



**INSTITUTE OF
HEALTH ECONOMICS**
ALBERTA CANADA

NERVE BLOCKS FOR NEUROPATHIC PAIN

SUMMARY OF THE LITERATURE

**Canadian Pain Society Special Interest Group on
Neuropathic Pain**

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PREFACE

During 2005 and 2006, the Canadian Pain Society Special Interest Group on Neuropathic Pain (NeP SIG) produced a clinical practice guideline on the pharmacological management of neuropathic pain. In 2007 the NeP SIG began developing a guideline on the use of other interventions for neuropathic pain, such as spinal cord stimulation, deep brain stimulation, nerve blocks (sympathetic blocks; nerve and nerve root blocks; trigger point blocks, epidural blocks, and other spinal injections); psychological treatments such as cognitive behavioural therapy, relaxation, biofeedback, meditation, hypnosis; physical and occupational therapy modalities/interventions such as graded exposure to stimulation, mirror visual reprogramming, stretching, exercises, acupuncture, transcutaneous electrical nerve stimulation, transcranial magnetic stimulation, and multidisciplinary pain management programs. In 2007, a survey of NeP SIG members was undertaken to help prioritize this list of interventions. The results of the survey indicated that among the aggressive treatments used for neuropathic pain, the following four were considered high priority by the NeP SIG members.

- Epidural blocks
- Nerve blocks
- Intravenous infusions
- Spinal cord stimulation

In order to facilitate the development of the NeP SIG guideline on interventions for neuropathic pain, the Institute of Health Economics was recruited to assist in gathering and rating the quality of the available scientific literature on these four abovementioned interventions.

SCOPE OF THE PAPER

This report is the fourth of a set of four documents that provide a summary and critical appraisal of the available published evidence from the international medical literature regarding the use of epidural blocks, nerve blocks, intravenous infusions, and spinal cord stimulation for the treatment of neuropathic pain.

This literature summary was conducted according to a predefined methodology that was formulated in consultation with NeP SIG representatives. It does not represent a systematic review of the literature on nerve blocks for the treatment of neuropathic pain; thus, no firm conclusions are offered on the safety or effectiveness of this intervention. In addition, the evidence was only summarized and no attempt was made to assess the veracity of the information contained within the included studies.

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METHODS

Inclusion criteria

Types of studies

Systematic reviews (SRs), randomized controlled trials (RCTs), and clinical practice guidelines (CPGs) were included.

Systematic reviews

An article was deemed to be a SR if it met all of the following criteria as defined by Cook et al.¹

- 1) Focused clinical question.
- 2) Explicit search strategy.
- 3) Use of explicit, reproducible, and uniformly applied criteria for article selection.
- 4) Critical appraisal of the included studies.
- 5) Qualitative or quantitative data synthesis.

Randomized and quasi-randomized controlled trials

RCTs were included. Trials using a quasi-random method of treatment allocation (quasi-randomized controlled trials), such as date of birth, day of the week, or medical record number, were also included.

Clinical practice guidelines

CPGs are most commonly defined as “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances”.² For a CPG to be valid, the evidence supporting its recommendations must be cited.^{2,3} Therefore, an article was deemed to be a CPG if it met all of the following criteria.

- 1) It contained the word ‘guideline’ or ‘recommendation’ in its title or introduction, or contained recommendations on managing patients with neuropathic pain in the form of advice or instructions.⁴
- 2) It was developed by at least two authors.
- 3) It was evidence-based.

CPGs that were not evidence-based, such as consensus statements that contained recommendations based only on expert opinion, were excluded.

Only CPGs formulated in countries with developed market economies were included since the health status, cultural norms, access to health care, and disease burden of individuals from countries with transitional or developing economies were likely to be too different from those of Canada to be clinically relevant. Countries deemed to have developed economies, as defined by the United Nations, were as follows: Australia, Canada, Japan, New Zealand, the United States of America, and Europe (except for

Albania, Bulgaria, Czech Republic, Hungary, Poland, Romania, Slovakia, Bosnia and Herzegovina, Croatia, Slovenia, the former Yugoslav Republic of Macedonia, Yugoslavia, Estonia, Latvia, Lithuania, Belarus, the Republic of Moldova, the Russian Federation, and Ukraine).⁵

Participants

Data were collected on adult patients (18 years of age or older) with a peripheral or central neuropathic pain condition of any duration. Studies that referred to ‘patients’ or ‘adult patients’ without providing a specific age range were also included. However, any study that clearly included patients under the age of 18 years was excluded.

Patients with cancer pain were excluded unless they had a defined post-surgical pain syndrome with neuropathic contribution, such as post-mastectomy pain. Patients with visceral pain, migraine, headache, fibromyalgia, or ischemic pain were excluded. Studies that included data for patients with neuropathic pain and those with non-neuropathic pain conditions were excluded unless the data subset for the patients with neuropathic pain could be separated from the aggregate data.

Index Intervention

Peripheral nerve blocks, sympathetic nerve blocks, regional nerve blocks, and paravertebral or trigger point blocks using any drug for the treatment of neuropathic pain. Diagnostic nerve blocks were not included. Given the overlap between diagnostic and non-diagnostic nerve blocks, a specific definition for diagnostic nerve blocks was not used. Nerve blocks were considered diagnostic if they were examined using a diagnostic study design, or if the study specifically stated that the nerve block was used for diagnostic purposes. All reports of nerve blocks that used an interventional study design were included, regardless of the length of follow up or number of treatments administered.

Comparative intervention

Any medical, mechanical, or surgical intervention designed to treat patients with neuropathic pain. Placebo and no treatment comparisons were also included. Studies that compared technical aspects of nerve blocks were excluded.

Literature search strategy

The medical literature was searched to identify relevant, publicly available SRs, RCTs, and CPGs published in English from January 1997 to May 2008 (see Appendix A for the search terms and databases used). Although the bibliographies of articles retrieved in hard copy form were not systematically searched for relevant references that may have been missed in the database searches (pearling), any additional relevant references accidentally uncovered during the examination of these full-text articles were retrieved.

Literature selection process

Study selection was conducted by one reviewer. Articles were excluded that, on the basis of their abstract, clearly did not meet the inclusion criteria. Copies of the full text of potentially eligible studies were retrieved. In some cases, when the full text of the article

was retrieved, closer examination revealed that it did not meet the inclusion criteria. Consequently, these papers were excluded (Appendix B).

Systematic reviews

In cases where multiple SRs on a single topic were identified that were of the same quality and had identical comparators and patient populations, only the most recently published SR was included. In cases where a SR described a particular subgroup of neuropathic pain patients (e.g. postherpetic neuropathy, radiculopathy) or used different or additional comparators to those of the most recent SR, both SRs were included.

Randomized and quasi-randomized controlled trials

RCTs or quasi-RCTs that covered the same interventions and patient groups detailed in the included SRs and were published after the end date of the search strategy of the included SRs were also included. Thus, the intent was only to update the included SRs. RCTs on conditions or interventions that were not within the scope of the included SRs were excluded. When overlapping patient groups were reported in RCTs, only the paper quoting the most complete data set was used.

Clinical practice guidelines

In cases where multiple CPGs on a single topic were identified that were of the same quality and had identical comparators and patient populations, only the most recently published CPG was included. In cases where a CPG described a particular subgroup of neuropathic pain patients (e.g. postherpetic neuropathy, radiculopathy) or used different or additional comparators to those of the most recent CPG, both CPGs were included.

In cases where multiple CPGs on a single topic were identified that had identical comparators but were of differing quality, only the highest quality CPG was included if it was also the most recent. If the highest quality CPG was not the most recent, then both the highest quality CPG and the most current CPG, regardless of its quality, were included.

Assessment methods

Study methodology appraisal

The included studies were assessed with respect to various aspects of methodology and reporting using checklists specific for each particular study type (Appendices C, D, and E). The quality assessments were undertaken independently by two reviewers. The checklists were operationalized by constructing dictionaries that explained each criterion. The two reviewers discussed the dictionaries with respect to the interpretation of questions prior to assessing the studies. Critical appraisal results for all included studies are tabulated in Appendices C, D, and E.

Systematic reviews

The included SRs were assessed using a checklist developed in-house that was adapted from a number of sources (Appendix C).⁶⁻⁹ This tool was chosen because it is more detailed and less subjective than other commonly used tools, such as the AMSTAR¹⁰ and Oxman and Guyatt¹¹ checklists, and the reviewers were very experienced in its use. Any disagreements in scoring between the two reviewers that

could not be resolved by discussion were referred to a third reviewer for mediation until consensus was reached.

The quality of SRs was assessed according to how well their methods excluded bias and confounding by examining: the search strategy used; how the data extraction, quality assessment of the included studies, and data analysis/synthesis were conducted; and whether the conclusions of the review match the results. Thus, the quality of the SR was rated numerically with respect to six quality subsections (grey boxes in checklist) as follows:

Good – six criteria met (✓✓✓✓✓✓), or five criteria met and one criterion ‘unclear’ (✓✓✓✓✓?).

Average – one criterion not met (✓✓✓✓✓×), or one criterion not met and one criterion ‘unclear’ (✓✓✓✓×?), or two criteria ‘unclear’ (✓✓✓✓??).

Poor – at least two criteria not met (✓✓✓✓××).

Randomized controlled trials

The included RCTs were assessed using the criteria list recommended in the method guidelines of the Cochrane Back Review Group for SRs¹² (Appendix D). This list has been used in a number of SRs¹³⁻¹⁵ in the field of chronic pain and includes all the criteria from the lists generated by Jadad et al.¹⁶ and Verhagen et al.¹⁷. It consists of internal and external validity criteria, as well as statistical criteria. The list was modified by removing items E (Was the care provider blinded?) and G (Was compliance acceptable?), since blinding of the care provider is not always possible for some of the neuropathic pain treatments being considered and compliance is not a relevant issue when nerve block is the sole treatment. In addition, some instructions were reworded or supplemented with more detailed criteria descriptions from Downs and Black¹⁸. A simple nominal rating scale was used such that the studies were scored as positive (yes), negative (no), or unclear (don’t know) for each quality criterion. Any disagreements in scoring between the two reviewers that could not be resolved by discussion were referred to a third reviewer for mediation until consensus was reached.

For descriptive purposes, the included RCTs were referred to as being good, moderate, or poor quality with respect to internal and external validity according to the total number of criteria met as follows:

- Internal validity (total number of criteria = 9) – good (≥ 7 criteria met), moderate (between 4 and 6 criteria met), poor (< 4 criteria met);
- External validity (total number of criteria = 6) – good (≥ 5 criteria met), moderate (3 or 4 criteria met), poor (< 3 criteria met).

Clinical practice guidelines

The included CPGs were assessed using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument¹⁹ (Appendix E). The AGREE instrument is an internationally developed, generic tool that is validated, transparent, and widely accepted, with satisfactory reliability for most domains. The instrument has 23 key items organized into six domains: scope and purpose (items 1-3); stakeholder involvement (items 4-7);

rigor of development (items 8-14); clarity of presentation (items 15-18); applicability (items 19-21); and editorial independence (items 22-23).

The tool is accompanied by a detailed User Guide that explains how to score the 23 items. Each guideline is assessed using a 4-point scale (ranging from 4 = “strongly agree” to 1 = “strongly disagree”) to rate each of the 23 items. These scores are then combined for each of the six domains and converted into standardized domain scores according to the following formula:

$$\text{Standardized domain score (\%)} = \frac{\text{obtained score} - \text{minimum possible score}}{\text{maximum possible score} - \text{minimum possible score}} \times 100$$

The six domain scores are independent and cannot be combined into a single score. Instead, appraisers can provide an overall assessment of the guideline according to the following categories:

- Strongly recommended;
- Recommended (with provisos or alterations);
- Would not be recommended;
- Unsure.

Two modifications were made to the AGREE tool to reduce the ambiguity and subjectivity associated with item scoring, and to enable the differentiation of good from poor quality guidelines.

- 1) A detailed set of instructions, or dictionary, based on the AGREE guidance was constructed using logical operators (AND, OR, NOT) to quantify what constitutes a score of 4, 3, 2, or 1 for each of the 23 items.
- 2) Seven “essential” criteria were identified for categorizing guidelines as good, moderate, or poor quality.²⁰
 - Item 8: Systematic search conducted
 - Item 10: Methods used to formulate recommendations described
 - Item 12: Link between recommendations and evidence
 - Item 13: External review by experts
 - Item 15: Specific, unambiguous recommendations
 - Item 22: Editorially independent from funder
 - Item 23: Conflicts of interest reported

The scores from the two reviewers were combined into an average quality score (maximum possible of 28 [7x4]), which was then rated as follows:

Good –score of 22 to 28;

Average –score of 15 to 21;

Poor –score 0 to 14.

Outcome measures and data extraction

Study profile information, as well as relevant safety and efficacy data, was extracted by one reviewer using standardized data extraction forms developed *a priori*.

SUMMARY OF THE LITERATURE

Fifty-one studies were identified that potentially met the inclusion criteria. On closer examination of the full text article, 37 of these studies were excluded and the reasons documented (Appendix B). Four SRs and four CPGs were included (Table 1). Six RCTs that were published after the end date of the search strategy of the included SR, covered the same interventions and patient groups detailed in the included SRs, and met the inclusion criteria were also included. When overlapping patient groups were reported in the RCTs, only the paper quoting the most complete data set was used.

Details of two potentially relevant studies that could not be retrieved in hard copy form before the report deadline (March 31, 2009) are listed in Appendix B, Table B.2.

Study profiles of the included studies are summarized in Tables 2 to 4. The relevant safety and efficacy data extracted from each of the included studies are tabulated in Tables 5 to 7.

Table 1: Summary of included studies

Study	Year	Quality Rating	Pain Condition/Treatment Comparisons
Systematic Reviews			
Carragee et al. ²¹	2008	Average (4/6)	Neck pain resulting from whiplash injuries and work-related injuries and strains; neck pain of unknown etiology in the general population
DePalma et al. ²²	2005	Average (4/6)	Lumbosacral radiculopathy
Forouzanfar et al. ²³	2002	Average (4/6)	Complex regional pain syndrome type I or reflex sympathetic dystrophy
Kumar et al. ²⁴	2004	Poor (3/6)	Herpes zoster and postherpetic neuralgia
Randomized Controlled Trials			
Becker et al. ²⁵	2007	<i>Internal validity</i> Good (8/9) <i>External validity</i> Good (6/6)	Unilateral lumbar radicular compression Epidural perineural injection autologous conditioned serum (n=32) vs triamcinolone 10 mg (n=25) vs triamcinolone 5 mg (n=27)
Bonetti et al. ²⁶	2005	<i>Internal validity</i> Moderate (6/9) <i>External validity</i> Moderate (4/6)	Acute or chronic low back pain with sciatica Periradicular steroid injection (n=80) vs intraforaminal O ₂ O ₃ injection (n=86)
Livingstone and Atkins ²⁷	2002	<i>Internal validity</i> Good (7/9) <i>External validity</i> Good (5/6)	Complex regional pain syndrome type I Intravenous regional blockade guanethidine 15 mg (n=27) vs saline (n=30)

Table 1: Summary of included studies (cont'd)

Study	Year	Quality Rating	Pain Condition/Treatment Comparisons
Randomized Controlled Trials (cont'd)			
Ng et al. ²⁸	2005	<i>Internal validity</i> Good (8/9) <i>External validity</i> Moderate (4/6)	Chronic lumbar radicular pain Periradicular injection bupivacaine plus methylprednisolone (n=43) vs bupivacaine (n=43)
Nishiyama et al. ²⁹	2006	<i>Internal validity</i> Good (7/9) <i>External validity</i> Poor (2/6)	Sudden deafness; postherpetic neuralgia Crossover trial (n=5 for postherpetic neuralgia) Stellate ganglion block (neurotropin vs mepivacaine)
Taskaynatan et al. ³⁰	2004	<i>Internal validity</i> Moderate (5/9) <i>External validity</i> Good (5/6)	Complex regional pain syndrome type I Intravenous regional Bier block methylprednisolone plus lidocaine (n=14) vs saline (n=11)
Clinical Practice Guidelines			
Ambrosio et al. ³¹ (Italy)	2006	Poor (14/28)	Chronic non-cancer pain >3 months' duration
Dubinsky et al. ³² (USA)	2004	Average (17/28)	Postherpetic neuralgia ≥ 8 weeks' duration
Hunter Integrated Pain Service ³³ (Australia)	2009	Poor (10/28)	Neuropathic pain, spinal and radicular pain, tissue ischemia pain, cancer pain
WCB Evidence Based Practice Group ³⁴ Canada	2004	Poor (11.5/28)	Complex regional pain syndrome

STUDY PROFILES – SYSTEMATIC REVIEWS

Table 2: Study profiles for *systematic reviews* on nerve blocks for neuropathic pain

Systematic Review	Population	Selection Criteria/Outcomes	Methods
<p>Carragee et al (2008)²¹</p> <p>Objective: To identify, critically appraise, and synthesize literature on surgical interventions for neck pain alone or with radicular pain in the absence of serious pathologic disease.</p> <p>Financial support: National Chiropractic Mutual Insurance Company (USA); Canadian Chiropractic Protective Association (Canada); State Farm Insurance Company (USA); Insurance Bureau of Canada; Länsförsäkringar (Sweden); The Swedish Whiplash Commission; Jalan Pacific, Inc. (Brazil); Amgen (USA). All funds received were unrestricted grants. Funders had no control in planning, research activities, analysis, or results.</p> <p>Conflict of interest: No benefits in any form were received from a commercial party related directly or indirectly to the subject of the manuscript.</p>	<p>Total number: Selective nerve root block for radicular neck pain: n = 97 (1 non-randomized comparative study) Extraforaminal root injection for radicular neck pain: n = 844 (1 case series study)</p> <p>Age: Not stated.</p> <p>Included conditions: Neck pain resulting from whiplash injuries and work-related injuries and strains; neck pain of unknown etiology in the general population.</p> <p>Excluded conditions: Neck pain resulting from fractures or dislocations, inflammatory arthritis, infection, tumours, and other non-musculoskeletal types of neck pain, except for diagnostic studies relating to ruling out fractures and dislocations in neck pain.</p>	<p>Intended comparators: Placebo, any active treatment.</p> <p>Study inclusion criteria: Original research studies and systematic reviews/meta-analyses published in peer-reviewed journals pertaining to the diagnosis, incidence, prevalence, determinants or risk factors, prevention, course, prognosis, treatment and rehabilitation, or economic costs of neck pain; studies containing data or findings specific to neck pain and/or disorders associated with neck pain; studies including at least 20 persons with neck pain or at risk for neck pain; systematic reviews of the literature on neck pain; conference proceedings, technical reports, unpublished manuscripts, guidelines, and book chapters with original data; clinical case series were included if they were judged to be of special relevance to the Neck Pain Task Force report.</p> <p>Study exclusion criteria: Studies on neck pain associated with serious local pathology or systemic disease; opinion articles, letters to the editor, and articles without scientific data or a report of their methodology; studies with no neck pain-specific data; case series (except as indicated in the inclusion criteria) and narrative review articles; guidelines without details of their methodology.</p> <p>Outcomes measured: Data or findings specific to neck pain and/or disorders associated with neck pain.</p>	<p>Literature search: <u>Time period:</u> From 1980 to 2005, plus additional key articles published in 2006 and early 2007. <u>Limits:</u> English, French, and Swedish language publications only. <u>Databases:</u> MEDLINE. <u>Other sources:</u> Additional reports were identified from reference lists of relevant studies.</p> <p>Data extraction: Data from studies judged as scientifically admissible were abstracted into evidence tables. If a study was related to more than one topic, it was included in more than one set of evidence tables. The evidence tables formed the basis for the review on each topic.</p> <p>Appraisal of study quality: Rotating pairs of Scientific Secretariat members performed independent, in-depth critical reviews of each article, identifying methodological strengths and weaknesses. After discussing each article in Scientific Secretariat meetings, consensus decisions were made about their scientific merit. Those judged to have adequate internal validity were included in the best evidence synthesis. Criteria used for appraising the methodological quality of the studies focused on sources of potential bias (selection bias, information bias, confounding) and compared these findings to the magnitude of any bias that would likely result in erroneous or misleading conclusions. Studies with such problems were not accepted in whole or in part into the best evidence synthesis.</p> <p>Data analysis: Qualitative.</p> <p>Conclusions supported by results: Yes. However, the evidence for the statements on efficacy regarding cervical injections was not clearly outlined in the body of the report.</p>

