes	No	NS	Yes	Yes
Cointerventions avoided or similar	Yes	NS	Yes	Yes	No	Don't know	No	Don't know	Yes	Yes	Yes	NS	Yes	Yes
Compliance acceptable in all groups	Yes	NS	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NS	Yes	Yes
Drop-out rate described and acceptable	Yes	NS	Yes	Yes	Yes	Yes	No	No	No	No	Yes	NS	Yes	Yes
Timing of outcome assessment in all groups similar	No	NS	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NS	Yes	Yes
Intention to treat analysis	5/11	NS	Yes	Yes	Yes	Yes	No	Yes	No	Don't know	No	NS	Yes	Yes
Score	5/11	NS	10/11	9/11	10/11	8/11	6/11	5/11	9/11	7/11	5/11	NS	11/11	11/11
Corrected Score	4/11	NS	10/11	9/11	10/11	8/11	6/11	5/11	9/11	7/11	5/11	NS	11/11	11/11

*Included by Chou and Huffman (35) and Datta et al (54)
✚Included by Datta et al (54), but not Chou and Huffman (35)
ΔIncluded by Chou and Huffman (35), but not Datta et al (54)
§Included in present review, but not Chou and Huffman (35)
NS = Not scored by APS-AAPM review

Neither of them were relevant to chronic low back pain management. Both studies compared facet joint nerve blocks and intraarticular injections with high volume injections with very short-term follow-up. Both the studies by Manchikanti et al (187,193,203,204) were shown to be of high quality even though one study with 2 reports (187,203) was not included in the analysis by Chou and Huffman (35), despite its publication prior to the search.

Among the studies evaluating radiofrequency neurotomy, only one study by Nath et al (196) was ideal and met the inclusion criteria by other evaluators (54). However, Chou et al (35,37) found multiple deficiencies with this study which was previously considered one of the best studies in the literature except for lack of long-term follow-up (54,213). Chou et al (35,37,41) misinterpreted Nath et al's (196) data. Chou and Huffman (35) reported the final scores in both groups were identical and there was no change in low back pain; however, Nath et al (196) showed clear and distinct differences between both groups in all aspects. The active treatment group showed statistically significant improvement, not only in back and leg pain, but also back and hip movement as well as sacroiliac joint pain. There was also significant improvement in quality of life variables, global perception of improvement, and generalized pain in the active treatment group. Further, Chou and Huffman (35) utilized conflicting numbers in the study at different places in their document, either 40 or 60, with the actual number being 40.

Chou and Huffman (35) included multiple inappropriate studies. Gallagher et al (197) randomly assigned 41 patients based on their response to diagnostic intraarticular blocks (equivocal or good response) to either sham or true denervation. A statistically significant difference in outcome was observed at one month only between sham and true radiofrequency denervation in those patients who obtained a definitive response to diagnostic blocks. This difference persisted for the duration of the 6 month follow-up.

van Kleef et al (199) assessed 15 patients in the radiofrequency treatment group with an 80° radiofrequency lesion of the dorsal ramus of the segmental nerve roots L3, L4, and L5, and 16 patients in the control group undergoing the same procedure without use of radiofrequency current. The authors (199) concluded that radiofrequency denervation results in significant short-term and long-term alleviation of pain and functional disability in a select group of patients with chronic low back pain. This study did not utilize controlled local anesthetic blocks, and used 50% relief as the criterion standard with a single block. Even so, the results were significantly better in the treatment group compared to placebo group (54,207-210).

Leclaire et al (201) randomly assigned patients to receive either RFA under fluoroscopic guidance (n = 36) or the same procedure without denervation (sham procedure) (n = 34). The authors concluded that, although RFA might provide short-term improvement in functional disability, the efficacy of the treatment has not been established. This study (201) used diagnostic nerve blocks to identify affected locations. The Leclaire study invited criticism because it failed to define the study population and had inappropriate diagnostic criteria (use of intraarticular injections to identify patients for radiofrequency neurotomy). Patients were evaluated with a single diagnostic block with 50% pain relief as the criterion standard. They considered any relief of one day duration during a 7-day period following a single diagnostic intraarticular injection as significant. Such an effect could be the result of many factors, including natural sequence. Thus, any results or conclusions based on this study would be erroneous. Interestingly, Gauci (214) requested from the authors of the study (201) an explanation on precisely what medical assessment groups should interpret from the study's results. Leclaire et al (215) responded, essentially agreeing to all the disadvantages described above stating that, "if we repeated our study today, we would use controlled medial branch blocks as the primary inclusion criteria to correctly identify patients with pain originating from the lumbar zygapophysial joint."

van Wijk et al (198) randomized 40 patients to radiofrequency or a sham treatment (n = 41). There was no difference between the 2 groups in the combined outcome measure or visual analogue score (VAS), although both groups showed improvement in VAS scores. The global perceived effect, however, improved in the radiofrequency group. The researchers observed that there was a lack of improvement in physical function despite reduction in pain scores. The authors concluded that in selected patients, radiofrequency facet denervation appears to be more effective than sham treatment. However, the van Wijk article was excluded from the review because of several weaknesses. The van Wijk study failed to utilize controlled diagnostic blocks and reasonable pain relief criteria. The study (198) has also been criticized for multiple deficiencies (216,217).

Surprisingly enough, van Wijk (218) in a follow-up study of 2 randomized trials evaluating psychological predictors of substantial pain reduction after minimally invasive radiofrequency and injection treatments for chronic low back pain, reached opposite conclusions, even though the data were the same. They concluded that minimally invasive treatment for chronic low back pain leads to significant pain reduction, including potential placebo effects.

Chou and Huffman (35) inappropriately excluded the study by Manchikanti et al (187,203). Manchikanti et al (203) in a randomized, double blind, controlled trial included 60 patients in Group I with local anesthetic and 60 patients in Group II with local anesthetic and steroid. The inclusion criteria were based on a positive response to diagnostic controlled comparative local anesthetic lumbar facet joint blocks. Outcome measures included numeric pain scores, Oswestry Disability Index (ODI), opioid intake, and work status. All outcome assessments were performed at baseline, 3 months, 6 months, and 12 months. The results showed significant improvement with significant pain relief (≥ 50%) and functional improvement (≥ 40%) observed in 82% in Group I, and 85% in Group II. Based on the results of the present study, it appears that patients might experience significant pain relief 44 to 45 weeks of one year, requiring approximately 3 to 4 treatments with an average relief of 15 weeks per episode of treatment. While limitations of this study include a lack of placebo control, the study included an active control in a randomized controlled trial, and the study met all the criteria with 60 patients in each group with

appropriate outcome measurements. The 2-year follow-up results which were also published (204) have illustrated the sustainability of the results with significant improvement observed in 85% of the patients in Group I and 90% in Group II over a 2-year period with 5 to 6 treatments with an average relief of 19 weeks per episode of treatment, and significant pain relief being experienced by patients from 82 to 84 weeks out of 104 weeks. This is the longest follow-up study of a controlled, randomized, double blind trial for therapeutic facet joint nerve blocks using strict selection criteria.

