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## REVIEW ARTICLE

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# “Evidence-Based Interventional Pain Medicine According to Clinical Diagnoses”: Update 2018

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### ■ Abstract

**Introduction:** Between 2009 and 2011 a series of 26 articles on evidence-based medicine for interventional pain medicine according to clinical diagnoses were published. The high number of publications since the last literature search justified an update.

**Methods:** For the update an independent 3rd party, specialized in systematic reviews was asked in 2015 to perform the literature search and summarize relevant evidence using Cochrane and GRADE methodology to compile guidelines on

interventional pain management. The guideline committee reviewed the information and made a last update on March 1st 2018. The information from new studies published after the research performed by the 3th party and additional observational studies was used to incorporate other factors such as side effects and complications, invasiveness, costs and ethical factors, which influence the ultimate recommendations.

**Results:** For the different indications a total of 113 interventions were evaluated. Twenty-seven (24%) interventions were new compared to the previous guidelines and the recommendation changed for only 3 (2.6%) of the interventions.

**Discussion:** This article summarizes the evolution of the quality of evidence and the strength of recommendations for the interventional pain treatment options for 28 clinical pain diagnoses. ■

**Key Words:** interventional pain management, evidence-based medicine, systematic review, GRADE, recommendations

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### INTRODUCTION

Clinical practice guidelines are statements that include recommendations intended to optimize patient care that

are established by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.<sup>1</sup> For guidelines to reflect the best available evidence, it is important that they be based on a comprehensive systematic review of all available evidence. Guidelines, though much appreciated by clinicians, may rapidly become outdated. Between 2009 and 2011, a series of articles were published on recommendations for diagnosis and treatment of 26 diagnoses. In particular, the evidence on interventional pain management techniques was analyzed and used as the basis for the recommendations. The recommendations were formulated according to a system adapted from Guyatt<sup>2</sup> by van Kleef et al.<sup>3</sup> For a detailed description of this scoring system, we refer the reader to van Kleef et al.<sup>3</sup> The guidelines were published in *Pain Practice*.<sup>4-29</sup> The large number of publications since the previous literature search justifies an update.

### Method of Reviewing the Literature

An independent company, Kleijnen Systematic Reviews (KSR), was asked to review the literature.

This review aimed to identify and summarize relevant evidence using Cochrane and Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology to inform guidelines on interventional pain management.<sup>30,31</sup> This objective was achieved by conducting a review of existing systematic reviews (SRs) and randomized controlled trials (RCTs) for the conditions outlined in the research question.

### RESEARCH QUESTION

What is the place for interventional pain management techniques in the treatment algorithm of the following conditions?

1. Trigeminal neuralgia
2. Cluster headache
3. Persistent idiopathic facial pain
4. Cervical radicular pain
5. Cervical facet pain
6. Cervicogenic headache
7. Whiplash-associated disorders
8. Occipital neuralgia
9. Thoracic radicular pain
10. Thoracic facet joint pain
11. Lumbosacral radicular pain
12. Failed back surgery syndrome
13. Pain due to spinal canal stenosis
14. Pain originating from the lumbar facet joints

15. Sacroiliac joint pain
16. Discogenic low back pain
17. Complex regional pain syndrome
18. Herpes zoster and postherpetic neuralgia
19. Painful diabetic polyneuropathy
20. Carpal tunnel syndrome
21. Meralgia paresthetica
22. Phantom pain
23. Traumatic plexus lesion
24. Chronic refractory angina pectoris
25. Ischemic pain in the extremities and Raynaud's phenomenon
26. Pain in chronic pancreatitis
27. Pain in patients with cancer

## METHODS

### Selection of the Literature

The search by the independent research company (KSR) was performed in 2015. The search covered the period 2010 to 2015.

### Inclusion Criteria

Studies that met the following criteria were eligible for inclusion.

**Participants.** Patients (adults or children) had any of the conditions under research.

**Interventions.** Interventional treatments were defined as procedures targeting the source of the patient's pain. The interventions discussed in the previous guideline were included, except for shoulder pain. Additionally, 2 new topics were added: failed back surgery syndrome and spinal canal stenosis. A list of treatments categorized by clinical diagnosis is presented in Appendix 1. When we identified RCTs of interventional treatments that were not listed in the protocol, the members of the guideline committee decided on inclusion in the review.

**Outcome.** Inclusion was not restricted based on outcome; any outcome was considered. The primary outcome, which is also most often used in SRs and RCTs, is pain reduction; improvement in function and quality of life were included as well. There is little information regarding medication use, but when available it was included.

**Study design.** SRs and RCTs were eligible for inclusion. If no relevant RCTs were identified for any prespecified

interventional technique of interest, then case-control or cohort studies were included.

### Literature Searches

Literature searches were conducted to identify relevant studies for each of the conditions of interest. The searches were carried out using a stepwise approach according to study design:

- SRs
- RCTs
- Observational studies (case-control or cohort studies)

SRs were identified by screening the in-house KSR pain database of SRs. This database consists of SRs identified by regular literature searches of a range of bibliographic databases. Additionally, a search for recent guidelines was undertaken.

