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## Interventions for treating pain and disability in adults with complex regional pain syndrome- an overview of systematic reviews (Review)

Ferraro MC, Cashin AG, Wand BM, Smart KM, Berryman C, Marston L, Moseley GL, McAuley JH, O'Connell NE

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## [Overview of Reviews]

# Interventions for treating pain and disability in adults with complex regional pain syndrome- an overview of systematic reviews

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## ABSTRACT

### Background

Complex regional pain syndrome (CRPS) is a chronic pain condition that usually occurs in a limb following trauma or surgery. It is characterised by persisting pain that is disproportionate in magnitude or duration to the typical course of pain after similar injury. There is currently no consensus regarding the optimal management of CRPS, although a broad range of interventions have been described and are commonly used. This is the first update of the original Cochrane review published in Issue 4, 2013.

### Objectives

To summarise the evidence from Cochrane and non-Cochrane systematic reviews of the efficacy, effectiveness, and safety of any intervention used to reduce pain, disability, or both, in adults with CRPS.

### Methods

We identified Cochrane reviews and non-Cochrane reviews through a systematic search of Ovid MEDLINE, Ovid Embase, Cochrane Database of Systematic Reviews, CINAHL, PEDro, LILACS and Epistemonikos from inception to October 2022, with no language restrictions. We included systematic reviews of randomised controlled trials that included adults (≥18 years) diagnosed with CRPS, using any diagnostic criteria.

Two overview authors independently assessed eligibility, extracted data, and assessed the quality of the reviews and certainty of the evidence using the AMSTAR 2 and GRADE tools respectively. We extracted data for the primary outcomes pain, disability and adverse events, and the secondary outcomes quality of life, emotional well-being, and participants' ratings of satisfaction or improvement with treatment.

### Main results

We included six Cochrane and 13 non-Cochrane systematic reviews in the previous version of this overview and five Cochrane and 12 non-Cochrane reviews in the current version. Using the AMSTAR 2 tool, we judged Cochrane reviews to have higher methodological quality than

non-Cochrane reviews. The studies in the included reviews were typically small and mostly at high risk of bias or of low methodological quality. We found no high-certainty evidence for any comparison.

There was low-certainty evidence that bisphosphonates may reduce pain intensity post-intervention (standardised mean difference (SMD) -2.6, 95% confidence interval (CI) -1.8 to -3.4,  $P = 0.001$ ;  $I^2 = 81\%$ ; 4 trials,  $n = 181$ ) and moderate-certainty evidence that they are probably associated with increased adverse events of any nature (risk ratio (RR) 2.10, 95% CI 1.27 to 3.47; number needed to treat for an additional harmful outcome (NNTH) 4.6, 95% CI 2.4 to 168.0; 4 trials,  $n = 181$ ).

There was moderate-certainty evidence that lidocaine local anaesthetic sympathetic blockade probably does not reduce pain intensity compared with placebo, and low-certainty evidence that it may not reduce pain intensity compared with ultrasound of the stellate ganglion. No effect size was reported for either comparison.

There was low-certainty evidence that topical dimethyl sulfoxide may not reduce pain intensity compared with oral N-acetylcysteine, but no effect size was reported.

There was low-certainty evidence that continuous bupivacaine brachial plexus block may reduce pain intensity compared with continuous bupivacaine stellate ganglion block, but no effect size was reported.

For a wide range of other commonly used interventions, the certainty in the evidence was very low and provides insufficient evidence to either support or refute their use. Comparisons with low- and very low-certainty evidence should be treated with substantial caution. We did not identify any RCT evidence for routinely used pharmacological interventions for CRPS such as tricyclic antidepressants or opioids.

### Authors' conclusions

Despite a considerable increase in included evidence compared with the previous version of this overview, we identified no high-certainty evidence for the effectiveness of any therapy for CRPS. Until larger, high-quality trials are undertaken, formulating an evidence-based approach to managing CRPS will remain difficult. Current non-Cochrane systematic reviews of interventions for CRPS are of low methodological quality and should not be relied upon to provide an accurate and comprehensive summary of the evidence.

## PLAIN LANGUAGE SUMMARY

### Which treatments are effective for the management of complex regional pain syndrome in adults?

#### Key messages

There is a critical lack of high-quality evidence for the benefits and risks of most treatments for adults with complex regional pain syndrome (CRPS). Larger, well-designed studies and higher-quality reviews are needed to provide accurate evidence for benefits and risks of treatments for adults with CRPS.

### What is complex regional pain syndrome?

CRPS is a disabling chronic pain condition. People with CRPS experience persistent pain, usually in the hands or feet, that is not proportionate in severity to any underlying injury. It often involves a variety of other symptoms in the affected body part such as swelling, discolouration, stiffness, weakness, and changes to skin quality.

### What did we want to find out?

A broad range of therapies are used to treat CRPS. The effects of these therapies are summarised across a number of Cochrane and non-Cochrane reviews. Our aim was to combine the information from these reviews into one accessible document. We specifically wanted to find out which treatments are effective in reducing pain and disability in adults with CRPS. We also wanted to find out whether these treatments cause any unwanted effects.

### What did we do?

We searched for Cochrane and non-Cochrane reviews in the medical literature using online databases, from their beginning to October 2011, in the previous version of this overview, and between October 2011 and October 2022 in the current version. We included reviews that evaluated any treatment aiming to reduce pain intensity and disability in adults with CRPS. We judged the quality of the included reviews and summarised their results. We also rated our confidence in the evidence included in the reviews, based on factors such as study methods and size.

## What did we find?

We included six Cochrane and 13 non-Cochrane systematic reviews in the previous version of this overview and five Cochrane and 12 non-Cochrane reviews in the current version. These reviews included evidence relating to a large range of treatments, including drugs, surgical procedures, rehabilitation, and complementary and alternative therapies. For most treatments, there were only a small number of published studies and the quality of these studies was low. The review evidence suggests the following:

- Compared with placebo (or 'dummy') treatment, bisphosphonates (a class of medicines that slow down bone loss) may reduce pain intensity shortly after treatment, but they are probably associated with some side effects.
- Compared with a placebo (or sham) treatment, blocking the branches of the sympathetic nervous system with an anaesthetic probably does not reduce pain intensity.
- There may not be any differences in the pain-reducing effects of a topical cream called dimethyl sulfoxide (DMSO) and an amino acid supplement called N-acetyl cysteine, but it is unclear whether either treatment works at all.
- One type of nerve block, called a brachial plexus block, may reduce pain intensity more than another type of block, called a bupivacaine stellate ganglion block.

For the majority of the commonly used drug, surgical, rehabilitation, and complementary and alternative therapies for CRPS, we found only very low-quality evidence or no evidence at all. As a result, we cannot be certain about their effects on pain and disability in CRPS.

## What are the limitations of the evidence?

All of the included non-Cochrane reviews were conducted in a way that affects the reliability of their findings. The studies included within both the Cochrane and non-Cochrane reviews had several limitations, particularly due to the small number of included participants. The results presented within this overview demonstrate unclear benefits and risks for most treatments for adults with CRPS.

## How up-to-date is this evidence?

This overview updates our previous overview. The evidence is up-to-date to October 2022.

## BACKGROUND

This is the first update of the original Cochrane review published in Issue 4, 2013.

### Description of the condition

Complex regional pain syndrome (CRPS) is a chronic pain condition that usually occurs distally in a limb, in response to trauma or surgery (Birklein 2015; Bruehl 2015). It is characterised by persisting pain that is disproportionate in magnitude or duration to the typical course of pain after similar injury (Bruehl 2010; Marinus 2011). The diagnostic label of CRPS was introduced in the 1990s by the International Association for the Study of Pain (IASP) (Merskey 1994). Iterative revisions to improve specificity have resulted in the current 'Budapest criteria' (Harden 2010), presented in Table 1. CRPS encompasses a variety of previous diagnostic labels including reflex sympathetic dystrophy (RSD), reflex neurovascular dystrophy, Sudeck's atrophy, causalgia and algodystrophy or algoneurodystrophy. CRPS is classified as a chronic primary pain condition in the International Classification of Diseases-11 (ICD-11) (Treede 2019).

The predominant feature of CRPS is severe and persistent pain in the affected limb which is accompanied, at least initially, by clear autonomic and inflammatory changes (Birklein 2017; Bruehl 2015). People with CRPS may present with some or all of the following symptoms and signs: sensory disturbances; temperature change; abnormal patterns of sweating; swelling and oedema; reduced joint range of motion; movement abnormalities such as weakness, tremor or dystonia; trophic changes such as skin atrophy or altered hair and nail growth; localised osteoporotic changes (Bruehl 2010; de Mos 2009; Krämer 2014; Shipton 2009); and alterations in body perception or schema (Lewis 2007; Lotze 2007; Moseley 2006).

CRPS can be classified into two main diagnostic subtypes: type I, in which no peripheral nerve injury can be identified, and type II, in which symptoms are associated with discrete peripheral nerve damage (Bruehl 2015), although this distinction is not always easily made (Ott 2018). In 2021, the IASP CRPS Special Interest Group published a consensus proposal of diagnostic updates to be included in the ICD-11 (Goebel 2021). These updates aim to resolve ambiguities in the IASP CRPS diagnostic criteria and include two important changes to CRPS subtypes: (i) that diagnostic signs of CRPS II must extend beyond any identified damaged nerve territory and, as such, should no longer be classed as a neuropathic pain condition in accordance with current criteria; and (ii) the addition of a third formal CRPS subtype "CRPS with Remission of Some Features" for patients who were previously documented as having fulfilled an IASP diagnosis but who no longer display the signs and symptoms required to meet these criteria.

The underlying pathophysiological mechanisms of CRPS are incompletely understood. Contemporary theories propose complex contributions from multiple systems including aberrant inflammatory and immune responses (Birklein 2014; Goebel 2013; Parkitny 2013), altered sympathetic nervous system function (Knudsen 2019), central sensitisation of nociceptive pathways (Eisenberg 2005), brain changes (Azqueta-Gavaldon 2020; Lee 2022), and genetic factors (Herlyn 2010; Van Rooijen 2012).

The incidence of CRPS has been estimated at between 5.5 and 26.2 cases per 100,000 people annually. It is three to four times more

common in women than in men and its incidence peaks at 50 to 70 years of age (de Mos 2007; Sandroni 2003). CRPS occurs most commonly following wrist fracture and, although rare, appears to occur spontaneously (de Mos 2007; de Mos 2008; Sandroni 2003). Data from higher methodological quality studies demonstrate a 3.7% to 14.0% incidence risk of CRPS within four months of wrist fracture (Rolls 2020). CRPS onset is most accurately predicted by early high pain intensity, irrespective of whether it develops after fracture (Moseley 2014) or after surgery (Bruehl 2022; Savaş 2018). Findings from studies investigating the clinical course of chronic CRPS are inconsistent but indicate that, in people with CRPS lasting 12 months or more, long-term outcomes are poor, with pain and motor dysfunction persisting beyond 12 months for 51% to 89% of patients (Johnson 2022).

CRPS has considerable societal and economic impacts. People with CRPS report that constant pain and functional decline lead to losses of identity, independence and integrity, and negatively affect personal relationships (Raja 2021). Between 30% to 40% of people working before the onset of CRPS do not return to work and, of those who do, between 27% to 35% return under reduced capacities (Johnson 2022). Limited data suggest that CRPS carries a substantial economic burden, with total individual annual healthcare costs increasing 2.17-fold after diagnosis (Elsamadic 2018).

### Description of the interventions

This overview includes systematic reviews of any intervention aimed at treating pain, disability or both in CRPS. In 2019, the European Pain Federation CRPS task force published standards to guide care (Goebel 2019), proposing three key elements for the treatment of CRPS: (i) pain management; (ii) physical and vocational rehabilitation; (iii) identifying and treating stress. A broad and varied range of interventions are used to manage one or all of these key elements in CRPS. These can be broadly grouped under pharmacotherapy (oral, intravenous or topical), interventional procedures, neuromodulation, rehabilitation, complementary and alternative therapies, and psychological therapies.

#### Oral, intravenous and topical pharmacotherapy

A variety of pharmacological interventions have been described for the treatment of CRPS and, in practice, combinations of these drugs are commonly used. Oral and intravenous pharmacological options can be divided into the following broad categories (Harden 2022; Mangnus 2022a):

- Anti-inflammatory therapies (e.g. non-steroidal anti-inflammatory drugs (NSAIDs) corticosteroids, cyclooxygenase-2 (Cox-2) inhibitors)
- Free radical scavengers (e.g. mannitol, vitamin C)
- Immunomodulators (e.g. tumour necrosis factor- $\alpha$  inhibitors, immunoglobulin)
- Anticonvulsants (e.g. pregabalin, gabapentin)
- Antidepressants and anxiolytics (e.g. amitriptyline, doxepin)
- Opioids (e.g. morphine, tramadol)
- N-methyl D-aspartate (NMDA) receptor antagonists (e.g. ketamine, memantine)
- Antihypertensives and  $\alpha$ -adrenergic antagonists (e.g. clonidine, phentolamine)

- Bisphosphonates (e.g. pamidronate, alendronate)
- Calcitonin

Topical analgesics are medications applied to body surfaces such as skin or mucous membranes (Derry 2017a). These treatments are applied to the skin as creams, or made into patches or plasters and stuck to the skin at the site of the affected tissues. Topical analgesics may include lidocaine patches, and creams containing local anaesthetic, capsaicin or dimethyl sulphoxide (DMSO).

### Interventional procedures

Interventional procedures such as intravenous sympathetic nerve blocks involve the infusion of pharmacological agents while the affected limb is tourniqueted and may use a variety of agents, such as guanethidine, lidocaine or clonidine (Harden 2022). Blocking of sympathetic nervous activity may be achieved by injection of anaesthetic directly into sympathetic neural structures such as the stellate ganglion or the lumbar sympathetic chain, or alternatively, into the epidural space (Nelson 2006; Wie 2021). Sympathectomy involves the destruction of sympathetic neural pathways chemically, through the injection of agents such as alcohol or phenol, or surgically, through excision or electrocoagulation (Nelson 2006; Straube 2013).

### Neuromodulation

Neuromodulation includes an array of invasive and non-invasive treatment approaches that aim to provide pain relief through targeted electrical stimulation of the nervous system (Knotkova 2021). Implanted spinal neuromodulation interventions involve the surgical implantation of electrodes into epidural space of the spinal cord or dorsal root ganglion (O'Connell 2021). Non-invasive forms of brain stimulation, such as transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) use electromagnetic coils and electrodes, respectively, to deliver electrical currents that modulate the neuronal excitability of underlying brain structures and associated neural networks (Knotkova 2021).

### Rehabilitation

Both occupational and physiotherapy rehabilitation are frequently used to treat CRPS and these incorporate a variety of approaches, sometimes used in isolation, but more commonly delivered in a multimodal format that may include manual therapy, tactile desensitisation, electrotherapy (including transcutaneous electrical nerve stimulation (TENS)), sensory-motor training (including graded motor imagery and mirror therapy), therapeutic exercise and pain education (Miller 2019).

### Complementary and alternative therapies

Complementary and alternative therapies are a broad set of healthcare practices that are not part of conventional medical care, and may have origins outside of Western practice (WHO 2023). Such approaches include acupuncture, Tai Chi and qigong (Urits 2021).

### Psychological therapies

Psychological therapies include cognitive behavioural therapy (CBT), acceptance and commitment therapy (ACT), counselling and relaxation techniques (Harden 2022; Williams 2020), or exposure-based treatments (Vlaeyen 2012).

## How the intervention might work

There are many possible therapeutic mechanisms for the broad range of potential interventions used to treat pain and disability in CRPS.

Oral, intravenous and topical pharmacotherapies aim to alter physiological pathways involved in the generation of pain, inflammation, peripheral and central sensitisation, abnormal sympathetic activity, motor disturbances or bone loss (Harden 2022; Mangnus 2022a).

Interventional procedures such as nerve blocks or sympathectomy are thought to reduce sympathetic symptoms by temporarily or permanently disrupting sympathetic nervous system output to the affected body area (Birklein 2017; Harden 2022).

Neuromodulation approaches, such as implanted spinal neuromodulation or non-invasive brain stimulation, seek to reduce pain by altering activity in areas of the central nervous system that are involved in the experience of pain (O'Connell 2018; O'Connell 2021).

Rehabilitation approaches typically include exercise regimes as well as passive techniques such as manual therapy, massage and various forms of electrotherapy to improve range of movement (ROM), strength, and functional use of the affected body part. CRPS-specific rehabilitation techniques aim to improve pain and function by altering cortical (brain) processing specific to the affected body part using strategies such as sensory-motor training, and tactile sensory discrimination training (Moseley 2012).

Complementary and alternative therapies are thought to reduce pain via a range of mechanisms. For acupuncture specifically, contemporary theories propose activation of endogenous opioid systems (Harris 2009) and alteration of brain activation patterns associated with pain processing (Scheffold 2015). Practices such as Tai Chi or qigong may exert analgesic effects by improving musculoskeletal health and body awareness, and relaxation (Kong 2016).

Psychological therapies primarily aim to manage pain, distress and disability by addressing the cognitive, behavioural and/or emotional aspects of living with the condition. They may target unhelpful pain-related behaviours and beliefs by improving self-efficacy, self-management skills and psychological flexibility (Williams 2020). Exposure-based treatments, such as 'exposure in vivo', combine psychological theory and rehabilitation to reduce disability specifically by targeting pain-related fear (den Hollander 2022).

## Why it is important to do this overview

There is no consensus regarding the optimal management of CRPS and a broad range of therapeutic interventions including pharmacological, interventional, psychological and rehabilitation treatments may be used clinically (Grieve 2019; Miller 2019). Several systematic reviews of interventions for CRPS have been published since the previous version of this overview (O'Connell 2013). The varied scope and methodology of these reviews may inhibit decision-makers' access to the evidence. Furthermore, information provided in current clinical guidelines from the Netherlands (Perez 2014), the UK (Goebel 2018), and US (Harden 2022) reflects both the evidence as well as pragmatic considerations such as country-

specific policies, access and healthcare pathways, and possibly the interests of key stakeholders. An updated single, accessible and rigorous summary of the evidence is required to support decision-making for patients, clinicians, and policymakers. This Cochrane overview aims to provide an updated critical summary of the systematic review evidence of all treatments for CRPS.

## OBJECTIVES

To summarise the evidence from Cochrane and non-Cochrane systematic reviews of the efficacy, effectiveness, and safety of any intervention used to reduce pain, disability, or both, in adults with complex regional pain syndrome.