3.2.2 Assessment of Systematic Reviews

Multiple systematic reviews were found in the literature search. Of these, the updated review by Datta et al (54) was considered as high quality for this evaluation. However, Datta et al (54) was published after Chou and Huffman's (35) search ended. Also, Manchikanti et al (76) was not utilized by Chou and Huffman (35). They did, however, utilize multiple systematic reviews (54,76, 92,97,161,185,186,202); but many of them had major deficiencies (Table 18).

Among the systematic reviews evaluating intraarticular injections, Staal et al (92,161) utilized 6

Table 18. *Quality ratings of systematic reviews evaluating lumbar facet joint interventions.*

	Boswell et al 2007 (185)♦		Geurts et al 2001 (184)♦		Niemisto et al 2003 (186)♦		Resnick et al 2005 (97)♦	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Search Method	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Yes
Comprehensive	Yes	Yes	Yes	Yes	Yes	Yes	No	Partial
Inclusion Criteria	Yes	Yes	Yes	Yes	Yes	Yes	No	Partial
Bias Avoided	Yes	Can't tell	Can't tell	Yes	Yes	Yes	No	Can't tell
Validity Criteria	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Validity Assessed	Yes	Partial	Yes	Yes	Yes	Yes	No	No
Methods for Combining Studies	No	Yes	Yes	Yes	Yes	Yes	No	Partial
Appropriately Combined	No	No	No	Yes	Yes	Yes	No	Can't tell
Conclusions Supported	Yes	No	No	Yes	Yes	Yes	No	Can't tell
Overall Quality	7/9	3/7	5/9	7/7	9/9	7/7	1/9	2/7
Corrected Score	7/9	5/9	5/9	9/9	9/9	9/9	1/9	2/9

	Slipman et al 2003 (202)♦		Datta et al 2009 (54) Δ§		Manchikanti et al 2008 (76)§		Staal et al 2008, 2009 (92♦,161Δ§)	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Search Method	No	Partial	Yes	NS	Yes	NS	Yes	Yes
Comprehensive	No	Partial	Yes	NS	Yes	NS	Yes	Yes
Inclusion Criteria	Yes	Yes	Yes	NS	Yes	NS	Yes	Yes
Bias Avoided	No	Can't tell	Yes	NS	Yes	NS	Yes	Yes
Validity Criteria	No	No	Yes	NS	Yes	NS	Yes	Yes
Validity Assessed	No	Partial	Yes	NS	Yes	NS	Yes	Yes
Methods for Combining Studies	No	Partial	No	NS	No	NS	Yes	Yes
Appropriately Combined	No	Can't tell	No	NS	No	NS	No	Yes
Conclusions Supported	No	Can't tell	Yes	NS	Yes	NS	No	Yes
Overall Quality	1/9	3/7	7/9	NS	7/9	NS	7/9	7/7

ΔNot available at the time of Chou's search

♦Included by Chou and Huffman (35), but not present review
§Included in present review, but not Chou and Huffman (35)
NS = Not scored by APS-AAPM review

weeks of pain relief as short-term and longer than 6 weeks as long-term, whereas Datta et al (54) utilized 80% pain relief with controlled diagnostic blocks as the inclusion criteria. However, Staal et al had no inclusion criteria based on the diagnostic validity. Boswell et al (185) utilized controlled diagnostic blocks as inclusion criteria; however, they included studies with single diagnostic blocks or no diagnostic blocks due to the paucity of the literature.

Lumbar facet joint nerve blocks were also evaluated by Staal et al (92,161), Manchikanti et al (76), Datta et al (54), and Boswell et al (185). The inclusion criteria and outcome criteria were similar to intraarticular injections. Datta et al (54) showed strong evidence for lumbar facet joint nerve blocks. Boswell et al (185) showed moderate evidence; however, Staal et al (92,161), including only one study by Manchikanti et al (193), concluded that there was no difference. Manchikanti et al (76) showed moderate evidence.

In reference to radiofrequency neurotomy, Geurts et al (184), which was considered by Chou and Huffman (35) to be high quality, scored lower in our reassessment—from 9 of 9 to 5 of 9. They concluded that there was moderate evidence that radiofrequency lumbar facet denervation was more effective for chronic low back pain than placebo. Niemisto et al (186), performed within the framework of the Cochrane Collaboration Back Review Group, was scored high by both evaluations; they concluded that there was conflicting evidence that radiofrequency denervation had a short-term effect on chronic low back pain. Slipman et al (202), a low quality systematic review, concluded that the evidence for radiofrequency denervation was moderate. Boswell et al (185) showed moderate to strong evidence for radiofrequency neurotomy. Manchikanti et al (76) showed moderate evidence.

3.2.3 Effectiveness

The reassessment of APS guidelines has shown results similar to that of Datta et al (54). As illustrated in Table 19, the evidence was negative in 2 of the 3 trials for short-term, whereas, long-term evidence assessment was not available in any of the studies. For medial branch blocks with study which was not included by Chou and Huffman (187,203,204) even though results were available at the time of the search criteria, and showed positive results both for short-term and long-term relief, whereas another study (193) which was rated as low quality by Chou and Huffman (35) showed positive results on a short-term basis and long-term results were not available. Nash et al (195) had no available data. For radiofrequency neurotomy 4 of the 5 studies were positive for short-term relief whereas for long-term relief 1 of the 2 studies was shown to be positive.

The evidence for intraarticular injections is in agreement with Chou and Huffman. However, the evidence is significantly different from that of Chou et al (35,37,41) based on their own criteria of grading with good, fair, and poor, for lumbar facet joint nerve blocks and radiofrequency neurotomy - fair.

Chou et al (35,37,41) also utilized outdated AHCPR guidelines (34) which have been removed from active practice in the United States.