The search strategies used to identify RCTs combined relevant search terms comprising indexed keywords (eg, medical subject headings [MeSH]) and text terms appearing in the titles and/or abstracts of database records for each of the target conditions. When searching for RCTs where the quantity of literature is likely to be large, the search strategies included an additional facet of search terms for the interventional treatments of interest for those particular conditions, for example, cancer pain, thoracic pain, and angina pectoris.

Search methods met best practice standards in SRs.<sup>32,33</sup> The search strategies were developed specifically for each database and the keywords adapted according to the configuration of each database. Where appropriate, searches were limited to remove animal studies. Searches were not limited by language or publication status.

#### 1. SRs and guidelines

The following databases were searched for the KSR pain database of SRs:

- Cochrane Database of Systematic Reviews (Wiley Online Library)
- Database of Abstracts of Reviews of Effects (Wiley Online Library)
- Medline In-Process Citations, Medline Daily Update (OvidSP)
- Embase (OvidSP)
- Cumulative Index to Nursing and Allied Health Literature (CINAHL; EBSCO)
- PsycINFO (OvidSP)

- Allied and Complementary Medicine Database (AMED; ProQuest)
- National Guideline Clearinghouse (for recent guidelines: [www.guideline.gov/](http://www.guideline.gov/))

#### 2. RCTs

The following databases were searched for RCTs and, where appropriate, included a search filter designed to identify RCTs:<sup>34</sup>

- Medline (OvidSP)
- Medline In-Process Citations, Medline Daily Update (OvidSP)
- PubMed (National Library of Medicine [NLM])
- Embase (OvidSP)
- Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley Online Library)

#### 3. Observational studies

If no evidence from SRs and RCTs was identified, the following databases were searched and included a search filter designed to identify observational studies:<sup>35</sup>

- Medline (OvidSP)
- Medline In-Process Citations, Medline Daily Update (OvidSP)
- PubMed (NLM)
- Embase (OvidSP)

**Reference Checking.** The bibliographies of identified research and review articles were checked for relevant studies.

**Handling of Citations.** Identified references were downloaded into Endnote reference management software Thomson Reuter (Scientific) LLC, London, UK for further assessment and handling. Individual records within the Endnote reference libraries were tagged with search information, such as searcher, date searched, database host, database searched, strategy name and iteration, theme, or search question. To save time removing duplicate records, as well as reviewer screening time, the results of searches for all chapters were combined into one Endnote library.

**Quality Assurance Within the Search Process.** The main Embase strategy for each search was independently peer reviewed by a second information specialist

using the Canadian Agency for Drugs and Technologies in Health Peer Review checklist.<sup>13</sup>

### Methods of Study Selection, Quality Assessment, and Data Extraction

**Study Selection.** Two KSR reviewers independently screened the titles and abstracts of all reports identified by the searches; any discrepancies were discussed and resolved by consensus. Full copies of all studies deemed potentially relevant were obtained. One reviewer assessed full text papers for inclusion, and a second reviewer checked the decision; any disagreements were resolved by consensus.

**Data Extraction.** Structured data extraction was performed using a Microsoft Access (Microsoft Corporation, Redmond, WA, U.S.A.) database that was developed specifically for the project. For interventional studies, details on the following parameters were extracted: participant characteristics, study design, brief inclusion and exclusion criteria, brief intervention details, details of outcomes assessed, and results. Data for pain and available functionality and quality of life were extracted by one KSR reviewer and checked by a second; any disagreement was resolved by consensus.

**Quality Assessment.** SRs were assessed for methodological quality using the ROBIS tool.<sup>36</sup> This tool aims to assess the risk of bias in SRs and includes domains covering study eligibility criteria, identification and selection of studies, data collection and study appraisal, synthesis and findings, and interpretation. Trials were assessed for methodological quality using the Cochrane Risk of Bias tool.<sup>31</sup> This includes items covering selection bias (random sequence generation and allocation concealment), performance bias (participant blinding), detection bias (blinding of outcome assessors), attrition bias (incomplete outcome data), and reporting bias (selective reporting). There was also an additional field for other sources of bias. For all tools, if at least 1 of the domains was rated as “high,” the study was considered at high risk of bias; if all domains were judged as “low,” the trial was considered at low risk of bias; otherwise the trial was considered to be at “unclear” risk of bias.

**Data Synthesis.** If sufficient studies assessing similar populations, interventions, comparators, and outcomes

were found, a formal meta-analysis was used to estimate summary measures of effect. GRADE methods were used to define the levels of evidence.

### Integration of the Evidence Before 2010 and New Publications Retrieved After 2015

The studies used in the previous 2010 guidelines were usually included in SRs that were identified. When studies were included in the previous guideline, but were not included in the most recent SR, the panel retrieved the publications used in the previous guideline. A member of the guidelines committee who was an epidemiologist judged the quality of studies that were withheld from the previous guideline.

### Last Update

Since the KSR search included studies published up to 2015, a new search of the abstracts was performed to identify more recent publications (until March 1, 2018) using the terms “diagnosis” and “intervention” for each diagnosis and for the different interventional pain management techniques.

When an SR was found, it was compared with the review reported up to 2015. If no new information was listed in the new SR, it was discarded. When new RCTs or important observational studies were found, they were discussed and included in the considerations paragraph, and a judgment was made to what extent this new information would influence (the strength of) the recommendations.