## METHODS

### Criteria for considering reviews for inclusion

#### Types of reviews

We included all Cochrane reviews of randomised controlled trials (RCTs) that assessed the effects of any intervention used to reduce pain or disability in adults with CRPS. We also chose to consider non-Cochrane reviews as, given the broad range of available treatments, to exclude them might have provided an incomplete summary of the available evidence. We therefore included non-Cochrane systematic reviews where they covered interventions that were not covered by identified Cochrane reviews or where they were more up-to-date. To be included, any non-Cochrane review was required to achieve a judgement of 'Yes' on the third criterion on the AMSTAR tool for assessing the quality of systematic reviews (Shea 2007), that is, "Was a comprehensive literature search performed?". We considered this a minimum requirement for a review to be systematic.

#### Types of participants

Participants were adults, 18 years or older, diagnosed with CRPS or an alternative descriptor for this condition (e.g. reflex sympathetic dystrophy, causalgia). We also included studies with participants with post-stroke shoulder-hand syndrome, which is considered a form of CRPS and is distinct from mechanical post-stroke shoulder pain. The use of formal diagnostic criteria for CRPS is inconsistent within the literature (Reinders 2002). Therefore, to avoid excluding reviews which contained relevant studies, we included reviews that did not use formally derived diagnostic criteria for CRPS. We included reviews of interventions for 'neuropathic pain' where studies specific to CRPS were presented and analysed separately, or in a subgroup analysis that was extractable. We did not consider comparisons that included participants with diagnoses other than CRPS.

#### Types of interventions

We included reviews of any intervention aimed at reducing pain, disability, or both, for CRPS.

#### Types of outcome measures

##### Primary outcomes

1. Pain intensity or severity, as measured using a visual analogue scale (VAS), numerical rating scale (NRS) or Likert scale.
2. Disability, measured through self-report scales or functional testing protocols.

3. Adverse events, including the number and nature of adverse event withdrawals and serious adverse events, where possible.

Pain intensity and disability outcomes could be presented and analysed as change on a continuous scale or in a dichotomised format as the proportion of patients in each group who achieved a predetermined threshold of improvement (for example, minimal clinically important difference (MCID), or recovery).

##### Secondary outcomes

1. Quality of life, measured using any validated tool.
2. Emotional well-being, measured using any validated tool.
3. Participant ratings of improvement or satisfaction with treatment, measured using any validated tool.

We grouped outcomes into post-intervention (up to 1 month post-treatment), short-term (> 1 month to 3 months post-treatment), medium-term (> 3 months to 6 months post-treatment) and long-term periods (> 6 months post-treatment). Where reviews reported outcome data for multiple time points within a period, we included a single effect per time period, taking the effect measured closest to the beginning of the period for post-intervention, and closest to the end of the period for all other time periods.

### Search methods for identification of reviews

#### Electronic searches

We searched electronic databases using a combination of controlled vocabulary (MeSH) and free-text terms. We incorporated search terms to target CRPS and systematic reviews but, because we wished to identify reviews that included any intervention, we did not include intervention-specific terms. We incorporated the [BMJ Clinical Evidence](#) search filter for systematic reviews. In the updated version of this overview, we searched Epistemonikos instead of the defunct DARE. For the previous and current versions, we searched the following databases:

- Ovid MEDLINE (1948 to 7 October 2022) ([Appendix 1](#));
- Ovid Embase (1980 to 7 October 2022) ([Appendix 2](#));
- Cochrane Database of Systematic Reviews Issue 10 of 12, October 2022 ([Appendix 3](#));
- Database of Abstracts of Reviews of Effects (DARE) (Issue 4 2011) ([Appendix 3](#));
- CINAHL (1982 October 2022) ([Appendix 4](#));
- PEDro (1929 to October 2022) ([Appendix 5](#));
- LILACS (All years to October 2022) ([Appendix 6](#));
- Epistemonikos (October 2011 to 10 October 2022) ([Appendix 7](#)).

The search results by source are presented for the previous and current versions of this overview in [Appendix 8](#).

#### Searching other sources

We handsearched the reference lists of all eligible reviews and relevant clinical guidelines to attempt to identify additional relevant reviews.

#### Language

The search attempted to identify and include all relevant studies, irrespective of language.

## Data collection and analysis

### Selection of reviews

Two overview authors (NOC and BW in the original overview; and MCF and AGC, KMS, CB or NOC in this updated overview) independently screened the titles and abstracts of identified studies and excluded studies that were clearly not relevant. Where it was not clear from the abstract whether a study was relevant, we checked the full review to confirm its eligibility. Two overview authors (NOC and BW in the original overview; and MCF and AGC, KMS, CB or NOC in this updated overview) independently applied the selection criteria to the full papers of identified reviews. Disagreement between overview authors was resolved through discussion. Where resolution was not achieved, a third overview author (JHM) considered the study(ies) in question.

### Data extraction and management

A pilot data extraction form was designed and piloted by three authors (MCF, AGC and NOC). Two overview authors (MCF and AGC, KMS, CB or NOC) independently extracted data using the finalised data extraction form. We resolved discrepancies by consensus. Where agreement could not be reached, a third overview author (JHM) considered the paper and we made a majority decision. The data extraction form included the following information:

- objectives of the review
- date of publication
- date of most recent search
- resources searched
- characteristics of the included participants (e.g. CRPS diagnostic criteria & subtypes)
- included interventions and comparators
- outcomes and time points assessed (primary and secondary)
- comparisons performed and meta-analysis details
- assessment of the risk of bias or methodological quality of the included evidence
- assessment of the certainty of included evidence

When data were presented in tabular or figure format, we extracted data from the included reviews. We planned to contact the authors of the reviews or the original study reports via email if the required information could not be extracted from the reports.

### Assessment of methodological quality of included reviews

Two authors (MCF and AGC, KMS, CB or NOC) used the Assessing the Methodological Quality of Systematic Reviews (AMSTAR 2; second version of the original AMSTAR) tool (to judge the methodological quality of the included reviews (Shea 2017) (see Appendix 9). We applied this to both Cochrane and non-Cochrane reviews. For this review, we assessed all 16 AMSTAR 2 domains, but considered the following seven domains 'critical':

- protocol registered before the commencement of the review (item 2)
- adequacy of the literature search (item 4)
- justification for excluding individual studies (item 7)
- risk of bias from individual studies being included in the review (item 9)
- appropriateness of meta-analytical methods (item 11)

- consideration of risk of bias when interpreting the results of the review (item 13)
- assessment of the presence and likely impact of publication bias (item 15)

To rate the overall confidence in the results of a review, we considered the potential impact of an inadequate rating detected in critical and non-critical items using the following criteria (Shea 2017):

- High (no or one non-critical weakness): high confidence means that the systematic review provides an adequate and comprehensive summary of the results of the available studies that address the question of interest.
- Moderate (more than one non-critical weakness): moderate confidence means that the review has more than one weakness but no critical flaws, and may provide an accurate summary of the results of the available studies that were included in the review.
- Low (one critical flaw with or without non-critical weaknesses): low confidence means that the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest.
- Critically low (more than one critical flaw with or without non-critical weaknesses): critically low confidence means that the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

We planned to downgrade the overall rating from moderate to low confidence where multiple non-critical weaknesses diminished confidence in the review.

### Assessment of the risk of bias and certainty of the evidence in included reviews

Included reviews assessed the methodological quality and risk of bias of included studies in several ways. We used the judgements made by the authors of the original reviews regarding the risk of bias and methodological quality of evidence and have reported it critically within the context of our assessment of the quality of the review itself. When reviews did not use GRADE (Schünemann 2020) to assess the certainty in the evidence, two reviewers (MCF and NOC) conducted these assessments for each type of intervention, each diagnostic group (CRPS I and II), and each outcome domain. For narratively reported comparisons, we only conducted GRADE assessments for those that reported no between-group differences, or between-group differences with an effect size and measure of precision, or a statement regarding statistical significance.

We used the following to assign GRADE judgements:

- Serious study limitations: we downgraded once if less than 75% of studies were at low risk of bias across all risk of bias criteria.
- Inconsistency: we downgraded once if point estimates varied widely across studies, confidence intervals showed minimal or no overlap, statistical tests for heterogeneity were statistically significant, or the  $I^2$  statistic was greater than 50%.
- Indirectness: we downgraded once if greater than 50% of participants were outside the target group.

- Imprecision: we downgraded once if there were fewer than 400 participants for continuous outcomes and fewer than 300 events for dichotomous data.
- Publication bias: we downgraded once where there was direct evidence of publication bias or if estimates of effect based on small scale, industry-sponsored studies raised suspicion of publication bias.

When the Cochrane Risk of Bias (ROB) tool was used to assess serious study limitations, we considered trials with a single domain at high risk of bias as being at high overall risk of bias. When other methodological quality tools were used, we followed their scoring system to evaluate overall quality. When no tool was used to evaluate risk of bias or methodological quality, we downgraded the certainty of evidence since, in our judgement, an absence of information regarding bias or quality represents a clear source of uncertainty.

We considered single trials to be inconsistent and imprecise, unless more than 400 participants were randomised for continuous outcomes or more than 300 for dichotomous outcomes. For imprecision, we retained one of the additional criteria used in the previous version of the overview (O'Connell 2013), by downgrading twice if the pooled sample size was < 50 participants per arm. Where conclusions were not made from a pooled analysis, the same rule was applied to the sample of the individual studies. We applied this criterion whether or not a positive result was reported for that intervention because, although small studies tend to produce positive results through publication biases, they may also return spurious negative results as a result of the play of chance (Moore 2010; Nüesch 2010).

We applied the following definitions regarding the certainty of the evidence (Balshem 2011):

- high: we are very confident that the true effect lies close to that of the estimate of the effect.
- moderate: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different.
- low: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
- very low: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

We decreased the certainty of evidence rating by one (-1), two (-2), or three (-3) levels, up to a maximum of -3, (or very low) for any criteria, based on the level of concern it raised. Where we found 'very serious' limitations for a given domain, we downgraded the certainty of evidence by two levels.

### Data synthesis

The precise comparisons presented were primarily determined by the content of the included reviews. For reviews that included a broad range of heterogeneous interventions, we grouped these pragmatically under pharmacotherapy, interventional procedures, neuromodulation, rehabilitation, and complementary and alternative therapy sections. Where data were provided by reviews in sufficient detail, we reported comparisons according to the Population, Intervention, Comparator, Outcome and Time

(PICOT), clearly stating where results applied to CRPS I, II or a mixed group. We reported a single measure of pain intensity where multiple measures were provided, prioritising pain at rest over pain with movement. Where measures of pain intensity were provided for multiple areas of the affected limb, we prioritised those closest to the extremity.

Where we deemed statistical pooling of interventions to be inappropriate in included reviews (e.g. by combining placebo controls with active controls), we reported the included interventions narratively. We did not calculate effect sizes where the necessary data were not reported in the review as this would have required the strong assumptions of equal numbers allocated to each group, zero attrition in each study and no protocol violations.

We planned to consider "responder" analyses based upon a 30% or greater reduction in pain to represent a moderately important benefit, and a 50% or greater reduction in pain intensity to represent a substantially important benefit, as suggested by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) guidelines (Dworkin 2008), for dichotomised outcomes (responder analyses). The IMMPACT thresholds are based on estimates of the degree of within-person change from baseline that participants might consider clinically important. There is little consensus or evidence regarding what the threshold should be for a clinically important difference in pain intensity based on the between-group difference post-intervention. The OMERACT 12 group have reported recommendations for a minimally important difference for pain outcomes (Busse 2015). They recommend a threshold of 10 mm on a 0 mm to 100 mm VAS as the threshold for minimal importance for average between-group change, though stress that this should be interpreted with caution as it remains possible that estimates which fall closely below this point may still reflect a treatment that benefits an appreciable number of patients. We planned to use this threshold but interpret it appropriately and cautiously.

### Overlap between reviews

To visually assess the overlap of primary studies across included reviews, we created a citation matrix using guidance from Pieper 2014. We followed recommendations in the Cochrane Handbook (Pollock 2022) to prioritise information from the "most comprehensive" reviews. First, we prioritised information from Cochrane reviews over non-Cochrane reviews. For non-Cochrane reviews, where reviews considered all interventions for CRPS, each review was compared to the most recent in order to establish whether the older review identified any RCTs that had not already been identified, or data which were not adequately reported in the most recent review. Where this was not the case, the older review was excluded. Similarly, where more than one review investigated the same intervention, or class of interventions, the equivalent process was followed. We only considered data from original studies presented in more than one included review once in any analysis.

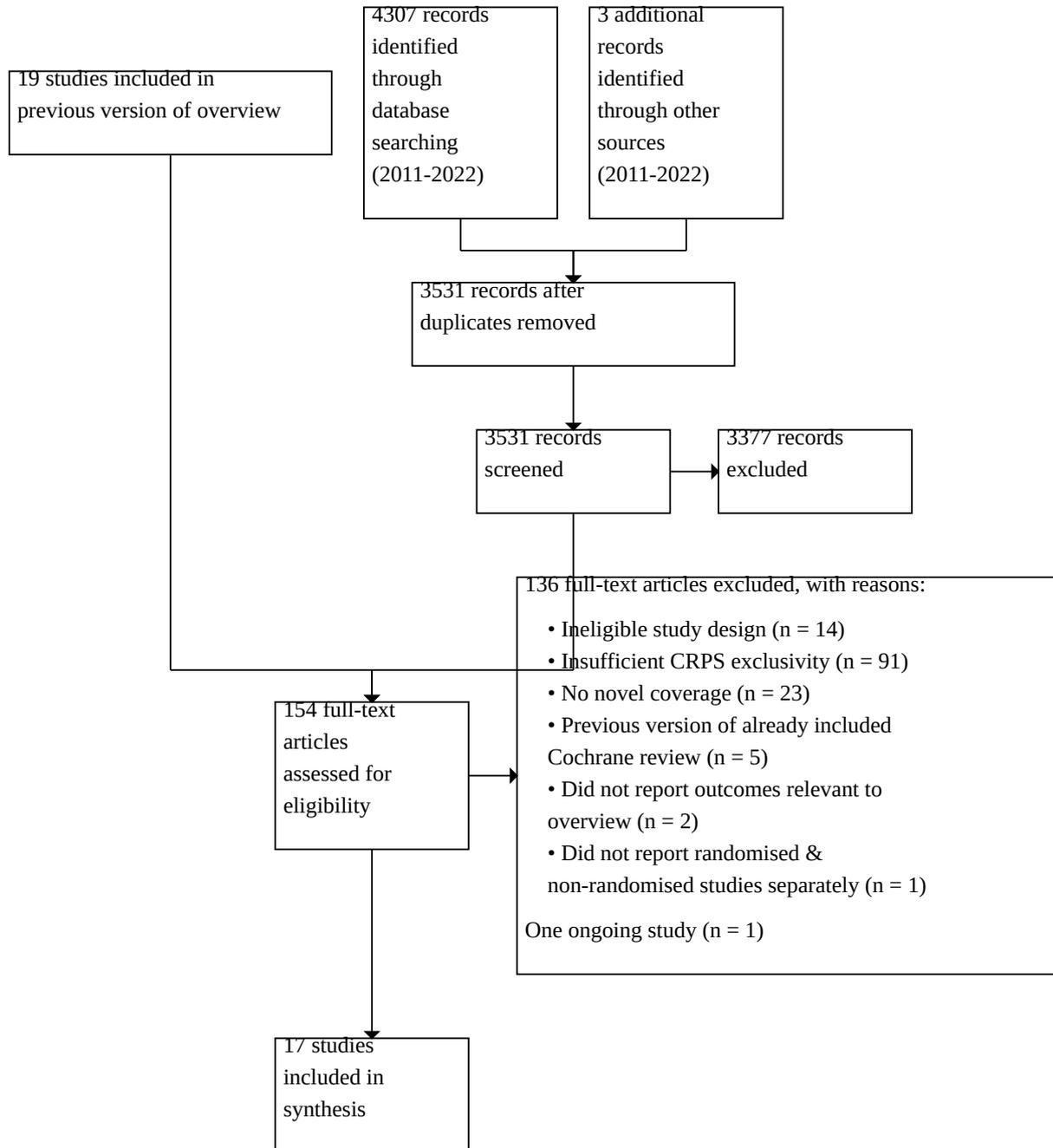
## RESULTS

See Figure 1 for a flow diagram of the search process. Our updated database search extended from October 2011 to October 2022. We identified 4307 records from the database searches and three additional records through citation alerts. After de-duplication (n

= 779) we screened the titles and abstracts of 3531 records, from which we screened full-text articles of 154 reviews for eligibility, together with 19 included reviews from the previous version of this

overview. Of these, 136 were excluded (see Table 2 for the reasons for exclusion) and one review was ongoing, leaving 17 included reviews.

**Figure 1. Study flow diagram**



## Description of included reviews

A list of the reviews and original studies which have contributed to this overview is presented in [Table 3](#) and a detailed description of the characteristics of the included reviews is presented in [Table 4](#).

We included 17 systematic reviews, including five Cochrane ([Challapalli 2005](#); [Moore 2014](#); [O'Connell 2016](#); [Straube 2013](#); [Smart 2022](#)) and 12 non-Cochrane systematic reviews ([Chauvineau 2005](#); [Chevreau 2017](#); [Cossins 2013](#); [Duong 2018](#); [Fassio 2022](#); [Fischer 2010](#); [Forouzanfar 2002](#); [Orhurhu 2019](#); [Peng 2018](#); [Smith 2005](#); [Tran 2010](#); [Xu 2016](#)). The median (range) year of review publication was 2014 (2002 to 2022). All included Cochrane reviews and only two of the non-Cochrane reviews ([Fassio 2022](#); [Orhurhu 2019](#)) established the review methods prior to conducting the review.

The five Cochrane reviews and seven of the 12 non-Cochrane reviews ([Chevreau 2017](#); [Cossins 2013](#); [Fassio 2022](#); [Fischer 2010](#); [Forouzanfar 2002](#); [Orhurhu 2019](#); [Peng 2018](#)) specified review outcomes of interest. All 12 reviews specified pain intensity as an outcome measure, two reviews ([Smart 2022](#); [Peng 2018](#)) specified disability or function as an outcome, eight reviews ([Challapalli 2005](#); [Chevreau 2017](#); [Fassio 2022](#); [Moore 2014](#); [O'Connell 2016](#); [Orhurhu 2019](#); [Smart 2022](#); [Straube 2013](#)) specified adverse events as an outcome, two reviews ([Smart 2022](#); [Chevreau 2017](#)) specified quality of life as an outcome and four reviews ([Fischer 2010](#); [Moore 2014](#); [Smart 2022](#); [Straube 2013](#)) specified a patient-reported rating of improvement or satisfaction with treatment as an outcome. Four reviews ([O'Connell 2016](#); [Smart 2022](#); [Chevreau 2017](#); [Orhurhu 2019](#)) specified their follow-up time points of interest.