Table 2: Study profiles for systematic reviews on nerve blocks for neuropathic pain (cont'd)

Systematic Review	Population	Selection Criteria/Outcomes	Methods
<p>DePalma et al. (2005)²²</p> <p>Objective: To critically review the best available trials of the utility of transforaminal epidural steroid injections or selective nerve root blocks to treat lumbosacral radiculopathy.</p> <p>Financial support: Not reported.</p> <p>Conflict of interest: None.</p>	<p>Total number: Transforaminal epidural steroid injections: n = 325 (5 randomized controlled trials)</p> <p>N.B. These constitute a subset of studies that are all included in Abdi et al. (2007)³⁵, which is one of the systematic reviews included in the companion literature summary on epidural injections.</p> <p>Age: Not stated.</p> <p>Included conditions: Lumbosacral radiculopathy.</p> <p>Excluded conditions: None stated.</p>	<p>Intended comparators: Placebo, any active treatment.</p> <p>Study inclusion criteria: Prospective randomized trials, in which one treatment arm received one or more fluoroscopically-guided selective nerve root corticosteroid injections (additional interventions were allowed provided they did not differ between groups).</p> <p>Study exclusion criteria: Not reported.</p> <p>Outcomes measured: Not specified.</p>	<p>Literature search: Time period: From 1966 to 2003. <u>Limits:</u> English language publications only. <u>Databases:</u> MEDLINE, EMBASE, <i>The Cochrane Library</i>. <u>Other sources:</u> Additional reports were identified from reference lists of retrieved studies.</p> <p>Data extraction: Information on inclusion criteria, randomization protocol, number of patients enrolled initially and at final analysis, statistical analysis used, technique, outcome measures, follow-up intervals, results, and reported complications were extracted, but the method of data extraction was not reported.</p> <p>Appraisal of study quality: The quality of individual studies was assessed using criteria from the Agency for Health Care and Policy Research.³⁶</p> <p>Data analysis: Qualitative.</p> <p>Conclusions supported by results: Yes.</p>

Table 2: Study profiles for systematic reviews on nerve blocks for neuropathic pain (cont'd)

Systematic Review	Population	Selection Criteria/Outcomes	Methods
<p>Forouzanfar et al. (2002)²³</p> <p>Objective: To ascertain appropriate therapies for complex regional pain syndrome type I based on a systematic review of the literature.</p> <p>Financial support: Not reported.</p> <p>Conflict of interest: Not reported.</p>	<p>Total number: <i>Reflex sympathetic dystrophy:</i> Placebo controlled trials; 7 RCTs Active controlled trials; 5 RCTs <i>Complex regional pain syndrome type I:</i> Placebo controlled trials; 2 RCTs Active controlled trials; 1 RCT</p> <p>Age: Not stated.</p> <p>Included conditions: Complex regional pain syndrome type I or reflex sympathetic dystrophy.</p> <p>Excluded conditions: None stated.</p>	<p>Intended comparators: Placebo, any active treatment.</p> <p>Study inclusion criteria: Double-blinded or single-blinded RCTs using pain intensity as the main outcome measure.</p> <p>Study exclusion criteria: Non-randomized studies, case reports, and clinical observations.</p> <p>Outcomes measured: Pain intensity.</p>	<p>Literature search: <u>Time period:</u> From January 1966 to June 2000. <u>Limits:</u> Dutch, German, and English language publications only. <u>Databases:</u> PubMed, MEDLINE, EMBASE, The Cochrane Library. <u>Other sources:</u> Additional reports were identified from reference lists of retrieved studies and review articles.</p> <p>Data extraction: Method not reported.</p> <p>Appraisal of study quality: RCTs assessed independently by two reviewers with De Vet et al. (1997)³⁷ scale. Disagreements were resolved by consensus. Unresolved disagreements were referred to a third reviewer.</p> <p>Data analysis: Qualitative.</p> <p>Conclusions supported by results: Yes.</p>
<p>Kumar et al. (2004)²⁴</p> <p>Objective: To evaluate and synthesize existing evidence for using nerve blocks with various injectants in treating pain of Herpes zoster and postherpetic neuralgia.</p> <p>Financial support: Supported in part by the University of Cincinnati, Cincinnati, Ohio, USA.</p> <p>Conflict of interest: Not reported.</p>	<p>Total number: Sympathetic blocks: n = 108 (two case series studies)</p> <p>Age: Not stated.</p> <p>Included conditions: Herpes zoster and postherpetic neuralgia.</p> <p>Excluded conditions: None stated.</p>	<p>Intended comparators: Placebo, any active treatment.</p> <p>Study inclusion criteria: RCTs, cohort studies, case-control studies, case series studies.</p> <p>Study exclusion criteria: Review articles, expert opinion, case reports; studies looking exclusively at other peripheral nerve blocks and local infiltrations.</p> <p>Outcomes measured: Pain relief.</p>	<p>Literature search: <u>Time period:</u> From 1966 to 2001. <u>Limits:</u> English language publications only. <u>Databases:</u> MEDLINE, EMBASE, Cochrane Clinical Trial databases. <u>Other sources:</u> Manual search of journal articles.</p> <p>Data extraction: Method not reported.</p> <p>Appraisal of study quality: The quality of individual studies was assessed using Methodologic Quality Score criteria.³⁸ Grades of recommendation were then made in accordance with the Oxford Centre for Evidence-Based Medicine.³⁹</p> <p>Data analysis: Semi-quantitative.</p> <p>Conclusions supported by results: Yes.</p>

STUDY PROFILES – RANDOMIZED CONTROLLED TRIALS

Table 3: Study profiles for *randomized controlled trials* on nerve blocks for neuropathic pain

Authors/Study Details	Intervention/Outcome Measures	Study Design/Execution
<p>Becker et al. (2007)²⁵ Germany</p> <p><u>Study design:</u> Prospective randomized, double-blind concurrently controlled trial.</p> <p><u>Follow-up:</u> 6, 10, and 22 weeks after the first injection.</p> <p><u>Study period:</u> Not stated.</p> <p><u>Setting:</u> Orthopaedic practice.</p> <p><u>Financial support:</u> None.</p>	<p>Epidural perineural injection (autologous conditioned serum (ACS)); n=32</p> <p>Epidural perineural injection (triamcinolone 10 mg); n=25</p> <p>Epidural perineural injection (triamcinolone 5 mg); n=27</p> <p>Epidural injection (ACS) <u>Injectant:</u> Conditioned autologous serum.</p> <p>Epidural injection (10 mg) <u>Injectant:</u> 1 mL of local anaesthetic plus 10 mg of triamcinolone.</p> <p>Epidural injection (5 mg) <u>Injectant:</u> 1 mL of local anaesthetic plus 5 mg of triamcinolone.</p> <p>Epidural ACS, 10 mg, and 5 mg groups <u>Procedure:</u> An oblique interlaminar approach with a 29 gauge spinal needle was used to enter the anterior epidural space and reach the selective 1 nerve root directly.</p> <p><u>Adjunct medications:</u> All pain medications were discontinued at the beginning of the trial. Patients received no additional medical therapy or physiotherapy. Ibuprofen was allowed for the treatment of pain during the trial.</p> <p><u>Subsequent treatments:</u> Patients were injected once per week for three consecutive weeks.</p> <p><u>Outcome measures:</u> Pain intensity (visual analog scale); Oswestry Disability Index score.</p> <p>There was no statistically significant difference between the groups with respect to age, sex distribution, duration of symptoms, pain score, or causes of compression signs (P>0.05).</p>	<p><u>Method of randomization:</u> Random number table.</p> <p><u>Time of randomization:</u> Not reported.</p> <p><u>Method of allocation concealment:</u> Allocation sequence was generated by a nurse not involved in the care of the patients and placed in sequentially numbered, sealed envelopes.</p> <p><u>Details of blinding:</u> Patients and outcome assessors were blinded. Blinding for the injection procedure was not possible for technical reasons.</p> <p><u>Participation rate:</u> Not reported.</p> <p><u>Eligibility rate for study:</u> Patients recruited consecutively.</p> <p><u>Intention-to-treat analysis:</u> Per protocol analysis as two patients refused further injections; four additional patients were excluded because of missing data.</p> <p><u>Crossovers:</u> None occurred.</p> <p><u>Provider:</u> Physician not otherwise involved in the care of the patients.</p> <p><u>Assessor details:</u> Physicians.</p> <p><u>Inclusion criteria:</u> Patients with unilateral lumbar radicular compression of at least 6 weeks' duration and moderate to severe pain intensity.</p> <p><u>Exclusion criteria:</u> Patients needing early surgery because of clinically remarkable pareses or unbearable pain; additional neurological illnesses, cervical myopathy, systemic bone or joint illnesses, previous epidural or epidural perineural injection to the affected nerve root in the last 3 months; cortisone or opioid use in the last 6 months.</p> <p><u>Conclusions supported by results:</u> Yes.</p>

Table 3: Study profiles for randomized controlled trials on nerve blocks for neuropathic pain (cont'd)

Authors/Study Details	Intervention/Outcome Measures	Study Design/Execution
<p>Bonetti et al. (2005)²⁶ Italy <u>Study design:</u> Prospective randomized, concurrently controlled trial. <u>Follow-up:</u> 1 week, 3 weeks, and 6 months after treatment. <u>Study period:</u> March 2001 to December 2003. <u>Setting:</u> Not reported. <u>Financial support:</u> Not stated.</p>	<p>Periradicular steroid injection; n=80 Intraforaminal O₂O₃ injection; n=86 The initial 306 patients were divided into two groups: those with disc disease (n=166) and those with non-disc disease (n=140). The latter group included patients with facet joint syndromes who received facet joint injections instead of periradicular steroid injections. The results for this group of patients are not summarized here. Periradicular steroid injection <u>Injectant:</u> 2 mL solution of methylprednisolone 80 mg without contrast medium. Intraforaminal O₂O₃ injection <u>Injectant:</u> 3 mL of O₂O₃ at a rate of 25 µg/mL close to the neural foramen. The needle was then retracted and another 5 mL was injected to involve the facet joint region. Computer tomography scans were used to check the correct distribution of the gas mixture. Periradicular steroid and intraforaminal O₂O₃ groups <u>Procedure:</u> A 9 cm 22 gauge needle was positioned 2 to 3 mm from the foraminal region, close to the ganglion of the affected nerve. Computed tomography scanning was used to check correct needle placement. <u>Subsequent treatments:</u> None stated. <u>Adjunct medications:</u> Not reported. <u>Outcome measures:</u> Pain relief. A statistical comparison of the baseline characteristics of the two groups was not reported.</p>	<p><u>Method of randomization:</u> Not reported. <u>Time of randomization:</u> Not reported. <u>Method of allocation concealment:</u> Not reported. <u>Details of blinding:</u> Not reported. <u>Participation rate:</u> Not reported. <u>Eligibility rate for study:</u> Not reported. <u>Intention-to-treat analysis:</u> By default as there were no dropouts or withdrawals during the treatment period. <u>Crossovers:</u> None occurred. <u>Provider:</u> Team of three neuroradiologists <u>Assessor details:</u> Two neurologists blinded to the type of treatment the patients received. <u>Inclusion criteria:</u> Patients with acute or chronic low back pain and sciatica that was unilateral or radiated along the innervation territories of L3, L4, L5, or S1. <u>Exclusion criteria:</u> Patients with bilateral lower back and sciatic nerve pain or with electromyographic features of neurogenic injury and/or denervation. <u>Conclusions supported by results:</u> Yes.</p>

Table 3: Study profiles for randomized controlled trials on nerve blocks for neuropathic pain (cont'd)

Authors/Study Details	Intervention/Outcome Measures	Study Design/Execution
<p>Livingstone and Atkins (2002)²⁷ United Kingdom <u>Study design:</u> Prospective randomized, double-blind concurrently controlled trial. <u>Follow-up:</u> 24 hours, 48 hours, and 1, 15, 20, and 30 weeks after each injection. <u>Study period:</u> Not stated. <u>Setting:</u> Not reported. <u>Financial support:</u> Project grant from the Arthritis Research Council.</p>	<p>Intravenous regional block (IVRB) (guanethidine 15 mg); n=27 IVRB (saline); n=30 Guanethidine IVRB <u>Injectant:</u> Guanethidine monosulphate 15 mg in 30 mL of 0.5% prilocaine. Saline IVRB <u>Injectant:</u> 30 mL of normal saline. Guanethidine & saline groups <u>Procedure:</u> A padded double-cuff tourniquet was applied to the upper arm which was elevated for two minutes before inflation of the proximal cuff to 250 mmHg and administration of the test solution. The total tourniquet time was 20 minutes. <u>Adjunct medications:</u> The patients started physiotherapy, with simple active and passive exercises only, within 48 hours of each block. <u>Subsequent treatments:</u> Further blocks were administered, up to a maximum of four, at weekly intervals until the dolorimetry ratio was ≥ 0.85. <u>Outcome measures:</u> Pain threshold (dolorimeter), verbal pain score, finger stiffness, grip strength, swelling. There was no statistically significant difference between the groups with respect to age, dolorimetry ratio, verbal pain score, finger stiffness, vasomotor instability score, grip ratio, and index finger or hand swelling ($P > 0.05$).</p>	<p><u>Method of randomization:</u> Coin toss. <u>Time of randomization:</u> Not reported. <u>Method of allocation concealment:</u> Coin toss performed by an independent clinician who took no further part in the study. <u>Details of blinding:</u> Treatments were drawn up immediately before injection by an independent clinician in a separate theatre suite. Both injections were of equal volume and colourless. <u>Participation rate:</u> 81.7% (67/82). <u>Eligibility rate for study:</u> 21.8% (82/377). Patients recruited consecutively. <u>Intention-to-treat analysis:</u> By default as there were no dropouts or withdrawals during the treatment period. <u>Crossovers:</u> None occurred. <u>Provider:</u> All injections administered by the same orthopaedic surgeon. <u>Assessor details:</u> Not reported. <u>Inclusion criteria:</u> Patients with complex regional pain syndrome type I (algodystrophy) of the hand after sustaining a Colles' fracture. <u>Exclusion criteria:</u> Surgical fixation of the Colles' fracture; presence of another injury of the upper limb; inability to cooperate with the assessment; pre-existing abnormality of the hand which would affect measurements; medication with known or possible anti-sympathetic effects; contraindication to sympathetic blockade; inability to receive an IVRB within two weeks of the initial assessment. <u>Conclusions supported by results:</u> Yes.</p>

Table 3: Study profiles for randomized controlled trials on nerve blocks for neuropathic pain (cont'd)

Authors/Study Details	Intervention/Outcome Measures	Study Design/Execution
<p>Ng et al. (2005)²⁸ United Kingdom <u>Study design:</u> Prospective randomized, double-blind concurrently controlled trial. <u>Follow-up:</u> 6 and 12 weeks after injection. <u>Study period:</u> November 2001 to June 2003. <u>Setting:</u> Spine specialist clinic at a university hospital. <u>Financial support:</u> None.</p>	<p>Periradicular injection (bupivacaine plus methylprednisolone); n=43 Periradicular injection (bupivacaine); n=43 Periradicular injection (bupivacaine plus methylprednisolone) <u>Injectant:</u> 2 mL of 0.25% bupivacaine with 40 mg of methylprednisolone. Periradicular injection (bupivacaine) <u>Injectant:</u> 2 mL of 0.25% bupivacaine. Bupivacaine plus methylprednisolone & bupivacaine alone groups <u>Procedure:</u> With the patient in a prone position, a 22 to 25 gauge needle was guided fluoroscopically towards the nerve root in the "safe triangle" (defined by the pedicle superiorly, spinal nerve medially, and vertebral body laterally). The nerve root was then visualized with contrast medium. The treatment agent was then injected slowly once a satisfactory neurogram was produced. <u>Adjunct medications:</u> Patients were asked not to alter their oral analgesic medication during the follow-up period without prior approval. <u>Subsequent treatments:</u> None. <u>Outcome measures:</u> Pain intensity (visual analog scale); Oswestry Disability Index score; walking distance; patient satisfaction. While baseline characteristics of the two groups were reported, a statistical comparison of the data was not reported.</p>	<p><u>Method of randomization:</u> Random number table. <u>Time of randomization:</u> Not reported. <u>Method of allocation concealment:</u> A member of the theatre staff who was not otherwise involved in the study placed the treatment assignments in opaque, prenumbered envelopes. The injectants were prepared in syringes sealed with opaque tape. <u>Details of blinding:</u> Patients, surgeons, and outcome assessors were blinded to treatment allocation. <u>Participation rate:</u> 97.8% (88/90). <u>Eligibility rate for study:</u> 89.1% (90/101). Patients recruited consecutively. <u>Intention-to-treat analysis:</u> Yes. Two patients in the bupivacaine plus steroid group and three patients in the bupivacaine group discontinued the trial at 6 weeks due to worsening symptoms and proceeded to discectomy (n=4) and repeat injection (n=1). The intention-to-treat analysis included these five patients. <u>Crossovers:</u> None occurred. <u>Provider:</u> All injections were performed by the same senior surgeon. <u>Assessor details:</u> Research fellow blinded to the type of treatment the patients received. <u>Inclusion criteria:</u> Patients with unilateral leg pain, where the leg pain intensity was at least comparable to the back pain, who had completed at least 6 weeks of non-operative management with non-steroidal anti-inflammatory medication and physical therapy with no apparent benefit; clinical symptoms consistent with the magnetic resonance imaging diagnosis of nerve root compression secondary to either lumbar disc herniation or foraminal stenosis. <u>Exclusion criteria:</u> Acute back trauma, cauda equina syndrome, active local skin infection, previous back operation, periradicular infiltration during the preceding 12 months, epidural injection within the last 3 months, pregnancy, allergy to treatment agents, anticoagulation treatment, inability to complete study questionnaire. <u>Conclusions supported by results:</u> Yes.</p>