The quality of the evidence found by KSR was maintained.

The strength of recommendation could be adapted based on the following factors:

- Studies published after 2015 providing relevant information
- Risk–benefit balance
- Values and preferences such as:
- Clinical relevance
- Invasiveness
- Technical requirements needed to perform the interventional pain management technique (degree of specialization, need for special equipment)
- The need for shared decision making.

Table 1 shows the classification of the quality of evidence, strength of recommendation, and description of the recommendations.

**Table 1. Classification of the Quality of Evidence, Strength of Recommendation, and Description of the Recommendation**

Quality of Evidence	Strength of Recommendation	Recommendation
High	Strong	Must (not) be used
Moderate	Moderate	Should (not) be used
Low	Weak	Could (not) be used
Very low	Very weak	Could (not) be considered

### Validation

The chapters were placed on a closed website. Members of the Dutch Society of Anesthesiologists; Flemish Association of Anesthesiological Pain Management; World Institute of Pain, Benelux section; and the educational committee of the World Institute of Pain were invited to give comments and feedback. All remarks from the Netherlands and Belgium were discussed in a plenary session. The comments from the educational committee were reviewed by the guideline committee. Where necessary, corrections were made.

### RESULTS

The search strategy resulted in a large number of references; for example, for the indications lumbar facet joint pain, sacroiliac joint pain, and discogenic pain, 10,333 records after deduplication were screened for inclusion in the study and 38 studies were finally included in our review (22 for lumbar facet pain, 6 for sacroiliac pain, and 10 for discogenic pain).

Table 2 summarizes the evolution of the evidence/recommendation for the different diagnoses and the relevant interventional pain management techniques. The studies included in the quality assessment and those used in the considerations, which may influence the strength of recommendation, are described in the individual chapters, which can be retrieved from <https://www.anesthesiologie.nl/publicaties/#filter=pijngeneeskunde>.

For the different indications, a total of 113 interventions were evaluated. Twenty-seven interventions (24%) were new compared to the 2010 guidelines, and the recommendation changed for only 3 (2.6%) of the interventions.

The scientific justification of the rating of the quality of evidence and the strength of recommendations can be retrieved from <https://www.anesthesiologie.nl/publicaties/#filter=pijngeneeskunde>.

## DISCUSSION

### Quality of Evidence

The large number of publications retrieved for this guideline project indicates the interest in the appropriate use of interventional pain management techniques. The quality of evidence may seem rather low and the strength of the recommendations weak. However, this must be viewed in the context of guideline methodology. GRADE rates evidence based on RCTs as high quality, but the confidence in evidence may be decreased for several reasons, such as:

- Study limitations
- Inconsistency of results
- Indirectness of evidence
- Imprecision
- Reporting bias

The quality of observational studies (eg, cohort and case-control studies) starts with a “low quality” rating; grading upwards may be warranted if the magnitude of the treatment effect is very large, if there is evidence of a dose-response relationship, or if all plausible biases would decrease the magnitude of apparent treatment.<sup>37</sup>

The fact that the quality of the evidence is rather low does not mean that the effect of the treatment is minimal; it indicates the need for clinical research. However, performing RCTs for (interventional) pain management techniques is hampered by several factors, such as difficulty in blinding the patient and interventionalist, patient refusal to enter a study with a risk of receiving a noneffective treatment, and ethical concern of withholding potential effective treatment from patients who suffer from chronic intolerable pain. This results in few selected RCTs, and when they are available they are downgraded because of risks of bias such as blinding and low number of participants.

The meaning of the GRADE rating is described in Table 3.

Strength of recommendation, quality of evidence, and size of the effect are not synonymous. When the quality of the evidence is low, this does not mean that the intervention is not effective. And the quality of the evidence may be high, indicating that the intervention is not effective.

The rating of the quality of evidence has a direct impact on the strength of recommendation. The members of the guideline committee considered factors such as risk for complications, degree of invasiveness, and