4.0 Therapeutic Sacroiliac Joint Interventions

Chou and Huffman (35) reported lack of evidence for sacroiliac joint steroid injections; however, they have not reviewed the evidence for radiofrequency neurotomy.

Rupert et al (68) reviewed the evidence for therapeutic sacroiliac joint interventions and judged it to be limited. Since there have not been any new studies and the evidence will not improve based on reassessment, we have not performed a reassessment of the evidence for therapeutic sacroiliac joint interventions. Rupert et al (68) concluded moderate evidence for diagnostic sacroiliac joint injections.

5.0 Intradiscal Electrothermal Therapy

Even though there are discrepancies in the evidence synthesis and analysis, along with recommendations, the evidence synthesis by ASIPP guidelines also has been scored at Level II-2 with a weak recommendation. Therefore, no reassessment analysis or discussion is provided in this manuscript.

6.0 Intrathecal Therapy

Chou and Huffman (35) concluded that in patients with failed back surgery syndrome (FBSS), there is insufficient evidence to judge the efficacy of intrathecal opioid therapy. Patel et al (67) performed a systematic review and were unable to find any randomized trials for consideration in the evidence synthesis. Since there have not been any new publications, no further analysis or discussion is provided in this manuscript.

Table 19. *Results of published randomized trials of facet joint interventions.*

Study	Study Characteristics	Methodological Quality Scoring		Participants	Pain Relief				Results	
		ASIPP	APS-AAPM		≤ 3 mos.	3 mos.	6 mos.	12 mos.	Short-term ≤ 6 mos.	Long-term > 6 mos.
INTRAARTICULAR INJECTIONS										
Carette et al 1991 (189)	RA, DB	10/11	8/11	Saline = 48 Steroid = 49	33% versus 42%	NA	15% versus 42%	NA	N	NA
Lilius et al 1989 (190,191)	RA	6/11	8/11	Intraarticular saline (8 mL) = 42 Intraarticular steroid (8 mL) = 28 Pericapsular steroid (8 mL) = 39	NA	NA	NA	NA	NA	NA
Fuchs et al 2005 (192)	RA, DB	7/11	6/11	SH = 30 TA = 30	SI	SI	SI	NA	P	NA
Nash 1989 (195)	RA, SB	2/11	2/11	N = 66	NA	NA	NA	NA	NA	NA
MEDIAL BRANCH BLOCKS										
Manchikanti et al 2001 (193)	RA	8/11	3/11	Group I non-steroid = 32 Group II steroid = 41	100%	75% versus 88%	75% versus 88%	NA	P	NA
Manchikanti et al 2008, 2010 (203,204)	RA, DB	10/11	NS	Group I – no steroid = 60 Group II – steroid = 60	NA	83% vs 82%	83% vs 93%	82% vs 85%	P	P
Nash 1989 (195)	RA, SB	2/11	2/11	N = 66	NA	NA	NA	NA	NA	NA
RADIOFREQUENCY NEUROTOMY										
Nath et al 2008 (196)	RA, DB	10/11	8/11	C = 20 * T = 20	NA	SI	SI	NA	P	NA
van Wijk et al 2005 (198)	RA, DB	11/11	11/11	C = 41 * T = 40	NA	39% versus 62%	NA	NA	P	NA
van Kleef et al 1999 (199)	RA, DB	9/11	7/11	C = 16 * T = 15	NA	25% vs 60%	19% vs 47%	13% vs 47%	P	N
Gallagher et al 1994 (197)	RA, DB	4/11	3/11	C = 12 * T = 18	SI = T	SI = T	SI = T	NA	P	NA
Leclaire et al 2001 (201)	RA, DB	10/11	9/11	C = 34 * T = 36	NSI	NSI	NA	NA	NA	NA
Tekin et al 2007 (200)	RA, DB	6/11	5/11	C = 20 * PRF = 20 CRF = 20	SI in all groups	SI in all groups	SI in all groups	SI in CRF only	P	P

* = control included bupivacaine; RA = randomized; DB = double blind; NS = not scored by APS-AAPM review; C = control; T = treatment; vs = versus; SI = significant improvement; NSI = no significant improvement; P = positive; SH = sodium hyaluronate; TA = triamcinolone acetonide; NA = not available; SB = single blind; PRF = pulsed radiofrequency; CRF = conventional radiofrequency

7.0 Spinal Cord Stimulation

Chou and Huffman (35) evaluated spinal cord stimulation and concluded that there was fair evidence for its effectiveness in FBSS. Spinal cord stimulation is primarily implanted in the United States for FBSS and complex regional pain syndrome (CRPS) (65,76,219-224).

It is important to note that NICE in its 2008 technology appraisal (225) recommended spinal cord stimulation for FBSS unequivocally.

7.1 Literature Search

Our literature search showed approximately 300 manuscripts with multiple systematic reviews and randomized trials evaluating the effectiveness of spinal cord stimulation in chronic pain (65,76,219-224,226-238).

7.2 Methodologic Quality Assessment

7.2.1 Assessment of Randomized Trials

Of 6 individual articles, 2 studies in 3 publications met the inclusion criteria for methodologic assessment (232,236,237). Among the other studies, one was a comparison of spinal cord stimulation electrode design (234); the second (238) was a study of spinal cord stimulation for axial low back pain, comparing dual with single percutaneous electrodes.

Table 20 shows the methodologic quality assessment of criteria for evaluating spinal cord stimulation in post lumbar surgery syndrome and the 2 randomized trials meeting the inclusion criteria by Chou and Huffman (35)

7.2.2 Assessment of Systematic Reviews

Multiple systematic reviews were identified (65,76,219-224,226-228); however, Frey et al (65) was published after the search was completed. Manchikanti et al (76) was published prior to the search; however, this study was not included in the evidence assessment. Table 21 illustrates the methodologic quality assessment of criteria of systematic reviews evaluating spinal cord stimulation.

Systematic reviews have been published evaluating the cost-effectiveness of spinal cord stimulation for FBSS (227,228). Taylor et al (227) found that initial health care acquisition costs were offset by a reduction in post implant health care resource demands and costs. Mean 5-year costs for FBSS were $29,123 in the intervention group compared to $38,029 in the control. Other investigators also showed similar findings illustrating the cost-effectiveness of spinal cord stimulation, even though initial health care acquisition costs are higher than other treatments (228-231).