Table 3: Study profiles for *randomized controlled trials* on nerve blocks for neuropathic pain (cont'd)

Authors/Study Details	Intervention/Outcome Measures	Study Design/Execution
<p>Nishiyama et al. (2006)²⁹ Japan <u>Study design:</u> Prospective randomized, concurrently controlled crossover trial. <u>Follow-up:</u> 15 minutes after each injection. <u>Study period:</u> Not stated. <u>Setting:</u> Not stated. <u>Financial support:</u> Not stated.</p>	<p>Crossover trial (n=15) Five patients had postherpetic neuralgia and 10 had sudden deafness. Only the results for the patients with postherpetic neuralgia are summarized here. Stellate ganglion block (neurotropin) <u>Injectant:</u> 3 mL of neurotropin in 3 mL of normal saline. Stellate ganglion block (mepivacaine) <u>Injectant:</u> 6 mL of 1% mepivacaine. Neurotropin & mepivacaine groups <u>Procedure:</u> Left stellate ganglion block was performed at C6 with a 25 gauge needle. <u>Adjunct medications:</u> Not reported. <u>Subsequent treatments:</u> Not reported. <u>Washout period:</u> Blocks scheduled twice a week; 10 to 15 injections were received by each patient over a period of 6 to 8 weeks. <u>Outcome measures:</u> Visual analog pain score.</p>	<p><u>Method of randomization:</u> First treatment of each patient was assigned by random numbers. <u>Time of randomization:</u> Not reported. <u>Method of allocation concealment:</u> Not reported. <u>Details of blinding:</u> Not reported. <u>Participation rate:</u> Not reported. <u>Eligibility rate for study:</u> Not reported. <u>Intention-to-treat analysis:</u> By default as there were no dropouts or withdrawals during the treatment period. <u>Crossovers:</u> All patients received both treatments as part of the study design. <u>Provider:</u> All injections administered by the same senior anaesthesiologist. <u>Assessor details:</u> Not reported. <u>Inclusion criteria:</u> Patients newly scheduled for left stellate ganglion block twice a week for sudden deafness or postherpetic neuralgia. <u>Exclusion criteria:</u> Not reported. <u>Conclusions supported by results:</u> Yes.</p>

Table 3: Study profiles for randomized controlled trials on nerve blocks for neuropathic pain (cont'd)

Authors/Study Details	Intervention/Outcome Measures	Study Design/Execution
<p>Taskaynatan et al. (2004)³⁰ Turkey</p> <p><u>Study design:</u> Prospective randomized, double-blind concurrently controlled trial.</p> <p><u>Follow-up:</u> 1 hour and 1.5 months after the first injection.</p> <p><u>Study period:</u> Not stated.</p> <p><u>Setting:</u> Hospital.</p> <p><u>Financial support:</u> Not reported.</p>	<p>Intravenous regional Bier block (IVRBB) (methylprednisolone plus lidocaine); n=14</p> <p>IVRBB (saline); n=11</p> <p>IVRBB (methylprednisolone plus lidocaine)</p> <p><u>Injectant:</u> 10 mL of 2% lidocaine and 40 mg of methylprednisolone in saline.</p> <p>IVRBB (saline)</p> <p><u>Injectant:</u> 100 mL of saline.</p> <p>Methylprednisolone plus lidocaine & saline groups</p> <p><u>Procedure:</u> A large vein in the cubital region was cannulated with a 22 gauge venous catheter. After the affected side was elevated and drained by using an elastic bandage, the cuff was inflated up to 100 mmHg above the patient's systolic blood pressure. The arm was then returned to the horizontal position and the test solution administered over 20 minutes under electrocardiogram monitoring.</p> <p><u>Adjunct medications:</u> Not reported.</p> <p><u>Subsequent treatments:</u> Treatments were applied once a week. Treatments were repeated until three sessions were completed unless significant adverse effects occurred or the patient chose not to continue.</p> <p><u>Outcome measures:</u> Pain intensity (visual analog scale), range of motion, edema, patient satisfaction.</p> <p>There was no statistically significant difference between the groups with respect to age, disease duration, pain intensity, range of motion, or edema (P>0.05).</p>	<p><u>Method of randomization:</u> Not reported.</p> <p><u>Time of randomization:</u> Not reported.</p> <p><u>Method of allocation concealment:</u> Envelopes. No further details reported.</p> <p><u>Details of blinding:</u> Patients and outcome assessors were blinded to treatment allocation.</p> <p><u>Participation rate:</u> Not reported.</p> <p><u>Eligibility rate for study:</u> Not reported.</p> <p><u>Intention-to-treat analysis:</u> Per protocol analysis as three patients withdrew from the study. In the methylprednisolone plus lidocaine group, one patient left because of syncope and one withdrew because of subjective palpitation. In the saline group, one patient withdrew because of subjective palpitation.</p> <p><u>Crossovers:</u> None occurred.</p> <p><u>Provider:</u> Not reported.</p> <p><u>Assessor details:</u> Physician blinded to the type of treatment the patients received.</p> <p><u>Inclusion criteria:</u> Patients with complex regional pain syndrome type I.</p> <p><u>Exclusion criteria:</u> Angina, myocardial infarction, peptic ulcer, diabetes mellitus, osteoporosis, cardiac conduction block or dysrhythmia; patients who had stellate ganglion block or IVRBB within the past month.</p> <p><u>Conclusions supported by results:</u> Yes.</p>

STUDY PROFILES – CLINICAL PRACTICE GUIDELINES

Table 4: Study profiles for *clinical practice guidelines* on nerve blocks for neuropathic pain

Guideline	Target Population	Selection Criteria/Outcomes	Methods
<p>Ambrosio et al. (2006)³¹</p> <p>Objective: To educate anaesthesia and intensive care specialists to consider chronic non-cancer pain as a disease rather than a symptom and to encourage them to individualize the optimum diagnostic and therapeutic approach according the actual model of disease management that focuses on patient's outcome, quality of care, and patient's information and involvement.</p> <p>Target users: Anaesthesia and intensive are specialists.</p> <p>Financial support: Not stated.</p> <p>Conflict of interest: Not stated.</p>	<p>Age: Not stated.</p> <p>Included conditions: Chronic non-cancer pain that extends 3 months beyond onset.</p> <p>Excluded conditions: Not stated.</p>	<p>Interventions: Pharmacologic treatments, intrathecal drug administration, non-pharmacologic treatments, physical therapy.</p> <p>Study inclusion criteria: All international and national scientific publications.</p> <p>Study exclusion criteria: Not stated.</p>	<p>Literature search: <u>Time Period:</u> Not stated. <u>Limits:</u> Not stated. <u>Databases:</u> Not stated. <u>Other sources:</u> Not stated.</p> <p>Appraisal of study quality: Not stated.</p> <p>Formulation of recommendations: Not stated.</p> <p>External review: Not stated.</p> <p>Evidence linked to recommendations: Yes.</p>
<p>Dubinsky et al. (2004)³²</p> <p>Objective: To determine which treatments provide benefit in terms of decreased pain and improved quality of life for patients with postherpetic neuralgia.</p> <p>Target users: Not stated.</p> <p>Financial support: Not stated.</p> <p>Conflict of interest: Not stated.</p>	<p>Age: Not stated.</p> <p>Included conditions: Postherpetic neuralgia of at least 8 weeks' duration.</p> <p>Excluded conditions: Not stated.</p>	<p>Interventions: Medical, interventional, and surgical treatment.</p> <p>Study inclusion/exclusion criteria: Articles that: addressed alleviation of pain in postherpetic neuralgia with a duration of at least 8 weeks after healing of the rash; were prospective, retrospective, or case series studies and provided clinical information on patients receiving treatment; provided detailed methodology and a clear outcome measure; had a primary purpose to demonstrate a decrease of pain related to postherpetic neuralgia; outlined treatment that was feasible in an outpatient setting.</p>	<p>Literature search: <u>Time period:</u> January 1960 to January 2004. <u>Limits:</u> Not stated. <u>Databases:</u> MEDLINE, the <i>Cochrane Database of Systematic Reviews</i>. <u>Other sources:</u> Additional reports were identified from reference lists of review articles and by searching MEDLINE using the names of authors who had published several articles on herpes zoster treatment.</p> <p>Appraisal of study quality: The evidence was graded. Disagreements among reviewers were resolved by consensus.</p> <p>Formulation of recommendations: Details not provided.</p> <p>External review: Peer review by the Quality Standards Subcommittee of the American Academy of Neurology, members of the American Academy of Neurology Member Review Network, and heads of sections of the American Academy of Neurology.</p> <p>Evidence linked to recommendations: Yes.</p>

Table 4: Study profiles for *clinical practice guidelines* on nerve blocks for neuropathic pain (cont'd)

Guideline	Target Population	Selection Criteria/Outcomes	Methods
<p>Hunter Integrated Pain Service (2009)³³</p> <p>Objective: To assist health professionals to provide better pain management for their patients.</p> <p>Target users: Health professionals.</p> <p>Financial support: Not stated.</p> <p>Conflict of interest: Not stated.</p>	<p>Age: Not stated.</p> <p>Included conditions: Neuropathic pain, spinal and radicular pain, tissue ischemia pain, cancer pain.</p> <p>Excluded conditions: Not stated.</p>	<p>Interventions: Medical, interventional, and surgical treatment.</p> <p>Study inclusion/exclusion criteria: Not stated.</p>	<p>Literature search: <u>Time period:</u> Not stated. <u>Limits:</u> Not stated. <u>Databases:</u> Not stated. <u>Other sources:</u> Not stated.</p> <p>Appraisal of study quality: Details not provided.</p> <p>Formulation of recommendations: Details not provided.</p> <p>External review: Details not provided.</p> <p>Evidence linked to recommendations: Yes.</p>
<p>Workers' Compensation Board Evidence Based Practice Group (2004)³⁴</p> <p>Objective: To develop reasonable and practical science-based clinical criteria for the diagnosis and treatment of chronic regional pain syndrome.</p> <p>Target users: Clinicians.</p> <p>Financial support: Not stated.</p> <p>Conflict of interest: Not stated.</p>	<p>Age: Not stated.</p> <p>Included conditions: Complex regional pain syndrome.</p> <p>Excluded conditions: Not stated.</p>	<p>Interventions: Medical, interventional, and surgical treatment.</p> <p>Study inclusion/exclusion criteria: Based on a non-systematic review of the literature, a compilation of expert opinion, and in-depth discussion with numerous practitioners who frequently see patients with chronic regional pain syndrome.</p>	<p>Literature search: <u>Time period:</u> Not stated. <u>Limits:</u> Not stated. <u>Databases:</u> Not stated. <u>Other sources:</u> Not stated.</p> <p>Appraisal of study quality: Evidence was graded according to listed criteria.</p> <p>Formulation of recommendations: Details not provided.</p> <p>External review: Details not provided.</p> <p>Evidence linked to recommendations: No.</p>

SUMMARY OF RELEVANT DATA – SYSTEMATIC REVIEWS

Table 5: Summary of relevant data extracted from *systematic reviews* on nerve blocks for neuropathic pain

Study/ Quality	Patients/ Pain Type	Comparators	Supporting Evidence*							Relevant Results/ Authors' Conclusions
			SR/MA	NR	RCT	NRCS	CS	G	Other	
Carragee et al (2008) ²¹ Quality rating: Average (4/6)	Total number: n = 97 for selective nerve root block (1 NRCS); n = 844 (1036 injections) for extraforaminal root injection (1 CS). Conditions reviewed: Radicular neck pain	No treatment				1 40	1 41			<p>Efficacy/effectiveness: Not reported.</p> <p>Safety: For <i>selective nerve root block</i>, pain at the injection site, non-spinal headache, and headache not associated with standing were all more frequent 1 week after injection, even after controlling for spontaneous events in the non-injection group. Increased pain at the injection site (23%), increased radicular pain (18%), light-headedness (14%), and increased spine pain, headache, or nausea (all 3% to 10%) were reported immediately after injection.</p> <p>For <i>fluoroscopically-guided extraforaminal root injection</i> of the cervical spine, there were no serious neurologic events. Transient pain or weakness occurred immediately after 6 of the 1036 injections (0.6%, 95% CI 0.2 to 1.0%). Adverse events seemed to be associated with anterior placement of the needle.</p> <hr/> <p>Authors' conclusions: There is evidence supporting short-term symptomatic improvement of radicular symptoms in patients not involved in litigation when treatment involves a short course of epidural or selective root injections with corticosteroids. There is no evidence that multiple injections (>3) or repeated courses are beneficial. (N.B. The supporting evidence for this statement was not clearly outlined in the body of the report).</p> <p>There is no evidence that the use of cervical root or epidural injections in patients with seriously symptomatic radiculopathy decreases the rate of open surgery.</p> <p>Cervical foraminal or epidural injections are associated with relatively frequent minor adverse events (5% to 20%); however, serious adverse events are very uncommon (<1%).</p>

Table 5: Summary of relevant data extracted from *systematic reviews* on nerve blocks for neuropathic pain (cont'd)

Study/ Quality	Patients/ Pain Type	Comparators	Supporting Evidence*							Relevant Results/ Authors' Conclusions
			SR/MA	NR	RCT	NRCS	CS	G	Other	
DePalma et al. (2005) ²² Quality rating: Average (4/6)	Total number: Transforaminal epidural steroid injections: n = 325 (5 RCTs) N.B. These constitute a subset of studies that are all included in Abdi et al. (2007) ³⁵ , which is one of the systematic reviews included in the companion literature summary on epidural injections. Conditions reviewed: Lumbosacral radiculopathy.	Placebo transforaminal epidural injection Anaesthetic transforaminal epidural injection Interlaminar epidural corticosteroid injection			5 42-46					<p>Efficacy/effectiveness: Periradicular epidural injection of corticosteroid and anaesthetic produced a statistically significant improvement in pain, straight leg raise test, lumbar flexion, and patient satisfaction at 2 weeks after injection, but not thereafter, compared with saline injection (1 RCT). A single epidural perineural corticosteroid injection was more effective at reducing pain than saline injection (1 RCT). Transforaminal epidural steroid injections were more effective in providing pain relief and improved quality of life compared with interlaminar epidural steroid injections (2 RCTs). Selective nerve root injections of corticosteroid and anaesthetic significantly reduced the need for surgery, compared with injections of anaesthetic alone (1 RCT).</p> <p>Safety: Headache occurred in 1.9% of patients (1 RCT; unclear if referring to all patients or only those in the index intervention arm). One episode of acute hypertension requiring administration of intravenous nicardipine (1 RCT; unclear which patient group this occurred in). One case of retroperitoneal hematoma in a patient who was on anticoagulation therapy (1 RCT; unclear which patient group this occurred in).</p> <hr/> <p>Authors' conclusions: There is limited to moderate evidence that transforaminal epidural steroid injections are a safe and effective adjunct treatment for lumbar radicular symptoms. However, more prospective, randomized, placebo-controlled studies using sham procedures are needed to provide conclusive evidence for the efficacy of transforaminal epidural steroid injections in treating lumbar radicular symptoms.</p>

Table 5: Summary of relevant data extracted from systematic reviews on nerve blocks for neuropathic pain (cont'd)

Study/ Quality	Patients/ Pain Type	Comparators	Supporting Evidence*						Relevant Results/ Authors' Conclusions	
			SR/MA	NR	RCT	NRCS	CS	G		Other
<p>Forouzanfar et al. (2002)²³</p> <p>Quality rating: Average (4/6)</p>	<p>Total number: Total number: <i>Reflex sympathetic dystrophy.</i> Placebo-controlled trials; 7 RCTs Active-controlled trials; 5 RCTs <i>Complex regional pain syndrome type I:</i> Placebo-controlled trials; 1 RCT Active-controlled trials; 1 RCT</p> <p>Conditions reviewed: Complex regional pain syndrome type I or reflex sympathetic dystrophy.</p>	<p><i>Placebo-controlled RCTs:</i> Epidural - clonidine Intravenous – phentolamine; phenylephrine; reserpine; guanethidine; droperidol; ketanserin; lidocaine Injection - lidocaine <i>Active-controlled RCTs:</i> Bretylium + lidocaine vs lidocaine; guanethidine vs lidocaine; guanethidine + lidocaine vs reserpine + lidocaine vs lidocaine; bupivacaine vs guanethidine; guanethidine vs topical dimethylsulphoxide</p>			<p>14 47-60</p>					<p>Efficacy/effectiveness: <u>Reflex sympathetic dystrophy:</u> <i>Placebo-controlled RCTs:</i> Epidural clonidine (300 or 700 µg) and intravenous ketanserin (10 mg bolus) both decreased pain significantly more than placebo (2 RCTs). Neither intravenous phentolamine 35 mg nor phenylephrine 500 µg were effective in achieving regional sympathetic block (1 RCT). There was no difference between intravenous reserpine (0.5 or 1.0 mg), intravenous guanethidine (10, 20, or 30 mg), intravenous droperidol (2.5 mg in 30 or 50 mL of saline), intravenous ketanserin (10 mg bolus), and placebo (4 RCTs). <i>Active-controlled RCTs:</i> Bretylium (1.5 mg/kg) plus 0.5% lidocaine block was more effective in reducing pain than 0.5% lidocaine alone (1 RCT). There was no difference between guanethidine (20 or 40 mg) and 0.5% lidocaine blocks (1 RCT). There was no difference between guanethidine (20 mg) and reserpine 1.25 mg blocks (1 RCT). There was no difference between stellate ganglion block with 0.5% bupivacaine and regional intravenous sympathetic block with guanethidine 20 mg (1 RCT). There was no difference between topical dimethylsulphoxide 50% and regional intravenous sympathetic block (injectant not stated) (1 RCT). <u>Complex regional pain syndrome type I:</u> <i>Placebo-controlled RCTs:</i> There was no difference between 1% lidocaine and placebo in achieving sympathetic ganglion block (1 RCT). <i>(cont'd next page)</i></p>

Table 5: Summary of relevant data extracted from *systematic reviews* on nerve blocks for neuropathic pain (cont'd)