## CRPS specificity of included reviews

Two Cochrane reviews ([O'Connell 2016](#); [Smart 2022](#)) included participants with CRPS only. The remaining three Cochrane reviews included a mix of neuropathic pain populations but included studies that were specific to CRPS I and CRPS II populations (or their alternative diagnostic labels). Of the non-Cochrane reviews, six were specific to CRPS I/RSD populations ([Chauvineau 2005](#); [Chevreau 2017](#); [Fassio 2022](#); [Fischer 2010](#); [Forouzanfar 2002](#); [Smith 2005](#)), four included both CRPS I/RSD and CRPS II/causalgia ([Cossins 2013](#); [Duong 2018](#); [Tran 2010](#); [Xu 2016](#)), one was specific to post-stroke shoulder-hand syndrome ([Peng 2018](#)), and one included mixed chronic pain conditions with CRPS reported separately ([Orhurhu 2019](#)). No included reviews were specific to CRPS II. Only trials specific to CRPS or its alternative diagnostic labels were included in this overview. Two of the seventeen included reviews restricted the minimum duration of CRPS to three months ([Moore 2014](#); [Orhurhu 2019](#)).

## Interventions evaluated in included reviews

Of the five Cochrane reviews, one review ([Moore 2014](#)) evaluated a specific pharmacological intervention (gabapentin); one review ([Smart 2022](#)) evaluated a broad range of rehabilitation interventions; and three reviews evaluated specific interventional techniques using a range of agents: systemic administration of local anaesthetic agents ([Challapalli 2005](#)), local anaesthetic sympathetic blockade ([O'Connell 2016](#)), and cervico-thoracic or lumbar sympathectomy ([Straube 2013](#)). Of the non-Cochrane reviews, four reviews evaluated distinct pharmacological classes or medicines: anti-inflammatory treatments ([Fischer 2010](#)); bisphosphonates ([Chauvineau 2005](#); [Chevreau 2017](#)) and ketamine ([Orhurhu 2019](#)). One review ([Fassio 2022](#)) evaluated

all pharmacological treatments, and one review ([Xu 2016](#)) evaluated all intravenous therapies. One review ([Peng 2018](#)) evaluated traditional manual acupuncture and one review ([Smith 2005](#)) evaluated a range of rehabilitation interventions including acupuncture. Four reviews ([Cossins 2013](#); [Duong 2018](#); [Forouzanfar 2002](#); [Tran 2010](#)) evaluated a broad range of pharmacological, interventional, neuromodulation, rehabilitation and complementary and alternative treatments.

## Comparisons

The five Cochrane reviews specified placebo (or sham) or other active treatments as comparators of interest, with three reviews ([Moore 2014](#); [O'Connell 2016](#); [Smart 2022](#)) also specifying no treatment as a comparator of interest. Eight of 12 non-Cochrane reviews ([Chauvineau 2005](#); [Cossins 2013](#); [Duong 2018](#); [Fischer 2010](#); [Forouzanfar 2002](#); [Smith 2005](#); [Tran 2010](#); [Xu 2016](#)) failed to specify a comparator of interest. Only two reviews ([O'Connell 2016](#); [Smart 2022](#)) specified a threshold for the between-group minimal clinically important difference.

## Risk of bias and methodological quality of included evidence

Fourteen reviews ([Challapalli 2005](#); [Chauvineau 2005](#); [Chevreau 2017](#); [Cossins 2013](#); [Duong 2018](#); [Fassio 2022](#); [Fischer 2010](#); [Forouzanfar 2002](#); [Moore 2014](#); [O'Connell 2016](#); [Orhurhu 2019](#); [Peng 2018](#); [Smart 2022](#); [Straube 2013](#)) used a formal tool to assess the risk of bias or methodological quality of the included evidence. Seven reviews ([Duong 2018](#); [Fassio 2022](#); [Moore 2014](#); [O'Connell 2016](#); [Orhurhu 2019](#); [Peng 2018](#); [Smart 2022](#)) used the Cochrane Risk of Bias tool ([Higgins 2011](#)) in its standard form or with modifications, three reviews ([Challapalli 2005](#); [Chevreau 2017](#); [Straube 2013](#)) used the Oxford Quality Score/Jadad scale ([Jadad 1996](#)), two reviews ([Cossins 2013](#); [Forouzanfar 2002](#)) used a 15-item methodological quality checklist ([de Vet 1997](#)), one review ([Fischer 2010](#)) used the 'Delphi list' ([Verhagen 1998](#)) and one review ([Chauvineau 2005](#)) used 'Aguilar's method' ([Cucherat 1997](#)). Three reviews ([Smith 2005](#); [Tran 2010](#); [Xu 2016](#)) failed to use any tool to assess the risk of bias or methodological quality of the included evidence.

## Certainty of included evidence

Five reviews ([Moore 2014](#); [O'Connell 2016](#); [Orhurhu 2019](#); [Smart 2022](#); [Straube 2013](#)) used GRADE to judge the overall certainty of evidence. One review ([Xu 2016](#)) determined levels of evidence for clinical guidelines using recommendations from [Guyatt 2006](#) and [Van Kleef 2009](#), and one review ([Cossins 2013](#)) determined the level of evidence using methods from [Van Tulder 1997](#).

## Methodological quality of included reviews

AMSTAR 2 ratings for the included reviews are summarised in [Table 5](#). Four Cochrane reviews ([Moore 2014](#); [O'Connell 2016](#); [Smart 2022](#); [Straube 2013](#)) were judged as high quality. One Cochrane review ([Challapalli 2005](#)) was judged as low quality because it did not account for risk of bias in primary studies when interpreting the results of the review, and because of several other non-critical weaknesses. Two non-Cochrane reviews were judged as low quality, either because it was not stated that review methods were established prior to conducting the review ([Cossins 2013](#)) or because review authors did not provide a list of excluded studies and justify the exclusions ([Orhurhu 2019](#)), in addition to other non-critical weaknesses. The remaining non-Cochrane reviews ([Chauvineau 2005](#); [Chevreau 2017](#); [Duong 2018](#); [Fassio](#)

2022; Fischer 2010; Forouzanfar 2002; Peng 2018; Smith 2005; Tran 2010; Xu 2016) were all judged as having critically low quality, due to multiple critical and non-critical weaknesses.

## Effect of interventions

A summary of effects for pain, disability and adverse event outcomes for all interventions is provided in Table 6, Table 7, Table 8, Table 9 and Table 10.

The outcomes reported below are only those for which data were available in included reviews. Where comparisons did not provide a time point for outcome measurement, we reported them as post-intervention. All included trials had a two-arm parallel-group design unless specified otherwise.

## Oral, intravenous and topical pharmacotherapy

### Anticonvulsants

#### Gabapentin

One Cochrane review, judged as high quality (Moore 2014) specifically investigated the effects of gabapentin in CRPS.

#### Oral gabapentin versus placebo

Moore 2014 included a single cross-over trial for this comparison (Van de Vusse 2004, n = 58, CRPS I ['IASP criteria']), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Moore 2014 reported no observed differences in the proportion of participants experiencing 'very much improved' Global Perceived Effect pain scores post-intervention (risk ratio (RR) 4.00, 95% CI 0.90 to 17.83, P = 0.07). We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and once for imprecision.

**Adverse events:** Moore 2014 reported increased incidence of participants experiencing at least one adverse event (RR 1.64, 95% CI 1.15 to 2.32), somnolence (RR 4.72, 95% CI 1.45 to 15.35) and dizziness (RR 9.44, 95% CI 2.32 to 38.39) in the gabapentin group, but there were no observed differences for peripheral oedema (RR 0.31, 95% CI 0.03 to 2.93) or ataxia (RR 9.0, 95% CI 0.5 to 162.53). We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

### Anti-inflammatory therapies

#### Corticosteroids

Two non-Cochrane reviews, judged as critically low quality (Duong 2018; Fischer 2010), included evidence on the effects of corticosteroids in CRPS.

#### Oral prednisolone versus oral piroxicam

Fischer 2010 included a single trial for this comparison (Kalita 2006, n = 60, post-stroke CRPS [diagnostic criteria not reported (NR)]), which they rated as high quality using the Delphi list.

**Disability:** Fischer 2010 reported no significant between-group differences post-intervention (Barthel Index, mean (standard deviation (SD)) prednisolone 1.97 (4.43), piroxicam 2.57; (5.56)). We judged the certainty in evidence as very low, downgraded once for inconsistency and twice for imprecision.

#### Continued oral prednisolone versus withdrawal of oral prednisolone

Duong 2018 included a single trial (enriched enrolment randomised withdrawal trial) for this comparison (Kalita 2016, n = 58, post-stroke CRPS [criteria NR]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Duong 2018 reported a between-group difference (visual analogue scale (VAS) mean (SD) 2.4 (1.0) vs 4.9 (2.1); P < 0.01) post-intervention in favour of continued oral prednisolone. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and twice for imprecision.

**Disability:** Duong 2018 reported no significant between-group differences in Barthel Index or Modified Rankin Scale scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and twice for imprecision.

#### Oral prednisone versus placebo

Fischer 2010 included a single trial for this comparison (Lukovic 2006, n = 60, CRPS I [criteria NR]), which they rated as poor quality using the Delphi list.

**Pain intensity:** Fischer 2010 reported no significant between-group differences post-intervention (VAS, mean (SD), prednisone 6.0 (0.4), placebo 5.9 (0.7)). We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and twice for imprecision.

#### Non-steroidal anti-inflammatory drugs (NSAIDs)

One non-Cochrane review, judged as critically low quality (Duong 2018) included evidence on the effects of NSAIDs in CRPS.

#### Intravenous parecoxib versus placebo

Duong 2018 included a single trial for this comparison (Breuer 2014, n = 20 upper limb CRPS [Harden 2007]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Duong 2018 reported no between-group differences post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

#### Free radical scavengers

##### Dimethyl sulfoxide (DMSO)

One non-Cochrane review, judged as critically low quality (Fischer 2010), included evidence on the effects of DMSO in CRPS.

#### Topical DMSO versus placebo

Fischer 2010 included two trials for this comparison (Goris 1987, n = 20, RSD [criteria NR], cross-over); Zuurmond 1996, n = 30, RSD [criteria NR]), which they rated as poor and high quality respectively, using the Delphi list.

**Pain intensity:** Fischer 2010 reported a significant between-group difference (VAS, median (range) DMSO 2.9 (-2.8 to 7.0), placebo 1.0 (-3.9 to 9.0)) post-intervention in favour of the DMSO group

for [Zuurmond 1996](#). We judged the certainty in evidence as very low, downgraded once for inconsistency and twice for imprecision.

**Participant ratings of improvement:** [Fischer 2010](#) reported improved patient-reported subjective clinical well-being in favour of the DMSO group post-intervention for [Goris 1987](#), but did not report between-group differences (GRADE assessment not possible).

#### Topical DMSO versus oral N-acetylcysteine

[Fischer 2010](#) included a single trial for this comparison ([Perez 2003](#), n = 146, CRPS I [criteria NR]), which they rated as high quality using the Delphi list.

**Pain intensity:** [Fischer 2010](#) reported no significant between-group differences post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as low, downgraded once for inconsistency and once for imprecision.

#### Mannitol

One non-Cochrane review, judged as critically low quality ([Fischer 2010](#)), included evidence on the effects of mannitol in CRPS.

#### Intravenous mannitol versus placebo

[Fischer 2010](#) included a single trial for this comparison ([Perez 2008](#), n = 41, CRPS I [criteria NR]), which they rated as high quality using the Delphi list.

**Pain intensity:** [Fischer 2010](#) reported no significant difference between groups (0 to 100 VAS, mean (SD), mannitol 53.1 (25.3), placebo 48 (31.8)) post-intervention. We judged the certainty in evidence as very low, downgraded once for inconsistency and twice for imprecision.

**Quality of life:** [Fischer 2010](#) reported no significant between-group differences in physical functioning (median (IQR) mannitol: 10.0 (-5.0 to 20), placebo: -5.0 (-10.0 to 15.0)) or social functioning (mannitol: 0.0 (-12.5 to 12.5), placebo: 0.0 (-25.0 to 12.5)) quality of life scores post-intervention. We judged the certainty in evidence as very low, downgraded once for inconsistency and twice for imprecision.

#### Bisphosphonates

Two non-Cochrane reviews, judged as critically low quality ([Chauvineau 2005](#); [Chevreau 2017](#)) specifically investigated the effects of bisphosphonates in CRPS, and another two non-Cochrane reviews, also judged as critically low quality ([Duong 2018](#); [Fassio 2022](#)) included evidence on the effects of bisphosphonates in CRPS. The following evidence was preferentially reported from [Chevreau 2017](#) after we identified what we judged to be inappropriate pooling of placebo- and active-controlled trials in the meta-analysis performed by [Fassio 2022](#).

#### Bisphosphonates versus placebo

[Chevreau 2017](#) included four trials for this comparison, testing oral alendronate ([Manicourt 2004](#), n = 40, lower limb CRPS I), intravenous pamidronate ([Robinson 2004](#), n = 27, upper and lower limb CRPS I), intravenous clodronate ([Varennna 2000](#), n = 32, upper and lower limb CRPS I), and intravenous neridronate ([Varennna 2013](#), n = 82, upper and lower limb CRPS I). The CRPS diagnostic

criteria were not reported for any of these trials. Using the Jadad scale, [Manicourt 2004](#), [Varennna 2000](#) and [Varennna 2013](#) were scored 5/5 and [Robinson 2004](#) was scored 3/5. [Fassio 2022](#) included an additional trial testing intramuscular neridronate ([Varennna 2021](#), n = 78, CRPS I [criteria NR]), which they rated at low overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Chevreau 2017](#) reported a between-group difference (standardised mean difference (SMD), -2.6, 95% confidence interval (CI) -1.8 to -3.4; P = 0.001; I<sup>2</sup> = 81%, 4 trials, n = 181) post-intervention in favour of bisphosphonates. [Fassio 2022](#) reported a clinically important between-group difference (0 to 100 VAS, mean difference (MD) -21.80; 95% CI -30.28 to -13.32) in favour of neridronate post-intervention. We judged the certainty in evidence as low, downgraded once for inconsistency and once for imprecision.

**Quality of life:** [Chevreau 2017](#) reported a between-group difference in SF-36 physical functioning scores in favour of bisphosphonates post-intervention for [Robinson 2004](#) but did not provide point estimates or measures of precision (GRADE assessment not possible).

**Adverse events:** [Chevreau 2017](#) reported a higher proportion of participants experiencing at least one adverse event in the bisphosphonate group (RR 2.10, 95% CI 1.27 to 3.47; number needed to treat for an additional harmful outcome (NNTH) 4.6, 95% CI 2.4 to 168.0; 4 trials, n = 181). [Fassio 2022](#) reported 26 adverse events in the neridronate group compared with 17 in the placebo group for [Varennna 2021](#) but did not provide point estimates or measures of precision (not included in GRADE assessment). We judged the certainty in evidence as moderate, downgraded once for imprecision.

#### Intranasal pamidronate versus intranasal calcitonin

[Chauvineau 2005](#) included a single trial for this comparison ([Cohen 1998](#), n = 14, upper limb algodystrophy [criteria NR]), which they rated moderate quality using 'Aguilar's method'.

**Pain intensity:** [Chauvineau 2005](#) reported no significant between-group differences in VAS scores at post-intervention, short-term and medium-term follow-up, but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

#### Intravenous pamidronate versus oral prednisolone

[Duong 2018](#) included a single trial for this comparison ([Eun Young 2016](#), n = 21, upper limb post-stroke CRPS [criteria NR]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Duong 2018](#) reported a between-group difference in VAS pain scores post-intervention in favour of pamidronate but did not provide point estimates or measures of precision (GRADE assessment not possible).

#### Calcitonin

One non-Cochrane review, judged as critically low quality ([Tran 2010](#)) included evidence on the effects of calcitonin in CRPS.

### Intranasal calcitonin versus placebo

[Tran 2010](#) included a single trial for this comparison ([Bickerstaff 1991](#), n = 38 upper limb CRPS [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** [Tran 2010](#) reported no between-group differences post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

### Calcitonin plus physiotherapy versus physiotherapy alone

[Tran 2010](#) included two trials for this comparison, testing subcutaneous calcitonin ([Gobelet 1986](#), n = 24 upper and lower limb CRPS [criteria NR]) and intranasal calcitonin ([Gobelet 1992](#), n = 66, upper and lower limbs CRPS [criteria NR]). No assessments of risk of bias or methodological quality were conducted.

**Pain intensity:** [Tran 2010](#) reported no between-group differences post-intervention for [Gobelet 1986](#) but did not provide point estimates or measures of precision. There was a significant between-group difference post-intervention (four-point pain scale, mean (SD) 0.45 (0.68) vs 0.69 (0.93)) in favour of calcitonin plus physiotherapy reported for [Gobelet 1992](#). We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

### Intranasal calcitonin versus oral paracetamol

[Tran 2010](#) included a single trial for this comparison ([Sahin 2006](#), n = 35, upper limb CRPS [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** [Tran 2010](#) reported no between-group differences post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

## Immunomodulators

### Immunoglobulin

One non-Cochrane review, judged as critically low quality ([Duong 2018](#)) included evidence on the effects of immunoglobulin in CRPS.

### Intravenous immunoglobulin versus placebo

[Duong 2018](#) included a single cross-over trial for this comparison ([Goebel 2010](#), n = 12, CRPS [[Harden 2007](#)]), which they rated at low overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Duong 2018](#) reported lower pain scores during treatment with intravenous immunoglobulin but did not provide between-group differences (GRADE assessment not possible).

**Participant ratings of improvement:** [Duong 2018](#) reported increased patient-reported improvement during treatment with intravenous immunoglobulin but did not provide between-group differences (GRADE assessment not possible).

### Infliximab

One non-Cochrane review, judged as critically low quality ([Xu 2016](#)) included evidence on the effects of the monoclonal antibody infliximab in CRPS.

### Intravenous infliximab versus placebo

[Xu 2016](#) included a single trial for this comparison ([Dirckx 2013](#), n = 13, CRPS I [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** [Xu 2016](#) reported no between-group differences post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Quality of life:** [Xu 2016](#) reported a significant between-group difference in EuroQol scores post-intervention in favour of intravenous infliximab, but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

### Lenalidomide

One non-Cochrane review, judged as critically low quality ([Duong 2018](#)) included evidence on effects of the thalidomide derivative and TNF- $\alpha$  antagonist lenalidomide in CRPS.

### Oral lenalidomide versus placebo

[Duong 2018](#) included a single trial for this comparison ([Manning 2014](#), n = 147, CRPS [[Harden 2007](#)]), which they rated at unclear overall risk of bias using the Cochrane ROB.

**Pain intensity:** [Duong 2018](#) reported no between-group differences in pain scores (proportion of participants with  $\geq 30\%$  improvement in pain from baseline) post-intervention, but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and once for imprecision.

**Disability:** [Duong 2018](#) reported no between-group differences in 'activity rating' post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and once for imprecision.