Table 20. *Methodological assessment of randomized clinical trials evaluating spinal cord stimulation in post lumbar surgery syndrome.*

	Kumar et al 2008, 2007 (232*,237#)		North et al 2005 (236)*	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Randomization	Yes	Yes	Yes	Yes
Concealed treatment allocation	Yes	Yes	Yes	Yes
Baseline group similarity	Yes	Yes	Yes	Don't know
Patient blinded	No	NA	No	NA
Care provider blinded	No	NA	No	NA
Outcome assessor blinded	No	Don't know	No	No
Cointerventions avoided or similar	Yes	Yes	Yes	Yes
Compliance acceptable in all groups	Yes	No	Yes	Yes
Drop-out rate described and acceptable	Yes	Yes	Yes	Yes
Timing of outcome assessment in all groups similar	Yes	Yes	Yes	Yes
Intention to treat analysis	Yes	No	Yes	No
Score	8/9	6/9	8/9	6/9

*included by Chou and Huffman (35) and Frey et al (65)
#included in present review, but not Chou and Huffman (35)
NA = not applicable

Table 21. *Quality ratings of systematic reviews evaluating spinal cord stimulation.*

	Mailis-Gagnon et al 2004 (222)♦		Taylor et al 2005, 2006 (220,225) ♦		Turner et al 2004 (221) ♦		Manchikanti et al 2008 (76)§		Frey et al 2009 (65) ♦§	
	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM	ASIPP	APS-AAPM
Search Method	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NS	Yes	NS
Comprehensive	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NS	Yes	NS
Inclusion Criteria	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NS	Yes	NS
Bias Avoided	Yes	Yes	Yes	Can't tell	Yes	Can't tell	Yes	NS	Yes	NS
Validity Criteria	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NS	Yes	NS
Validity Assessed	Yes	Yes	Yes	Yes	Yes	Partial	Yes	NS	Yes	NS
Methods for Combining Studies	Yes	Yes	Yes	Yes	Yes	Yes	No	NS	No	NS
Appropriately Combined	Yes	Yes	Yes	Yes	Yes	Yes	No	NS	No	NS
Conclusions Supported	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NS	Yes	NS
Overall Quality	9/9	7/7	9/9	5/7	9/9	5/7	7/9	NS	7/9	NS
Corrected Score	9/9	9/9	9/9	8/9	9/9	7/9	7/9	NS	7/9	NS

♦Included by Chou and Huffman (35), but not present review
ΔNot available at the time of Chou's search
§Included in present review, but not by Chou and Huffman (35)
NS = Not scored by APS-AAPM review

7.2.3 Effectiveness

Similar to the assessment by Chou and Huffman (35), based on grading of evidence of good, fair, and poor, there appears to be fair evidence for spinal cord stimulation in post lumbar surgery syndrome.

8.0 Integrity

The goals of integrity include transparency, accountability, consistency, and independence. None of these criteria appear to have been adequately achieved in the evaluation of Chou and Huffman (35). Reasons for this failure to uniformly meet the goals of integrity may be because of a lack of clear information and a possible conflict of interest.

8.1 Transparency

The Chou and Huffman (35) guidelines were published in May 2009, but were submitted in October 2008 by a multidisciplinary panel of 23 experts convened in 2004 to formulate low back pain recommendations. It appears that the research was performed at Oregon Evidence-Based Practice Center – an organization sponsored by AHRQ, the employer of Chou and Huffman (35). Further, it shows that the activity was supported by the APS. However, no other disclaimers are provided as to the nature of the financial support from government, as well as from APS to all or some authors. In 2007, they also recruited 2 or 3 additional experts in the areas of interventional therapy or surgery to participate in the development of the recommendations. Some of the authors withdrew their names; however, no such disclosure was provided. Of the final 13 authors, there appears to be only 2 interventional pain physicians.

The major investigators appear to be Chou and Huffman. While Chou is an internal medicine physician without clinical practice experience in interventional techniques, Huffman is a social worker. Based on public records, it appears that she left the Oregon Effectiveness Healthcare program in 2007. Even then, the research extended into 2008 and manuscripts were not published until 2009.

In a press release regarding the APS guidelines, the guidelines were stated to be from the American Pain Society and the American College of Physicians. However, no such reference was ever made in future articles of interventional techniques. Finally, each and every table in Chou and Huffman's document (35) shows them as the analysis of APS-AAPM.

Consequently, the results of background investigation illustrate that transparency was lacking in multiple areas.

8.2 Accountability

Accountability has not been provided appropriately: their conflict of interest policies, their process for prioritization of the literature, their peer review of evidence synthesis, and their recommendations and updating of the recommendations consistent with the current literature were not appropriately utilized.

8.3 Consistency

There is evidence of seemingly inconsistent review of the literature and an inexplicable use of inclusion and exclusion criteria rather than a standardized approach.

8.4 Independence

Finally, independence was compromised because at least 2 of the initial experts in interventional techniques withdrew their names from publication due to serious misgivings; this was not publicized.

Discussion

This critical reassessment reviewed APS guidelines for therapeutic interventional techniques developed by Chou and Huffman (35), published as multiple manuscripts (35,37,41). In this critical analysis and reassessment, the same principles described by Chou and Huffman (35) were utilized. The results of this critical assessment agreed with the conclusions of APS guidelines and their assessment with fair evidence for spinal cord stimulation and post lumbar surgery syndrome and poor evidence for lumbar intraarticular facet joint injections, lumbar interlaminar epidural injections, sacroiliac joint injections, intradiscal electrothermal therapy, caudal epidural injections for pain without disc herniation, spinal endoscopic adhesiolysis, and intrathecal therapy. However, the reevaluation provided different results for multiple techniques. Based on this re-evaluation, utilizing the very criteria described by Chou and Huffman (35), with grading of good, fair, or poor the evidence was fair for lumbar therapeutic facet joint nerve blocks, caudal epidural injections in managing chronic low back pain of disc herniation, percutaneous adhesiolysis in post lumbar surgery syndrome; lumbar radiofrequency neurotomy, and transforaminal epidurals in radicular pain. However, the addition of new evidence will change the evidence to good from fair for caudal epidural injections in disc herniation, and adhesiolysis, and fair from poor for caudal epidural in other conditions.

Chou and Huffman (35) exhibited multiple deficiencies due to inappropriate evaluation in multiple areas, inclusion of inappropriate studies, and exclusion of appropriate studies. Further, they also utilized multiple outdated guidelines, applied inappropriate evidence assessment criteria, used a methodologic quality assessment without weighted values, had inadequate conflict management, and their conclusions have minimal value for clinical aspects and patient values.