Study/ Quality	Patients/ Pain Type	Comparators	Supporting Evidence*							Relevant Results/ Authors' Conclusions
			SR/MA	NR	RCT	NRCS	CS	G	Other	
Forouzanfar et al. (2002) ²³ (cont'd)										<p><i>Active-controlled RCTs:</i> Lidocaine sympathetic block decreased pain significantly more than diphenhydramine block (1 RCT).</p> <p>Safety: Not reported.</p> <hr style="border-top: 1px dashed black;"/> <p>Authors' conclusions: There is limited to no evidence for the efficacy of sympathetic blocks (stellate ganglion block or regional intravenous sympathetic block) in the treatment of patients with complex regional pain syndrome type I or reflex sympathetic dystrophy.</p>

Table 5: Summary of relevant data extracted from *systematic reviews* on nerve blocks for neuropathic pain (cont'd)

Study/ Quality	Patients/ Pain Type	Comparators	Supporting Evidence*							Relevant Results/ Authors' Conclusions
			SR/MA	NR	RCT	NRCS	CS	G	Other	
Kumar et al. (2004) ²⁴ Quality rating: Poor (3/6)	Total number: n = 108 for sympathetic blocks Conditions reviewed: Postherpetic neuralgia	Not applicable					2 61,62			<p>Efficacy/effectiveness: One study found that sympathetic blocks were beneficial (injectant not stated). One study found that sympathetic blocks with local anaesthetic were less effective in the immediate post-block period than somatic blocks in patients with pain >1 years' duration.</p> <p>Safety: Not reported.</p> <hr style="border-top: 1px dashed black;"/> <p>Authors' conclusions: Evidence for the use of sympathetic blocks is supported by case series studies only. The response of postherpetic neuralgia to sympathetic blocks is unclear at this time. They may be considered useful, but lack good quality randomized controlled trials.</p>

CS - case series study; G - guideline; NR – non-systematic/narrative review; NRCS – non-randomized comparative study; RCT – randomized controlled trial; SR/MA – systematic review/meta-analysis

*The integers listed in the Supporting Evidence columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

SUMMARY OF RELEVANT DATA – RANDOMIZED CONTROLLED TRIALS

Table 6: Summary of relevant data extracted from *randomized controlled trials* on nerve blocks for neuropathic pain

Study/Quality Rating	Interventions/Study Population	Relevant Results/Authors' Conclusions
<p>Becker et al. (2007)²⁵ Prospective randomized, double-blind concurrently controlled trial Quality rating: <i>Internal validity</i> Good (8/9) <i>External validity</i> Good (6/6)</p>	<p>Epidural perineural injection (autologous conditioned serum (ACS)); n=32 Epidural perineural injection (triamcinolone 10 mg); n=25 Epidural perineural injection (triamcinolone 5 mg); n=27 <u>Patient diagnosis:</u> Unilateral lumbar radicular compression <u>Mean age:</u> Combined patient groups: 53.9 years (range 29 to 81) <u>Sex distribution:</u> Combined patient groups: M/F = 52 (61.9%)/32 (38.1%) <u>Pre-treatment mean visual analog scale pain score (scale 0 to 100):</u> ACS - 78; Triamcinolone 10 mg - 85; Triamcinolone 5 mg - 82 <u>Mean duration of pain:</u> Combined patient groups: ≥6 weeks <u>Disc pathology:</u> Not reported. <u>Patient co-morbidities:</u> Not stated. <u>Co-interventions:</u> All pain medications were discontinued at the beginning of the trial. Patients received no additional medical therapy or physiotherapy. Ibuprofen was allowed for the treatment of pain during the trial: the average dose was 1200 mg/day, with no statistically significant difference in usage between the three groups.</p>	<p><u>Lost to follow-up:</u> 0% <u>Outcomes:</u> Patients in all three treatment groups experienced a statistically significant reduction in pain and disability. At the 12- and 22-week follow-up, ACS injections produced a greater improvement in pain score compared with both triamcinolone groups, but statistical significance was observed only at week 22 in direct comparison to the triamcinolone 5 mg group (mean difference -13.5; P=0.046). There were no statistically significant differences between the two triamcinolone dosages with respect to pain or disability scores during the 6 months of the study. <u>Adverse events:</u> ACS (n=32): headache (3.1%); Triamcinolone 10 mg (n=25): headache (4.0%); Triamcinolone 5 mg (n=27): headache (3.7%).</p> <hr style="border-top: 1px dashed black;"/> <p>Authors' conclusions ACS is a promising new treatment option for patients with unilateral lumbar radicular compression. The decrease in pain was pronounced, clinically remarkable, and potentially superior to steroid injection.</p>

Table 6: Summary of relevant data extracted from *randomized controlled trials* on nerve blocks for neuropathic pain (cont'd)

Study/Quality Rating	Interventions/Study Population	Relevant Results/Authors' Conclusions
<p>Bonetti et al. (2005)²⁶ Prospective randomized, concurrently controlled trial Quality rating: <i>Internal validity</i> Moderate (6/9) <i>External validity</i> Moderate (4/6)</p>	<p>Periradicular steroid injection; n=80 Intraforaminal O₂O₃ injection; n=86 Patient <u>diagnosis</u>: Acute or chronic low back pain and sciatica <u>Mean age</u>: Not separately reported for disc disease group. <u>Sex distribution</u>: Not separately reported for disc disease group. <u>Pre-treatment mean visual analog scale pain score</u>: Not stated. <u>Duration of pain</u>: Not stated. <u>Disc pathology</u>: Not separately reported for disc disease group. <u>Patient co-morbidities</u>: Not stated. <u>Co-interventions</u>: Not stated.</p>	<p>Periradicular steroid injection versus intraforaminal O₂O₃ injection: <u>Lost to follow-up</u>: 0% <u>Outcomes</u>: At 1 week follow up, 80% of patients treated with periradicular steroid and 84.8% of patients treated with intraforaminal O₂O₃ had total remission (100% reduction) of pain. At 6 weeks' follow up, 67.5% of patients treated with periradicular steroid and 77.9% of patients treated with intraforaminal O₂O₃ had total remission (100% reduction) of pain. At 6 months' follow up, 57.5% of patients treated with periradicular steroid and 74.4% of patients treated with intraforaminal O₂O₃ had total remission (100% reduction) of pain (P=0.0021). <u>Adverse events</u>: None of the patients experienced arachnoiditis, meningitis, paraparesis, paraplegia, sensory disorders, bowel/bladder dysfunction, headache, or epilepsy.</p> <hr style="border-top: 1px dashed black;"/> <p>Authors' conclusions Oxygen-ozone treatment was highly effective in relieving acute and chronic lower back pain and sciatica. The gas mixture can be administered as a first treatment to replace epidural steroids.</p>

Table 6: Summary of relevant data extracted from *randomized controlled trials* on nerve blocks for neuropathic pain (cont'd)

Study/Quality Rating	Interventions/Study Population	Relevant Results/Authors' Conclusions
<p>Livingstone and Atkins (2002)²⁷ Prospective randomized, double-blind concurrently controlled trial Quality rating: <i>Internal validity</i> Good (7/9) <i>External validity</i> Good (5/6)</p>	<p>Intravenous regional blockade (IVRB) (guanethidine 15 mg); n=27 IVRB (saline); n=30 <u>Patient diagnosis:</u> Complex regional pain syndrome type I (algodystrophy) of the hand <u>Mean age:</u> Guanethidine: 61.7 years (standard error of the mean (SEM) 2.1); Saline: 61.6 years (SEM 2.5) <u>Sex distribution:</u> Guanethidine: M/F = 1 (3.7%)/26 (96.3%); Saline: M/F = 2 (7.1%)/28 (93.3%) <u>Pre-treatment mean dolorimetry ratio:</u> Guanethidine: 0.7 (SEM 0.03); Saline: 0.7 (SEM 0.02) <u>Mean time to diagnosis of algodystrophy:</u> Guanethidine: 9.1 weeks (SEM 0.25); Saline: 9.2 weeks (SEM 0.10) <u>Patient co-morbidities:</u> Not stated. <u>Co-interventions:</u> The patients started physiotherapy, with simple active and passive exercises only, within 48 hours of each block.</p>	<p>Guanethidine IVRB (53 blocks in 27 patients) versus saline IVRB (61 blocks in 30 patients): There was no significant difference between the two groups in terms of the number of IVRBs required. <u>Lost to follow-up:</u> 0% <u>Outcomes:</u> There was a significant improvement in the mean dolorimetry ratio after the blocks in both groups, but there was no significant difference between the two groups up to one week after injection. At 24 hours after the block, there was a significant reduction in the proportion of patients in both groups complaining of pain at rest. The improvement was still evident at one week in the saline group, but not the guanethidine group. This was also the case for pain on exercise, with only the saline group experiencing significant improvement (P=0.035) at one week, compared with baseline values. At 24 hours, 48 hours, and 1 week after injection, dolorimetry ratios, verbal pain scores, finger stiffness, grip strength, and swelling in both groups were significantly improved, compared to baseline values, but there was no difference in the degree of improvement between the groups. At 6 months' follow up, both groups showed continuing improvement with no difference in terms of pain, finger tenderness, finger stiffness, or grip strength. The guanethidine group experienced more pain in the affected hand (P=0.025) and at six months had more vasomotor instability (P<0.0001), compared with the saline group. <u>Adverse events:</u> Not reported.</p> <hr/> <p>Authors' conclusions Guanethidine IVRB offers no significant analgesic advantage over a normal saline placebo block in the treatment of early complex regional pain syndrome type I of the hand after fracture of the distal radius. It does not improve the outcome of this condition and may delay the resolution of vasomotor instability, compared with placebo.</p>

Table 6: Summary of relevant data extracted from *randomized controlled trials* on nerve blocks for neuropathic pain (cont'd)

Study/Quality Rating	Interventions/Study Population	Relevant Results/Authors' Conclusions
<p>Ng et al. (2005)²⁸ Prospective randomized, double-blind concurrently controlled trial</p> <p>Quality rating: <i>Internal validity</i> Good (8/9) <i>External validity</i> Moderate (4/6)</p>	<p>Periradicular injection (bupivacaine plus methylprednisolone); n=43 Periradicular injection (bupivacaine); n=43</p> <p><u>Patient diagnosis:</u> Unilateral chronic lumbar radicular pain</p> <p><u>Mean age:</u> Bupivacaine plus methylprednisolone: 51.2 years (standard deviation (SD) 14.5); Bupivacaine: 49.7 years (SD 17.1)</p> <p><u>Sex distribution:</u> Bupivacaine plus methylprednisolone: M/F = 22 (55.0%)/18 (45.0%); Bupivacaine: M/F = 21 (51.2%)/20 (48.8%)</p> <p><u>Pre-treatment mean visual analog scale pain score (scale 0 to 100):</u> Bupivacaine plus methylprednisolone: Leg – 73.0 (interquartile range 60.0 to 80.0); Back – 38.1 (interquartile range 10.0 to 50.0); Bupivacaine: Leg – 76.9 (interquartile range 60.0 to 82.5); Back – 34.4 (interquartile range 10.0 to 50.0)</p> <p><u>Mean duration of pain:</u> Bupivacaine plus methylprednisolone: 16.9 months (interquartile range 6.3 to 19.5); Bupivacaine: 12.0 months (interquartile range 6.0 to 18.5)</p> <p><u>Disc pathology:</u> Bupivacaine plus methylprednisolone: L3 – 5.0%; L4 – 37.5%; L5 – 32.5%; S1 – 25%; Bupivacaine: L3 – 7.3%; L4 – 34.2%; L5 – 46.3%; S1 – 12.2%;</p> <p><u>Patient co-morbidities:</u> Not stated.</p> <p><u>Co-interventions:</u> Patients were asked not to alter their oral analgesic medication during the follow-up period without prior approval.</p>	<p>Bupivacaine plus methylprednisolone (n=40) versus bupivacaine alone (n=41)</p> <p><u>Lost to follow-up:</u> Bupivacaine plus methylprednisolone – 10.0% (2/43); Bupivacaine – 7.0% (3/43);</p> <p><u>Outcomes:</u> There was no statistically significant difference between the two groups at 3 months' follow-up with respect to mean change in disability score, back or leg pain score, or walking distance.</p> <p>Duration of symptoms was negatively correlated with mean change in Oswestry Disability Index (P=0.03).</p> <p><u>Intention-to-treat analysis:</u> In the bupivacaine plus steroid group (n=43), 35% of patients achieved at least 10% reduction on disability score at 3 months, compared with 55% in the bupivacaine group (n=43). A reduction of at least 20 mm for leg pain visual analog scale occurred in 41.5% of bupivacaine plus steroid patients and 47.5% of bupivacaine patients.</p> <p><u>Adverse events:</u> No complications occurred in either treatment group.</p> <hr/> <p>Authors' conclusions Periradicular infiltration is a safe and simple procedure that can be performed as a day case to provide short-term pain relief. Clinical improvement occurred in both groups of patients. Corticosteroids did not provide any additional benefit over local anaesthetic in patients with chronic radicular pain.</p>

Table 6: Summary of relevant data extracted from *randomized controlled trials* on nerve blocks for neuropathic pain (cont'd)

Study/Quality Rating	Interventions/Study Population	Relevant Results/Authors' Conclusions
<p>Nishiyama et al. (2006)²⁹</p> <p>Prospective randomized concurrently controlled crossover trial</p> <p>Quality rating: <i>Internal validity</i> Good (7/9) <i>External validity</i> Poor (2/6)</p>	<p>Stellate ganglion block (neurotropin); n=5 Stellate ganglion block (mepivacaine); n=5</p> <p><u>Patient diagnosis:</u> Five patients had postherpetic neuralgia and 10 had sudden deafness. Only the results for the patients with postherpetic neuralgia are summarized here.</p> <p><u>Mean age:</u> Not separately reported for postherpetic neuralgia group.</p> <p><u>Sex distribution:</u> Not separately reported for postherpetic neuralgia group.</p> <p><u>Pre-treatment mean visual analog scale pain score (ranged 0 to 100):</u> Not clear from reported data.</p> <p><u>Mean duration of pain:</u> 14 days (standard deviation 7.0) for postherpetic neuralgia group.</p> <p><u>Location of pain:</u> Not reported.</p> <p><u>Patient co-morbidities:</u> Not stated.</p> <p><u>Co-interventions:</u> Not stated.</p>	<p><u>Lost to follow-up:</u> 0%</p> <p><u>Outcomes:</u> The visual analog pain score decreased significantly after each treatment, without any differences between the agents.</p> <p><u>Adverse events:</u> Neurotropin (n=94 injections): Horner's sign on the block side (100%); Mepivacaine (n=94 injections): Horner's sign on the block side (51.1%) (P<0.001) Horner's sign did not occur in any patient on the non-block side. Separate data were not reported for the five neuropathic pain patients.</p> <hr style="border-top: 1px dashed black;"/> <p>Authors' conclusions The stellate ganglion injection of neurotropin decreased the visual analog pain score of patients with postherpetic neuralgia to the same extent as mepivacaine, but with a decreased incidence of Horner's sign.</p>

Table 6: Summary of relevant data extracted from *randomized controlled trials* on nerve blocks for neuropathic pain (cont'd)

Study/Quality Rating	Interventions/Study Population	Relevant Results/Authors' Conclusions
<p>Taskaynatan et al. (2004)³⁰ Prospective randomized, double-blind concurrently controlled trial. Quality rating: <i>Internal validity</i> Moderate (5/9) <i>External validity</i> Good (5/6)</p>	<p>Intravenous regional Bier block (IVRBB) (methylprednisolone plus lidocaine); n=14 IVRBB (saline); n=11 <u>Patient diagnosis:</u> Complex regional pain syndrome type I. <u>Mean age:</u> Combined patient groups: 22.3 years (standard deviation (SD) 1.6) <u>Sex distribution:</u> Combined patient groups: Male = 100% <u>Pre-treatment mean visual analog scale pain score (scale 0 to 10):</u> Methylprednisolone plus lidocaine: 5.7 (SD 1.0); Saline: 4.8 (SD 1.1) <u>Mean duration of pain:</u> Combined patient groups: 3.1 months (SD 1.4) <u>Location of pain:</u> Not reported. <u>Patient co-morbidities:</u> Not stated <u>Co-interventions:</u> A standard exercise program that included range of motion, stretching and strengthening, and contrast bath were applied to all patients daily, except weekends.</p>	<p>Bupivacaine plus methylprednisolone (n=12) versus saline (n=10) <u>Lost to follow-up:</u> Methylprednisolone plus lidocaine – 14.3% (2/14); Saline – 9.1% (1/11) <u>Outcomes:</u> There was no statistically significant difference in pain scores at 1 hour and 1.5 months after injection, compared to baseline values, in either treatment group. Range of motion and volumetric measures improved during the inpatient period in both groups, compared to baseline values, but the improvements were not evident at the 1.5 month follow up. There were no differences between the treatment groups with respect to mean change in visual analog score after each session. There were no differences between the treatment groups with respect to mean change in visual analog score, range of motion, or volumetric measures at the end of the inpatient period. There was no difference in patient satisfaction between the treatment groups at any assessment period. <u>Adverse events:</u> Transient burning pain exacerbation and erythematous flat macular rash occurred in all patients. Nausea, dizziness, tinnitus, flushing, and pruritus in the affected limb were also reported and were more likely in the study group.</p> <hr/> <p>Authors' conclusions Bier block with methylprednisolone and lidocaine does not provide long-term benefit in patients with complex regional pain syndrome I, and its short-term benefit is not superior to saline placebo.</p>

SUMMARY OF RELEVANT DATA – CLINICAL PRACTICE GUIDELINES

Table 7: Summary of relevant data extracted from *clinical practice guidelines* on nerve blocks for neuropathic pain

Guideline/ Quality Rating	Synopsis of Recommendations	Supporting Evidence*						
		SR/MA	NR	RCT	NRCS	CS	G	Other
Ambrosio et al. (2006) ³¹ (Italy) Quality rating: Poor (14/28)	Guanethidine may be useful in complex regional pain syndromes with a documented sympathetic component.					1 63		1 64
Dubinsky et al. (2004) ³² (United States) Quality rating: Average (17/28)	The effectiveness of stellate ganglion block in the treatment of postherpetic neuralgia is unproven.					Refer- ences for CS studies not provided		
Hunter Integrated Pain Service (2009) ³³ Quality rating: Poor (10/28)	Nerve block techniques for early neuropathic pain are generally simple to perform with a low risk of significant side effects. The potential benefit in early neuropathic pain is high (preventing progression to persistent pain). Therefore, despite the inadequacy of the evidence base, a case can be made to consider procedural intervention in acute (<3 months' duration) and subacute (3 to 6 months' duration) neuropathic pain not responding to initial oral anti-neuropathic therapy. However, if procedural intervention is used, it should be part of a multi-modal "whole person" approach. Further research is clearly needed in this area.	3 24,53,65						

Table 7: Summary of relevant data extracted from *clinical practice guidelines* on nerve blocks for neuropathic pain (cont'd)

Guideline/ Quality Rating	Synopsis of Recommendations	Supporting Evidence*					
		SR/MA	NR	RCT	NRCS	CS	G
Workers' Compensation Board Evidence Based Practice Group (2004) ³⁴ Quality rating: Poor (11.5/28)	<ol style="list-style-type: none"> 1. In a patient who meets the criteria for chronic regional pain syndrome (CRPS), up to three sympathetic blocks will be authorized to allow the attending physician to determine whether the patient has sympathetically mediated pain. 2. Additional blocks should be undertaken only if there is evidence from the first three that the patient has sympathetically mediated pain. 3. The physician who performs each sympathetic block should document: <ol style="list-style-type: none"> a. Measurable evidence that a sympathetic blockade in the target limb was achieved – e.g., hand/foot temperature before and after the block, observed color changes and/or venodilation. b. The extent and duration of the patient's pain relief, based on a pain diary. 4. A patient should be seen by a physical or occupational therapist during the time interval when a sympathetic block would be expected to have an effect – i.e., within a few hours of the block. The therapist should document the functional status of the patient's symptomatic limb during the therapy session. 5. The attending physician or the physician performing sympathetic blocks should correlate the information previously described in #3 and #4 to determine whether a block has produced the intended effects on pain, function, and observable manifestations of CRPS. <p>Treatment Phases</p> <p>Treatment is divided into 6-week phases. A maximum of three phases may be authorized. The second phase will be authorized only if the first phase has led to demonstrable functional improvement. The third phase may be authorized only if the first and second phases have led to demonstrable functional improvement.</p> <ol style="list-style-type: none"> 1. In the first 6-week phase, up to five sympathetic blocks will be authorized (along with other accepted conservative measures such as medication management). 2. During the second 6-week phase, a total of three sympathetic blocks will be authorized. 3. Up to three more sympathetic blocks may be authorized for patients who go on to the third phase of treatment. 	Not provided					

*The integers listed in the Supporting Evidence columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

APPENDIX A: SEARCH STRATEGY

The literature search was conducted by the IHE Research Librarian from May 5 to 12, 2008. Major electronic databases used included *The Cochrane Library*, the NHS Centre for Reviews and Dissemination (CRD Databases: NHS EED, HTA, DARE), PubMed, EMBASE, and AMED (Allied and Complementary Medicine). In addition, relevant library collections, web sites of practice guideline clearing houses, regulatory agencies, evidence-based resources, and HTA related agency resources were searched (Table A.1). Internet search engines were also used to locate grey literature.