## NMDA receptor antagonists

### Ketamine

One non-Cochrane review, judged as low quality ([Orhurhu 2019](#)) specifically investigated the effects of ketamine infusions for CRPS.

### Intravenous ketamine versus placebo

[Orhurhu 2019](#) included two trials for this comparison ([Schwartzman 2009](#), n = 60, CRPS I & II [[Bruehl 1999](#)]; [Sigtermans 2009](#), n = 19, CRPS I [[Bruehl 1999](#)/[Merskey 1994](#)]), which they rated at unclear and high overall risk of bias respectively using the Cochrane ROB tool.

**Pain intensity:** [Orhurhu 2019](#) reported a clinically important between-group difference post-intervention in favour of ketamine (weighted mean difference (WMD), 0-10 NRS, -2.38, 95% CI -3.53 to -1.23;  $I^2 = 34.9\%$ ;  $\text{Tau}^2 = 0.34$ ; 2 trials, n = 79) but no between-group difference at medium-term (WMD -0.55, 95% CI -1.50 to 0.39;  $I^2 = 0\%$ ; 2 trials, n = 79). We judged the certainty in evidence as very low, downgraded once for serious study limitations and twice for imprecision.

## Magnesium

One non-Cochrane review, judged as very low quality (Duong 2018) included evidence on the effects of magnesium for CRPS.

### Intravenous and intramuscular magnesium versus placebo

Duong 2018 included two trials for this comparison (Fischer 2013, n = 56, CRPS [criteria NR], intravenous magnesium, cross-over); Van der Plas 2013, n = 22, CRPS [criteria NR], intramuscular magnesium), which they rated at unclear overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Duong 2018 reported no between-group differences on numeric rating scale scores (11-point NRS) scores at post-intervention, short-term and medium-term follow-up for Fischer 2013, but did not provide numerical data. An improvement in NRS scores was reported in the intramuscular magnesium group for Van der Plas 2013, but no between-group differences were provided (GRADE assessment not possible). We judged the certainty in evidence for Fischer 2013 as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

### Memantine

One non-Cochrane review, judged as low quality (Cossins 2013) included evidence of the effects of memantine for CRPS.

### Oral memantine plus oral morphine versus placebo plus oral morphine

Cossins 2013 included a single trial for this comparison (Gustin 2010, n = NR ('small'), upper limb CRPS [Merskey 1994]), which they rated as high quality using a 15-item quality checklist (de Vet 1997).

**Pain intensity:** Cossins 2013 reported a significant between-group difference in VAS scores post-intervention in favour of the memantine and morphine group but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for inconsistency and twice for imprecision.

## Other pharmacological therapies

### Botulinum toxin A

One non-Cochrane review, judged as critically low quality (Duong 2018) included evidence on the effects of botulinum toxin A in CRPS.

### Intradermal/subcutaneous botulinum toxin A versus placebo

Duong 2018 included a single trial for this comparison (Safarpour, n = 8, CRPS [Harden 2007]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Duong 2018 reported no between-group differences in Brief Pain Inventory scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Participant satisfaction with treatment:** Duong 2018 reported no between-group differences in Patient Satisfaction Scale scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Adverse events:** Duong 2018 reported increased pain on injection in the botulinum toxin A group but did not provide between-group differences (GRADE assessment not possible).

### Isosorbide dinitrate

One non-Cochrane review, judged as critically low quality (Duong 2018) included evidence on the effects of the nitrate isosorbide dinitrate in CRPS.

### Topical isosorbide dinitrate versus placebo

Duong 2018 included a single trial for this comparison (Groeneweg 2009, n = 24, upper limb CRPS [criteria NR]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Duong 2018 reported no between-group differences post-intervention, but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Disability:** Duong 2018 reported no between-group differences in Disabilities of the Arm, Shoulder and Hand (DASH) scores post-intervention, but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

### Sarpogrelate hydrochloride

One non-Cochrane review, judged as critically low quality (Tran 2010) included evidence on the effects of the serotonin receptor antagonist sarpogrelate hydrochloride in CRPS.

### Oral sarpogrelate hydrochloride plus conventional care versus conventional care alone

Tran 2010 included a single trial for this comparison (Ogawa 1998, n = 30, CRPS [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** Tran 2010 reported no between-group differences in VAS scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

### Tadalafil

One non-Cochrane review, judged as critically low quality (Tran 2010) included evidence on the effects of the phosphodiesterase-5 inhibitor tadalafil in CRPS.

### Oral tadalafil versus placebo

Tran 2010 included a single trial for this comparison (Groeneweg 2008, n = 24 lower limb CRPS [Bruehl 1999]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** Tran 2010 reported a between-group difference post-intervention in favour of the tadalafil group (VAS, tadalafil 15% reduction vs placebo 0%, P = 0.004, measures of variance NR). We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

## Interventional procedures

### Neuraxial therapy

#### Epidural clonidine

One non-Cochrane review, judged as critically low quality (Tran 2010) included evidence on the effects of epidural pharmacological administration in CRPS.

#### Epidural clonidine (300 µg and 700 µg) versus placebo

Tran 2010 included a single three-arm cross-over trial for this comparison (Rauck 1993, n = 26, upper and lower limb CRPS [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** Tran 2010 reported a significant between-group difference in VAS scores in favour of both clonidine groups post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

#### Epidural clonidine 300 µg versus epidural clonidine 700 µg

Two arms of the same three-arm cross-over trial (Rauck 1993) provided data for this comparison.

**Pain intensity:** Tran 2010 reported no significant between-group differences in VAS scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Adverse events:** Tran 2010 reported a significant between-group increase in the number of participants experiencing sedation in the 700 µg clonidine group but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

#### Intrathecal pharmacological administration

One non-Cochrane review, judged as critically low quality (Duong 2018) included evidence on the effects of intrathecal administration of a range of pharmacological agents in CRPS.

#### Intrathecal baclofen 'fast' (0.75 mg/mL<sup>-1</sup>) versus 'slow' (3 mg/mL<sup>-1</sup>) infusions

Duong 2018 included a single cross-over trial for this comparison (Van der Plas 2011, n = 14, CRPS [criteria NR]), which they rated at low overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Duong 2018 reported no between-group differences in NRS scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for inconsistency and twice for imprecision.

**Participant rating of improvement:** Duong 2018 reported no between-group differences in Global Impression Scale scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for inconsistency and twice for imprecision.

**Adverse events:** Duong 2018 reported an increase in adverse events in the 'fast' baclofen infusion group but did not provide between-group differences (GRADE assessment not possible).

#### Intrathecal clonidine versus intrathecal adenosine

Duong 2018 included a single cross-over trial for this comparison (Rauck 2015, n = 20, upper and lower limb CRPS [Harden 2007]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Duong 2018 reported no between-group differences in 'pain success' (proportion of participants reporting > 30% decrease in pain from baseline) post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Participant rating of improvement:** Duong 2018 reported no between-group differences in patient-reported global assessment of effect scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

#### Intrathecal glycine versus placebo

Duong 2018 included a single cross-over trial for this comparison (Munts 2009, n = 18, CRPS [criteria NR]), which they rated at unclear overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Duong 2018 reported no between-group differences in NRS scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Disability:** Duong 2018 reported no between-group differences in Radboud Skills Questionnaire or Walking Skills Questionnaire scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Participant rating of improvement:** Duong 2018 reported no between-group differences in participant-reported Global Impression Scale scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Adverse events:** Duong 2018 reported no between-group differences in adverse events but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

#### Intrathecal methylprednisolone versus placebo

Duong 2018 included a single cross-over trial for this comparison (Munts 2010, n = 10, CRPS [criteria NR]), which they rated at unclear overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Duong 2018 reported no between-group differences in NRS scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as

very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Participant rating of improvement:** [Duong 2018](#) reported no between-group differences in Global Impression Scale scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Adverse events:** [Duong 2018](#) reported an increase in myoclonus in the intrathecal methylprednisolone group but did not provide between-group differences (GRADE assessment not possible).

### **Intravenous Regional Blockade (IVRB)**

One Cochrane review, judged as low quality ([Challapalli 2005](#)) specifically investigated the effects of IVRB in CRPS, and five non-Cochrane reviews, judged as critically low quality ([Fassio 2022](#); [Fischer 2010](#); [Forouzanfar 2002](#); [Tran 2010](#); [Xu 2016](#)) included evidence on the effects of IVRB using a range of pharmacological agents in CRPS.

#### **Atropine IVRB versus placebo**

[Tran 2010](#) included a single cross-over trial for this comparison ([Glynn 1993](#), n = 30, CRPS [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** [Tran 2010](#) reported no between-group difference in VAS scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and twice for imprecision.

#### **Droperidol IVRB versus placebo**

[Xu 2016](#) included a single cross-over trial for this comparison ([Kettler 1988](#), n = 6, RSD [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** [Xu 2016](#) reported no between-group difference post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and twice for imprecision.

#### **Guanethidine IVRB versus placebo**

[Xu 2016](#) included three trials for this comparison ([Blanchard 1990](#), n = 21, RSD; [Livingstone 2002](#), n = 57, upper limb CRPS I; [Ramamurthy 1995](#), n = 60, RSD) (criteria NR). No assessments of risk of bias or methodological quality were conducted.

**Pain intensity:** [Xu 2016](#) reported no significant between-group differences post-intervention for [Blanchard 1990](#) and [Ramamurthy 1995](#), but there was a significant increase in pain intensity in the IVRB group at medium-term follow-up for [Livingstone 2002](#). Point estimates or measures of precision were not reported for any of the comparisons. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Adverse events:** [Xu 2016](#) reported minimal changes in blood pressure in the IVRB group for [Blanchard 1990](#) (no between-group differences provided), and no between-group differences in

adverse events for [Ramamurthy 1995](#) (point estimates or measures of precision not provided). At medium-term follow-up, a significant between-group difference in the incidence of vasomotor instability was reported in the IVRB group for [Livingstone 2002](#) but point estimates or measures of precision were not provided. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### **Ketanserin IVRB versus placebo**

[Forouzanfar 2002](#) identified two cross-over trials for this comparison ([Bounameaux 1984](#), n = 9, RSD; [Hanna 1989](#), n = 9, RSD) (criteria NR), which they rated as low quality using [de Vet 1997](#) criteria.

**Pain intensity:** [Forouzanfar 2002](#) reported no significant between-group differences in pain scores post-intervention for [Bounameaux 1984](#), but there was a significant between-group difference in VAS scores for [Hanna 1989](#). Point estimates or measures of precision were not provided for either comparison. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### **Lidocaine IVRB versus placebo**

[Challapalli 2005](#) identified a single cross-over trial for this comparison ([Wallace 2000](#), n = 16, CRPS I & II [criteria NR]), which they rated 3/5 using the Jadad scale.

**Pain intensity:** [Challapalli 2005](#) reported no statistically significant within group reduction in spontaneous pain post-intervention, but no between-group differences were provided (GRADE assessment not possible).

**Adverse events:** [Challapalli 2005](#) reported a significant between-group difference in light-headedness, with an increased incidence in the IVRB group, but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and twice for imprecision.

#### **Methylprednisolone and lidocaine bier block versus placebo**

[Fischer 2010](#) identified a single study for this comparison ([Taskaynatan 2004](#), n = 22, CRPS I [criteria NR]), which they rated as high quality using the Delphi list.

**Pain intensity:** [Fischer 2010](#) reported no significant between-group differences post-intervention (VAS, mean (SD) 5.7 (1.3), placebo 4.8 (0.9)). We judged the certainty in evidence as very low, downgraded once for inconsistency, and twice for imprecision.

#### **Guanethidine plus lidocaine IVRB versus reserpine plus lidocaine IVRB versus lidocaine IVRB alone**

[Xu 2016](#) identified a three-arm cross-over trial for this comparison ([Rocco 1989](#), n = 12 [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** [Xu 2016](#) reported no between-group differences post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and twice for imprecision.

**Adverse events:** Xu 2016 reported mild depression and diarrhoea in the reserpine group but did not provide between-group differences (GRADE assessment not possible).

#### **Lidocaine IVRB versus lidocaine IVRB with 30 mg, 60 mg or 120 mg ketorolac**

Xu 2016 identified a four-arm cross-over trial for this comparison (Eckmann 2011, n = 12, lower limb CPRS [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** Xu 2016 reported pain reductions in all three ketorolac groups but did not provide between-group differences with placebo (GRADE assessment not possible).

**Adverse events:** Xu 2016 reported a higher incidence of mild drowsiness, faintness, and shakiness with ketorolac administration, but did not provide between-group differences (GRADE assessment not possible).

#### **Parecoxib, lidocaine and clonidine IVRB versus lidocaine and clonidine IVRB versus intravenous parecoxib, lidocaine and clonidine**

Fassio 2022 identified a single three-arm study for this comparison (Frade 2005, n = 30, CRPS I [criteria NR]), which they rated at unclear overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Fassio 2022 reported a significant between-group difference post-intervention in favour of the parecoxib, lidocaine and clonidine IVRB group compared with both comparator groups but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and twice for imprecision.

#### **Local anaesthetic sympathetic blockade (LASB)**

One Cochrane review, judged as high quality (O'Connell 2016) specifically investigated the effects of LASB using a range of pharmacological agents on CRPS.

#### **Lidocaine stellate ganglion block versus placebo**

O'Connell 2016 included two trials for this comparison (Aydemir 2006, n = 25, upper limb CRPS I [Bruehl 1999], 3-arm trial; Price 1998, n = 7, upper and lower limb CRPS I & II [Merskey 1994], cross-over), both rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported no between-group differences in VAS scores post-intervention for both studies (Aydemir 2006 and Price 1998), but individual between-group estimates were not provided by the trial authors. The review authors judged the certainty in evidence as moderate, downgraded once for imprecision.

#### **Lidocaine stellate ganglion block versus stellate ganglion ultrasound**

Two arms of the same three-arm cross-over trial (Aydemir 2006) provided data for this comparison.

**Pain intensity:** O'Connell 2016 reported no significant between-group differences in VAS scores post-intervention, but between-group estimates were not provided by the trial authors. The review authors judged the certainty in evidence as low, downgraded once for inconsistency and once for imprecision.

#### **Bupivacaine stellate ganglion block versus guanethidine IVRB**

O'Connell 2016 included a single trial for this comparison (Bonelli 1983, n = 19, RSD [criteria NR]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported no significant between-group differences in 100-mm linear scale scores post-intervention but did not provide point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and once for imprecision.

#### **Botulinum toxin A plus bupivacaine sympathetic block versus bupivacaine sympathetic block alone**

O'Connell 2016 included a single cross-over trial for this comparison (Carroll 2009, n = 9, lower limb CRPS I [Merskey 1994]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported a significant reduction in 10-cm VAS scores in the botulinum toxin A group post-intervention, but the trial authors did not report between-group differences (GRADE assessment not possible).

**Adverse events:** O'Connell 2016 reported that a single participant experienced nausea and emesis in the botulinum toxin A group but no between-group difference was provided (GRADE assessment not possible).

#### **Lidocaine and clonidine sympathetic block of the lumbar plexus versus pulsed radiofrequency of the lumbar plexus**

O'Connell 2016 included a single trial for this comparison (Freitas 2013, n = 40, lower limb CRPS I [Bruehl 1999]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported no significant between-group differences post-intervention but did not provide point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and once for imprecision.

#### **Lidocaine stellate ganglion block versus oral prednisone**

O'Connell 2016 included a single trial for this comparison (Lim 2007, n = 38, upper limb post-stroke CRPS I [criteria NR]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported no between-group differences in hand pain post-intervention (0 to 3 scale, MD 0.00, 95% CI -0.35 to 0.35). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and once for imprecision.

#### **Lidocaine sympathetic block versus lidocaine and clonidine IVRB**

O'Connell 2016 included a single trial for this comparison (Nascimento 2010, n = 43, upper limb CRPS I [Merskey 1994]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported no significant between-group differences in 0-10 cm VAS scores post-intervention but did not provide point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded

once for serious study limitations, once for inconsistency and once for imprecision.

**Adverse events:** O'Connell 2016 reported an increase in the incidence of dizziness in the lidocaine sympathetic block group but did not provide point estimates or measures of precision (GRADE assessment not possible).

#### **Ropivacaine/triamcinolone thoracic sympathetic block versus subcutaneous ropivacaine/triamcinolone**

O'Connell 2016 included a single trial for this comparison (Rocha 2014, n = 36, upper limb CRPS [Merskey 1994/Harden 2010]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported no observed between-group differences post-intervention (Brief Pain Inventory, 0 to 10 scale, MD -1.25, 95% CI -3.20 to 0.70), but there was a clinically important between-group difference in favour of the sympathetic block group at long-term follow-up (MD -2.39, 95% CI -4.72 to -0.06). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and once for imprecision.

**Adverse events:** O'Connell 2016 reported an increase in the incidence of dyspnoea in the sympathetic block group compared with the subcutaneous ropivacaine/triamcinolone group (24% vs 6%) but did not provide point estimates or measures of precision (GRADE assessment not possible).

#### **Continuous bupivacaine stellate ganglion block versus continuous bupivacaine brachial plexus block**

O'Connell 2016 included a single trial for this comparison (Toshniwal 2012, n = 33, upper limb CRPS I [Bruehl 1999]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported a significant between-group difference in pain scores (0 to 10 scale, 0.7 vs 3.3) in favour of continuous brachial plexus block post-intervention, but no measures of precision were provided. The review authors judged the certainty in evidence as low, downgraded once for inconsistency and once for imprecision.

**Adverse events:** O'Connell 2016 reported an increase in the incidence of positive catheter tip culture (61.1% vs 8.3%) and decreased catheter migration (5.2% vs 7.1%) in the sympathetic block group, but no effect size measures of precision were provided (GRADE assessment not possible).

#### **Lidocaine image-guided versus lidocaine nonimage-guided stellate ganglion block**

O'Connell 2016 included a single trial for this comparison (Yoo 2012, n = 42, upper limb post-stroke CRPS [Harden 2010]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported no observed between-group differences (VAS, 0 to 10 scale, MD -0.58, 95% CI -1.51 to 0.35) post-intervention. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, once for imprecision, and once for indirectness.

**Adverse events:** O'Connell 2016 reported an increase in the incidence of haematoma at injection site (24% vs 6%) in the non-image guided block compared with the image-guided block, but

did not provide point estimates or measures of precision (GRADE assessment not possible).

#### **Stellate ganglion block plus rehabilitation versus rehabilitation alone.**

O'Connell 2016 included a single trial for this comparison (Zeng 2003, n = 60, post-stroke shoulder-hand syndrome [criteria NR]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported no observed between-group differences post-intervention (Verbal Rating Scale 0 to 10 scale, MD 0.2, 95% CI -1.3 to 1.7). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and once for imprecision.