There were differences in rating strengths for multiple therapeutic interventional techniques utilizing the most recent literature from the evaluations performed during the ASIPP guideline preparation process. Discrepancies and deficiencies in the process of guidelines development must be challenged and corrected as they can deny patient access to effective, appropriate, and vital pain relief. For methodologists it may appear to be appropriate, but for clinicians and patients who are suffering with pain, accurate determination of the evidence is essential.

ASA updated practice guidelines for chronic pain management (44) provided significant evidence and strong recommendation for multiple interventional techniques including epidural injections, medial branch or facet joint nerve blocks and spinal cord stimulation.

1.0 Misinterpretation of Randomized Trials and Inordinate Focus on Placebo-Control

The authors (35,37,41) focused extensively on placebo controls. However, injecting high doses of sodium chloride solution into a closed space or over a nerve is not a true placebo. A true placebo can only be administered by injecting the solution, which is the same amount as the active solution, in an area which is away from the epidural space or nerve root. There is general confusion regarding placebo control for almost all therapeutic trials. Further, placebo-controlled neural blockades are not viable, even though they continue to be misinterpreted (211,212,239-245). It is a common practice in interventional pain management, especially by those with a lack of understanding and bias to focus only on methodology and to erroneously report inaccurate conclusions referring to any local anesthetic injection as a placebo.

The differences among various types of placebo injections have been demonstrated, as well as injections into various structures. The experimental and clinical findings from investigation of the electrophysiological effects of 0.9% sodium chloride solution and dextrose 5% in water solution illustrate the potential inaccuracy created by 0.9% sodium chloride solution versus 5% dextrose (244,245). In addition, the effect of sodi-

um chloride solution when injected into the disc, the facet joint, or paraspinal muscles have been shown to be variable. Indahl et al (211,212) in their evaluation of the electromyographic response of the porcine multifidus musculature after nerve stimulation (212) and interaction between the porcine lumbar intervertebral disc, zygapophysial joint, and paraspinal muscles (211), showed that stimulation of the disc and the facet joint capsule produced contractions in the multifidus fascicles (212). They also demonstrated that the introduction of lidocaine into the facet joint resulted in a significantly reduced electromyographic response with the most drastic reduction seen when stimulating the facet joint capsule. Further, the introduction of physiologic saline into the zygapophysial joint reduced the stimulation pathway from the intervertebral disc to the paraspinal musculature (211). Consequently, they hypothesized that the paraspinal muscle activation caused by nerve stimulation in the annulus fibrosis of the lumbar intervertebral disc could be altered by saline injection into a zygapophysial joint. Thus, it is essential to rule out zygapophysial joint pain prior to discography or administration of epidural injections. Epidural saline has been illustrated to provide therapeutic benefit (246-252). In addition, the immediate relief of pain after injection suggesting a strong placebo effect and also which does not differ in efficacy from treatment with diadynamic currents or roentgen irradiation – about 60% of patients gaining pain relief in the short-term from both treatments (253,254). Lilius et al (190) reported 23% of the patients with persistent benefit up to 3 months after the injection, irrespective of the type of the injection with high volumes.

Taking into consideration all the pitfalls associated with interpreting of placebo-control, multiple deficiencies in the methodologic quality assessment of individual studies and systematic reviews, and available new evidence, there is significantly superior evidence available, including good evidence for caudal epidural injections for disc herniation and discogenic pain, fair evidence for lumbar spinal stenosis and post lumbar surgery syndrome, and fair evidence for transforaminal epidural injections in managing disc herniation and radiculitis.

2.0 Epidural Steroid Injections

Lumbar epidural injections are performed by 3 approaches: caudal, interlaminar, and transforaminal. The injections are used for various types of pathology, including disc herniation and/or radiculitis, discogenic pain without disc herniation, spinal stenosis, and lumbar post surgery syndrome. Thus, the procedure and indications are variable. Chou et al (35,37,41) performed extensive searches and looked at multiple systematic reviews (91-98) and identified 40 randomized trials (112-150). However, similar to previous systematic reviews, they combined interlaminar epidural injections with caudal, even though there is no evidence that they work in the same manner. This follows the classic approach of methodology, which looks at all epidural injections as one, which leads to inappropriate opinions (77,78,92, 102,107,111,161). The authors who have separated the 3 modalities of epidural injections (59,60,62,94,100) have shown significantly better evidence for caudal epidural even compared to transforaminal epidural injections there is no significant evidence for lumbar interlaminar epidural injections thus far. However, there have not been any appropriately performed studies that conduct a head to head comparison among the 3 types of injections for various pathological conditions. While the reassessment agrees with Chou et al (35,37,41) concerning evidence for lumbar interlaminar epidural injections and caudal epidural injections in patients without disc herniation, the reassessment reached different conclusions regarding caudal epidural injections, and transforaminal epidural injections for disc herniation. The authors based their evidence synthesis for the caudal approach on poorly performed studies. Of the multiple studies utilized by Chou et al (35,37,41), most of them were of low quality without clinical relevance.

2.1 Caudal Epidural Injections

Chou and Huffman (35) described that they identified multiple trials which were placebo controlled (114,118-136) and claimed that several were of higher quality (114,117,118,121,122,124,126,130, 132,135,140). However, there are multiple problems with this interpretation. Dashfield et al (140) was not a placebo-controlled trial as the authors themselves have identified. On close examination, Zahaar (136) was also not placebo-controlled. It was stated by Chou and Huffman (35) that they utilized sodium chloride solution; however, Zahaar (136) injected 30 mL of solution, which was a local anesthetic diluted with 2 mL of 4% Carbocaine and 28 mL of sodium chloride solution, thus it can not be considered a sodium chloride solution. Béliveau (119) also did not use an injection of only sodium chloride solution; it was combined with procaine 0.5% in normal saline or 40 mL of procaine 0.5% in normal saline with 2 mL of methylpredniso-

lone, for a total injection of 42 mL in each group. As already mentioned, the injection of sodium chloride is not inert in the epidural space or into the joints (211,212,246-254). Wilson-MacDonald et al (135) had a good design, but it was not placebo control as they injected extra epidural steroid and bupivacaine. Kraemer et al (128), reporting the results of 2 trials with 3 injections in one week, compared their new technique of epidural perineural injection administered blindly with a conventional epidural injection technique and with a third group, who received a paravertebral local anesthetic injection. Once again, the effects of paravertebral injection have been illustrated and they are not benign (211,212), thus this is not a true placebo. Rogers et al (133) employed either local anesthetic alone or local anesthetic with steroids. They used sodium chloride solution as a diluent. Thus, multiple studies (119,128,133,135,136,140) were not placebo injections as claimed by Chou and Huffman (35).