**Table 2. Summary of the Recommendations\***

Treatment	Recommendations in 2010†	GRADE Level of Evidence in 2015	Recommendations in 2018
Trigeminal neuralgia			
Microvascular decompression		Very low	Very weak
Stereotactic radiosurgery		Very low	Very weak
Radiofrequency treatment of the ganglion Gasseri	2 B+	Low	Weak
Pulsed radiofrequency	2 B–	Very low	Very weak
Cluster headache			
Uni- or bilateral injection of nervus occipitalis		Not graded	Very weak
Radiofrequency treatment of ganglion pterygopalatinum	2 C+	Very low	Weak
Stimulation of ganglion pterygopalatinum		Very low	Very weak
Occipital nerve stimulation	2 C+	Low	Very weak
Persistent idiopathic facial pain			
Pulsed radiofrequency of ganglion pterygopalatinum	2 C+	Very low	Very weak
Radiofrequency of ganglion pterygopalatinum		Very low	Very weak
Cervical radicular pain			
Interlaminar epidural corticosteroid administration	2 B+	Moderate	Weak
Transforaminal epidural preservative-free dexamethasone	2 B– (not dexamethasone)	Very low	Very weak
Pulsed radiofrequency treatment adjacent to de DRG	1 B+	Moderate	Moderate
Radiofrequency treatment adjacent to de DRG	2 B+	Moderate	Weak
Spinal cord stimulation	0	Not graded	Very weak
Cervical facet joint pain			
Intra-articular corticosteroid administration	0	Low	Weak against
Therapeutic (repetitive) cervical medial branch injections of local anesthetic with or without corticosteroid	2 B+	Moderate	Weak
Radiofrequency treatment of ramus medialis of the ramus dorsalis	2 C+	Low	Weak
Cervicogenic headache			
Injection of the nervus occipitalis major with local anesthetic with or without steroid	1 B+	Moderate	Weak
Injection of atlanto-axial joint with local anesthetic with or without steroid	2 C–	Not graded	Weak against
Radiofrequency treatment of cervical ramus medialis	2 B+/-	Very low	Very weak
Pulsed radiofrequency treatment of nervus occipitalis major		Low	Weak
Pulsed radiofrequency treatment of atlanto-axial joint		Not graded	Very weak
Pulsed radiofrequency of cervical DRG (C2–C3)	0		
Whiplash-associated disorder			
Botulinum toxin injections	2 B–	Moderate	Moderate against
Radiofrequency treatment of cervical ramus medialis of the ramus dorsalis	2 B+	Low	Moderate
Intra-articular corticosteroid injections	2 C–	Very low	Very weak against
Occipital neuralgia			
A single infiltration of the nervi occipitales with local anesthetic and corticosteroids	2 C+	Very low	Very weak
Pulsed radiofrequency of the nervi occipitales	2 C+	Very low	Weak
Pulsed radiofrequency adjacent to the DRG	0		
Peripheral nerve stimulation	2 C+	Very low	Very weak
Botulinum toxin injections	2 C+/-	Very low	Very weak
Stimulation of the nervi occipitales	2 C+	Very low	Very weak
Thoracic radicular pain syndrome			
Intercostal nerve blocks	0	Not graded	Not applicable
(Pulsed) radiofrequency of thoracic DRG	2 C+	Low	Weak
Pain originating from the thoracic facet joint			
Addition of corticosteroids to local anesthetic for thoracic medial branch blocks		High	Moderate against
Lumbosacral radicular pain			
Epidural corticosteroid administration (interlaminar, transforaminal contained herniation, and transforaminal extruded herniation)		Moderate	Weak
Epidural TNF- $\alpha$ inhibitors		Low	Weak against
Radiofrequency treatment adjacent to lumbar DRG	2 A–	Moderate	Moderate against
Pulsed radiofrequency treatment adjacent to lumbar DRG	2 C+	Moderate	Moderate
Failed back surgery syndrome			
Adhesiolysis	2 B+/-	Very low	Very weak
Epiduroscopy	2 B+/-	Moderate	Weak
Spinal cord stimulation (tonic)	2 A+	Moderate	Moderate
Spinal cord stimulation (HF-10)		Not graded	Moderate
Subcutaneous stimulation as add-on to spinal cord stimulation		Not graded	Very weak
Pain originating from the lumbar facet joints			
Intra-articular injection of local anesthetic with or without corticosteroid	2 B+/-	Low	Very weak
Radiofrequency treatment of the ramus medialis of the ramus dorsalis	1 B+	Low	Weak
Pulsed radiofrequency treatment of ramus medialis of the ramus dorsalis		Low	Very weak against

Table 2. (Continued)