#### **Lidocaine and bupivacaine stellate ganglion block plus conventional care versus conventional care alone**

O'Connell 2016 included a single trial for this comparison (Rodriguez 2005, n = 82, upper limb CRPS I & II [Merskey 1994; Reinders 2002]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** O'Connell 2016 reported a between-group difference (at least 50% pain reduction, absolute risk reduction 17%; number needed to treat for an additional beneficial outcome (NNTB) = 6) at short-term follow-up in favour of the stellate ganglion block group but did not provide point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and once for imprecision.

#### **Sympathectomy**

One Cochrane review, judged as high quality (Straube 2013) specifically investigated the effects of cervico-thoracic or lumbar sympathectomy for CRPS.

#### **Percutaneous radiofrequency thermal lumbar sympathectomy versus phenol lumbar sympathetic neurolysis**

Straube 2013 identified a single study for this comparison (Manjunath 2008, n = 20, CRPS [Bruehl 1999]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** Straube 2013 reported no significant between-group differences post-intervention or at medium-term follow-up but did not provide point estimates or measures of precision. The review authors judged the certainty in evidence as very low (reasons for downgrading evidence NR).

**Adverse events:** Straube 2013 reported that all participants experienced post-injection soreness, one participant in the phenol group experienced post-sympathectomy neuralgia, and one participant in the phenol group experienced paraesthesia during needle positioning but did not provide between-group differences (GRADE assessment not possible).

#### **Neuromodulation**

##### **Implanted spinal neuromodulation interventions**

Two non-Cochrane reviews, judged as critically low quality (Duong 2018; Tran 2010) included evidence on the effects of implanted spinal neuromodulation interventions in CRPS.

### Standard, burst, 500 Hz and 1000 Hz spinal cord stimulation versus placebo

**Duong 2018** identified a single five-arm cross-over trial for this comparison (**Kriek 2017**, n = 40, CRPS [**Harden 2007**]), which was rated at low overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** **Duong 2018** reported significant between-group differences post-intervention in favour of all SCS (spinal cord stimulation) groups compared with placebo but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for inconsistency and twice for imprecision.

**Participant ratings of improvement:** **Duong 2018** reported significant between-group differences in Global Perceived Effect post-intervention in favour of all SCS groups compared with placebo but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for inconsistency and twice for imprecision.

### SCS versus dorsal root ganglion stimulation (DRGS)

**Duong 2018** identified a single study for this comparison (**Deer 2017**, n = 146, lower limb CRPS [**Harden 2007**]), which was rated at high overall risk of bias using the Cochrane ROB tool.

**Quality of life:** **Duong 2018** reported significant between-group differences in the physical component, general health and social functioning scales of the SF-36 at long-term follow-up in favour of DRGS, but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Participant satisfaction with treatment:** **Duong 2018** reported no between-group differences in patient satisfaction at long-term follow-up, but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Adverse events:** **Duong 2018** reported no between-group differences in adverse events at long-term follow-up but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

### Spinal cord stimulation plus physiotherapy versus physiotherapy alone

**Tran 2010** identified three separate reports of a single trial for this comparison (**Kemler 2000**, n = 54; **Kemler 2004**, n = NR; **Kemler 2008**, n = NR [all **Bruehl 1999**]). No assessments of risk of bias or methodological quality were conducted.

**Pain intensity:** **Tran 2010** reported a between-group difference (VAS, mean (SD) 2.4 (2.5) vs 0.2 (1.4); P < 0.001) in favour of SCS at medium-term follow-up (**Kemler 2000**), and a significant between-group difference was maintained at long-term follow-up (**Kemler 2004**), but point estimates or measures of precision were not provided for this time point. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Disability:** **Tran 2010** reported no between-group differences in functional status at medium-term follow-up but did not provide point estimates or measures of precision (**Kemler 2000**). We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Quality of life:** **Tran 2010** reported no between-group differences in quality of life at medium-term follow-up but did not provide point estimates or measures of precision (**Kemler 2000**). We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Participant ratings of improvement:** **Tran 2010** reported a significant between-group difference in GPE scores (proportion achieving 6/7 GPE, 36% vs 6%, measures of variance NR) in favour of SCS at medium-term follow-up (**Kemler 2000**), and a significant between-group difference was maintained at long-term follow-up (**Kemler 2004**), but point estimates and measures of precision were not provided for this time point. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency and twice for imprecision.

**Adverse events:** **Tran 2010** reported that 42% of participants in the SCS group experienced a device-related complication over the five-year study period (**Kemler 2000**; **Kemler 2004**; **Kemler 2008**), but did not provide between-group differences or measures of precision (GRADE assessment not possible).

### Non-invasive brain stimulation

One non-Cochrane review, judged as low quality (**Cossins 2013**) included evidence on the effects of non-invasive brain stimulation in CRPS.

### Repetitive transcranial magnetic stimulation (rTMS) versus placebo

**Cossins 2013** identified two trials for this comparison (**Picarelli 2010**, n = NR [**Merskey 1994**]; **Pleger 2004**, n = NR [**Merskey 1994**], cross-over), which they rated as high quality using a 15-item quality checklist (**de Vet 1997**).

**Pain intensity:** **Cossins 2013** reported significant between-group differences in VAS scores in favour of rTMS post-intervention for both **Picarelli 2010** and **Pleger 2004** but the positive effect was not sustained at medium-term follow-up for **Picarelli 2010**. Point estimates or measures of precision were not provided for these comparisons. We judged the certainty in evidence as very low, downgraded once for inconsistency and twice for imprecision.

### Rehabilitation

One Cochrane review, judged as high quality (**Smart 2022**) specifically investigated the effects of a broad range of rehabilitation/physiotherapy interventions for CRPS.

### Sensory-motor training strategies

#### Graded Motor Imagery

#### Graded motor imagery (GMI) versus standard care

**Smart 2022** identified three trials for this comparison (**Moseley 2004**, n = 13, upper limb CRPS I [**Bruehl 1999**]; **Moseley 2006**, upper and lower limb CRPS I [**Bruehl 1999**] n = 37, **Schreuders 2014**, n = 18, upper limb CRPS I [**Bruehl 1999**]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported a clinically important between-group difference (VAS 0-100, MD -14.45, 95% CI -23.02 to -5.87,  $P = 0.001$ ;  $I^2 = 29\%$ ; 2 trials,  $n = 49$ ) in favour of GMI post-intervention ([Moseley 2004](#), [Moseley 2006](#)). At short-term follow-up, no between-group differences were reported for [Schreuders 2014](#) but numerical data were not reported by the trial authors. At medium-term follow-up there was a clinically important between-group difference in favour of GMI (MD -21.00, 95% CI -31.17 to -10.83) reported for [Moseley 2006](#). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** [Smart 2022](#) reported a between-group improvement in patient-specific functional scale scores (0 to 10 scale, MD 1.87, 95% CI 1.03 to 2.71,  $P < 0.001$ ;  $I^2 = 41\%$ ; 2 trials,  $n = 49$ ) in favour of GMI post-intervention ([Moseley 2004](#), [Moseley 2006](#)). There was also a between-group difference at medium-term follow-up in favour of GMI (MD 2.30, 95% CI 1.12 to 3.48,  $P < 0.001$ ) reported for [Moseley 2006](#). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### GMI versus waiting-list control

[Smart 2022](#) identified a single cross-over trial for this comparison ([Strauss 2021](#),  $n = 22$ ; upper limb CRPS II [criteria NR by trial authors]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported no evidence of between-group differences post-intervention (0 to 10 VAS, MD -0.58, 95% CI -1.94 to 0.78). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Adverse events:** [Smart 2022](#) reported increased swelling of the affected limb in two participants and increased pain in 12 participants during training, and increased pain after completing training in two participants, but no other numerical data were reported by the trial authors. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### Mirror therapy

##### Mirror therapy versus placebo

[Smart 2022](#) identified a single three-arm trial for this comparison ([Cacchio 2009a](#),  $n = 24$ , upper limb post-stroke CRPS I [[Bruehl 1999](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported that seven out of eight participants in the mirror therapy group experienced reduced pain (0-100 VAS, median change -51 mm, range -70 to -18) compared with one out of eight in the placebo group post-intervention, but the review authors stated they could not calculate an effect size due to missing between-group data. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

##### Mirror therapy plus stroke rehabilitation versus placebo mirror therapy plus stroke rehabilitation

[Smart 2022](#) identified a single study for this comparison ([Cacchio 2009b](#),  $n = 48$ , upper limb post-stroke CRPS I [[Bruehl 1999](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported a clinically important between-group differences in favour of the mirror therapy group post-intervention (0-10 VAS, MD -2.9, 95% CI -4.23 to -1.57;  $P < 0.001$ ) and at medium-term follow-up (MD -3.4, 95% CI -4.71 to -2.09;  $P < 0.001$ ). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** [Smart 2022](#) reported significant between-group differences in Wolf Motor Function test scores in favour of the mirror therapy group post-intervention (0 to 5 scale, MD -1.9, 95% CI -2.36 to -1.44;  $P < 0.001$ ) and at medium-term follow-up (MD -2.3, 95% CI -2.88 to -1.72;  $P < 0.001$ ). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

##### Mirror therapy versus mental imagery

[Smart 2022](#) included the 3-arm trial by [Cacchio 2009a](#) for this comparison.

**Pain intensity:** [Smart 2022](#) reported that seven out of eight participants in the mirror therapy group experienced reduced pain on movement (0-100 VAS, median change -51 mm, range -70 to -18) compared with two out of eight in the mental imagery group post-intervention, but the review authors reported they could not calculate an effect size due to missing between-group data. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

##### Mirror therapy plus stroke rehabilitation versus stroke rehabilitation alone

[Smart 2022](#) identified two studies for this comparison ([Saha 2021](#),  $n = 38$ , post-stroke upper limb CRPS [criteria NR by trial authors]; [Vural 2016](#),  $n = 30$ , post-stroke upper limb CRPS I [[Veldman 1993](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported a clinically important between-group difference (0-10 NRS, MD -1.40, 95% CI -2.26 to -0.54;  $P < 0.001$ ) in favour of mirror therapy post-intervention for [Saha 2021](#) and a between-group difference (median within group change, 0 to 10 VAS, 3 vs 1) in favour of mirror therapy post-intervention for [Vural 2016](#), but the review authors stated they could not determine an effect size for the latter trial because of missing point estimates and measures of precision. The review authors judged the certainty in evidence as very low, downgraded twice for serious study limitations, and once for imprecision.

**Disability:** [Smart 2022](#) reported an improvement in Functional Independence Measure (FIM) scores (18 to 126 scale, MD 21.95, 95% CI 9.71 to 34.19;  $P < 0.001$ ) in favour of the mirror therapy group post-intervention for [Saha 2021](#) and an improvement in Fugl-Meyer Assessment hand scores (0-14 scale, median within-group change 3 vs 0) in favour of mirror therapy post-intervention for [Vural 2016](#), but the effect size and measures of precision were

not reported by authors of the latter trial. The review authors judged the certainty in evidence as very low, downgraded twice for serious study limitations, and once for imprecision.

#### **Mirror visual feedback plus medical management versus contrast baths plus medical management**

[Smart 2022](#) identified a single 3-arm trial for this comparison ([Sarkar 2017](#),  $n = 30$ , upper and lower limb CRPS [[Harden 2007](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported a clinically important between-group difference (11-point NRS, MD  $-2.65$ , 95% CI  $-3.14$  to  $-2.16$ ;  $P < 0.001$ ) in favour of the mirror visual feedback group post-intervention. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### **Mirror visual feedback plus medical management versus contrast baths and exercise plus medical management**

[Smart 2022](#) included the same three-arm trial by [Sarkar 2017](#) for this comparison.

**Pain intensity:** [Smart 2022](#) reported a clinically important between-group difference (11-point NRS, MD  $-2.60$ , 95% CI  $-3.08$  to  $-2.12$ ;  $P < 0.001$ ) in favour of the mirror visual feedback group post-intervention. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### **Virtual reality**

##### **Virtual body swapping with mental rehearsal versus 'watching movement only'**

[Smart 2022](#) identified a single three-arm trial for this comparison ([Hwang 2014](#),  $n = 39$ , upper and lower limb CRPS I & II [[Bruehl 1999](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported no between-group differences in the 11-point pain scale post-intervention, but numerical data were not reported by the trial authors. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

##### **Virtual body swapping with mental rehearsal versus mental rehearsal only**

[Smart 2022](#) included the same three-arm trial by [Hwang 2014](#) for this comparison.

**Pain intensity:** [Smart 2022](#) reported no between-group differences in 11-point pain scale scores post-intervention, but numerical data were not reported by the trial authors. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

##### **Virtual body swapping with mental rehearsal versus virtual body swapping alone**

[Smart 2022](#) identified a single trial for this comparison ([Jeon 2014](#),  $n = 10$ , upper and lower limb CRPS I [[Harden 2007](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported no between-group differences post-intervention, but numerical data were not reported by the trial authors. [Smart 2022](#) judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### **Virtual reality versus sham virtual reality**

[Smart 2022](#) identified a single trial for this comparison ([Lewis 2021](#),  $n = 45$ , upper limb CRPS [[Harden 2010](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported a between-group difference post-intervention (11-point NRS, MD  $1.2$ ; SMD  $0.7$ ) but stated the effect size could not be confirmed due to missing measures of variance. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### **Tactile discrimination**

##### **Four tactile discrimination training protocols compared with each other**

[Smart 2022](#) identified a single four-arm cross-over trial for this comparison ([Moseley 2009](#),  $n = 10$ ; upper limb CRPS I [[Bruehl 1999](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported no between-group differences in 100-mm VAS scores post-intervention, but numerical data were not reported by the trial authors. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Adverse events:** [Smart 2022](#) reported increased pain during tactile discrimination training, but no between-group differences were provided. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### **Prism adaptation**

##### **Prism adaptation treatment versus placebo**

[Smart 2022](#) identified a single trial for this comparison ([Halicka 2021](#),  $n = 49$ ; upper limb CRPS I [[Harden 2010](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported no evidence of benefit over placebo in 11-point NRS scores post-intervention or at medium-term follow-up, but the trial authors did not report mean differences and 95% CIs. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Participant ratings of improvement:** [Smart 2022](#) reported no evidence of benefit over placebo in Patient's Global Impression of Change scores post-intervention or at medium-term follow-up, but the trial authors did not report median differences with measures of variation. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

## Electrophysical agents

### Stellate ganglion ultrasound versus placebo

**Smart 2022** identified a single three-arm trial for this comparison (**Askin 2014**,  $n = 45$ ; upper limb CRPS I [**Bruehl 1999**]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** **Smart 2022** reported no evidence of between-group differences in 10-cm VAS scores post-intervention, but the trial authors did not report point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** **Smart 2022** reported no evidence of between-group differences in DASH scores post-intervention, but the trial authors did not report point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

### Stellate ganglion ultrasound versus TENS

**Smart 2022** identified a single trial for this comparison (**Hazneci 2005**,  $n = 30$ ; upper limb RSD [**Kozin 1992**]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** **Smart 2022** reported a clinically important between-group difference (0-10 VAS, MD 2.13, 95% CI 1.47 to 2.79;  $P < 0.001$ ) in favour of TENS post-intervention. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

### Electromagnetic field therapy (EMF) versus placebo

**Smart 2022** identified three trials for this comparison (**Benedetti 2018**,  $n = 30$ , upper and lower limb CRPS I [**Harden 2007**], **Büyükturan 2018**,  $n = 42$ , upper limb CRPS I [**Harden 2007**]; **Durmus 2004**,  $n = 40$ , upper limb CRPS I [**Merskey 1994**]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** **Smart 2022** reported no between-group differences in 10-cm VAS scores post-intervention for **Durmus 2004** (effect size could not be calculated by review authors due to missing data), but there were clinically important between-group differences for **Benedetti 2018** (10-cm VAS, MD -2.2, 95% CI -1.99 to -2.41;  $P < 0.001$ ) and **Büyükturan 2018** (10-cm VAS 1.6, 95% CI 0.83 to 2.37,  $P < 0.001$ ) post-intervention, both in favour of the EMF groups. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** **Smart 2022** reported that for **Benedetti 2018** there was a between-group difference in lower limb disability post-intervention (Maryland Foot Score, 0 to 100, MD 14.4, 95% CI 11.36 to 17.44;  $P < 0.001$ ;  $n = 18$ ) in favour of EMF, and a between-group difference in upper limb disability post-intervention (DASH, 0-100, MD -14.0 95% CI -4.41 to -23.59;  $P < 0.004$ ;  $n = 12$ ) in favour of placebo. There was no between-group difference on Quick-DASH scores post-intervention reported for **Büyükturan 2018** (0 to 100, MD 2, 95% CI -3.91 to 7.91). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Adverse events:** **Smart 2022** reported there were no adverse events for **Benedetti 2018**. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

### TENS versus placebo

**Smart 2022** identified a single trial for this comparison (**Bilgili 2016**,  $n = 30$ , upper limb CRPS I [**Merskey 1994**]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** **Smart 2022** reported no observed between-group differences in 10-cm VAS scores post-intervention (MD -9, 95% CI -18.5 to 0.5;  $P = 0.074$ ) in favour of TENS post-intervention. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** **Smart 2022** reported no observed between-group differences in Duruöz Hand Index scores (scoring NR) (MD -3.6, 95% CI -13.38 to 6.18;  $P = 0.48$ ) post-intervention. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

### Laser therapy versus interferential therapy

**Smart 2022** identified a single trial for this comparison (**Dimitrijevic 2014**,  $n = 50$ , upper and lower limb CRPS I [**Harden 2005**]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** **Smart 2022** reported a between-group difference (0 to 100 VAS, MD -8.6, 95% CI -16.27 to -0.93;  $P = 0.03$ ) in favour of laser therapy post-intervention. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Adverse events:** **Smart 2022** reported there were no adverse events. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

### CO<sub>2</sub> bath therapy and exercise versus exercise alone

**Smart 2022** identified a single trial for this comparison (**Mucha 1992**,  $n = 40$ , upper limb algodystrophy [criteria NR]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** **Smart 2022** reported a between-group difference in pain post-intervention in favour of the CO<sub>2</sub> bath group, but numerical data were not reported by the trial authors. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

### Whirlpool baths versus neuromuscular electrical stimulation

**Smart 2022** identified a single trial for this comparison (**Devrimsel 2015**,  $n = 60$ , upper limb CRPS I [**Harden 2010**]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** **Smart 2022** reported a between-group difference (10-cm VAS, MD -0.65, 95% CI -1.03 to -0.27;  $P < 0.001$ ) in favour of the whirlpool bath group post-intervention. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Adverse events:** [Smart 2022](#) reported there were no adverse events. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### **Fluidotherapy plus stroke rehabilitation versus stroke rehabilitation alone**