High volumes used in some of these studies disrupt adhesions and provide a "washing effect" which may remove inflammatory mediators from around nerves. As described above, there are multiple effects elicited with injection into discs, facet joints, or paraspinal muscles along with effects of dextrose and sodium chloride solution into nerve sheaths (211,212,244-247,249-252). In fact, Kraemer et al (128) described that it was not difficult for them to get patients' consent for potential saline injection alone because there had been reports about the success of epidural saline in sciatica (246,247,249-252).

As illustrated above, multiple caudal epidural injections were inappropriately included in the evaluation, were not placebo control as described, and utilized large amounts of solutions which is clinically not appropriate.

Zahaar's study (136) was very poorly performed, evaluating 2 different pathologies – herniated nucleus pulposus and spinal stenosis, with utilization of high volumes (sterile saline with local anesthetic with or without steroid 30 mL) injected blindly without fluoroscopic guidance and without any imaging studies to demonstrate contrast spread. Consequently, based on studies that show a lack of appropriate delivery of injectate in caudal epidural injections in a significant proportion of patients, the results of this study must be vigorously questioned (255-259).

In Ackerman and Ahmad's study (112), the authors stated that the candidates were randomized into one of 3 arms: caudal, interlaminar, or transforaminal. However, no rationale was given to why each of the arms was chosen. It is also unclear if the patients were informed about the possible difference in therapeutic efficacy or if they were chosen by a physician irrespective of the nature of the pathology or severity. It is also difficult to understand the rationale for transforaminals. They utilized the L5 nerve root instead of the S1 nerve root, which might be more appropriate for L5/S1 disc herniation with S1 nerve root irritation. Further, the authors also injected very high volumes of solutions with 3 mL of contrast, followed by 5 mL of normal saline and triamcinolone, which is a high volume for transforaminal injections. Similarly, they also injected 20 mL to 30 mL of normal saline for caudal epidural injection.

As illustrated in the results section, the present evidence, utilizing Chou and Huffman's criteria with grading of good, fair, and poor, there is fair evidence for the therapeutic effectiveness of caudal epidural injections, in patients with disc herniation or radiculitis with or without steroids, for short-term and long-term relief. However, with addition of new studies the evidence is good for therapeutic effectiveness of caudal epidural injections in disc herniation or radiculitis in contrast to Chou and Hoffman grading of only poor.

Further, utilizing Chou and Huffman's criteria with grading good, fair, and poor, the evidence is poor for the therapeutic effectiveness of caudal epidural injections in post-surgery syndrome for short-term and long-term relief. However, addition of new studies will change the level of evidence to fair.

Finally, based on Chou and Huffman's criteria with grading of good, fair, and poor, the evidence is poor for the therapeutic effectiveness of caudal epidural injections in discogenic pain. However, addition of new studies will change the level of evidence to fair.

2.2 Lumbar Interlaminar Epidural Injections

Even though our reassessment had no significant differences with Chou and Huffman's (35) evaluation, multiple studies which were described as true placebos were in essence not placebos. Cuckler et al (123), in their evaluation of a double-blind randomized trial conducted from 1978 to 1980 and published in 1985, utilized a flawed process by considering local anesthetic injection as a placebo. Cuckler et al (123) also utilized either 2 mL of sterile water containing 80 mg of methylprednisolone acetate combined with 5 mL of 1% procaine or 2 mL of saline combined with 5 mL of 1% procaine, thus, this is not a placebo-controlled trial. Other variables include that the procedure was

performed with a blind technique between L3 and L4 in the lateral decubitus position on the affected side with the inability to reach the targeted area in almost half of the patients (258,260-268). Other flaws of this study include its small sample size, poor methodology, and inadequate outcome assessments. They also failed to provide detailed data on significant pain relief and performed their evaluation at only 2 points.

Carette et al's (122) study has been described as the best study evaluating the role of epidural steroids. This is true methodologically. It has been used as a landmark study to deny the effectiveness of all types of epidural injections. They studied 158 patients with injections of either 80 mg, 2 mL of methylprednisolone acetate mixed with 8 mL of isotonic saline, or 1 mL of isotonic saline. They used the lateral position, entering the epidural space between L3/4 without fluoroscopy. The results showed that at 3 weeks, the ODI score had improved slightly in the methylprednisolone group compared to the placebo group, along with significant difference noted with finger-to-floor distance and sensory deficits, which were greater in the methylprednisolone group. However, after 6 weeks, the only a significant difference was the improvement in leg pain, which was greater in the methylprednisolone group. There were no significant differences after 3 months. Problems with this study include the lack of fluoroscopy and the targeted delivery of the medication due to highly variable flow patterns in the lumbar interlaminar epidural space (252,254-262).

Arden et al (118) in a study published in 2005, which included 228 patients, presumably administered injection without fluoroscopy and in the lateral position between L3/4 or L4/5. The active group received epidural steroids via the lumbar route of 80 mg of triamcinolone acetonide and 10 mL of 0.25% bupivacaine at weeks 0, 3, and 6. The placebo group received injections of 2 mL of normal saline into the intraspinous ligament. They reported that 60 patients achieved a 75% improvement on the ODI before week 6 and therefore did not receive 3 injections. The patients were assessed at multiple points. The primary outcome measure was the reduction of 75% of ODI from baseline, with secondary outcome measures of VAS and short-form 36 (SF-36); however, based on the available literature, a reduction of 75% from baseline on the ODI is an unusual and unrealistic outcome measure as the literature considers a clinically important difference much lower than that or at best, 50% improvement. Even so, they reported a statistically significant improvement in self-reported function compared with placebo at 3 weeks. However, they reported that by 6 weeks, the benefit of epidural steroids was lost and at all subsequent visits, there were no differences between the groups on any measurable outcome, but at 52 weeks, 32.5% of the active group and 29.6% of the placebo group had achieved a 75% improvement in ODI. They included 1/3 of the patients who were acute. It is very difficult to assess the impact of the results. Even then, it is in the placebo range.