Treatment	Recommendations in 2010†	GRADE Level of Evidence in 2015	Recommendations in 2018
Spinal canal stenosis			
Spinal cord stimulation		Very low	Very weak
Pulsed radiofrequency treatment adjacent to DRG		Moderate	Moderate
Epidural local injections (without steroids)		Low	Weak
Epidural corticosteroid injections		High	Moderate against
Sacroiliac joint pain			
Intra-articular corticosteroid injections	1 B+	Low	Weak
Radiofrequency treatment of rami dorsalis and lateralis (palisade)	2 C+	Very low	Very weak
Radiofrequency treatment of rami dorsalis and lateralis (palisade) SIJ pain due to ankylosing spondylitis		Moderate	Moderate
Radiofrequency treatment of rami dorsalis and lateralis (simplicity)		Not graded	Moderate against
Pulsed radiofrequency treatment of rami dorsalis and lateralis	2 C+	Not graded	Very weak
Radiofrequency treatment of ramus dorsalis at L4–L5 and cooled radiofrequency of the ramus lateralis	2 B+	Low	Weak
Cooled radiofrequency treatment of ramus dorsalis at L4–L5 and ramus lateralis		Moderate	Moderate
Discogenic pain			
Intradiscal methylene blue injection		Moderate	Weak
Intradiscal corticosteroid injection	2 B–	Low	Weak against
Intradiscal radiofrequency treatment	2 B+/-	Low	Weak against
Intradiscal electrothermal therapy		Low	Weak
Intradiscal pulsed radiofrequency treatment	2 B+/-	Very low	Very weak
Intradiscal biacuplasty	0	Moderate	Moderate
Disctrode	0		
Radiofrequency treatment of ramus communicans	2 B +	Very low	Very weak against
Complex regional pain syndrome			
Sympathetic blocks with local anesthetics	2 B+	Moderate	Moderate against
Thoracic block (T2–T3) with ropivacaine and triamcinolone		Low	Weak
IV regional blocks with guanethidine	2 A–	Moderate	Moderate against
Spinal cord stimulation	2 B+	Moderate	Moderate
DRG stimulation (for lower extremity CRPS)		Moderate	Moderate
Peripheral nerve stimulation	2 C+	Very low	Very weak
Low-dose IV ketamine		Moderate	Weak
Herpes zoster and postherpetic neuralgia			
Acute phase: epidural injection of corticosteroid with local anesthetics	2 B+	Moderate	Moderate
Acute phase: paravertebral injections of corticosteroids with local anesthetics		Moderate	Moderate
Acute phase: repeated epidural injections of corticosteroid with local anesthetics and epinephrine		Moderate	Weak
Acute phase: stellate ganglion block	2 C+	Low	Weak
Treatment of postherpetic neuralgia: epidural corticosteroid injections or combined therapy with intrathecal midazolam	0	Low	Weak
Treatment of postherpetic neuralgia: sympathetic nerve block	2 C+	Very low	Very weak against
Treatment of postherpetic neuralgia: spinal cord stimulation	2 C+	Very low	Very weak
Treatment of postherpetic neuralgia: pulsed radiofrequency on intercostal nerve		Moderate	Moderate
Treatment of postherpetic neuralgia: pulsed radiofrequency adjacent to DRG		Very weak	Moderate
Treatment of postherpetic neuralgia: intrathecal administration of corticosteroid		Low	Strong against
Treatment of postherpetic neuralgia: lumbar sympathetic block		Very low	Very weak
Painful diabetic polyneuropathy			
Spinal cord stimulation	2 C+	Moderate	Moderate
Lumbar sympathetic block		Very low	Very weak
Meralgia paresthetica			
Infiltration of LFCB with local anesthetic with or without corticosteroid	2 C+	Very low	Very weak
Pulsed radiofrequency of LFCB	0	Very low	Very weak
Spinal cord stimulation	0	Not graded	Very weak
Carpal tunnel syndrome			
Intracarpal corticosteroid injection(s)	1 B+	Moderate	Moderate
Pulsed radiofrequency treatment of median nerve	0	Very low	Very weak
Phantom pain			
Pulsed radiofrequency treatment of the most tender part of the neuroma	0	Very low	Very weak
Spinal cord stimulation	0	Very low	Very weak
DRG stimulation		Very low	Very weak
Traumatic plexus lesion			
Spinal cord and DRG stimulation	0	Not graded	Very weak
Chronic refractory angina pectoris			
Spinal cord stimulation	2 B+	Low	Weak

**Table 2. (Continued)**

Treatment	Recommendations in 2010†	GRADE Level of Evidence in 2015	Recommendations in 2018
Raynaud's phenomenon			
Radiofrequency of T2–T3 and T2 thermolesion with a local application of phenol	2 C+	Very low	Very weak
Spinal cord stimulation		Very low	Very weak
Ischemic pain of the extremities			
Sympathectomy	2 B+/-	Not graded	Very weak
Spinal cord stimulation	2 B+/-	High	Moderate
Chronic pancreatitis			
Plexus coeliacus block with local anesthetic and corticosteroid		Low	Weak against
Splanchnic nerve block	2 C+ (radiofrequency)	Very low	Very weak
Spinal cord stimulation	2 C+	Very low	Very weak
Pain in patients with cancer			
Intrathecal drug administration	2 B+	Moderate	Weak
Epidural drug administration	2 C+	Very low	Very weak
Spinal cord stimulation		Very low	Very weak
Cervical percutaneous cordotomy	2 C+	Very low	Very weak
Neurolytic plexus coeliacus block	2 A+	High	Strong
Neurolytic plexus hypogastricus block	2 C+	Low	Weak
Intrathecal phenolization of lower sacral roots of cauda equina (lower end block)	0	Very low	Very weak
Kyphoplasty	2 B+	Not graded	Very weak
Vertebroplasty	2 B+	Very low	Very weak

\*2010 recommendations as reported in the previous guideline; the level of evidence in 2015 as identified by independent evaluation using GRADE; and the strength of recommendation as updated by the Guideline Committee in 2018, taking into consideration newer publications and potential risks for side effects and complications.

†A is the highest level of evidence (various RCTs of good quality), B stands for RCTs with methodological limitations or large observational studies and C stands for observational studies or case series.<sup>7</sup>

CRPS, chronic regional pain syndrome; DRG, dorsal root ganglion; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HF-10, High frequency 10-kHz stimulation; LFCB, lateral femoral cutaneous nerve; SIJ, sacroiliac joint; TNF- $\alpha$ , tumor necrosis factor- $\alpha$ .

**Table 3. Interpretation of the Quality of Evidence**

High	Much confidence that real effect is close to observed effect
Moderate	Moderate confidence that real effect is close to observed effect, but there is a possibility that it is substantially different
Low	Restricted confidence that real effect is close to observed effect, the real effect can be substantially different than the observed effect
Very low	Little confidence that real effect is close to observed effect; the real effect is probably substantially different from the observed effect

technical requirements to formulate a strength of recommendation. A treatment option with low-quality evidence and a weak recommendation may be preferred over a treatment with high-quality evidence when the former has fewer risks for complications and/or is less invasive.