Medical Subject Headings (MeSH) terms relevant to this topic include: Pain; Peripheral nervous system diseases; Neuralgia; Complex regional pain syndromes; Nerve Block; Infusions, Intravenous; Analgesia, Epidural.

Table A.1: Databases and search terms used in the search strategy

Database	Edition/Date Searched	Search Terms
Databases		
<i>The Cochrane Library</i> http://www.thecochranelibrary.com	May 5, 2008	(((neuropath* OR neurogenic) AND pain) OR neuralgia* OR "reflex system dystrophy" Or "reflex sympathetic dystrophy" OR "diabetic neuropathy" OR "peripheral neuropathy" OR radiculopath* or plexopath* or" complex regional pain syndrome" OR causalgia OR ("multiple sclerosis" and pain) OR sciatica OR (("nerve injury" OR "nerve injuries") and pain) OR syringomyelia OR "brachial plexus injury" OR "brachial plexus injuries" OR "phantom limb" OR amputation OR "post mastectomy" OR "post stroke" OR ("spinal cord" and pain) or (sacroiliac and pain)):ti,ab,kw and ("nerve block" or "nerve blocks" or "nerve blockade" or "medial branch block" or "medial branch blocks" or "intravenous infusion" or "intravenous infusions" or "IV infusion" or "IV infusions" or "spinal nerve stimulation" or "spinal cord stimulation" OR "sympathetic block" or "sympathetic blocks" or "sympathetic blockade" or "epidural block" or "epidural blocks" or "epidural blockade" Or "epidural steroid injection" or tfesi or "epidural steroid injections" or "paravertebral block" or "paravertebral blocks" or "paravertebral injection" or "paravertebral injections" or "paraspinal block" or "paraspinal blocks" or "paraspinal injection" or "paraspinal injections" or "stellate ganglion block" or nonpharmacologic* or non-pharmacologic*):ti,ab, from 1997 to 2008
EMBASE –Ovid platform (Licensed resource)	May 5, 2008	See Note 1 for EMBASE search
MEDLINE/PubMed	May 5, 2008	See Note 2 for MEDLINE search PubMed searched for in process citations. (search[tiab] OR medline[tiab] OR systematic review[tiab] OR metaanalys*[tiab] OR randomized[tiab] or clinical trial[ti]) AND (in process[sb] OR pubmednotmedline[sb] OR publisher[sb]) added to textword search

<p>Web of Science – ISI platform (Licensed resource)</p> <p>BIOSIS Previews – ISI platform (licensed resource)</p>	<p>May 5, 2008</p>	<p>neuropath* OR neurogenic OR neuralgia* OR “reflex system dystrophy” OR “reflex sympathetic dystrophy” OR “diabetic neuropathy” OR “peripheral neuropathy” OR radiculopath* OR plexopath* OR “complex regional pain syndrome” OR causalgia OR “multiple sclerosis” OR sciatica OR “nerve injury” OR “nerve injuries” OR syringomyelia OR “brachial plexus injury” OR “brachial plexus injuries” OR “phantom limb” OR amputation OR “post mastectomy” OR “post stroke” OR “spinal cord” OR sacroiliac</p> <p>AND pain</p> <p>AND “nerve block” or “nerve blocks” or “nerve blockade” or “medial branch block” or “medial branch blocks” or “intravenous infusion” or “intravenous infusions” or “IV infusion” or “IV infusions” or “spinal nerve stimulation” or “spinal cord stimulation” OR “sympathetic block” or “sympathetic blocks” or “sympathetic blockade” or “epidural block” or “epidural blocks” or “epidural blockade” Or “epidural steroid injection” or tfsi or “epidural steroid injections” or “paravertebral block” or “paravertebral blocks” or “paravertebral injection” or “paravertebral injections” or “paraspinal block” or “paraspinal blocks” or “paraspinal injection” or “paraspinal injections” or “stellate ganglion block” or nonpharmacologic* or non-pharmacologic*</p> <p>AND random* or "systematic review" or "practice guideline" or search* or "technology assessment" or "clinical trial" or double-blind* or meta-analys* or metaanalys*</p>
<p>CRD Databases (Results from DARE and HTA portions only)</p>	<p>May 5, 2008</p>	<p>neuropath* OR neurogenic OR neuralgia* OR “reflex system dystrophy” OR “reflex sympathetic dystrophy” OR “diabetic neuropathy” OR “peripheral neuropathy” OR radiculopath* OR plexopath* OR “complex regional pain syndrome” OR causalgia OR “multiple sclerosis” OR sciatica OR “nerve injury” OR “nerve injuries” OR syringomyelia OR “brachial plexus injury” OR “brachial plexus injuries” OR “phantom limb” OR amputation OR “post mastectomy” OR “post stroke” OR “spinal cord” OR sacroiliac</p> <p>AND pain</p> <p>AND “nerve block” or “nerve blocks” or “nerve blockade” or “medial branch block” or “medial branch blocks” or “intravenous infusion” or “intravenous infusions” or “IV infusion” or “IV infusions” or “spinal nerve stimulation” or “spinal cord stimulation” OR “sympathetic block” or “sympathetic blocks” or “sympathetic blockade” or “epidural block” or “epidural blocks” or “epidural blockade” Or “epidural steroid injection” or tfsi or “epidural steroid injections” or “paravertebral block” or “paravertebral blocks” or “paravertebral injection” or “paravertebral injections” or “paraspinal block” or “paraspinal blocks” or “paraspinal injection” or “paraspinal injections” or “stellate ganglion block” or nonpharmacologic* or non-pharmacologic*</p> <p>Year published 1997 – 2008 OR Published date 1997 - 2008</p>
<p>AMED</p>	<p>May 5, 2008</p>	<p>See Note 3 for AMED search</p>

CINAHL	May 5, 2008	<p>(MH "Pain+") or pain</p> <p>AND</p> <p>(MH "Peripheral Nervous System Diseases+") OR (MH "Facial Neuralgia") OR (MH "Trigeminal Neuralgia") OR (MH "Nervous System Diseases+") OR (MH "Reflex Sympathetic Dystrophy") or (MH "Complex Regional Pain Syndromes+") OR (MH "Radiculopathy") or (MH "Polyradiculopathy") or (MH "Polyradiculoneuritis") OR (MH "Multiple Sclerosis") OR (MH "Syringomyelia") OR (MH "Brachial Plexus Neuropathies+") OR (MH "Phantom Limb") or (MH "Phantom Pain") OR (MH "Amputation+") OR (MH "Somatosensory Disorders+") or neuralgia* or neuropath* or neurogenic or "reflex sympathetic dystrophy" or "complex regional pain syndrome" or radiculopath* or plexopath* or polyradiculopath* or causalgia or sciatica</p> <p>AND</p> <p>(MH "Nerve Block") OR (MH "Infusions, Intravenous") or (MH "Infusions, Intraspinal+") OR (MH "Central Nervous System Stimulants") OR (MH "Sympatholytics+") OR (MH "Analgesia, Epidural") or (MH "Infusions, Epidural") or (MH "Injections, Epidural+") OR (MH "Injections, Intraspinal") OR (MH "Ganglionic Blockers") OR "nerve block" or "nerve blocks" or "nerve blockade" or "sympathetic block" or "sympathetic blocks" or "sympathetic blockade" or "intravenous infusion" or "iv infusion" or "intravenous infusions" or "iv infusions" or "spinal nerve stimulation" or "spinal cord stimulation" or "epidural block" or "epidural blocks" or "epidural blockade" or "medial branch block" or "medial branch blocks" or "medical branch blockade" or "epidural steroid injection" or "epidural steroid injections" or tfesi or "paravertebral block" or "paravertebral blocks" or "paraspinal block" or "paraspinal blocks" or "paravertebral infusion" or "paravertebral infusions" or "paraspinal infusion" or "paraspinal infusions" or "ganglion block" or nonpharmacologic* or non-pharmacologic*</p> <p>AND</p> <p>(MH "Meta Analysis") OR (MH "Systematic Review") OR (MH "Practice Guidelines") OR (MH "Clinical Trials") or (MH "Double-Blind Studies") Or random* OR "systematic review" or "practice guideline" or search* or "technology assessment" or "clinical trial" or double-blind* or meta-analys* or metaanalys*</p>
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Theses Canada portal	May 7, 2008	Neuropathic; neuralgia; neuropathy; complex regional; reflex sympathetic; causalgia; radiculopathy; blockade; epidural; nerve block; nerve blocks; spinal cord stimulation Title keyword Pain and nerve and treatment Any keyword
National Library for Health	May 7, 2008	Neuropathic pain; neuralgia; neuropathy; complex regional; reflex sympathetic; causalgia; radiculopathy; nerve block; nerve blockade; nerve blocks; epidural block(s,ade); spinal cord stimulation; iv infusion(s); intravenous infusions(s)
Proquest Dissertations and Theses	May 7, 2008	TITLE(neuropathic pain) TITLE(neuralgia or neuropathy or causalgia) AND (treat* or therap*) TITLE(complex regional) OR TITLE (reflex sympathetic) TITLE (nerve block or nerve blocks or nerve blockade) TITLE(epidural block or epidural blocks or epidural blockade) TITLE(iv infusion or iv infusions or intravenous infusion or intravenous infusions)
Guidelines		
AMA Clinical Practice Guidelines http://www.topalbertadors.org/TOP/CPG/CPGTopics.htm	May 7, 2008	Browsed list of guidelines
CMA Infobase http://mdm.ca/cpgsnew/cpgs/index.asp	May 7, 2008	Neuropathic; neuropathy; neurogenic; neuralgia; pain; nerve; nerves; intravenous; block; stimulation; epidural
National Guideline Clearinghouse http://www.ngc.gov	May 7, 2008	"neuropathic pain"; "complex regional pain syndrome"; nerve block; nerve blocks; intravenous infusion; spinal nerve stimulation; spinal cord stimulation; sympathetic block; sympathetic blocks; epidural Clinical specialty; neurology
Guidelines International Network	May 7, 2008	Neuropathic pain; neuralgia; neuropathy; nerve block; nerve blockade; blockade; epidural; infusion; stimulation; complex regional; reflex; causalgia; radiculopathy; polyradiculopathy
New Zealand Guidelines Group http://www.nzgg.org.nz	May 7, 2008	Browsed list of guidelines.
SIGN http://www.sign.ac.uk	May 7, 2008	Browsed list of guidelines.
Clinical Trials		
ClinicalTrials.gov (US) http://clinicaltrials.gov/	May 7, 2008	Neuropathic pain and nerve block; Epidural block; Neuralgia pain block; Causalgia pain block Spinal cord stimulation Iv infusions pain; intravenous infusions pain Complex regional pain syndrome Reflex sympathetic dystrophy Radiculopathy

CenterWatch Clinical Trials Listing Service http://www.centerwatch.com/	May 7, 2008	Neuropathic pain Nerve block (s/ade) Epidural block (s/ade) Spinal cord stimulation Intravenous (IV) infusion pain CRPS Reflex sympathetic
metaRegister of Controlled Trials (mRCT) http://www.controlled-trials.com/mrct/	May 12, 2008	Neuropathic pain and block Neuralgia Nerve block (s/ade) and pain Epidural block (s/ade) pain Epidural nerve pain Spinal cord stimulation Complex Regional pain syndrome Reflex sympathetic Iv infusion and pain; intravenous infusion and pain
HTA resources		
AETMIS http://www.aetmis.gouv.qc.ca	May 12, 2008	Neuropathic pain; neuralgia; causalgia; neuropathy; nerve; epidural; stimulation; pain syndrome; sympathetic; intravenous
CADTH http://www.cadth.ca	May 12, 2008	Neuropathic; neuralgia; causalgia; neuropathy; nerve; epidural; stimulation; pain syndrome; sympathetic; intravenous
Institute for Clinical and Evaluative Sciences (ICES), Ontario http://www.ices.on.ca/	May 12, 2008	Browsed list of reports
Health Technology Assessment Unit At McGill http://www.mcgill.ca/tau/	May 12, 2008	Browsed list of reports
Medical Advisory Secretariat http://www.health.gov.on.ca/english/providers/program/mas/mas_mn.html	May 12, 2008	Browsed list of analyses and recommendations
CCE http://www.med.monash.edu.au/healthservices/cce/	May 12, 2008	Browsed list of current evidence reviews
ASERNIP-S http://www.surgeons.org/asernip-s/	May 12, 2008	Browsed list of publications
WorksafeBC http://www.worksafebc.com/health_care_providers/related_information/evidence_based_medicine/default.asp	May 12, 2008	Browsed list of systematic reviews

NIHR Health Technology Assessment Programme http://www.ncchta.org	May 12, 2008	Browsed HTA research
NZHTA http://nzhta.chmeds.ac.nz/publications.htm	May 12, 2008	Browsed list of publications
NICE (UK) http://www.nice.org.uk/	May 12, 2008	Neuropathic; neuralgia; causalgia; neuropathy; nerve; block; epidural; stimulation; pain; sympathetic; intravenous
MSAC http://www.msac.gov.au/	May 12, 2008	Browsed lists of current and completed assessments
National Horizon Scanning Centre http://www.pcpoh.bham.ac.uk/publichealth/horizon	May 12, 2008	Browsed lists of publications and technology briefings
AHRQ http://www.ahrq.gov	May 12, 2008	Browsed lists of technology assessments and evidence reports
California Technology Assessment Forum (CTAF) http://www.ctaf.org	May 12, 2008	Browsed list of assessments
Euroscan	May 12, 2008	Browsed list of technology reports

“*” is a truncation character that retrieves all possible suffix variations of the root word e.g. surg* retrieves surgery, surgical, surgeon, etc.