[Smart 2022](#) identified a single trial for this comparison ([Ozcan 2019](#),  $n = 32$ , upper limb post-stroke CRPS I [[Harden 2010](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported no between-group differences in 10-cm VAS scores post-intervention, but the trial authors did not report point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** [Smart 2022](#) reported no between-group differences in FIM scores post-intervention, but the trial authors did not report point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### **Exposure-based interventions**

##### **Pain exposure physical therapy versus usual physiotherapy**

[Smart 2022](#) identified a single trial for this comparison ([Barnhoorn 2015](#),  $n = 56$ , upper and lower limb CRPS I [[Harden 2007](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported no significant between-group differences (1 to 10 VAS, MD 0.61, 95% CI -0.70 to 1.92) at long-term follow-up. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** [Smart 2022](#) reported no observed between-group differences in upper limb (DASH, 0 to 100 scale, MD 6.47, 95% CI -5.97 to 18.90) and lower limb (Lower Limb Tasks Questionnaire, 0 to 40 scale, MD 5.11, 95% CI -0.45 to 10.68) disability scores at long-term follow-up. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Quality of life:** [Smart 2022](#) reported no observed between-group differences in EuroQol-5D index scores (maximum score 1, MD -0.01, 95% CI -0.10 to 0.08) at long-term follow-up. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

##### **Exposure in vivo versus usual physiotherapy**

[Smart 2022](#) identified a single trial for this comparison ([den Hollander 2016](#),  $n = 46$ , upper and lower limb CRPS I [[Merskey 1994](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported clinically important between-group differences in Neuropathic Pain Scale scores in favour of the exposure intervention post-intervention (0 to 10, MD -2.04 95% CI -3.01 to -1.07;  $P = 0.001$ ) and at medium-term follow-up (MD -2.82,

95% CI -4.18 to -1.46;  $P = 0.001$ ). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** [Smart 2022](#) reported between-group differences in upper limb disability post-intervention (Radboud Skills Questionnaire, 0-5, MD -1.08, 95% CI -1.60 to -0.56;  $P = 0.001$ ) and at medium-term follow-up (MD -1.30, 95% CI -0.92 to -1.69;  $P = 0.001$ ); and a significant between-group difference in lower limb disability at medium-term follow-up (Walking Ability Questionnaire, 0 to 10, MD -3.62, 95% CI -6.78 to -0.47;  $P = 0.02$ ) but no between-group differences post-intervention. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Quality of life:** [Smart 2022](#) reported between-group differences in SF-36 physical component summary scores (SF-36 PCS, 0 to 100, MD 25.93, 95% CI 15.92 to 35.91,  $P = 0.001$ ) and mental component summary (SF-36 MCS, 0 to 100, MD 16.23, 95% CI 6.85 to 25.63;  $P = 0.001$ ) post-intervention and at medium-term follow-up (SF-36 PCS: MD 22.64, 95% CI 10.15 to 35.13;  $P = 0.001$ ; SF-36 MCS: MD 19.63, 95% CI 10.78 to 28.47;  $P = 0.001$ ), all in favour of the exposure intervention. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### **Multimodal physiotherapy**

##### **Physiotherapy versus minimal care**

[Smart 2022](#) identified a single three-arm trial for this comparison ([Oerlemans 1999](#),  $n = 135$ , upper limb CRPS I [[Veldman 1993](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported a between-group difference in pain intensity in favour of physiotherapy post-intervention and no between-group differences at long-term follow-up, but the trial authors did not report point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** [Smart 2022](#) reported a between-group difference in disability in favour of physiotherapy at long-term follow-up (Impairment Level Sum Score, 5-50, MD -3.7, 95% CI -7.13 to -0.27,  $P = 0.03$ ). There were no between-group differences for several measures of upper limb disability (Radboud Skills Questionnaire, modified Greentest, Radboud Dexterity Test) at long-term follow-up. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Quality of life:** [Smart 2022](#) reported no between-group differences in health-related quality of life (Sickness Impact Profile) at long-term follow-up but the trial authors did not report numerical data. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

##### **Physiotherapy versus occupational therapy**

[Smart 2022](#) included the same three-arm trial by [Oerlemans 1999](#) for this comparison.

**Pain intensity:** [Smart 2022](#) reported no between-group differences at long-term follow-up, but the trial authors did not report point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** [Smart 2022](#) reported no between-group differences for several measures of upper limb disability (Impairment Level Sum Score, Radboud Skills Questionnaire, modified Greentest, Radboud Dexterity Test) at long-term follow-up, but the trial authors did not report point estimates or measures of precision. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Quality of life:** [Smart 2022](#) reported no between-group differences in health-related quality of life (Sickness Impact Profile) at long-term follow-up, but the trial authors did not report point estimates or measures of precision. We judged the certainty in evidence for this comparison as very low, downgraded once for serious study limitations, once for inconsistency and once for imprecision.

#### Upper limb aerobic exercise and physiotherapy versus physiotherapy alone

[Smart 2022](#) identified a single trial for this comparison ([Topcuoglu 2015](#), n = 40, upper limb post-stroke CRPS I [[Bruehl 1999](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported a clinically important between-group difference in daytime pain post-intervention (10-cm VAS, MD -1.9, 95% CI -3.23 to -0.57; P < 0.005). The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### Other physiotherapy-based interventions

##### Manual lymphatic drainage therapy versus conventional care

[Smart 2022](#) identified two trials for this comparison ([Duman 2009](#), n = 34, upper limb RSD [[Bruehl 1999](#)]; [Uher 2000](#), n = 40, lower limb CRPS I [criteria NR]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported no between-group differences post-intervention for either study but were unable to extract accurate numerical data to calculate an effect size. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

##### Electro-acupuncture and massage versus rehabilitation

[Smart 2022](#) identified a single trial for this comparison ([Li 2012a](#), n = 120, post-stroke shoulder-hand syndrome [[Steinbrocker 1948](#)]), which they rated at high overall risk of bias using the Cochrane ROB tool.

**Pain intensity:** [Smart 2022](#) reported a clinically important between-group difference in pain on movement post-intervention (NRS, MD -1.70, 95% CI -2.09 to -1.31; P = 0.01) and at short-term follow-up (MD -1.40, 95% CI -1.78 to -1.02; P < 0.001) in favour of the electro-acupuncture and massage group. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Disability:** [Smart 2022](#) reported no between-group differences in Fugl-Meyer hand scores post-intervention, or in Fugl-Meyer upper limb scores at short-term follow-up, but no point estimates or measures of precision were provided. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

**Adverse events:** [Smart 2022](#) reported there were no adverse events. The review authors judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision.

#### Complementary and alternative therapies

##### Acupuncture

One non-Cochrane review, judged as critically low quality ([Peng 2018](#)) specifically investigated the effects of acupuncture in shoulder-hand syndrome. Another two non-Cochrane reviews, also judged as critically low quality ([Forouzanfar 2002](#); [Smith 2005](#)) included evidence on the effects of acupuncture in CRPS.

##### Acupuncture versus sham acupuncture

[Forouzanfar 2002](#) identified three trials for this comparison ([Fialka 1993](#), n = 14, RSD; [Kho 1995](#), n = 28, RSD; [Korpan 1999](#), n = 14, CRPS I) (criteria NR for all trials), which they rated as low quality using [de Vet 1997](#) criteria. [Smith 2005](#) identified an additional trial for this comparison ([Ernst 1995](#), n = 14, CRPS I [criteria NR]) but no assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** [Forouzanfar 2002](#) reported no significant between-group differences in VAS scores for two studies post-intervention ([Fialka 1993](#); [Kho 1995](#)) and a significant between-group difference in VAS scores for one study ([Korpan 1999](#)) in favour of the acupuncture group post-intervention but did not provide point estimates or measures of precision. [Smith 2005](#) reported a reduction in VAS scores in favour of the acupuncture group post-intervention for [Ernst 1995](#) but provided no measure of statistical significance (GRADE assessment not possible). We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and once for imprecision (three studies).

**Participant ratings of improvement:** [Smith 2005](#) reported an improvement in patient subjective success scores in favour of the acupuncture group post-intervention but did not provide point estimates or measures of precision (GRADE assessment not possible).

##### Traditional manual acupuncture plus rehabilitation versus rehabilitation alone

[Peng 2018](#) identified 20 trials of participants with shoulder-hand syndrome for this comparison (diagnostic criteria provided where reported): [Chai 2016](#), n = 118; [Chang 2005](#), n = 80 ([Kozin 1992](#)); [Chen 2015](#), n = 94 ([Miao 1996](#)); [Gao 2016](#), n = 100; [Li 2012b](#), n = 60 ([Miao 1996](#)); [Li 2015a](#), n = 92; [Liang 2016](#), n = 30; [Liao 2006](#), n = 90; [Niu 2015](#), n = 108 ([Miao 1996](#)); [Shang 2008](#), n = 80 ([Miao 1996](#)); [Shen 2014](#), n = 60 ([Miao 1996](#)); [Sun 2012](#), n = 60 ([Miao 1996](#)); [Tie 2016](#), n = 100 ([Miao 1996](#)); [Wan 2013](#), n = 120 ([Miao 1996](#)); [Wang 2017a](#), n = 142; [Wu 2014](#), n = 200 ([Miao 1996](#)); [Xu 2015](#), n = 80 ([Miao 1996](#)); [Zhao 2004](#), n = 54; [Zhang 2015](#), n = 92; [Zhong 2011](#) ('Zhu' criteria). The review authors judged all trials at unclear overall risk of bias.

**Pain intensity:** Peng 2018 reported a clinically important between-group difference (VAS, MD 1.49, 95% CI 1.15 to 1.82;  $I^2 = 71\%$ ;  $\text{Tau}^2 = 0.17$ ; nine trials,  $n = 834$ ) in favour of manual acupuncture post-intervention. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, once for imprecision and once for indirectness.

**Disability:** Peng 2018 reported a between-group difference in upper limb disability (Fugl-Meyer Assessment, MD 8.42, 95% CI 6.74 to 10.10;  $I^2 = 94\%$ ;  $\text{Tau}^2 = 13.07$ , 20 trials,  $n = 1918$ ) in favour of manual acupuncture post-intervention. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, once for imprecision and once for indirectness.

### Qigong

One non-Cochrane review, judged at critically low quality (Smith 2005) included evidence on the effects of qigong in CRPS.

#### Qigong versus placebo

Smith 2005 identified a single trial for this comparison (Wu 1999,  $n = 26$ , upper and lower limb CRPS I [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** Smith 2005 reported a significant between-group difference in the number of participants who reported a decrease in pain (VAS, 91% vs 36%, magnitude of decrease not specified) but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, downgraded once for serious study limitations, once for inconsistency, and twice for imprecision.

### Relaxation therapy

One non-Cochrane review, judged at critically low quality (Smith 2005) included evidence on the effects of relaxation therapy in CRPS.

#### Autogenic relaxation training plus home treatment versus home treatment alone

Smith 2005 identified a single trial for this comparison (Fialka 1996,  $n = 18$ , upper CRPS I [criteria NR]). No assessment of risk of bias or methodological quality was conducted.

**Pain intensity:** Smith 2005 reported no significant between-group differences in VAS scores post-intervention but did not provide point estimates or measures of precision. We judged the certainty in evidence as very low, once for serious study limitations, once for inconsistency, and twice for imprecision.

### Other interventions

#### Occlusal splints

One non-Cochrane review, judged as low quality (Cossins 2013) included evidence on the effects of occlusal splints in CRPS.

#### Occlusal splint versus control (not specified)

Cossins 2013 identified a single trial for this comparison (Fischer 2008,  $n = \text{NR}$ , upper limb CRPS I [Bruehl 1999]). which they rated as high quality using de Vet 1997 criteria.

**Pain intensity:** Cossins 2013 reported no significant between-group differences in NRS scores post-intervention but did not provide

point estimates or measures of precision. We judged the certainty in evidence as very low, once for inconsistency and twice for imprecision.

## DISCUSSION

### Summary of main results

Our objective was to provide an overview of Cochrane and non-Cochrane systematic review evidence of all interventions for treating pain and disability in adults with CRPS. We included data from 17 systematic reviews and synthesised the results reported for 127 RCTs. Despite a considerable increase in included evidence, the findings of this overview do not differ largely from those of the previous version. There are very few well-designed, well-reported, and large RCTs of the many interventions proposed for the treatment of CRPS. We found moderate-certainty evidence that, compared with placebo, local anaesthetic sympathetic blockade probably does not reduce pain intensity, and that bisphosphonates probably increase the risk of experiencing an adverse event of any nature. A summary of results from comparisons for which there is only low- or very low-certainty evidence is presented in Appendix 10. The critical lack of high-quality evidence prevents us from drawing any firm conclusions regarding the efficacy or effectiveness of any intervention for treating pain and disability in adults with CRPS.

### Overall completeness and applicability of evidence

We included both Cochrane and non-Cochrane reviews to ensure that this overview represents a comprehensive summary of all eligible systematic reviews published prior to the search dates. However, because we used published systematic reviews instead of original trials as the sole evidence source, and only five included reviews were published within the last five years, important trial evidence may have been excluded. The inclusion of two broad systematic reviews of pharmacotherapy (Fassio 2022) and physiotherapy (Smart 2022) published close to our search dates may mitigate this issue to some degree. Despite the inclusion of a large body of data from 17 reviews including the results from a total of 127 RCTs, we identified several factors that limit the overall completeness and applicability of the evidence at both review and trial levels.

The included evidence investigated a broad range of pharmacological, interventional, and rehabilitation treatments. Many of the included trials were small, involved short follow-up periods and were exploratory. Long-term (> 6 months) results were reported for only five included trials, offering limited information about the ongoing utility of most interventions. We found few instances where a specific intervention was tested in more than a single trial. Many included trials tested interventions against active comparators without prior evidence of efficacy using placebo control. We did not identify any RCT evidence for routinely used pharmacological interventions for CRPS such as tricyclic antidepressants or opioids. The description of included interventions in non-Cochrane reviews was poor although, in some instances, this may have been due to the inadequate reporting of original trials.

Several of the included reviews and trials were published before the current diagnostic criteria for CRPS (Harden 2010). This increases the risk that these studies included participants who would not

fulfil a diagnosis of CRPS under current diagnostic criteria. Although we aimed to include evidence on all CRPS subtypes and report results for each subtype separately, reviews did not always clearly distinguish between CRPS I and CRPS II. Additionally, few of the included reviews reported comprehensive demographic and clinical data on the included participants. These factors represent a source of clinical heterogeneity and make it difficult to establish for whom the evidence may be applicable.

The selection and reporting of outcome measures was inconsistent across RCTs and reviews, particularly between Cochrane and non-Cochrane reviews. Five non-Cochrane reviews failed to specify outcomes of interest and only two non-Cochrane reviews registered the selection of outcome measures before conducting the review. This increases the risk of selective outcome reporting (Stewart 2012) and makes it difficult to ascertain whether the absence of many of the outcomes of interest to this overview were missing in original trials, or simply not reported in reviews. Of the reviews that specified outcomes of interest to this overview, all selected pain intensity as the primary outcome. Few data were available for other overview outcomes such as quality of life and participant satisfaction with treatment. The definition and reporting of adverse events was inadequate, limiting our ability to make any firm conclusions regarding the safety of the included interventions. We also found the reporting of results to be poor. In many instances, results were reported narratively without providing quantitative data such as between-group estimates and their measures of precision. Without adequate reporting of such data, it is difficult to establish the clinical importance of many of the positive effects reported in this overview.

### Quality of the evidence

At the review level, we identified important differences in the quality of Cochrane and non-Cochrane reviews. While the inclusion of non-Cochrane reviews ensured a more comprehensive summary of the published evidence, it also reduced the overall quality of evidence within this overview.

We used the AMSTAR 2 tool to assess the quality of included reviews. Four of five Cochrane reviews were judged as high quality due to their consistent and transparent methods used to search and select studies, perform analyses, and assess the risk of bias and certainty of evidence. In all instances, these methods were prespecified before the commencement of the review. We judged 10 of 12 non-Cochrane reviews as critically low quality, with most included reviews failing to satisfy all or most of the critical AMSTAR 2 criteria. Notably, only one non-Cochrane review (Orhurhu 2019) was judged to fully satisfy item 2 - "Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?". Failure to adhere to a prospectively developed protocol increases the risk of bias in the review (Shea 2017). That Cochrane reviews had better AMSTAR 2 ratings than non-Cochrane reviews is unremarkable considering Cochrane reviews have been demonstrated to have higher methodological rigour and more complete reporting than non-Cochrane reviews (Dosenovic 2018; Goldkuhle 2018; Page 2016). The low quality of the non-Cochrane reviews was striking and represents a body of evidence synthesis of limited utility for guiding CRPS care. The suboptimal review methods and reporting compound the already substantial limitations with the quality of the primary trial evidence in CRPS.

The included reviews assessed the risk of bias or methodological quality of included trials using a range of different assessment tools, limiting our ability to make comparative statements on individual domains across trials. The Cochrane ROB tool (Higgins 2011) was used in three of the five Cochrane reviews, but in only four of the seven non-Cochrane reviews published since its advent. Critically, three non-Cochrane reviews failed to conduct any assessment of risk of bias or methodological quality. We made two important observations regarding the risk of bias judgements using the Cochrane ROB tool across Cochrane and non-Cochrane reviews. First, the use of non-Cochrane risk of bias or methodological quality tools may have resulted in inappropriately positive quality ratings. For example, Cossins 2013 rated two small rTMS trials (Picarelli 2010; Pleger 2004) as 'high' quality using a 15-item methodological quality checklist (de Vet 1997), whereas the same two studies were rated at high overall risk of bias in a Cochrane review (O'Connell 2018). Second, when the Cochrane ROB tool was used in non-Cochrane reviews, we were not confident that it was applied appropriately. For example, Smart 2022 judged Bilgili 2016 at high risk of bias for random sequence allocation and blinding domains, whereas Duong 2018 judged Bilgili 2016 at low risk of bias for the same domains. While we only reported the results of Bilgili 2016 using data extracted from Smart 2022, it is possible that these inconsistencies were applied throughout Duong 2018, a review which contributed substantial data to this overview.

Use of the GRADE approach to assess the certainty of evidence was high for Cochrane reviews (four of five), but very low for non-Cochrane reviews (one of 12). This may in part be explained by the publication of several reviews before the advent of the GRADE system. We attempted to mitigate this issue by conducting additional GRADE assessments for reviews where they were missing. Across this overview, the highest certainty of evidence for any comparison was moderate, with the majority of comparisons judged as very low.