For example, in the judgment of epidural corticosteroid injections for the treatment of spinal canal stenosis, high-quality evidence based on several SRs of 13 studies showed no significant difference in pain reduction between the groups treated with corticosteroids compared to the group treated with local anesthetics. This observation, together with considerations on the potential side effects and complications of corticosteroids, led to the recommendation against the

use of corticosteroids. The epidural administration of local anesthetics alone is recommended.

Another example is in the treatment of postherpetic neuralgia. Pulsed radiofrequency treatment of the dorsal root ganglion has a very weak quality of evidence, but this treatment is documented to be rather easy to perform and safe; therefore, the strength of the recommendation is upgraded to moderate.

### Further Research

When the recommendation is very low, there is a high need for more research.

Each intervention that received a very weak recommendation should be performed in the context of a study, which means at least the systematic recording of

- Patient characteristics
- Diagnostic process
- Treatment, including the details of the technique concerned
- Evaluation of the result (preferably VAS, Euro-Qol, and a complaint-specific scale over 3, 6, and 12 months)
- Recording of side effects and complications
- Systematic reporting of the results.



The aim is thus to accumulate information that enables estimation of the value of the technique when it has been applied to a larger number of patients. If these results are positive, they may then lead to the justification for a prospective randomized study.<sup>3</sup>

### Critical Look at Guidelines

Guidelines have gained in popularity because clinicians have easy access to the recommendations that may facilitate their daily work. These guidelines may have an immense impact, because they act as a standard of care and may be used to devise national and local protocols, measure physician performance, and evaluate adherence to standards. They can also be used as expert testimony in cases of litigation and malpractice.<sup>38</sup> There are, however, some points that deserve attention.

The recommendations formulated in guidelines are valid for a specific patient population; however, they may not be valid for the individual patient with comorbidities. This stresses the role of the clinician to select a treatment based on the complete medical picture of the patient.

Furthermore, there is an increasing number of guidelines that are not performed according to the rigorous methodology advocated by scientific groups such as the Cochrane collaboration. A recent article in the *European Journal of Anaesthesiology* described the different factors that may influence the interpretation of the literature.<sup>38</sup> The authors listed a methodological shortage in many published SRs, the apparent ignorance among reviewers and editors of scientific journals to methodological issues and shortcomings of SRs, the influence of sponsors on research outcome, financial links of principal investigators of clinical trials that are strongly associated with a positive clinical trial outcome, conflicts of interest and lack of methodological knowledge of peer reviewers, scientific fraud promoted by the financial incentives of scientific publications, and the poor quality of published clinical trials.<sup>38</sup>

### Towards an Integrated Treatment Plan

Pain is a complex physical, psychosocial, ethnocultural, affective-cognitive, and environmental phenomenon. No single treatment can influence all these aspects and, therefore, a multidisciplinary and multimodal approach has been advocated. For the management of chronic pain discussed in this guideline, a stepwise approach is indicated. Firstly, conservative treatment options should

be used to their full extent. Secondly, interventional treatment can be used. In the design of a treatment algorithm, the first parameter to consider is the efficacy of the treatment, but secondarily the grade of invasiveness of the intervention should be taken into consideration. As stated earlier, quality of evidence is not synonymous with effectiveness and use of healthcare resources.

The correct application of interventional pain management techniques requires an excellent knowledge of the neuroanatomy, experience in the interpretation of the images obtained during the procedure, and adequate training. It is obvious that a more complicated intervention can only be performed by a well-trained and experienced physician. Therefore, it is preferred that such interventions be performed in specialized centers.<sup>39</sup>

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### CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

### REFERENCES

1. Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice Guidelines. *Clinical*

*Practice Guidelines We Can Trust*. Washington, DC: National Academies Press; 2011.