; separates search terms that were searched separately

Note 1: EMBASE Search Strategy

1. pain.mp. or POSTOPERATIVE PAIN/ or exp PAIN/
2. exp Neuropathic pain/
3. 1 or 2
4. exp NEURALGIA/
5. exp Neuropathy/
6. (neuropath\$ or neurogenic or neuralgia\$.mp.
7. reflex sympathetic dystrophy.mp.
8. complex regional pain syndrome\$.mp.
9. exp Radiculopathy/
10. (radiculopath\$ or plexopath\$.mp.
11. exp Nervous System Injury/
12. post stroke.mp.
13. causalgia.mp.
14. Multiple Sclerosis/
15. exp Spinal Cord Disease/
16. sciatic nerve/
17. peripheral nerve/
18. peripheral nerve injur\$.mp.
19. brachial plexus/
20. (sciatica or ischialgia).mp.
21. exp spinal cord/

22. exp Nervous System Tumor/
23. exp Agnosia/
24. exp amputation/
25. post mastectomy.mp.
26. exp Somatosensory Disorder/
27. or/4-25
28. 3 and 27
29. (non-pharmacologic\$ adj2 (treatment\$ or intervention\$ or therap\$)).mp.
30. exp nerve block/
31. nerve block\$.mp.
32. medial branch block\$.mp.
33. intravenous drug administration/
34. ((intravenous or iv) adj1 infusion\$).mp.
35. spinal cord stimulation/
36. ((spinal cord or spinal nerve) adj1 stimulat\$).mp.
37. sympathetic blocking/
38. sympathetic block\$.mp.
39. exp epidural anesthesia/
40. epidural block\$.mp.
41. (epidural steroid injection\$ or tfesi).mp.
42. epidural drug administration/
43. ((paravertebral or paraspinal) adj1 (block\$ or injection\$)).mp.
44. stellate ganglion block\$.mp.
45. or/29-44
46. 28 and 45
47. meta-analysis.mp.
48. (medline or pubmed or search\$).mp.
49. systematic\$ review\$.mp.
50. (technology assessment\$ or hta).mp.
51. practice guideline.mp.
52. clinical pathway/
53. consensus development.mp. or consensus statement.ti.
54. or/47-53
55. 46 and 54
56. random\$.tw. or placebo\$.mp. or double-blind\$.tw. or trial.ti.
57. controlled clinical trial/ or randomized controlled trial/
58. 56 or 57
59. 46 and 58
60. 55 or 59
61. limit 60 to yr="1997 - 2008"

Note 2: MEDLINE Search Strategy

1. pain.mp. or exp Pain/ or Pain, Postoperative/
2. neuropath\$.mp.
3. neurogenic.mp.
4. exp peripheral nervous system diseases/ or brachial plexus neuropathies/ or complex regional pain syndromes/ or diabetic neuropathies/ or neuralgia/ or sciatica/
5. Facial Neuralgia/
6. Trigeminal Neuralgia/
7. neuralgia\$.mp.
8. reflex sympathetic dystrophy.mp.
9. exp polyradiculopathy/
10. (radiculopath\$ or plexopath\$).mp.
11. complex regional pain syndromes/ or causalgia/ or reflex sympathetic dystrophy/

12. thalamic.mp.
13. post stroke.mp.
14. exp Multiple Sclerosis/
15. Syringomyelia/
16. Sciatic Nerve/ or Peripheral Nerves/
17. peripheral nerve injur\$.mp.
18. exp Brachial Plexus/ or brachial plexus injury pain syndrome.mp. or exp Brachial Plexus Neuropathies/
19. (sciatica or ischialgia).mp.
20. exp Spinal Cord/
21. exp Spinal Cord Diseases/
22. exp Nervous System Neoplasms/
23. Phantom Limb/
24. amputation/
25. post mastectomy.mp.
26. somatosensory disorders/ or hyperalgia/ or hyperesthesia/ or paresthesia/
27. (complex regional pain syndrome\$ or reflex sympathetic dystrophy\$ or causalgia).mp.
28. or/2-27
29. 1 and 28
30. (non-pharmacologic\$ adj2 (treatment\$ or intervention\$ or therap\$)).mp.
31. exp Nerve Block/
32. nerve block\$.mp.
33. Infusions, Intravenous/
34. ((intravenous or iv) adj1 infusion\$).mp.
35. Anesthetics, Local/
36. spinal nerve stimulat\$.mp.
37. spinal cord stimulat\$.mp.
38. sympathetic block\$.mp.
39. Analgesia, Epidural/
40. Injections, Epidural/
41. epidural block\$.mp.
42. medial branch block\$.mp.
43. (epidural steroid injection\$ or tfesi).mp.
44. ((paravertebral or paraspinal) adj1 (block\$ or injection\$)).mp.
45. stellate ganglion block\$.mp.
46. or/30-45
47. 29 and 46
48. meta-analysis.mp.pt.
49. (medline or pubmed or search\$).mp.
50. systematic\$ review\$.mp.
51. (technology assessment\$ or hta).mp.
52. practice guideline.mp.pt. or guideline.pt.
53. critical pathways/
54. consensus development conference.pt. or consensus statement.ti.
55. or/48-54
56. 47 and 55
57. Clinical trial.pt. or randomized.ab. or placebo.ab. or clinical trials/ or randomly.ab. or trial.ti.
58. 47 and 57
59. 56 or 58
60. limit 59 to yr="1997 - 2008"

Note 3: AMED Search Strategy

1. pain.mp. or exp Pain/
2. (neuropath\$ or neurogenic or neuralgia\$).mp.
3. exp peripheral nervous system disease/
4. (reflex sympathetic dystrophy or complex regional pain syndrome\$).mp.
5. (radiculopath\$ or plexopath\$).mp.
6. causalgia.mp.
7. post stroke.mp.
8. thalamic.mp.
9. multiple sclerosis/
10. exp spinal cord disease/
11. exp spinal cord injuries/
12. exp peripheral nerves/
13. peripheral nerve injur\$.mp.
14. (sciatica or ischialgia).mp.
15. spinal cord/
16. exp nervous system neoplasms/
17. hyperalgesia/ or paresthesia/ or phantom limb/
18. amputation/
19. post mastectomy.mp.
20. or/2-19
21. 1 and 20
22. ((non-pharmacologic\$ or nonpharmacologic\$) adj2 (treatment\$ or intervention\$ or therap\$)).mp.
23. nerve block/
24. nerve block\$.mp.
25. medial branch block\$.mp.
26. ((intravenous or iv) adj1 infusion\$).mp.
27. ((spinal nerve or spinal cord) adj2 stimulat\$).mp.
28. sympathetic block\$.mp.
29. analgesia epidural/
30. epidural block\$.mp.
31. (epidural steroid injection\$ or tfesi).mp.
32. ((paravertebral or paraspinal) adj1 (block\$ or injection\$)).mp.
33. stellate ganglion block\$.mp.
34. or/22-33
35. meta-analys\$.mp. or search\$.tw. or review.pt. or systematic review.mp.
36. random\$.mp.
37. practice guidelines/ or practice guideline\$.mp.
38. or/35-37
39. 21 and 34 and 38
40. limit 39 to yr="1997 - 2008"

APPENDIX B: EXCLUDED STUDIES AND STUDIES NOT RETRIEVED BY THE REPORT DEADLINE

Table B.1: Summary of excluded studies on *nerve blocks* (listed in alphabetical order of first author)

Study	Study Type	Reason for Exclusion
Systematic reviews		
Abram SE. Neural blockade for neuropathic pain. <i>The Clinical Journal of Pain</i> 2000; 16(2 Suppl):S56-S61.	Quasi-systematic review	Included studies not critically appraised.
Agency for Healthcare Research and Quality. Management of chronic central neuropathic pain following traumatic spinal cord injury. Report No. 45. 2001. Available: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hst at1.chapter.64890	Systematic review	Included studies on children/adolescents (>13 years of age).
Albazaz R. Complex regional pain syndrome: A review. <i>Annals of Vascular Surgery</i> 2008; 22(2):297-306.	Quasi-systematic review	Included studies not critically appraised.
Alper BS, Lewis PR. Treatment of postherpetic neuralgia: a systematic review of the literature. <i>The Journal of Family Practice</i> 2002; 51(2):121-8.	Systematic review	Literature searches conducted up to October 2000. Superseded by Kumar et al. (2004) ²⁴ .
Berg AP, Rosenquist RW. Complications of peripheral nerve blocks. <i>Techniques in Regional Anesthesia and Pain Management</i> 2007; 11(3):133-40.	Narrative review	Search strategy not described. Included studies not critically appraised.
Bernstein RM. Injections and surgical therapy in chronic pain. <i>Clinical Journal of Pain</i> 2001; 17(4 Suppl):S94-S104.	Quasi-systematic review	Included studies not critically appraised.
Bhargava A, DePalma MJ, Ludwig S, Gelb D, Slipman CW. Injection therapy for lumbar radiculopathy. <i>Current Opinion in Orthopedics</i> 2005; 16(3):152-7.	Systematic review	Literature searches conducted from December 2003 to January 2005. Included DePalma et al. (2005) ²² , but review of lower quality and search strategy more limited than the DePalma et al. (2005) review.
Cepeda MS, Lau J, Carr DB. Defining the role of local anesthetic sympathetic blockade in complex regional pain syndrome: A narrative and systematic review. <i>The Clinical Journal of Pain</i> 2002; 18(4):216-33.	Systematic review	Literature searches conducted up to 1999. Superseded by Forouzanfar et al. (2002) ²³ .
Cepeda MS, Carr DB, Lau J. Local anaesthetic sympathetic blockade for complex regional pain syndrome. <i>Cochrane Database of Systematic Reviews</i> 2005; Issue 4. Art. No.: CD004598. DOI: 10.1002/14651858.CD004598.pub2	Systematic review	Inclusion criteria encompassed studies on children. Included the same studies as Forouzanfar et al. (2002) ²³ .
Chan PSL, Clark AJ. Postherpetic neuralgia: Review of treatment modalities. <i>Pain Research and Management</i> 2000; 5(1):69-74.	Quasi-systematic review	Included studies not critically appraised.

Day M. Sympathetic blocks: the evidence. <i>Pain Practice</i> 2008; 8(2):98-109.	Systematic review	The study population included patients with fibromyalgia, headache, cancer, myofascial, ischemia, and pancreatitis related pain; the results for neuropathic pain could not be separated from the aggregate data.
Eisenberg E, Geller R, Brill S. Pharmacotherapy options for complex regional pain syndrome. <i>Expert Review of Neurotherapeutics</i> 2007; 7(5):521-31.	Narrative review	Search strategy not described. Included studies not critically appraised.
Halbert J, Crotty M, Cameron ID. Evidence for the optimal management of acute and chronic phantom pain: A systematic review. <i>The Clinical Journal of Pain</i> 2002; 18(2):84-92.	Systematic review	None of the included studies addressed nerve blocks for pain lasting more than 2 weeks after limb amputation.
Harden RN. Pharmacotherapy of complex regional pain syndrome. <i>American Journal of Physical Medicine & Rehabilitation</i> 2005; 84(3 Suppl):S17-S28.	Narrative review	Search strategy not described. Included studies not critically appraised.
Hempstall K, Nurmikko TJ, Johnson RW, A'Hern RP, Rice ASC. Analgesic therapy in postherpetic neuralgia: A quantitative systematic review. <i>PLoS Medicine</i> 2005; 2(7):e164.	Systematic review	Does not include studies on nerve blocks for neuropathic pain.
Hord ED, Oaklander L. Complex regional pain syndrome: A review of evidence-supported treatment options. <i>Current Pain and Headache Reports</i> 2003; 7(3):188-96.	Narrative review	Search strategy not described. Included studies not critically appraised.
Kemler MA. Complex regional pain syndrome type I. <i>Pain Reviews</i> 2001; 8(1):35-45.	Quasi-systematic review	Included studies not critically appraised.
Kingery WS. A critical review of controlled clinical trials for peripheral neuropathic pain and complex regional pain syndromes. <i>Pain</i> 1997; 73(2):123-39.	Systematic review	Literature searches conducted up to 1996. Superseded by Forouzanfar et al. (2002) ²³ .
Luijsterburg PA, Verhagen AP, Ostelo RW, Van Os TA, Peul WC, Koes BW. Effectiveness of conservative treatments for the lumbosacral radicular syndrome: a systematic review. <i>European Spine Journal</i> 2007; 16(7):881-99.	Systematic review	Literature searches conducted up to May 2004. The single relevant study was included in DePalma et al. (2005) ²² .
McQuay HJ, Moore RA, Eccleston C, Morley S, De C Williams AC. Systematic review of outpatient services for chronic pain control. <i>Health Technology Assessment</i> 1997; 1(6):1-137. Available: http://www.ncchta.org/execsumm/summ106.htm	Systematic review	Literature searches conducted up to May 1993. Superseded by Forouzanfar et al. (2002) ²³ .
Middleton WJ. Lumbar sympathetic block: A review of complications. <i>Techniques in Regional Anesthesia and Pain Management</i> 1998; 2(3):137-46.	Narrative review	Search strategy not described. Included studies not critically appraised.
Nelemans PJ, deBie RA, deVet HC, Sturmans F. Injection therapy for subacute and chronic benign low back pain. <i>Spine</i> 2001; 26(5):501-15.	Systematic review	Does not include studies on nerve blocks for neuropathic pain.
Nelson DV, Stacey BR. Interventional therapies in the management of complex regional pain syndrome. <i>Clinical Journal of Pain</i> 2006; 22(5):438-42.	Narrative review	Search strategy not described. Included studies not critically appraised.

Peloso PMJ, Gross A, Haines T, Trinh K, Goldsmith CH, Burnie SJ, Cervical Overview Group. Medicinal and injection therapies for mechanical neck disorders. <i>Cochrane Database of Systematic Reviews</i> 2007, Issue 3. Art. No.: CD000319. DOI: 10.1002/14651858.CD000319.pub4	Systematic review	Does not include studies on nerve blocks for neuropathic pain.
Perez RS, Kwakkel G, Zuurmond WW, de Lange JJ. Treatment of reflex sympathetic dystrophy (CRPS type 1): a research synthesis of 21 randomized clinical trials. <i>Journal of Pain and Symptom Management</i> 2001; 21(6):511-26.	Systematic review	Literature searches conducted up to 2000. Superseded by Forouzanfar et al. (2002) ²³ .
Rowbotham MC. Pharmacologic management of complex regional pain syndrome. <i>Clinical Journal of Pain</i> 2006; 22(5):425-29.	Narrative review	Search strategy not described. Included studies not critically appraised.
Van Zundert J, Harney D, Joosten EAJ, Durieux ME, Patijn J, Prins MH, Van Kleef M. The role of the dorsal root ganglion in cervical radicular pain: Diagnosis, pathophysiology, and rationale for treatment. <i>Regional Anesthesia and Pain Medicine</i> 2006; 31(2):152-67.	Systematic review	Does not include studies on nerve blocks for neuropathic pain.
Vroomen PC, de Krom MC, Slofstra PD, Knottnerus JA. Conservative treatment of sciatica: a systematic review. <i>Journal of Spinal Disorders</i> 2000; 13(6):463-9.	Systematic review	Does not include studies on nerve blocks for neuropathic pain.
Wunderlich RP. Pathophysiology and treatment of painful diabetic neuropathy of the lower extremity. <i>Southern Medical Journal</i> 1998; 91(10):894-98.	Quasi-systematic review	Included studies not critically appraised.
Randomized controlled trials		
Arakawa M, Aoyama Y, Ohe Y. Epidural bolus injection with alkalinized lidocaine improves blockade of the first sacral segment—a brief report. <i>Canadian Journal of Anaesthesia</i> 2002; 49(6):566-70.	Randomized controlled trial	Only included surgical patients.
Goebel A, Lawson A, Allen S, Glynn C. Buprenorphine injection to the stellate ganglion in the treatment of upper body chronic pain syndromes. <i>European Journal of Pain</i> 2008; 12(3):266-74.	Randomized controlled trial	The study population included patients with non-neuropathic pain conditions; the results for patients with neuropathic pain could not be separated from the aggregate data.
Kanai A, Suzuki A, Kobayashi M, Hoka S. Intranasal lidocaine 8% spray for second-division trigeminal neuralgia. <i>British Journal of Anaesthesia</i> 2006; 97(4):559-63.	Randomized controlled trial	Condition not described in the included systematic reviews.
Lemos L, Flores S, Oliveira P, Almeida A. Gabapentin supplemented with ropivacain block of trigger points improves pain control and quality of life in trigeminal neuralgia patients when compared with gabapentin alone. <i>Clinical Journal of Pain</i> 2008; 24(1):64-75.	Randomized controlled trial	Condition not described in the included systematic reviews.
Shulman M, Lubenow TR, Nath HA, Blazek W, McCarthy RJ, Ivankovich AD. Nerve blocks with 5% butamben suspension for the treatment of chronic pain syndromes. <i>Regional Anesthesia and Pain Medicine</i> 1998; 23(4):395-401.	Randomized controlled trial	The study population included patients with non-neuropathic pain conditions; the results for patients with neuropathic pain could not be separated from the aggregate data.

Wolff AP, Wilder Smith OH, Crul BJ, van de Heijden MP, Groen GJ. Lumbar segmental nerve blocks with local anesthetics, pain relief, and motor function: a prospective double-blind study between lidocaine and ropivacaine. <i>Anesthesia and Analgesia</i> 2004; 99(2):496-501.	Randomized controlled trial	Described the nerve blocks administered as diagnostic segmental nerve root blocks.
Yee J, Leo RJ, Karuza J, Calkins E. Pain relief produced by sphenopalatine ganglion block in a heterogeneous population of chronic pain patients. <i>American Journal of Pain Management</i> 1998; 8(2):44-8.	Randomized controlled trial	The study population included patients with non-neuropathic pain conditions; the results for patients with neuropathic pain could not be separated from the aggregate data.
Zambello A. Epidural steroid injection vs paravertebral O ₂ O ₃ infiltration for symptomatic herniated disc refractory to conventional treatment: A prospective randomized study. <i>Rivista Italiana di Ossigeno-Ozonoterapia</i> 2006; 5(2):123-7.	Randomized controlled trial	Paravertebral injectant not described in the included systematic reviews. N.B. This study is included in the companion literature summary on epidural injections.
Guidelines		
Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J, Klüber-Moffett J, Kovacs F, et al. on behalf of the COST B13 Working Group on Guidelines for Chronic Low Back Pain. European guidelines for the management of chronic non-specific low back pain. 2004. Available: http://www.kovacs.org/Imágenes/EuropeanGuidelinesCHRONIC.LBP.pdf .	Guideline	Non-specific chronic low back pain only. Radicular pain not included.
American Society of Anesthesiologists. Practice guidelines for chronic pain management. A report by the American Society of Anesthesiologists Task Force on Pain Management, Chronic Pain Section. <i>Anesthesiology</i> 1997; 86(4):995-1004.	Guideline	Does not specifically address nerve blocks for neuropathic pain.
Boswell MV, Trescot AM, Datta S, Schultz DM, Hansen HC, Abdi S, et al. Interventional techniques: evidence-based practice guidelines in the management of chronic spinal pain. <i>Pain Physician</i> 2007; 10(1):7-111.	Guideline	Does not include nerve blocks.
Dworkin RH, Backonja M, Rowbotham MC, Allen RR, Argoff CR, Bennett GJ, et al. Advances in neuropathic pain: diagnosis, mechanisms, and treatment recommendations. <i>Archives of Neurology</i> 2003; 60(11):1524-34.	Guideline	Does not include nerve blocks.
Institute for Clinical Systems Improvement (ICSI). Assessment and management of chronic pain. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2007. Available: http://www.ngc.gov/summary/summary.aspx?doc_id=10724&nbr=005586&string=%22neuropathic+pain%22	Guideline	Does not specifically address neuropathic pain.
Netherlands Society of Rehabilitation Specialists and the Netherlands Society of Anaesthesiologists. Guideline: Complex regional pain syndrome type I. 2006. Available: http://www.cbo.nl/product/richtlijnen/folder20021023121843/rl_crps_eng_07.pdf	Guideline	Included studies on children.

New Zealand Accident Compensation Corporation. Common peroneal nerve block. 2005. Available: http://www.acc.co.nz/for-providers/interventional-pain-management/interventions/intervention-index/WCM1_033907	Guideline	Included studies on children/adolescents (>12 years of age).
New Zealand Accident Compensation Corporation. Intravenous (IV) regional sympathetic block. 2005. Available: http://www.acc.co.nz/for-providers/interventional-pain-management/interventions/intervention-index/WCM1_033928	Guideline	Included studies on children/adolescents (>12 years of age).
New Zealand Accident Compensation Corporation. Sympathetic ganglion block. 2005. Available: http://www.acc.co.nz/for-providers/interventional-pain-management/interventions/intervention-index/WCM1_033973	Guideline	Included studies on children/adolescents (>12 years of age).
New Zealand Accident Compensation Corporation. Trigeminal nerve block. 2005. Available: http://www.acc.co.nz/for-providers/interventional-pain-management/interventions/intervention-index/WCM1_034132	Guideline	Included studies on children/adolescents (>12 years of age).
North American Spine Society. <i>Diagnosis and treatment of degenerative lumbar spinal stenosis</i> . Burr Ridge, IL, USA: North American Spine Society; 2007. Available from: http://www.spine.org/Documents/NASSCG_Stenosis.pdf	Guideline	Does not specifically address nerve blocks for neuropathic pain.
Sanders SH, Harden RN, Vicente PJ. Evidence-based clinical practice guidelines for interdisciplinary rehabilitation of chronic non-malignant pain syndrome patients. <i>Pain Practice</i> 2005; 5:303-15.	Guideline	Does not specifically address neuropathic pain.
Stanton-Hicks M, Baron R, Boas R, Gordh T, Harden N, Hendler N, et al. Complex Regional Pain Syndromes: guidelines for therapy. <i>Clinical Journal of Pain</i> 1998; 14(2):155-66.	Consensus statement	Not an evidence-based guideline.
The College of Physicians and Surgeons of Ontario. Evidence-Based Recommendations for Medical Management of Chronic Non-malignant Pain. 2000. Available: https://www.cpso.on.ca/uploadedFiles/policies/guidelines/methadone/MedicalManagementPain.pdf	Guideline	Same interventions and patient groups as Dubinsky et al. (2004) ³² , but guideline of lower quality and not as current.