Wilson-MacDonald et al (135) compared lumbar epidural steroid injections to intraspinous ligament steroid injections to assess whether the steroid's epidural location was responsible for the subsequent effects. They concluded that there was no difference in the rate of subsequent surgery through the follow-up period. However, properly performed studies under fluoroscopic visualization should yield different results, similar to the results obtained from caudal epidural injections. Ackerman and Ahmad (112), even though their procedures were not performed appropriately, showed 60% of the patients improved at their 24-week follow-up in the interlaminar group, compared to 57% in the caudal group, and 83% in the transforaminal group. Recent studies evaluating the effectiveness of interlaminar epidural injections in the lumbar and cervical spine yielded improved results, with effectiveness in a significant proportion of the patients suffering with either disc herniation or discogenic pain. This is emerging evidence and indicates that appropriately performed studies will change the concept and also provide different results than are believed at the present time (269-272).

2.3 Transforaminal Epidural Injections

Similar to lumbar interlaminar and caudal epidural injections, transforaminal epidural injections also have been misunderstood. The authors of systematic reviews (62,76,91,94-96) have focused and placed inordinate importance on the manuscript by Karppinen et al (126). Even though this is a very well performed methodologically high quality manuscript, the results are not final. However, Karppinen et al (126) has been criticized as controversial, regarding the terminology of the procedure itself, the technique utilized, randomization, and the outcome results (166). The appropriate terminology is transforaminal epidural injection rather than periradicular infiltration. Periradicular infiltration describes a selective nerve root block or a ventral ramus block for diagnostic purposes, which would be inappropriate in this situation considering the large volumes of injectate utilized. The target delivery was compromised by high

volumes of bupivacaine mixed with methylprednisolone, essentially providing a washout effect either with bupivacaine or with sodium chloride solution. Their process of randomization was also flawed in that patients were recruited from general practitioners on the basis that they presumably were suffering from sciatica. These patients might differ from patients in interventional pain management settings or even surgical settings. In addition, the MRI classification of symptomatic discs was highly variable, with a significant number of patients having either a normal disc or a bulge, and with most patients having a disc extrusion. Transforaminal epidural steroid injections are not indicated in patients with disc bulging or normal discs; they are only indicated in patients with disc herniation or proven radiculitis. Their statistical interpretation is very difficult to understand because they reported in means rather than the proportion of patients with significant pain relief and improvement in functional status.

As described in the above section about placebo effects, one cannot consider an injection of several mL of sodium chloride solution with or without steroids as a placebo due to the inherent effects of sodium chloride solution when injected into the epidural space, over the nerve roots, or into the muscles and joints (211,212,247,249-254).

The study by Ackerman and Ahmad (112) which was considered as a high quality study by Chou and Huffman (35) for caudal and interlaminar epidural injections was excluded in the evidence synthesis for transforaminal epidural injections. Despite its numerous flaws, the study showed 83% of the patients improved at their final follow-up of 24 weeks.

As illustrated in the results sections based on the available evidence and utilizing Chou and Huffman's (35) criteria, the evidence appears to be fair, based on grading of good, fair, and poor in managing lumbar nerve root pain with transforaminal epidural injections.

Consequently, our reassessment has shown multiple deficiencies in their analysis and inappropriate conclusions.

3.0 Percutaneous Adhesiolysis

Chou and Huffman (35) stated that the term "failed back surgery syndrome" is commonly used to refer to a heterogenous group of conditions characterized by chronic disabling low back pain, with or without leg pain, following one or more spinal surgeries. They also described adhesiolysis. They described adhesiolysis and forceful epidural injections synonymously as they also disrupt epidural adhesions or fibrosis; however, they continue to consider sodium chloride solution injection as a placebo. They inappropriately scored systematic reviews and also provided inappropriate evidence for one study despite their consideration of the study as higher quality (117). They reported that there was a 0% response rate with epidural steroids; however, this is inaccurate as 33% of the patients in the epidural group experienced significant improvement for less than 3 months. After 3 months there was no significant improvement noted. They also misclassified the study by Heavner et al (176) as low quality. They failed to include the one-year follow-up available for evaluating endoscopic adhesiolysis, rather they included a preliminary report. They also utilized a study by Dashfield et al (140) which delivered steroids through endoscope or with a caudal approach under fluoroscopy; however, very few patients in this study had adhesions.

As illustrated in the results section based on Chou and Huffman's (35) grading of good, fair, and poor and the analysis of the included studies, there is at least fair evidence for percutaneous lumbar epidural adhesiolysis for short-term and long-term relief, whereas it may be considered poor for long-term improvement with spinal endoscopic adhesiolysis, and fair for short-term improvement of 6 months. However, with inclusion of more recent studies (173,174) and systematic reviews (66,76) the evidence is good for percutaneous adhesiolysis as opposed to only fair assessed by Chou and Hoffman (35).

Consequently, our reassessment has shown errors in their evaluation. We also added newly published randomized trials and the systematic reviews which obviously provided evidence that is different from that of Chou and Huffman (35).

4.0 Facet Joint Injection, Therapeutic Medial Branch Block, and Radiofrequency Neurolysis

Chou and Huffman (35) concluded that there was no evidence for the efficacy of facet joint injections or medial branch blocks. They further said the evidence was poor for radiofrequency neurotomy for lumbar facet joint pain. The present evaluation agrees with assessment of intraarticular injections. However, evidence was fair for medial branch blocks and radiofrequency thermoneurolysis, based on their own criteria.

There were multiple issues related to this evaluation, such as misunderstandings of Nath et al's article

(196) and exclusion of the one-year follow-up of therapeutic medial branch blocks (203). The final results are now available for the 2-year follow-up (204), which shows that these effects are in fact sustainable.

The manuscripts by Leclaire et al (201) and van Wijk et al (198) received heavy weight, but they have been extensively criticized. In fact, Chou and Huffman (35) in their description of radiofrequency denervation of the medial branch of the primary dorsal ramus versus sham or placebo for facet joint origin concluded that interpretation of the results was controversial because the trials used uncontrolled facet joint blocks to select patients and that the radiofrequency denervation technique might have been suboptimal in some of the trials, thus leading to the judgement that the level of evidence was poor. However, Chou and Huffman (35) discarded the diagnosis of facet joint pain utilizing controlled local anesthetic blocks based on poorly conducted cryoneurolysis that did not have any relevance to facet joint pain (273,274). They also concluded that for presumed facet joint pain, intraarticular radiofrequency denervation was superior to extraarticular radiofrequency denervation in one small trial; however, there is no clinical or anatomical basis for intraarticular radiofrequency. Further, all so-called sham lesions are not really placebo-controlled because the nerve was stimulated, irritated, and finally injected with local anesthetic.