2. Guyatt G, Gutterman D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an American College of Chest Physicians task force. *Chest*. 2006;129:174–181.
3. van Kleef M, Mekhail N, van Zundert J. Evidence-based guidelines for interventional pain medicine according to clinical diagnoses. *Pain Pract*. 2009;9:247–251.
4. van Kleef M, van Genderen WE, Narouze S, et al. 1. Trigeminal neuralgia. *Pain Pract*. 2009;9:252–259.
5. van Kleef M, Lataster A, Narouze S, et al. Evidence-based interventional pain medicine according to clinical diagnoses. 2. Cluster headache. *Pain Pract*. 2009;9:435–442.
6. Cornelissen P, van Kleef M, Mekhail N, et al. Evidence-based interventional pain medicine according to clinical diagnoses. 3. Persistent idiopathic facial pain. *Pain Pract*. 2009;9:443–448.
7. Van Zundert J, Huntoon M, Patijn J, et al. 4. Cervical radicular pain. *Pain Pract*. 2009;10:1–17.
8. van Eerd M, Patijn J, Lataster A, et al. 5. Cervical facet pain. *Pain Pract*. 2010;10:113–123.
9. van Suijlekom H, Van Zundert J, Narouze S, et al. 6. Cervicogenic headache. *Pain Pract*. 2010;10:124–130.
10. van Suijlekom H, Mekhail N, Patel N, et al. 7. Whiplash-associated disorders. *Pain Pract*. 2010;10:131–136.
11. Vanelderden P, Lataster A, Levy R, et al. 8. Occipital neuralgia. *Pain Pract*. 2010;10:137–144.
12. Huygen F, Patijn J, Rohof O, et al. 9. Painful shoulder complaints. *Pain Pract*. 2010;10:318–326.
13. van Kleef M, Stolker RJ, Lataster A, et al. 10. Thoracic pain. *Pain Pract*. 2010;10:327–338.
14. Van Boxem K, Cheng J, Patijn J, et al. 11. Lumbosacral radicular pain. *Pain Pract*. 2010;10:339–358.
15. van Kleef M, Vanelderden P, Cohen SP, et al. 12. Pain originating from the lumbar facet joints. *Pain Pract*. 2010;10:459–469.
16. Vanelderden P, Szadek K, Cohen SP, et al. 13. Sacroiliac joint pain. *Pain Pract*. 2010;10:470–478.
17. Patijn J, Janssen M, Hayek S, et al. 14. Coccygodynia. *Pain Pract*. 2010;10:554–559.
18. Kallewaard JW, Terheggen MA, Groen GJ, et al. 15. Discogenic low back pain. *Pain Pract*. 2010;10:560–579.
19. van Eijs F, Stanton-Hicks M, Van Zundert J, et al. Evidence-based interventional pain medicine according to clinical diagnoses. 16. Complex regional pain syndrome. *Pain Pract*. 2011;11:70–87.
20. van Wijck AJ, Wallace M, Mekhail N, et al. Evidence-based interventional pain medicine according to clinical diagnoses. 17. Herpes zoster and post-herpetic neuralgia. *Pain Pract*. 2011;11:88–97.
21. Pluijms W, Huygen F, Cheng J, et al. Evidence-based interventional pain medicine according to clinical diagnoses. 18. Painful diabetic polyneuropathy. *Pain Pract*. 2011;11:191–198.
22. Patijn J, Vallejo R, Janssen M, et al. Carpal tunnel syndrome. *Pain Pract*. 2011;11:297–301.
23. Patijn J, Mekhail N, Hayek S, et al. Meralgia paresthetica. *Pain Pract*. 2011;11:302–308.
24. Wolff A, Vanduyndhoven E, van Kleef M, et al. 21. Phantom pain. *Pain Pract*. 2011;11:403–413.
25. van Dongen R, Cohen SP, van Kleef M, et al. 22. Traumatic plexus lesion. *Pain Pract*. 2011;11:414–420.
26. Vissers KC, Besse K, Wagemans M, et al. 23. Pain in patients with cancer. *Pain Pract*. 2011;11:453–475.
27. van Kleef M, Staats P, Mekhail N, et al. 24. Chronic refractory angina pectoris. *Pain Pract*. 2011;11:476–482.
28. Devulder J, van Suijlekom H, van Dongen R, et al. 25. Ischemic pain in the extremities and Raynaud's phenomenon. *Pain Pract*. 2011;11:483–491.
29. Puylaert M, Kapural L, Van Zundert J, et al. 26. Pain in chronic pancreatitis. *Pain Pract*. 2011;11:492–505.
30. Cochrane Collaboration Training. *Cochrane Handbook for Systematic Reviews of Interventions*; 2018. Available at: <https://training.cochrane.org/handbook>.
31. Guyatt GH, Oxman AD, Vist G, et al. GRADE guidelines: 4. Rating the quality of evidence—study limitations (risk of bias). *J Clin Epidemiol*. 2011;64:407–415.
32. Higgins J, Green S. 2011. *Cochrane Handbook for Systematic Reviews of Interventions*. Available at: <http://handbook-5-1.cochrane.org>. Accessed March 26, 2015
33. Centre for Reviews and Dissemination. *Systematic Reviews: CRD's guidance for undertaking reviews in health care* [Internet]. 2009. York: University of York. <http://www.york.ac.uk/inst/crd/SysRev/!SSL!/WebHelp/SysRev3.htm>. (accessed March 26, 2015).
34. Wong SS, Wilczynski NL, Haynes RB. Developing optimal search strategies for detecting clinically sound treatment studies in EMBASE. *J Med Libr Assoc*. 2006;94:41–47.
35. Scottish Intercollegiate Guidelines Network (SIGN). 2013. *Search filters: observational studies [Embase (OvidSP)] [Internet]*. Edinburgh: SIGN. <http://www.sign.ac.uk/methodology/filters.html#obs> (accessed March 26, 2015).
36. Whiting P, Davies D, Savovic J, et al. *Developing ROBIS—A New Tool to Assess the Risk of Bias in Systematic Reviews* [Unpublished]. York, U.K.: Bristol School of Social and Community Medicine; 2014.
37. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–926.
38. Afshari A, De Hert S. Pitfalls of clinical practice guidelines in the era of broken science: let's raise the standards. *Eur J Anaesthesiol*. 2018;35:903–906.
39. Van Zundert J, Raj P, Erdine S, et al. Application of radiofrequency treatment in practical pain management: state of the art. *Pain Pract*. 2002;2:269–278.