Table B.2: Summary of potentially relevant studies on *nerve blocks* that could not be retrieved by the report deadline (listed in alphabetical order of first author)

Study	Abstract
Randomized controlled trials	
<p>Aydemir K. The effects of stellate ganglion block with lidocaine and ultrasound in complex regional pain syndrome: A randomized, double blind, placebo controlled study. <i>Journal of Rheumatology and Medical Rehabilitation</i> 2006; 17(3):193-200.</p>	<p>Objective: The purpose of this study was to investigate the efficacies of stellate ganglion blockage (SGB) with lidocaine and ultrasound in complex regional pain syndrome (CRPS).</p> <p>Methods: Twenty-five patients were divided into three groups. Treatment modalities including Transcutaneous electrical nerve stimulation (TENS), contrast bath, pneumatic compression and exercise were applied to all patients for 21 sessions. In addition; in group 1 SGB with lidocaine and in group 2 SGB with ultrasound were applied. Sham SGB and ultrasound were applied to third group. The evaluations were performed before and after treatment and one month later with the following parameters: Spontaneous pain, provocative pain, edema, finger pulp-distal palmar crease distance (FPD), grip strength, functional hand scale (FHS) and Keitel score.</p> <p>Results: Improvements in edema, FPD, FHS, Keitel score and grip strength were statistically significant in ultrasound blockage group. Improvements in FPD, FHS and Keitel score were statistically significant in lidocaine blockage group. While improvements in FPD, FHS and Keitel score were statistically significant in the control group, the improvement in the Keitel score was lost at the final assessment.</p> <p>Conclusion: We suggest that the SGB with either ultrasound or lidocaine is effective in CRPS. Ultrasound can be preferred because of its advantages of being practical, non-invasive and having no significant complications.</p>
<p>bdel-Raouf M. Radiologically-guided steroid injection in the management of failed back surgery syndrome: Role of selective nerve root injection, epidurography, and their combination. <i>Egyptian Journal of Anaesthesia</i> 2004; 20(1):77-81.</p>	<p>Background: This study was designed to evaluate the radiologically-guided selective nerve root/s steroid injection, epidurography and their combination in the management of pain in patients with FBSS.</p> <p>Methods: The study was carried out on 60 female patients suffering from failed back surgery syndrome (FBSS). Patients were randomly allocated into one of three equal groups (n= 20, each). In S Group: 1 ml containing 1 mg betamethasone dipropionate and 2.5 mg betamethasone sodium phosphate followed by 1 ml lidocaine 1% were injected through each needle after radiological confirmation of desired nerve root/s. In E group 2 ml containing 2 mg betamethasone dipropionate and 5 mg betamethasone sodium phosphate followed by 6 ml lidocaine 1% were injected epidurally. In C group, combined selective nerve root and epidural steroid injection was done. The following parameters were evaluated: the duration of the procedure; the incidence of immediate (2 hours), delayed (one week), and long-term (six months) pain relief; and the incidence of dural puncture or bloody aspirate.</p> <p>Results: Procedure duration was [30.32 (2.1)], [19.35 (2.3)], and [31.35 (3.1)] minutes in groups S, E, and C, respectively with significantly shorter duration in group E compared to either group S or group C (p < 0.01). Dural puncture was not encountered in any patient. All patients in the three groups showed immediate pain relief. The incidence of delayed and long-term pain relief in the combined group was significantly higher than the other two groups, with no significant statistical difference between group S and group E.</p> <p>Conclusion: Radiologically-guided combined transforaminal selective nerve root and epidural steroids injection is associated with higher percentage of delayed and long term relief of both sciatic and back pain in patients with FBSS compared to either technique used alone.</p>

APPENDIX C: QUALITY ASSESSMENT CHECKLIST FOR SYSTEMATIC REVIEWS⁶⁻⁹

Study Question

The research question should be established a priori.

Reported:

The objectives of the review are clearly stated in the abstract, introduction, or methods.

Partially reported:

The objectives of the review are stated in:

- the abstract, introduction, or methods but are vague or unclear; or
- a section of the report other than the abstract, introduction, or methods.

Not reported:

The objectives are not stated in any section of the review.

Inclusion/Exclusion Criteria

The participants, interventions, outcome measures, and types of studies considered for analysis should be established a priori.

Reported:

All four elements (participants, interventions, outcome measures, types of studies) are reported in the abstract, introduction, or methods section of the review.

Partially reported:

Only three of the four elements are reported in the abstract, introduction, or methods section.

Not reported:

Less than three of the four elements are reported in the abstract, introduction, or methods section; or

- The first mention of any of these elements occurs in the results section.

Search Strategy

Electronic databases

Reported:

At least one electronic database was searched and the names of the databases are provided.

Partially reported:

At least one electronic database was searched but the names are not provided.

Not reported:

Electronic databases were not searched or are not mentioned in the review.

Quality subsection 1: At least MEDLINE and EMBASE

Yes:

Both MEDLINE and EMBASE were searched.

Unclear:

It was unclear whether MEDLINE and EMBASE were searched because a complete list of all the electronic databases searched is not provided.

No:

The review stated that neither MEDLINE nor EMBASE was searched;

- Neither MEDLINE nor EMBASE is mentioned in the complete list of electronic databases searched; or
- Only one of the two the databases was searched.

Other sources

Reported:

At least one additional resource or method, other than searching electronic databases, was used to identify relevant literature (e.g. pearling or review of reference lists in retrieved articles, hand searching of journals).

Partially reported:

Other resource or methods were used but details are not provided.

Not reported:

The review did not use other resource or methods to identify relevant literature or does not mention it.

Data Extraction

Data extraction method

Reported:

The data extraction process is described.

Partially reported:

A data extraction process is mentioned but no details are provided.

Not reported:

A data extraction process was not used or described.

Quality subsection 2: Standardized method

Yes:

The data categories extracted are listed or the use of a standardized data extraction form is mentioned.

Unclear:

The review states that a standardized data extraction process was used but does not list the data categories extracted or mention the use of a standardized data extraction form.

No:

The data categories extracted are not listed or the use of a standardized data extraction form is not mentioned.

Quality subsection 3: Independent data extraction by at least two reviewers

Yes:

Data were extracted independently by at least two reviewers.

Unclear:

The number of reviewers who extracted data is not stated.

No:

Data were extracted by:

- only one reviewer; or
- one reviewer and checked by another.

Quality Assessment

Criteria used to assess the validity of included studies

Reported:

A quality assessment tool or checklist was used and details are provided (e.g. name or source).

Partially reported:

A quality assessment tool or checklist was used but no details are provided.

Not reported:

A quality assessment tool or checklist was not used or mentioned; or

- Studies were only categorized according to a level of evidence hierarchy.

Quality subsection 4:**Independent quality assessment by at least two reviewers***Yes:*

The quality of the included studies was assessed independently by at least two reviewers.

Unclear:

The number of reviewers who appraised study quality is not stated.

No:

Studies were assessed by:

- only one reviewer; or
- one reviewer and checked by another.

Inter-rater agreement*Reported:*

The review provides a statement of the degree of difference/equivalence between the reviewers or a statistical measure of inter-rater agreement.

Partially reported:

The review mentions that inter-rater agreement was measured but does not provide a statement of the degree of difference/equivalence or a statistical measure of inter-rater agreement.

Not reported:

The review does not provide any information on inter-rater agreement.

Data Analysis/Synthesis

Only ONE of the three methods for data analysis/synthesis can be assessed. Select the data analysis type according to the definitions below. Only score the quality subsection that pertains to the particular data analysis method used in the review.

Qualitative review:

A narrative summary of the study results with no statistical analysis or pooling of results.

Quality subsection 5a:

Study quality used in analysis or discussion of study results

Yes:

Results of the included studies are discussed or analyzed in terms of their quality.

Unclear:

- Study quality was assessed but is either not used at all or is only used to analyze some of the included studies.
- The review mentions selective inclusion of 'quality' studies, but without further assessment of their quality (e.g. only RCTs were included but the robustness of their execution was not assessed).

No:

- The results of the included studies are not discussed or analyzed in terms of their quality.
- Study quality was not assessed.

Semi-quantitative review:

Incorporates a statistical analysis of individual studies without pooling the results (e.g. relative risks calculated for individual study outcomes) or pooling of results using only descriptive statistics (e.g. median, mean, mode, frequency).

Quality subsection 5b: Confidence interval/measures of dispersion reported

Yes:

Confidence intervals or measures of dispersion (range, standard deviation, standard error of the mean) are reported for all relevant analyses.

Unclear:

- Confidence intervals or measures of dispersion are only reported for some of the relevant analyses.
- Confidence intervals are reported for all relevant analyses, but the level of confidence is not specified (e.g. unclear if 95% or 99% confidence intervals were calculated).
- Measures of dispersion are reported for all relevant analyses but the type is not specified (e.g. standard deviation or standard error).

No:

Confidence intervals or measures of dispersion are not reported.

Meta-analysis:

A pooled effect estimate is calculated for at least two studies. Reviews that contain a meta-analysis of some studies and a qualitative analysis of the remaining studies are considered a 'meta-analysis'.

Quality subsection 5c: Precision of results reported

Yes:

Confidence intervals are reported for all pooled effect estimates.

Unclear:

- Confidence intervals are reported for some but not all pooled effect estimates.
- Confidence intervals are reported for all pooled effect estimates but the level of confidence is not specified (e.g. unclear if 95% or 99% confidence intervals were calculated).

No:

Confidence intervals are not reported.

Quality subsection 5d: Test of study heterogeneity conducted

Yes:

A statistical analysis of study heterogeneity is reported for all pooled studies.

Unclear:

- A statistical analysis of study heterogeneity is reported for some but not all pooled studies.
- Heterogeneity was examined visually or a statistical analysis of study heterogeneity is reported for all pooled studies, but the type of model used is not specified (e.g. fixed-effect or random-effects).

No:

A statistical analysis of study heterogeneity was not conducted.

Test for publication bias

Reported:

Publication bias was analysed or a reason provided for why it was not.

Partially reported:

- The review mentions analysing publication bias but does not present the results.
- The review states that publication bias was not analysed but does not explain why.

Not reported:

There was no mention of analysing publication bias.

Concluding Section

Potential methodological limitations

Reported:

The methodological limitations or advantages of the review are described in a separate section or paragraph.

Partially reported:

The description of the methodological limitations or advantages of the review is cursory (e.g. single sentence or no separate paragraph or section).

Not reported:

There is no mention of the potential methodological limitations or advantages of the review.

Clinical application of results

The clinical application of results is considered adequate if all of the following four elements are present in the concluding section (includes discussion) or statement of the review: treatment, treatment effect, patient group, and comparator.

Reported:

All four elements are present.

Partially reported:

Only three of the four elements are present.

Not reported:

Less than three of the four elements are present.

Incorporation of methodological quality

The review should take into account the methodological quality of the included studies when formulating the conclusions.

Reported:

The methodological quality of the included studies is mentioned in the concluding section (includes discussion) or statement of the review.

Partially reported:

The study types, as designated by a level of evidence hierarchy category, are mentioned in the concluding section (includes discussion) or statement of the review, but not the quality of the studies.

Not reported:

The methodological quality of the included studies is not mentioned in the concluding section (includes discussion) or statement of the review.

Quality subsection 6: Conclusions supported by results

Yes:

The conclusions drawn by the authors of the review are supported by the evidence presented in the results section.

Unclear:

Some, but not all, of the conclusions drawn by the authors of the review are supported by the evidence presented in the results section.

No:

The conclusions drawn by the authors of the review are not supported by the evidence presented in the results section.

Conflict of Interest and Funding

Conflict of interest

Reported:

A statement of conflict of interest (if any) is provided.

Partially reported:

A conflict of interest is mentioned but details are not provided.

Not reported:

A statement of conflict of interest (if any) is not provided.

Sources of funding

Reported:

- Funding sources are mentioned; or
- The review was developed without external funding (e.g. authors employed by a university or volunteered time to produce a Cochrane Review).

Partially reported:

External funding is mentioned but details are not provided.

Not reported:

Funding sources are not mentioned.

Quality Rating

SRs were rated on how well their methods excluded bias and confounding by examining: the search strategy used; how the data extraction, quality assessment of the included studies, and data analysis/synthesis were conducted; and whether the conclusions of the review matched the results. The SRs were rated with respect to six essential quality criteria (grey boxes above) as follows:

Good – six criteria met (✓✓✓✓✓✓), or five criteria met and one criterion ‘unclear’ (✓✓✓✓✓?).

Average – one criterion not met (✓✓✓✓✓×), or one criterion not met and one criterion ‘unclear’ (✓✓✓✓✓×?), or two criteria ‘unclear’ (✓✓✓✓✓??).

Poor – at least two criteria not met (✓✓✓✓××).

N.B. For a criterion to have been ‘met’, it must be scored as ‘yes’ (✓). For meta-analyses, the two applicable quality subsections (5c and 5d) are counted as a single quality criterion. Therefore, to meet the fifth quality criterion for meta-analyses both 5c and 5d must be scored as ‘yes’ (✓).

Table C.1: Quality assessment results for included systematic reviews

Review Characteristic		Carragee et al. (2008) ²¹	DePalma et al. (2005) ²²	Forouzanfar et al. (2002) ²³
Study question established a priori		●	●	●
Inclusion/exclusion criteria		◐	◐	●
Search strategy	Electronic databases	●	●	●
	<i>1. At least MEDLINE and EMBASE</i>	X	✓	✓
	Other sources	●	●	●
Data extraction	Data extraction method	●	●	◐
	<i>2. Standardized method</i>	✓	✓	X
	<i>3. Independent data extraction by at least two reviewers</i>	?	X	?
Quality assessment	Criteria used to assess the validity of included studies	●	●	●
	<i>4. Independent quality assessment by at least two reviewers</i>	✓	?	✓
	Inter-rater agreement for quality assessment	◐	◐	◐
Data analysis/synthesis	Qualitative review	●	●	●
	<i>5a. Study quality used in analysis or discussion of study results</i>	✓	✓	✓
	Semi-quantitative review	N/A	N/A	N/A
	<i>5b. Confidence intervals or measures of dispersion reported</i>	N/A	N/A	N/A
	Meta-analysis	N/A	N/A	N/A
	<i>5c. Precision of results reported</i>	N/A	N/A	N/A
	<i>5d. Test of homogeneity conducted</i>	N/A	N/A	N/A
Test for publication bias		◐	◐	◐
Concluding section	Potential methodological limitations/advantages	●	◐	●
	Clinical application of results	●	◐	◐
	Incorporation of methodological quality	●	●	●
	<i>6. Conclusions supported by results</i>	✓	✓	✓
Conflict/funding	Conflict of interest (if any)	●	●	◐
	Sources of funding	●	◐	◐
Quality rating	Six criteria (search at least two databases; standardized data extraction; independent data extraction and quality rating by two reviewers; appropriate data synthesis; conclusions supported by results)	4/6 Average	4/6 Average	4/6 Average

Key for quality of reporting: Reported: ●; Partially reported: ◐; Not reported: ○; Not applicable: N/A

Key for quality of review subsections (grey sections of table): Yes = ✓; Unclear = ?; No = X

Table C.1: Quality assessment results for included systematic reviews (cont'd)

Review Characteristic		Kumar et al. (2004) ²⁴
Study question established a priori		•
Inclusion/exclusion criteria		•
Search strategy	Electronic databases	•
	<i>1. At least MEDLINE and EMBASE</i>	✓
	Other sources	•
Data extraction	Data extraction method	◐
	<i>2. Standardized method</i>	X
	<i>3. Independent data extraction by at least two reviewers</i>	?
Quality assessment	Criteria used to assess the validity of included studies	•
	<i>4. Independent quality assessment by at least two reviewers</i>	?
	Inter-rater agreement for quality assessment	◐
Data analysis/synthesis	Qualitative review	N/A
	<i>5a. Study quality used in analysis or discussion of study results</i>	N/A
	Semi-quantitative review	•
	<i>5b. Confidence intervals or measures of dispersion reported</i>	✓
	Meta-analysis	N/A
	<i>5c. Precision of results reported</i>	N/A
	<i>5d. Test of homogeneity conducted</i>	N/A
Test for publication bias		◐
Concluding section	Potential methodological limitations/advantages	•
	Clinical application of results	◐
	Incorporation of methodological quality	•
	<i>6. Conclusions supported by results</i>	✓
Conflict/funding	Conflict of interest (if any)	◐
	Sources of funding	•
Quality rating	Six criteria (search at least two databases; standardized data extraction; independent data extraction and quality rating by two reviewers; appropriate data synthesis; conclusions supported by results)	3/6 Poor

Key for quality of reporting: Reported: •; Partially reported: ◐; Not reported: ◐; Not applicable: N/A

Key for quality of review subsections (grey sections of table): Yes = ✓; Unclear = ?; No = X

APPENDIX D: QUALITY ASSESSMENT CHECKLIST FOR RANDOMIZED CONTROLLED TRIALS

(Adapted from the list recommended in the method guidelines of the Cochrane Back Review Group¹², with additional guidance derived from Downs and Black¹⁸.)

Patient Selection

- A. *Were the eligibility criteria specified?*
Inclusion and/or exclusion criteria should be given.
- B. *Treatment allocation*
1) *Was a method of randomization performed?*
Studies stating that patients were randomized should be answered 'yes' except where the method of randomization would not ensure random allocation. Methods of allocation using date of birth, date of admission, hospital numbers, or alternation are not regarded as appropriate.
2) *Was the treatment allocation concealed?*
Assignment generated by an independent person not responsible for determining the eligibility of the patients.
- C. *Were the groups similar at baseline regarding the most important prognostic indicators?*
To receive a 'yes', groups must be similar at baseline regarding age, sex distribution, duration of pain, and at least one of the following: patient comorbidities, mobility, health-related quality of life, or pain intensity.