Leclaire et al (215), in a recent letter to the editor of Pain Practice, acknowledged multiple deficiencies in their study; many consider this a retraction of their manuscript. They elaborated that the results of their research have been interpreted by the UK Institute of Clinical Excellence as evidence that radiofrequency neurotomy is ineffective as a treatment for low back pain which they are of the opinion is an inappropriate use of the conclusions of their study given that the authors themselves have serious reservation about their own study. Further, they added that contemporary reviews that rejected their study with the dated approach as inappropriate or invalidated (54,275). They also acknowledged the value of controlled local anesthetic blocks and false-positive rates. They stated that if they repeated their study today, they would use controlled medial branch blocks as the primary inclusion criteria to correctly identify patients with pain originating from the lumbar zygapophysial joints. They also discussed needle positioning and lesioning. Their final conclusion was that the study should be viewed as a precursor to more effective diagnostic and therapeutic strategies in the management of zygapophysial joint pain and must be interpreted only in its historical context of what methodology has been shown to be invalid. Further, they stated that only selection criteria based on controlled medial branch blocks with high grade relief consistent with the physiologic effects of the anesthetic and an appropriate multiplanar fluoroscopic radiofrequency neurotomy technique should be used to produce valid studies on this treatment for chronic low back pain.

van Wijk et al (198) also generated 2 letters to the editor (216,217). Bogduk (217) commented that the radiographs published by van Wijk et al (198) indicate not only that the electrodes were placed perpendicular to the target nerves, but also that they were lateral to the actual location of the nerve. In these locations the lesions produced were destined to fail to coagulate the nerves adequately, if at all. Consequently, the study of van Wijk et al (198) amounts to comparing one sham with another. Gofeld (216) also pointed out that uncontrolled single blocks, such as those used in the van Wijk study, yields 27% false-positive results. Furthermore, he emphasized that the electrodes were 1) definitely not positioned "parallel the nerves"; 2) placed at the base of the transverse process, and not at the base of the superior articular process, and therefore too lateral from the nerve; and 3) too far posteriorly as in the lateral view (that is, on the mamilloaccessory ligament) which insulates medial branches and L5 posterior primary ramus from radiofrequency electrodes. Lastly, the authors accepted that 22 gauge electrodes with a 5-mm active tip could produce an insufficient lesion size, but managed to execute lesions using this electrode without position adjustments, thus generating very limited lesions. Finally, van Wijk et al (218) contradicted their own reports of lack of effectiveness by showing that radiofrequency neurotomy and placebo injections were effective.

Gallagher et al (197) and also Van Kleef et al (199) faced substantial criticism for various methodological reasons.

Thus, our reassessment appropriately reached different conclusions with fair evidence-based on Chou and Huffman's (35) criteria for therapeutic lumbar facet joint nerve blocks, and radiofrequency neurotomy and same conclusion with poor for intraarticular injections.

As illustrated in the results section the evidence for intraarticular injections is in agreement with Chou and Huffman. However, our analysis showed that the evidence is significantly different from that of Chou et al based on their own criteria with grading of good, fair, and poor, for lumbar facet joint nerve blocks and radiofrequency neurotomy which is fair.

5.0 Spinal Cord Stimulation

Chou and Huffman (35) evaluated multiple systematic reviews and 2 randomized trials and concluded that there was fair evidence for spinal cord stimulation in FBSS, despite spinal cord stimulation being unequivocally recommended by NICE in its 2008 technology appraisal.

Chou (270) published an editorial entitled "Generating Evidence on Spinal Cord Stimulation for Failed Back Surgery Syndrome" which he felt was not yet fully charged. Chou felt that even though there is significant evidence of clinical and cost effectiveness there are still deficiencies. Chou also criticized that Kumar et al (232,237) had a deficiency since they utilized conventional medical management as a comparator, even though patients had already failed such treatment and would probably continue to do so, thus, stacking results in favor of spinal cord stimulation. Chou thought that the cost effectiveness studies fall short in several areas since the original studies do not reflect actual costs. The editorial could be interpreted that Chou believes that systematic reviews do not have much value. He concluded that it is quite conceivable that future studies might lead to different conclusions regarding clinical effectiveness and that we do not know with any degree of certainty whether spinal cord stimulation "is worth it." He recommended that studies adhering to guidelines for sound cost effectiveness analysis are clearly needed as are trials comparing spinal cord stimulation to interdisciplinary rehabilitation or other promising alternatives. Considering that most patients fail conservative management, including interdisciplinary management, the idea appears to be only cosmetic and a reason to continue to oppose spinal cord stimulation.

In response to the editorial by Chou (276), North et al (277) disagreed with Chou's contentions. Justifiably, North et al (277) concluded that it was unfair to discredit the conclusions of the studies that meet review criteria. It was implied that Chou must either discredit the review or turn away from the review and look to his opinions, which are of course subject to error and bias – the very problem the systematic review process is designed to reduce. North et al (277) concluded that editorials would do well to follow the fact checking procedures employed by researchers who conduct systematic reviews.

6.0 Assessment of Integrity

As detailed in the results section, the goals of integrity including transparency, accountability, consistency, and independence were not met.

The authors and organizations had apparent conflicts of interest, withdrawal of physicians was not listed, and involvement of multiple societies without financial disclosures may have compromised integrity.

Transparency was lacking along with a lack of accountability, consistency, and finally, a lack of independence.

7.0 Conclusion

The reassessment of any and all guidelines is an essential part of modern medicine. Chou and Huffman (35) have performed an extensive analysis. However, due to inappropriate evaluations, the inclusion of inappropriate studies, and the exclusion of appropriate studies, it appears that their evidence synthesis lack rigour and therefore reaches inappropriate conclusions. reached conclusions.

In summary criticisms can be leveled at the study of Chou and Huffman (35). Their study displays misleading results due to lack of methodological rigour and fact check. A careful reanalysis of the data leads to significantly different results as described.

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Disclosures

Dr. Hirsch is a consultant for Cardinal Healthcare. He is a minor shareholder in Medtronic and Cardinal Healthcare. He serves on the Steering Committee for KAVIAR trial (volunteer position) and on the Data and Safety Monitoring Board (DSMB): CEEP trial (volunteer position). Dr. Datta receives research support from Sucampo Pharmaceuticals and an honorarium from Smith and Nephew.

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