## APPENDIX 1

### Eligible Populations and Interventions

Population	Interventional treatments
Trigeminal neuralgia	Surgical microvascular decompression Stereotactic radiation therapy, gamma knife Percutaneous balloon microcompression Radiofrequency treatment of the Gasserian ganglion Pulsed RF treatment of the Gasserian ganglion
Cluster headache	RF treatment of the pterygopalatine ganglion (sphenopalatinum) Occipital nerve stimulation
Persistent idiopathic facial pain	Pulsed RF treatment of the ganglion pterygopalatinum (sphenopalatinum)
Cervical radicular pain	Interlaminar epidural corticosteroid administration Transforaminal epidural corticosteroid administration RF treatment adjacent to the cervical ganglion spinale (DRG) Pulsed RF treatment adjacent to the cervical ganglion spinale (DRG)
Cervical facet pain	Spinal cord stimulation Intra-articular injections Therapeutic (repetitive) cervical ramus medialis (medial branch) of the ramus dorsalis block (local anesthetic with or without corticosteroid) RF treatment of the cervical ramus medialis (medial branch) of the ramus dorsalis
Cervicogenic headache	Injection of nervus occipitalis major with corticosteroid + local anesthetic Injection of atlanto-axial joint with corticosteroid + local anesthetic RF treatment of the cervical ramus medialis (medial branch) of the ramus dorsalis Pulsed RF treatment of the cervical ganglion spinale (DRG) (C2 to C3)
Whiplash-associated disorders	Botulinum toxin type A Intra-articular corticosteroid injection RF treatment of the cervical ramus medialis (medial branch) of the ramus dorsalis
Occipital neuralgia	Single infiltration of the nervi occipitales with local anesthetic and corticosteroids Pulsed RF treatment of the nervi occipitales Pulsed RF treatment of the cervical ganglion spinale (DRG) Subcutaneous stimulation of the nervi occipitales Botulinum toxin A injection
Thoracic pain	Intercostal block RF treatment of thoracic ganglion spinale (DRG) Pulsed RF treatment of thoracic ganglion spinale (DRG)
Lumbosacral radicular pain	Interlaminar epidural corticosteroid administration Transforaminal epidural corticosteroid administration in "contained herniation" Transforaminal epidural corticosteroid administration in "extruded herniation" RF lesioning adjacent to the lumbar ganglion spinale (DRG) Pulsed RF treatment adjacent to the lumbar ganglion spinale (DRG) Spinal cord stimulation (FBSS only) Adhesiolysis-epiduroscopy
Pain originating from the lumbar facet joints	Intra-articular corticosteroid injections RF treatment of the lumbar rami mediales (medial branches) of the dorsal ramus
Sacroiliac joint pain	Therapeutic intra-articular injections with corticosteroids and local anesthetic RF treatment of rami dorsales and rami laterals Pulsed RF treatment of rami dorsales and rami laterals Cooled/RF treatment of the rami laterales
Coccygodynia	Local injections corticosteroids/local anesthetic Intradiscal corticosteroid injections, ganglion impar block, RF ganglion impar, caudal block Neurostimulation
Discogenic low back pain	Intradiscal corticosteroid administration RF treatment of the discus intervertebralis Intradiscal electrothermal therapy Biacuplasty Distrode RF of the ramus communicans
Complex regional pain syndrome	Intravenous regional block guanethidine Ganglion stellatum (stellate ganglion) block Lumbar sympathetic block Plexus brachialis block Epidural infusion analgesia Spinal cord stimulation Peripheral nerve stimulation
Herpes zoster and post-herpetic neuralgia	Interventional pain treatment of acute herpes zoster Epidural corticosteroid injections

**Appendix A. (Continued)**

Population	Interventional treatments
	Sympathetic nerve block
	One-time epidural corticosteroid injection
	Repeated paravertebral injections
	Sympathetic nerve block
	Epidural corticosteroid injections
	Sympathetic nerve block
	Intrathecal injection
	Spinal cord stimulation
Painful diabetic polyneuropathy	Spinal cord stimulation
Carpal tunnel syndrome	Local injections with corticosteroids
	Pulsed RF treatment median nerve
Meralgia parasthetica	Lateral femoral cutaneous nerve (LFCN) infiltration with local anesthetic $\pm$ corticosteroid
	Pulsed RF treatment of LFCN
	Spinal cord stimulation
Phantom pain	Pulsed RF treatment of the stump neuroma Pulsed RF treatment adjacent to the spinal ganglion (DRG)
	Spinal cord stimulation
Traumatic plexus lesion	Spinal cord stimulation
Pain in patients with cancer	Intrathecal medication delivery
	Epidural medication delivery
	Cervical cordotomy
	Neurolytic plexus coeliacus block
	Neurolytic nervus splanchnicus block
	Neurolytic plexus hypogastricus block
	Intrathecal phenolization of lower sacral roots of cauda equine
	Vertebroplasty
	Kyphoplasty
Chronic refractory angina pectoris	Spinal cord stimulation
Ischemic pain of the extremities and Raynaud's phenomenon	Sympathectomy
	Spinal cord stimulation
Pain in chronic pancreatitis	RF nervus splanchnicus block
	Spinal cord stimulation

DRG, dorsal root ganglion; FBSS, failed back surgery syndrome; RF, radiofrequency.