Interventions

- D. *Were the index and control interventions explicitly described?*
The description should include (when applicable) type, modality, application technique, intensity, and duration as well as the number and frequency of sessions so that others can replicate the treatment. If any of the treatments are described by name only, with no further detail given, the question should be answered 'no'.
- E. *Were co-interventions avoided or comparable?*
Co-interventions should either be avoided in the trial design or comparable between the index and control groups.
- F. *Was the patient blinded to the intervention?*
For studies where the patients would have no way of knowing which intervention they received, this should be answered 'yes'. For studies that do not state whether blinding was attempted, the answer should be 'unclear'.

Outcome Measurement

G. *Was the outcome assessor blinded to the intervention?*

For studies where the outcome assessor would have no way of knowing which intervention the patients received, this should be answered 'yes'. For studies that do not state whether blinding was attempted, the answer should be scored as 'unclear'.

H. *Were the outcome measures relevant?*

Outcome measures should be clearly described. Relevant measures for non-malignant chronic pain include changes in pain, mobility, and pain pressure threshold; generic functional status; global measure of improvement; and return to work.

I. *Were adverse effects described?*

Each event should be described and correctly attributed to the allocated treatment. If it was explicitly reported that no adverse events occurred then a 'yes' should be scored. When adverse events are described but not clearly attributed to a particular treatment, the answer should be scored as 'unclear'.

J. *Was the withdrawal/dropout rate described and acceptable?*

Patients included in the study but who did not complete the observation period or were not included in the analysis must be described. If the numbers of patients lost to follow-up were not reported, the question should be answered as 'unclear'. If the proportion lost to follow-up was too small ($\leq 10\%$ in each treatment group for short-term follow-up and $\leq 20\%$ for long-term follow-up) to affect the main findings, the question should be answered 'yes'. (**Note:** These percentages are arbitrary and are not supported by literature).

K. *Timing of follow-up measurements*

1) *Was a short-term follow-up measurement performed?*

Outcome assessment at the end of the intervention period.

2) *Was a long-term follow-up measurement performed?*

Outcome assessment >3 months after randomization.

L. *Was the timing of the outcome assessment comparable in both groups?*

The timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments. Where follow-up was the same for all study patients, the answer should be 'yes'. If the results were adjusted to account for different lengths of follow-up (for example by survival analysis), the answer should be 'yes'. Studies where differences in follow-up were ignored should be answered 'no'.

Statistics

M. *Was the sample size for each group described?*

Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions.

N. *Did the analysis include an intention-to-treat analysis?*

All randomized patients are reported/analysed for the most important effect measurements (minus missing values) irrespective of non-compliance and co-interventions.

O. *Were point estimates and measures of variability presented for the primary outcome measures?*

Both point estimates and measures of variability should be presented separately for each important outcome. In non-normally distributed data the median and inter-quartile range should be reported. In normally distributed data the mean plus standard error, standard deviation, or confidence interval should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered 'yes'.

Quality Rating

For descriptive purposes, the included RCTs were referred to as being good, moderate, or poor quality with respect to internal and external validity according to the total number of criteria met as follows.

- Internal validity (total number of criteria = 9) – good (≥ 7 criteria met), moderate (between 4 and 6 criteria met), poor (< 4 criteria met).
- External validity (total number of criteria = 6) – good (≥ 5 criteria met), moderate (3 or 4 criteria met), poor (< 3 criteria met).

Table D.1: Quality assessment results for included randomized controlled trials

Study Characteristic		Becker et al. (2007) ²⁵	Bonetti et al. (2005) ²⁶	Livingstone & Atkins (2002) ²⁷	Ng et al. (2005) ²⁸
Patient Selection	A. Were the eligibility criteria specified?	✓	✓	✓	✓
	B1. Was randomization performed adequately?	✓	?	✓	✓
	B2. Was treatment allocation concealed?	✓	?	✓	✓
	C. Were the groups similar at baseline?	✓	?	✓	?
Interventions	D. Were the index and control interventions explicitly described?	✓	✓	✓	✓
	E. Were co-interventions avoided or comparable?	✓	?	?	?
	F. Was the patient blinded to the intervention?	✓	✓	✓	✓
Outcome measurement	G. Was the outcome assessor blinded to the intervention?	✓	✓	?	✓
	H. Were the outcome measures relevant?	✓	✓	✓	✓
	I. Were adverse events described?	✓	?	×	✓
	J. Was the withdrawal/dropout rate described and acceptable?	✓	✓	✓	✓
	K1. Was a short-term follow-up measurement performed?	✓	✓	✓	✓
	K2. Was a long-term follow-up measurement performed?	✓	✓	✓	×
	L. Was the timing of the outcome assessment comparable in both groups?	✓	✓	✓	✓
Statistics	M. Was the sample size for each group described?	✓	✓	✓	✓
	N. Did the analysis include an intention-to-treat analysis?	×	✓	✓	✓
	O. Were point estimates and measures of variability presented for the primary outcome measures?	✓	×	✓	✓

Key: Yes = ✓; No = ×; Unclear = ?; Not applicable or not possible because of the nature of the intervention = NA

Internal validity criteria: b, e, f, g, h, j, l, n; External validity criteria: a, c, d, i, k; Statistical criteria: m, o

Table D.1: Quality assessment results for included randomized controlled trials (cont'd)

Study Characteristic		Nishiyama et al. (2006) ²⁹	Taskaynatan et al. (2004) ³⁰
Patient Selection	A. Were the eligibility criteria specified?	×	✓
	B1. Was randomization performed adequately?	✓	?
	B2. Was treatment allocation concealed?	✓	?
	C. Were the groups similar at baseline?	?	✓
Interventions	D. Were the index and control interventions explicitly described?	?	✓
	E. Were co-interventions avoided or comparable?	?	✓
	F. Was the patient blinded to the intervention?	✓	✓
Outcome measurement	G. Was the outcome assessor blinded to the intervention?	?	✓
	H. Were the outcome measures relevant?	✓	✓
	I. Were adverse events described?	✓	✓
	J. Was the withdrawal/dropout rate described and acceptable?	✓	×
	K1. Was a short-term follow-up measurement performed?	✓	✓
	K2. Was a long-term follow-up measurement performed?	×	×
	L. Was the timing of the outcome assessment comparable in both groups?	✓	✓
Statistics	M. Was the sample size for each group described?	✓	×
	N. Did the analysis include an intention-to-treat analysis?	✓	?
	O. Were point estimates and measures of variability presented for the primary outcome measures?	✓	✓

Key: Yes = ✓; No = ×; Unclear = ?; Not applicable or not possible because of the nature of the intervention = NA

Internal validity criteria: b, e, f, g, h, j, l, n; External validity criteria: a, c, d, i, k; Statistical criteria: m, o

APPENDIX E: QUALITY ASSESSMENT CHECKLIST FOR CLINICAL PRACTICE GUIDELINES

(Adapted from The Agree Collaboration¹⁹.)

Scope and Purpose (Items 1,2,3)

Item 1 – Guideline objectives

Information about the clinical condition, target population, and expected health benefit should be provided in the objectives statement.

4 – All three elements reported (condition, target population, health benefit).

3 – Two elements reported.

2 – Unclear or only one element reported.

1 – Objectives of the guideline are not provided.

Item 2 – Clinical question

Information about the intervention and clinical condition should be provided.

4 – Two elements reported (intervention, clinical condition).

3 – One element reported.

2 – Unclear.

1 – Information about the clinical question is not provided.

Item 3 – Target population

Information about the age (defined as “adults” or by an age range), comorbidity, and clinical description (if applicable) of the target population should be provided.

4 – All applicable elements reported (age, comorbidity, clinical description). In cases where at least one element is not applicable, the guideline is scored 4 only if all of the remaining applicable elements are present. For example, if comorbidity is not applicable, the guideline will only score 4 if age and clinical description are provided.

3 – One applicable element not reported.

2 – Unclear or two applicable elements not reported.

1 – Information about the target population is not provided.

Stakeholder Involvement

Item 4 - Relevant professional groups

Information about the composition of the guideline development group (GDG) and the discipline (job title, university department, etc.) and relevant expertise (particular area of skill, e.g. methodologist, occupational medicine) of its members should be provided.

- 4 – All three elements (composition of the entire GDG; discipline and expertise of all GDG members) are reported.
- 3 – Composition of the entire GDG is provided but two elements (discipline and relevant expertise) reported for only some of its members.
- 2 – Unclear or composition of the entire GDG is provided but only one element (discipline and relevant expertise) reported for all of its members.
- 1 – Information about the GDG is not provided or composition of the entire GDG is provided but one element (discipline or relevant expertise) reported only for some of its members.

Item 5 - Patients' perspectives

- 4 – Patient perspectives incorporated and methods reported.
- 3 – Patient perspectives discussed but methods not reported.
- 2 – Unclear.
- 1 – Patient perspectives not incorporated.

Item 6 - Target users defined

- 4 – Target users explicitly defined by specialty, e.g. general practitioners, neurologists, physiotherapists.
- 3 – Target users defined in broad terms, e.g. practitioners treating patients with chronic pain.
- 2 – Unclear.
- 1 – Target users not defined.

Item 7 - Piloted among target users

- 4 – Guideline piloted among target users and methods reported.
- 3 – Guideline piloted among target users but methods not reported.
- 2 – Unclear.
- 1 – Guideline not piloted among target users.

Rigour of Development

Item 8 - Systematic methods used to search for evidence

Information about the search terms used, sources consulted, and date limits of the literature searches should be provided.

- 4 – All three elements reported (search terms, sources, date limits).
- 3 – Two elements reported.
- 2 – Unclear or one element reported.
- 1 – Information about the methods used to search for evidence is not provided.

Item 9 - Selection criteria

4 – Inclusion/exclusion criteria described and reasons for excluding (or including) evidence clearly stated.

3 – Inclusion/exclusion criteria described but reasons for excluding evidence (or including) are not stated.

2 – Unclear.

1 – Inclusion/exclusion criteria not stated.

Item 10 - Methods used to formulate recommendations

Information on the methods used to formulate the recommendations, resolve disagreements, and reach final decisions should be provided.

4 – All three elements reported (formulation of recommendations, resolving disagreements, reaching final decisions).

3 – Two elements reported.

2 – Unclear or only one element reported.

1 – Information about the methods used to formulate the recommendations is not provided.

N.B. In cases where the guideline was written by a single author, the guideline is scored as follows:

4 – The methods used to formulate the recommendations are reported.

2 – Unclear.

1 – Information about the methods used to formulate the recommendations is not provided.

Item 11 - Consideration of benefits, side effects, and risks

Information on the benefits, side effects, and risks of the recommendations should be provided.

4 – All applicable elements reported (benefits, side effects, risks). In cases where at least one element is not applicable, the guideline is scored 4 only if all of the remaining applicable elements are present. For example, if side effects are not applicable, the guideline will only score 4 if benefits and risks are provided.

3 – One applicable element not reported.

2 – Unclear or two applicable elements not reported.

1 – Information about the benefits, side effects, and risks not stated.

Item 12 - Link between recommendations and the supporting evidence

4 – Each recommendation is explicitly linked to the references on which it is based.

3 – Only some of the recommendations are explicitly linked to the references on which they are based.

2 – Unclear.

1 – No explicit link between each recommendation and the references on which it is based.

Item 13 - External review

4 – Externally reviewed by independent clinical and methodological experts and methods reported.

3 – Externally reviewed and one of the following criteria met: methods reported, reviewers included clinical and methodological experts.

2 – Unclear or externally reviewed but none of the following criteria met: methods reported, reviewers included clinical and methodological experts.

1 – Not externally reviewed or no statement about external review.

Item 14 - Procedure for updating the guideline

4 – Statement about updating the guideline and methods reported.

3 – Statement about updating the guideline but methods not reported.

2 – Unclear.

1 – Guideline will not be updated or no statement about updating the guideline.

Clarity and Presentation

Item 15 - Specific, unambiguous recommendations

The recommendations were considered adequate if all of the following three elements were present: management or treatment, patient group, clinical situation.

4 – All three elements reported.

3 – Two elements reported.

2 – Unclear or one element reported.

1 – None of the elements reported.

Item 16 - Different management options presented

4 – Different management options were considered to be adequately presented if the comparators for each intervention were stated in the guideline. For example, massage therapy is more effective than relaxation therapy in patients with chronic low back pain.

3 – The comparators were stated for only some of the interventions.

2 – Unclear.

1 – The comparators for the interventions were not stated.

Item 17 - Key recommendations identifiable

4 – Key recommendations summarized and identifiable.

3 – Key recommendations reported but not summarized or highlighted for easy identification.

2 – Unclear.

1 – Key recommendations not identifiable.

Item 18 - Additional support materials provided

4 – Additional support materials provided.

3 – Additional support materials provided but not easily available e.g. published in a journal that is not open access.

2 – Unclear.

1 – Additional support materials not provided.

Applicability

Item 19 - Organizational barriers discussed

4 – Not applicable or organizational barriers discussed and required changes are outlined.

3 – Organizational barriers mentioned but required changes are not outlined.

2 – Unclear.

1 – Organizational barriers not discussed.

Item 20 - Resource implications considered

4 – Not applicable or resource implications discussed and the effects on resources are outlined.

3 – Resources implications mentioned but the effects on resources are not outlined (or are only outlined for some interventions).

2 – Unclear.

1 – Resource implications not discussed.

Item 21 - Key review criteria presented

4 – Key review criteria presented and specific thresholds provided.

3 – Key review criteria discussed but specific thresholds not provided.

2 – Unclear.

1 – Key review criteria not presented.

Editorial Independence

Item 22 - Editorially independent from funding body

4 – Developed without external funding or details of financial support provided plus an explicit statement that the funding body has not influenced the final recommendations.

3 – Details of financial support provided but no statement about the funding body's influence on guideline development.

2 – Unclear or no details about financial support.

1 – Funding body potentially influenced the final recommendations.

Item 23 - Conflicts of interest reported

4 – Details of the affiliations and conflicts of interest (if any) of the development group are provided.

3 – Details of conflicts of interest (if any) are provided but without a list of the development group’s affiliations.

2 – Unclear or a list of the development group’s affiliations is provided but without details on conflicts of interest (if any).

1 – Details of the affiliations and conflicts of interest (if any) of the development group are not provided.

Quality Rating

Guidelines were rated on how well their methods excluded bias by examining the search strategy used; how the recommendations were formulated and presented; whether the recommendations were directly linked to the evidence; the external review process; and whether conflicts of interest and funding sources were reported. The average quality rating score (maximum possible score is 28 (7 x 4)) for these criteria was derived by dividing the sum of the scores given by each reviewer by the number of reviewers. The guideline was then rated as follows (grey rows in Table E.1).

Good – average score of 22 to 28;

Average – average score of 15 to 21;

Poor – average score 0 to 14.

Standardized Domain Scores

These scores for each of the six domains were combined and converted into standardized domain scores according to the following formula (Table E.2).

$$\text{Standardized domain score (\%)} = \frac{\text{obtained score} - \text{minimum possible score}}{\text{maximum possible score} - \text{minimum possible score}} \times 100$$

Table E.1: AGREE tool quality assessment results for included clinical practice guidelines (two appraisers)

Guideline Characteristic		Ambrosio et al. (2006) ³¹		Dubinsky et al. (2004) ³²	
Scope/ purpose	1.Objectives	3	3	4	2
	2. Clinical question	3	3	3	4
	3. Target population	2	2	2	2
Stakeholder involvement	4. Relevant professional groups represented	2	2	1	2
	5. Patients' perspectives included	2	1	2	1
	6. Target users defined	4	4	1	1
	7. Piloted among target users	2	2	2	1
Rigour of development	8. Systematic search conducted	1	1	4	4
	9. Selection criteria described	1	1	4	3
	10. Methods used to formulate recommendations described	1	1	1	2
	11. Benefits, side effects, risks considered	4	2	4	3
	12. Link between recommendations and evidence	4	3	4	4
	13. External review by experts	1	1	2	2
	14. Updating procedure described	1	1	1	1
Clarity/ presentation	15. Specific, unambiguous recommendations	4	3	1	3
	16. Different management options presented	3	3	4	3
	17. Key recommendations easily identifiable	3	3	1	4
	18. Additional support materials provided	4	2	1	4
Applicability	19. Organizational barriers discussed	3	2	1	1
	20. Resource implications considered	1	1	1	1
	21. Key review criteria presented	1	1	1	1
Editorial independ- ence	22. Editorially independent from funder	2	2	2	2
	23. Conflicts of interest reported	2	2	2	1
Quality Rating	Seven criteria (systematic search, method of formulating recommendations, recommendations-evidence link, external review, clear recommendations, editorial independence, conflict of interest)	14 Poor		17 Average	

Table E.1: AGREE tool quality assessment results for included clinical practice guidelines (two appraisers) (cont'd)

Guideline Characteristic		Hunter Integrated Pain Service (2009) ³³		WCB Evidence Based Practice Group (2004) ³⁴	
Scope/ purpose	1.Objectives	3	2	4	2
	2. Clinical question	4	4	3	2
	3. Target population	2	1	2	1
Stakeholder involvement	4. Relevant professional groups represented	1	1	1	1
	5. Patients' perspectives included	2	1	2	1
	6. Target users defined	3	1	3	1
	7. Piloted among target users	2	1	2	1
Rigour of development	8. Systematic search conducted	1	1	1	1
	9. Selection criteria described	1	1	2	1
	10. Methods used to formulate recommendations described	1	1	1	2
	11. Benefits, side effects, risks considered	3	1	4	1
	12. Link between recommendations and evidence	4	1	1	2
	13. External review by experts	2	1	2	1
	14. Updating procedure described	2	1	1	1
Clarity/ presentation	15. Specific, unambiguous recommendations	1	1	4	2
	16. Different management options presented	1	1	1	1
	17. Key recommendations easily identifiable	1	1	4	2
	18. Additional support materials provided	1	1	1	1
Applicability	19. Organizational barriers discussed	1	1	1	1
	20. Resource implications considered	1	1	1	1
	21. Key review criteria presented	1	1	4	1
Editorial independ- ence	22. Editorially independent from funder	2	1	2	1
	23. Conflicts of interest reported	2	1	2	1
Quality Rating	Seven criteria (systematic search, method of formulating recommendations, recommendations-evidence link, external review, clear recommendations, editorial independence, conflict of interest)	10 Poor		11.5 Poor	

Table E.2: AGREE tool standardized domain scores (%) for included clinical practice guidelines (two appraisers)

AGREE Domain	Ambrosio et al. (2006)³¹	Dubinsky et al. (2004)³²	Hunter Integrated Pain Service (2009)³³	WCB Evidence Based Practice Group (2004)³⁴
Scope and purpose	44	61	56	44
Stakeholder involvement	46	13	17	17
Rigour of development	21	60	17	17
Clarity and presentation	71	54	0	33
Applicability	17	0	0	17
Editorial independence	33	25	17	17

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