### Potential biases in the overview process

We considered several biases during the overview processes and attempted to reduce them in several ways. This overview was conducted according to a published protocol (O'Connell 2011), and we have highlighted differences between the current version, previous version and published protocol of this overview. We used a comprehensive search strategy which was designed and implemented under expert guidance by the Cochrane Pain, Palliative and Supportive Care Review Group. While we have attempted to identify all eligible reviews using a comprehensive search strategy, it remains possible that we may have missed some key literature.

Two authors independently assessed the reviews for inclusion, extracted data and conducted GRADE and AMSTAR 2 assessments, resolving disagreements through recourse to a third reviewer, where necessary. As two of the included Cochrane reviews were authored by members of this overview team (O'Connell 2016: NOC, BMW; Smart 2022: KMS, MCF, BMW, NOC), there may have been a risk of potential bias with review and appraisal of this work. We were unable to reallocate all extraction tasks to members who were not authors on the original reviews, however no authors conducted AMSTAR 2 quality assessments for their own reviews.

Our application of GRADE judgements to comparisons where they were missing introduces an element of subjective judgement. It

was found to be particularly difficult because judgements were informed by data reported in the included reviews rather than the original studies, and because reviews assessed and reported study risk of bias or quality in different ways. We have tried to be consistent in our judgements across all comparisons but it should be recognised that these judgements are open to interpretation. The decision to downgrade twice for imprecision based on a sample size of less than 50 participants per arm may appear to be overly punitive. However, this is based on the observation that studies of this size are potentially more biased than those with 50 to 200 participants, which themselves are at risk of bias (Moore 2010).

In the current version of this overview, we did not reconduct analyses using trial report data where we identified inconsistencies or where reporting of effects was poor. While we acknowledge that doing this may have improved the accuracy of effect estimates, we are confident that such analyses would not have meaningfully changed any of the overview's conclusions.

### Agreements and disagreements with other studies or reviews

We did not identify any published overviews of all interventions for treating pain and disability in adults with CRPS. The most up-to-date systematic review of all interventions for CRPS (Duong 2018) concluded that there is supporting evidence for bisphosphonates and short courses of oral steroids, and emerging evidence for a range of medical interventions, most notably ketamine, intravenous immunoglobulin, intrathecal administration of clonidine, adenosine and baclofen, and dorsal root ganglion stimulation, although the review authors reported that further confirmatory RCTs were warranted.

Our conclusions for the efficacy of bisphosphonates largely concur with those of Duong 2018, however, given the small number of total participants and significant heterogeneity in the included analysis from Chevreau 2017, we have graded this evidence as low certainty. Appropriate use of more stringent criteria to assess serious study limitations, such as the Cochrane ROB tool, may have downgraded the certainty of evidence for this comparison to very low. We note that the observed standardised mean difference for the pooled effect (-2.6) is considerably larger than effect sizes commonly seen in chronic pain trials and, as such, should be interpreted with caution. Accordingly, we would suggest that while the efficacy of bisphosphonates is promising according to these data, the current evidence is uncertain and requires further investigation. It is noteworthy that a series of unpublished industry-sponsored bisphosphonate trials (NCT02504008; NCT03530345; NCT03560986) have been terminated early for futility.

Our conclusion for oral steroids differs to that of Duong 2018, likely because their conclusion was partly based on positive effects on composite CRPS symptom scores rather than only specific pain or disability scales. Our overview only identified very low-certainty evidence of no effect of oral prednisone compared with placebo (Lukovic 2006), and very low-certainty evidence that continuing oral prednisolone therapy results in greater pain reductions than withdrawing oral prednisolone (Kalita 2016).

For ketamine, we found very low-certainty evidence of clinically important effects compared with placebo at post-intervention, but not short-term follow-up. Using updated GRADE criteria, we downgraded the certainty of evidence for this comparison from the

previous version of this overview. It is remarkable that, despite no new published RCT evidence since 2009, CRPS has been reported as the most common indication for ketamine in pain clinics (Mangnus 2022b). That this widespread practice may have been largely informed by two RCTs with a combined 79 participants is alarming. Further RCTs are urgently needed to resolve uncertainties surrounding ketamine's medium- to long-term benefits, as well as efforts to improve active surveillance to collect ongoing safety data given the unknown harms of repeated dosing (Short 2018).

Since publication of Duong 2018, the promising effects of intravenous immunoglobulin have been tested in a large placebo-controlled RCT of 111 participants with longstanding CRPS (Goebel 2017). The observed benefits in Goebel 2010 were not replicated, with no differences found between immunoglobulin and placebo. These findings demonstrate the importance of replication studies and emphasise the inability of small exploratory trials to provide reliable evidence of efficacy.

In contrast to Duong 2018, we found no evidence of promise for intrathecal administration of clonidine, adenosine or baclofen. We did not identify placebo-controlled comparisons for these agents and based our conclusions on two comparative effectiveness trials (Rauck 2015; Van der Plas 2011). There was very low-certainty evidence of little to no between-group differences on pain intensity. We propose that a higher level of evidence is required to warrant further investigation and other interventions should be prioritised for future research.

Based on evidence from both their review and the previous version (Tran 2010), Duong 2018 concluded that there is no strong evidence to support the use of a range of pharmacological interventions including NSAIDs, magnesium, botulinum toxin A, lenalidomide, isosorbide dinitrate, mannitol, tadalafil, sarpogrelate, and gabapentin; and no evidence to support the use of IVRB using guanethidine, reserpine, droperidol, ketanserin, atropine, lidocaine-methylprednisolone, or ketorolac. Because most of the evidence for these interventions in this overview was derived from these reviews, our conclusions are broadly in agreement.

Duong 2018 concluded that dorsal root ganglion stimulation (DRGS) holds promise for refractory CRPS and recommended further confirmatory trials to validate its benefits. This conclusion was based on improvements in a composite efficacy and safety outcome compared with conventional spinal cord stimulation. Separate pain intensity scores were not reported and, as such, we cannot make comparisons for this outcome. While improvements in quality of life were observed at long-term follow-up, we found the certainty in evidence to be very low, and emphasise the difficulty of interpreting these positive effects in the absence of placebo-controlled trials. It is notable that a Cochrane review (O'Connell 2021) identified no trials testing DRGS against placebo in any chronic pain condition.

We found no up-to-date systematic reviews focusing on specific rehabilitation or physiotherapy interventions for CRPS with which to draw comparisons. A 2017 review of mirror therapy and graded motor imagery for CRPS (Méndez-Rebolledo 2017) reported that, while both interventions demonstrated consistent reductions in pain intensity and disability in CRPS I, the evidence was limited, owing primarily to small sample sizes and clinical heterogeneity. The review concluded that there is insufficient

evidence to recommend the use of these therapies over other CRPS I treatments. We would broadly concur with these conclusions and recommend that further trials be conducted.

## AUTHORS' CONCLUSIONS

### Implications for practice

#### For adults with CRPS

The evidence regarding the effectiveness of most interventions used to treat pain and disability in CRPS is very uncertain.

We found low-certainty evidence that, on average, treatment with bisphosphonates may reduce pain intensity compared with placebo, but is probably associated with an increased risk of experiencing an adverse effect.

We found moderate-certainty evidence that, on average, blocking the activity of the sympathetic nerves using lidocaine anaesthetic probably does not reduce pain intensity more than a placebo intervention, and low-certainty evidence that it may not be more effective than ultrasound.

We also found that other commonly used treatments such as ketamine infusions, spinal cord stimulation, graded motor imagery and mirror therapy may reduce pain intensity more than placebo or other active controls, however the evidence is very uncertain.

While there is a lack of evidence for adverse events, the risk of harm likely varies between invasive, drug and non-drug treatments and may be an important consideration to guide the choice of management.

#### For clinicians

There is insufficient high-certainty evidence on which to base comprehensive clinical guidance on the management of CRPS. Current non-Cochrane systematic reviews are unlikely to provide an unbiased representation of the available RCT evidence.

We found moderate- or low-certainty evidence for only two placebo-controlled comparisons:

- There was low-certainty evidence bisphosphonates may reduce pain intensity post-intervention, and moderate-certainty evidence that they are probably associated with increased adverse events of any nature. The included studies used a range of bisphosphonates with different routes of administration, and were primarily used in early onset CRPS I. As such, it is unclear whether the observed effects are likely to apply to long-standing CRPS, or CRPS with associated neural tissue injury. Further investigations of this medicine class are warranted.
- There was moderate-certainty evidence that lidocaine local anaesthetic sympathetic blockade probably does not reduce pain intensity compared with placebo.

We found only low-certainty evidence for three effectiveness comparisons:

- compared with oral N-acetylcysteine, topical DMSO may not reduce pain intensity.
- compared with ultrasound of the stellate ganglion, lidocaine stellate ganglion may not reduce pain intensity.

- compared with continuous bupivacaine stellate ganglion block, continuous brachial plexus block may reduce pain intensity.

While there was evidence of efficacy or effectiveness for routinely used interventions for CRPS such as intravenous ketamine, spinal cord stimulation, graded motor imagery and mirror therapy, the very low-certainty of the evidence suggests that the true effects of these interventions are likely to be substantially different from the estimates of effect. These results should be interpreted with caution and do not reliably aid clinical decision-making. We did not identify any RCT evidence for commonly used pharmacological interventions such as tricyclic antidepressants or opioids.

While adverse event data are lacking for most included interventions, consideration of the probable risk of treatment-related harms may be important for guiding patient management. Based on findings from this overview, managing CRPS using an evidence-based approach will remain difficult until further larger, well-conducted trials are undertaken.

### For policy-makers and funders

The available evidence relating to treatments for CRPS is very uncertain. Policy and funding decisions should not be made on the basis of findings from current non-Cochrane reviews due to their low methodological quality. There is insufficient evidence to support or refute the use of the majority of routinely used interventions for pain intensity and disability in CRPS. Funders might prioritise CRPS research calls that enable consortia of researchers to leverage funding for high-quality clinical trials that aim to meaningfully resolve key clinical uncertainties. Until such research is undertaken, clinical guidelines for the treatment of CRPS will continue to be informed largely by consensus.

### Implications for research

#### Design of future systematic reviews

There is a clear need to improve the methodological quality of systematic reviews of treatments for CRPS. In planning for future reviews, authors should follow methodological guidance for systematic reviews outlined in the Cochrane Handbook (Higgins 2021). Careful consideration of the review Population, Intervention, Comparison(s), Outcome and Time (PICOT) is required when formulating the review question. Rather than limiting the scope of a review to a single CRPS subtype, authors should aim to include evidence on all CRPS subtypes, and report results separately. This will ensure no important evidence is excluded. In order to minimise duplication of reviews and reporting bias, methods should be established in a protocol prior to the conduct of the review and registered on open databases such as PROSPERO (Cashin 2021). To facilitate transparent, complete and accurate reporting of what was done, reviews should adhere to the PRISMA reporting guideline (Page 2021). Authors should clearly describe the included interventions in accordance with published guidance (Hoffmann 2017) in order to improve the usability of the review by clinicians, patients and policy makers.

#### Design of randomised trials

We have identified that there is very low-certainty evidence for most interventions used to treat pain and disability in CRPS. It is unlikely that further small, short-term studies testing poorly-defined interventions will meaningfully improve this uncertainty. There is an urgent need for adequately powered, high-quality

randomised controlled trials, tested over clinically-relevant time frames. There are many challenges to addressing this problem. Given the relatively low incidence of CRPS, it remains difficult to recruit adequate numbers into clinical trials. The best chance of solving this issue may be through multicentre, international collaborative research projects which recruit from much larger clinical populations. The use of telehealth trials could facilitate this. Recruitment targets may be more easily met through alterations to trial design parameters (Parmar 2016) and Bayesian approaches to increase statistical power (Partington 2022), and efficiency could be maximised by testing two or more interventions in a single factorial trial (Kahan 2022).

Future trials should use established diagnostic criteria (Harden 2010) and specify the type and aetiology of CRPS under investigation (Goebel 2021). Comprehensive reporting of participant characteristics, including those that stratify health opportunities and outcomes (O'Neill 2014), will help to assess the generalisability of findings. Trial interventions must be carefully selected based on major clinical uncertainty or rigorous pilot research. There is a critical need for industry-independent placebo-controlled replication trials of intravenous ketamine and bisphosphonates, and trials of routinely used pharmacological interventions such as tricyclic antidepressants and opioids. Trials testing pragmatic, multimodal models of functional restoration, such as those endorsed by clinical guidelines (Bruehl 2022), against minimal or no care should be also prioritised. Trialists should consider optimal strategies for reporting pain in clinical trials (Busse 2015) and measure outcomes specified in the core set for CRPS (Grieve 2017). There is also a clear need to improve the measurements and reporting of adverse events in the field. Trial reports should fully adhere to CONSORT guidance (Schulz 2010) and interventions should be described in sufficient detail to allow replication by using the TIDIER guidelines (Hoffmann 2014).

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## Editorial and peer-reviewer contributions

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The following people conducted the editorial process for this article:

- Sign-off Editor (final editorial decision): Prof Christopher Eccleston, Centre of Pain Research, University of Bath, Bath, UK
- Contact Editor (editorial guidance): Associate Professor McKenzie Ferguson, PaPaS Editor, Southern Illinois University Edwardsville, USA
- Managing Editor (selected peer reviewers, collated peer-reviewer comments, provided editorial guidance to authors, edited the article): Jessica Thomas, Anna Erskine (Oxford University Hospitals (OUH) NHS Foundation Trust, Oxford, UK)
- Assistant Managing Editor (conducted editorial checks and supported editorial team): Kerry Harding (Oxford University Hospitals (OUH) NHS Foundation Trust, Oxford, UK)
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## REFERENCES

### References to included reviews

#### Challapalli 2005

Challapalli V, Tremont-Lukats I, McNicol ED, Lau J, Carr DB. Systemic administration of local anesthetic agents to relieve neuropathic pain. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No: CD003345. [DOI: [10.1002/14651858.CD003345.pub2](https://doi.org/10.1002/14651858.CD003345.pub2)]

#### Chauvineau 2005

Chauvineau V, Codine P, Herisson C, Pellas F, Pelissier J. What is the place of biphosphonates in the treatment of complex regional pain syndrome I? [Quelle est la place des biphosphonates dans le traitement de l'algodystrophie sympathique réflexe? Analyse critique de la littérature]. *Annales de Réadaptation et de Médecine Physique* 2005;**48**(3):150-7. [DOI: [10.1016/j.annrmp.2004.11.004](https://doi.org/10.1016/j.annrmp.2004.11.004)]

#### Chevreau 2017

Chevreau M, Romand X, Gaudin P, Juvin R, Baillet A. Bisphosphonates for treatment of complex regional pain syndrome type 1: a systematic literature review and meta-analysis of randomized controlled trials versus placebo. *Joint Bone Spine* 2017;**84**(4):393-9. [DOI: [10.1016/j.jbspin.2017.03.009](https://doi.org/10.1016/j.jbspin.2017.03.009)]

#### Cossins 2013

Cossins L, Okell RW, Cameron H, Simpson B, Poole HM, Goebel A. Treatment of complex regional pain syndrome in adults: a systematic review of randomized controlled trials published from June 2000 to February 2012. *European Journal of Pain* 2013;**17**(2):158-73. [DOI: [10.1002/j.1532-2149.2012.00217.x](https://doi.org/10.1002/j.1532-2149.2012.00217.x)]

#### Duong 2018

Duong S, Bravo D, Todd KJ, Finlayson RJ, Tran DQ. Treatment of complex regional pain syndrome: an updated systematic review and narrative synthesis. *Canadian Journal of Anesthesia* 2018;**65**(6):658-84. [DOI: [10.1007/s12630-018-1091-5](https://doi.org/10.1007/s12630-018-1091-5)]

#### Fassio 2022

Fassio A, Mantovani A, Gatti D, Rossini M, Viapiana O, Gavioli I, et al. Pharmacological treatment in adult patients with CRPS-I: a systematic review and meta-analysis of randomized controlled trials. *Rheumatology* 1 February 2022 [Epub ahead of print]. [DOI: [10.1093/rheumatology/keac060](https://doi.org/10.1093/rheumatology/keac060)]

#### Fischer 2010

Fischer SGL, Zuurmond WWA, Birklein F, Loer SA, Perez RSGM. Anti-inflammatory treatment of complex regional pain syndrome. *Pain* 2010;**151**(2):251-6. [DOI: [10.1016/j.pain.2010.07.020](https://doi.org/10.1016/j.pain.2010.07.020)]

#### Forouzanfar 2002

Forouzanfar T, Koke AJ, van Kleef M, Weber WE. Treatment of complex regional pain syndrome type I. *European Journal of Pain* 2002;**6**(2):105-22. [DOI: [10.1053/eujp.2001.0304](https://doi.org/10.1053/eujp.2001.0304)]

#### Moore 2014

Moore RA, Wiffen PJ, Derry S, Rice ASC. Gabapentin for chronic neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2014, Issue 4. Art. No: CD007938. [DOI: [10.1002/14651858.CD007938.pub3](https://doi.org/10.1002/14651858.CD007938.pub3)]

#### O'Connell 2016

O'Connell NE, Wand BM, Gibson W, Carr DB, Birklein F, Stanton TR. Local anaesthetic sympathetic blockade for complex regional pain syndrome. *Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No: CD004598. [DOI: [10.1002/14651858.CD004598.pub4](https://doi.org/10.1002/14651858.CD004598.pub4)]

#### Orhurhu 2019

Orhurhu V, Orhurhu MS, Bhatia A, Cohen SP. Ketamine infusions for chronic pain: a systematic review and meta-analysis of randomized controlled trials. *Anesthesia & Analgesia* 2019;**129**(1):241-54. [DOI: [10.1213/ANE.0000000000004185](https://doi.org/10.1213/ANE.0000000000004185)]

#### Peng 2018

Peng L, Zhang C, Zhou L, Zuo HX, He XK, Niu YM. Traditional manual acupuncture combined with rehabilitation therapy for shoulder hand syndrome after stroke within the Chinese healthcare system: a systematic review and meta-analysis. *Clinical Rehabilitation* 2018;**32**(4):429-39. [DOI: [10.1177/0269215517729528](https://doi.org/10.1177/0269215517729528)]

#### Smart 2022

Smart KM, Ferraro MC, Wand BM, O'Connell NE. Physiotherapy for pain and disability in adults with complex regional pain syndrome (CRPS) types I and II. *Cochrane Database of Systematic Reviews* 2022, Issue 5. Art. No: CD010853. [DOI: [10.1002/14651858.CD010853.pub3](https://doi.org/10.1002/14651858.CD010853.pub3)]

#### Smith 2005

Smith TO. How effective is physiotherapy in the treatment of complex regional pain syndrome type I? A review of the literature. *Musculoskeletal Care* 2005;**3**(4):181-200. [DOI: [10.1002/msc.9](https://doi.org/10.1002/msc.9)]

#### Straube 2013

Straube S, Derry S, Moore RA, Cole P. Cervico-thoracic or lumbar sympathectomy for neuropathic pain and complex regional pain syndrome. *Cochrane Database of Systematic Reviews* 2013, Issue 9. Art. No: CD002918. [DOI: [10.1002/14651858.CD002918.pub3](https://doi.org/10.1002/14651858.CD002918.pub3)]

#### Tran 2010

Tran DQH, Duong S, Bertini P, Finlayson R. Treatment of complex regional pain syndrome: a review of the evidence. *Canadian Journal of Anesthesia* 2010;**57**(2):149-66. [DOI: [10.1007/s12630-009-9237-0](https://doi.org/10.1007/s12630-009-9237-0)]

#### Xu 2016

Xu J, Yang J, Lin P, Rosenquist E, Cheng J. Intravenous therapies for complex regional pain syndrome: a systematic review. *Anesthesia & Analgesia* 2016;**122**(3):843-56. [DOI: [10.1213/ANE.0000000000000999](https://doi.org/10.1213/ANE.0000000000000999)]

## References to excluded reviews

### Aamir 2020

Aamir A, Girach A, Sarrigiannis PG, Hadjivassiliou M, Paladini A, Varrassi G, et al. Repetitive magnetic stimulation for the management of peripheral neuropathic pain: a systematic review. *Advances in Therapy* 2020;**37**(3):998-1012. [DOI: [10.1007/s12325-020-01231-2](https://doi.org/10.1007/s12325-020-01231-2)]

### Aiyer 2016

Aiyer R, Barkin RL, Bhatia A. Treatment of neuropathic pain with venlafaxine: a systematic review. *Pain Medicine* 2017;**18**(10):1999-2012. [DOI: [10.1093/pm/pnw261](https://doi.org/10.1093/pm/pnw261)]

### Aiyer 2018

Aiyer R, Mehta N, Gungor S, Gulati A. A systematic review of NMDA receptor antagonists for treatment of neuropathic pain in clinical practice. *Clinical Journal of Pain* 2018;**34**(5):450-67. [DOI: [10.1097/AJP.0000000000000547](https://doi.org/10.1097/AJP.0000000000000547)]

### Andreae 2015

Andreae MH, Carter GM, Shaparin N, Suslov K, Ellis RJ, Ware MA, et al. Inhaled cannabis for chronic neuropathic pain: a meta-analysis of individual patient data. *The Journal of Pain* 2015;**16**(12):1221-32. [DOI: [10.1016/j.jpain.2015.07.009](https://doi.org/10.1016/j.jpain.2015.07.009)]

### Azari 2012

Azari P, Lindsay DR, Briones D, Clarke C, Buchheit T, Pyati S. Efficacy and safety of ketamine in patients with complex regional pain syndrome: a systematic review. *CNS Drugs* 2012;**26**(3):215-28.

### Birse 2012

Birse F, Derry S, Moore RA. Phenytoin for neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 5. Art. No: CD009485. [DOI: [10.1002/14651858.CD009485.pub2](https://doi.org/10.1002/14651858.CD009485.pub2)]

### Boyчук 2015

Boyчук DG, Goddard G, Mauro G, Orellana MF. The effectiveness of cannabinoids in the management of chronic nonmalignant neuropathic pain: a systematic review. *Journal of Oral & Facial Pain and Headache* 2015;**29**(1):7-14.

### Boyd 2019

Boyd A, Bleakley C, Hurley DA, Gill C, Hannon-Fletcher M, Bell P, et al. Herbal medicinal products or preparations for neuropathic pain. *Cochrane Database of Systematic Reviews* 2019, Issue 4. Art. No: CD010528. [DOI: [10.1002/14651858.CD010528.pub4](https://doi.org/10.1002/14651858.CD010528.pub4)]

### Brookes 2017

Brookes ME, Eldabe S, Batterham A. Ziconotide monotherapy: a systematic review of randomised controlled trials. *Current Neuropharmacology* 2017;**15**(2):217-31. [DOI: [10.2174/1570159X14666160210142056](https://doi.org/10.2174/1570159X14666160210142056)]

### Brunner 2009

Brunner F, Schmid A, Kissling R, Held U, Bachmann LM. Bisphosphonates for the therapy of complex regional pain

syndrome I - systematic review. *European Journal of Pain* 2009;**13**(1):17-21. [DOI: [10.1016/j.ejpain.2008.03.005](https://doi.org/10.1016/j.ejpain.2008.03.005)]

### Buksnys 2020

Buksnys T, Armstrong N, Worthy G, Sabatschus I, Boesl I, Buchheister B, et al. Systematic review and network meta-analysis of the efficacy and safety of lidocaine 700 mg medicated plaster vs. pregabalin. *Current Medical Research and Opinion* 2020;**36**(1):101-15. [DOI: [10.1080/03007995.2019.1662687](https://doi.org/10.1080/03007995.2019.1662687)]

### Bussa 2015

Bussa M, Guttilla D, Lucia M, Mascaro A, Rinaldi S. Complex regional pain syndrome type I: a comprehensive review. *Acta Anaesthesiologica Scandinavica* 2015;**59**:685-97. [DOI: [10.1111/aas.12489](https://doi.org/10.1111/aas.12489)]

### Casale 2021

Casale R. Capsaicin 179-mg cutaneous patch in the treatment of post-surgical neuropathic pain: a scoping review of current evidence and place in therapy. *Expert Review of Neurotherapeutics* 2021;**21**(10):1147-58. [DOI: [10.1080/14737175.2021.1974842](https://doi.org/10.1080/14737175.2021.1974842)]

### Cepeda 2005

Cepeda MS, Carr D B, Lau J. Local anesthetic sympathetic blockade for complex regional pain syndrome. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No: CD004598. [DOI: [10.1002/14651858.CD004598.pub2](https://doi.org/10.1002/14651858.CD004598.pub2)]

### Chaparro 2012

Chaparro LE, Wiffen PJ, Moore RA, Gilron I. Combination pharmacotherapy for the treatment of neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 7. Art. No: CD008943. [DOI: [10.1002/14651858.CD008943.pub2](https://doi.org/10.1002/14651858.CD008943.pub2)]

### Collins 2010

Collins S, Sigtermans MJ, Dahan A, Zuurmond WW, Perez RS. NMDA receptor antagonists for the treatment of neuropathic pain. *Pain Medicine* 2010;**11**(11):1726-42. [DOI: [10.1111/j.1526-4637.2010.00981.x](https://doi.org/10.1111/j.1526-4637.2010.00981.x)]

### Connolly 2015

Connolly SB, Prager JP, Harden RN. A systematic review of ketamine for complex regional pain syndrome. *Pain Medicine* 2015;**16**(5):943-69. [DOI: [10.1111/pme.12675](https://doi.org/10.1111/pme.12675)]

### Cooper 2017

Cooper TE, Chen J, Wiffen PJ, Derry S, Carr DB, Aldington D, et al. Morphine for chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2017, Issue 5. Art. No: CD011669. [DOI: [10.1002/14651858.CD011669.pub2](https://doi.org/10.1002/14651858.CD011669.pub2)]

### Corrigan 2012

Corrigan R, Derry S, Wiffen PJ, Moore RA. Clonazepam for neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 5. Art. No: CD009486. [DOI: [10.1002/14651858.CD009486.pub2](https://doi.org/10.1002/14651858.CD009486.pub2)]

**Daly 2009**

Daly AE, Bialocerkowski A. Does evidence support physiotherapy management of adult Complex Regional Pain Syndrome Type One? A systematic review. *European Journal of Pain* 2009;**13**(4):339-53. [DOI: [10.1016/j.ejpain.2008.05.003](https://doi.org/10.1016/j.ejpain.2008.05.003)]

**David 2018**

David MC, Moraes AA, Costa ML, Franco CI. Transcranial direct current stimulation in the modulation of neuropathic pain: a systematic review. *Neurological Research* 2018;**40**(7):557-65. [DOI: [10.1080/01616412.2018.1453190](https://doi.org/10.1080/01616412.2018.1453190)]

**De Souza 2015**

De Souza NS, Martins AC, Bastos VH, Orsini M, Leite MA, Teixeira S, et al. Motor imagery and its effect on complex regional pain syndrome: an integrative review. *Neurology International* 2015;**7**(3):5962. [DOI: [10.4081/ni.2015.5962](https://doi.org/10.4081/ni.2015.5962)]

**Deer 2020**

Deer TR, Hunter CW, Mehta P, Sayed D, Grider JS, Lamer TJ, et al. A systematic literature review of dorsal root ganglion neurostimulation for the treatment of pain. *Pain Medicine* 2020;**21**(8):1581-9. [DOI: [10.1093/pm/pnaa005](https://doi.org/10.1093/pm/pnaa005)]

**Derry 2012a**

Derry S, Gill D, Phillips T, Moore RA. Milnacipran for neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 3. Art. No: CD008244. [DOI: [10.1002/14651858.CD008244.pub2](https://doi.org/10.1002/14651858.CD008244.pub2)]

**Derry 2012b**

Derry S, Moore RA. Topical capsaicin (low concentration) for chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 9. Art. No: CD010111. [DOI: [10.1002/14651858.CD010111](https://doi.org/10.1002/14651858.CD010111)]

**Derry 2013**

Derry S, Rice AS, Cole P, Tan T, Moore RA. Topical capsaicin (high concentration) for chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2013, Issue 2. Art. No: CD007393. [DOI: [10.1002/14651858.CD007393.pub3](https://doi.org/10.1002/14651858.CD007393.pub3)]

**Derry 2014**

Derry S, Wiffen PJ, Moore RA, Quinlan J. Topical lidocaine for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2014, Issue 7. Art. No: CD010958. [DOI: [10.1002/14651858.CD010958.pub2](https://doi.org/10.1002/14651858.CD010958.pub2)]

**Derry 2015a**

Derry S, Phillips T, Moore RA, Wiffen PJ. Milnacipran for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2015, Issue 7. Art. No: CD011789. [DOI: [10.1002/14651858.CD011789](https://doi.org/10.1002/14651858.CD011789)]

**Derry 2015b**

Derry S, Wiffen PJ, Aldington D, Moore RA. Nortriptyline for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2015, Issue 1. Art. No: CD011209. [DOI: [10.1002/14651858.CD011209.pub2](https://doi.org/10.1002/14651858.CD011209.pub2)]

**Derry 2016**

Derry S, Stannard C, Cole P, Wiffen PJ, Knaggs R, Aldington D, et al. Fentanyl for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 20176, Issue 10. Art. No: CD011605. [DOI: [10.1002/14651858.CD011605.pub2](https://doi.org/10.1002/14651858.CD011605.pub2)]

**Derry 2017b**

Derry S, Rice ASC, Cole P, Tan T, Moore RA. Topical capsaicin (high concentration) for chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2017, Issue 1. Art. No: CD007393. [DOI: [10.1002/14651858.CD007393.pub4](https://doi.org/10.1002/14651858.CD007393.pub4)]

**Derry 2019**

Derry S, Bell RF, Straube S, Wiffen PJ, Aldington D, Moore RA. Pregabalin for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2019, Issue 1. Art. No: CD007076. [DOI: [10.1002/14651858.CD007076.pub3](https://doi.org/10.1002/14651858.CD007076.pub3)]

**Di Stefano 2021**

Di Stefano G, Di Lionardo A, Di Pietro G, Cruccu G, Truini A. Pharmacotherapeutic options for managing neuropathic pain: a systematic review and meta-analysis. *Pain Research and Management* 2021;**2021**:1-13. [DOI: [10.1155/2021/6656863](https://doi.org/10.1155/2021/6656863)]

**Dirckx 2012**

Dirckx M, Stronks DL, Groeneweg G, Huygen FJ. Effect of immunomodulating medications in complex regional pain syndrome: a systematic review. *Clinical Journal of Pain* 2012;**28**(4):355-63. [DOI: [10.1097/AJP.0b013e31822efe30](https://doi.org/10.1097/AJP.0b013e31822efe30)]

**Duarte 2020**

Duarte RV, Nevitt S, McNicol E, Taylor RS, Buchser E, North RB, et al. Systematic review and meta-analysis of placebo/sham controlled randomised trials of spinal cord stimulation for neuropathic pain. *Pain* 2020;**161**(1):24-35. [DOI: [10.1097/j.pain.0000000000001689](https://doi.org/10.1097/j.pain.0000000000001689)]

**Duehmke 2017**

Duehmke RM, Derry S, Wiffen PJ, Bell RF, Aldington D, Moore RA. Tramadol for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2017, Issue 6. Art. No: CD003726. [DOI: [10.1002/14651858.CD003726.pub4](https://doi.org/10.1002/14651858.CD003726.pub4)]

**Dworkin 2013**

Dworkin RH, O'Connor AB, Kent J, Mackey SC, Raja SN, Stacey BR, et al. Interventional management of neuropathic pain: NeuPSIG recommendations. *Pain* 2013;**154**(11):2249-61. [DOI: [10.1016/j.pain.2013.06.004](https://doi.org/10.1016/j.pain.2013.06.004)]

**Dykukha 2021**

Dykukha I, Malessa R, Essner U, Überall MA. Nabiximols in chronic neuropathic pain: a meta-analysis of randomized placebo-controlled trials. *Pain Medicine* 2021;**22**(4):861-74. [DOI: [10.1093/pm/pnab050](https://doi.org/10.1093/pm/pnab050)]

**Eccleston 2015**

Eccleston C, Hearn L, de C Williams AC. Psychological therapies for the management of chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2015, Issue 10. Art. No: CD011259. [DOI: [10.1002/14651858.CD011259.pub2](https://doi.org/10.1002/14651858.CD011259.pub2)]

**Fabregat 2013**

Fabregat G, De Andrés J, Villanueva-Pérez VL, Asensio-Samper JM. Subcutaneous and perineural botulinum toxin type A for neuropathic pain: a descriptive review. *Clinical Journal of Pain* 2013;**29**(11):1006-12. [DOI: [10.1097/AJP.0b013e31827eafff](https://doi.org/10.1097/AJP.0b013e31827eafff)]

**Finnerup 2015**

Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurology* 2015;**14**(2):162-73. [DOI: [10.1016/S1474-4422\(14\)70251-0](https://doi.org/10.1016/S1474-4422(14)70251-0)]

**Galafassi 2021**

Galafassi GZ, de Aguiar PH, Simm RF, Franceschini PR, Prist Filho M, Pagura JR, et al. Neuromodulation for medically refractory neuropathic pain: spinal cord stimulation, deep brain stimulation, motor cortex stimulation, and posterior insula stimulation. *World Neurosurgery* 2021;**146**:246-60. [DOI: [10.1016/j.wneu.2020.11.048](https://doi.org/10.1016/j.wneu.2020.11.048)]

**Gallagher 2015**

Gallagher HC, Gallagher RM, Butler M, Buggy DJ, Henman MC. Venlafaxine for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2015, Issue 8. Art. No: CD011091. [DOI: [10.1002/14651858.CD011091.pub2](https://doi.org/10.1002/14651858.CD011091.pub2)]

**Gaskell 2014**

Gaskell H, Moore RA, Derry S, Stannard C. Oxycodone for neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2014, Issue 6. Art. No: CD010692. [DOI: [10.1002/14651858.CD010692.pub2](https://doi.org/10.1002/14651858.CD010692.pub2)]

**Gaskell 2016**

Gaskell H, Derry S, Stannard C, Moore RA. Oxycodone for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No: CD010692. [DOI: [10.1002/14651858.CD010692.pub3](https://doi.org/10.1002/14651858.CD010692.pub3)]

**Gibson 2017**

Gibson W, Wand BM, O'Connell NE. Transcutaneous electrical nerve stimulation (TENS) for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2017, Issue 9. Art. No: CD011976. [DOI: [10.1002/14651858.CD011976.pub2](https://doi.org/10.1002/14651858.CD011976.pub2)]

**Grabow 2003**

Grabow TS, Tella PK, Raja SN. Spinal cord stimulation for complex regional pain syndrome: an evidence-based medicine review of the literature. *Clinical Journal of Pain* 2003;**19**(6):371-83. [DOI: [10.1097/00002508-200311000-00005](https://doi.org/10.1097/00002508-200311000-00005)]

**Hearn 2012**

Hearn L, Derry S, Moore RA. Lacosamide for neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 2. Art. No: CD009318. [DOI: [10.1002/14651858.CD009318.pub2](https://doi.org/10.1002/14651858.CD009318.pub2)]

**Hearn 2014a**

Hearn L, Derry S, Phillips T, Moore RA, Wiffen PJ. Imipramine for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2014, Issue 5. Art. No: CD010769. [DOI: [10.1002/14651858.CD010769.pub2](https://doi.org/10.1002/14651858.CD010769.pub2)]

**Hearn 2014b**

Hearn L, Moore RA, Derry S, Wiffen PJ, Phillips T. Desipramine for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2014, Issue 9. Art. No: CD011003. [DOI: [10.1002/14651858.CD011003.pub2](https://doi.org/10.1002/14651858.CD011003.pub2)]

**Hoydonckx 2019**

Hoydonckx Y, Costanzi M, Bhatia A. A scoping review of novel spinal cord stimulation modes for complex regional pain syndrome. *Canadian Journal of Pain* 2019;**3**(1):33-48. [DOI: [10.1080/24740527.2019.1574536](https://doi.org/10.1080/24740527.2019.1574536)]

**Iskedjian 2007**

Iskedjian M, Bereza B, Gordon A, Piwko C, Einarson TR. Meta-analysis of cannabis based treatments for neuropathic and multiple sclerosis-related pain. *Current Medical Research and Opinion* 2007;**23**(1):17-24. [DOI: [10.1185/030079906X158066](https://doi.org/10.1185/030079906X158066)]

**Jadad 1995**

Jadad AR, Carroll D, Glynn CJ, McQuay HJ. Intravenous regional sympathetic blockade for pain relief in reflex sympathetic dystrophy: a systematic review and a randomized, double-blind crossover study. *Journal of Pain and Symptom Management* 1995;**10**(1):13-20. [DOI: [10.1016/0885-3924\(94\)00064-R](https://doi.org/10.1016/0885-3924(94)00064-R)]

**Jin 2015**

Jin Y, Xing G, Li G, Wang A, Feng, Tang Q, et al. High frequency repetitive transcranial magnetic stimulation therapy for chronic neuropathic pain: a meta-analysis. *Pain Physician* 2015;**18**(6):E1029-46.

**Ju 2017**

Ju ZY, Wang K, Cui HS, Yao Y, Liu SM, Zhou J, et al. Acupuncture for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2017, Issue 2. Art. No: CD012057. [DOI: [10.1002/14651858.CD012057.pub2](https://doi.org/10.1002/14651858.CD012057.pub2)]

**Julian 2020**

Julian T, Syeed R, Glasgow N, Angelopoulou E, Zis P. B12 as a treatment for peripheral neuropathic pain: a systematic review. *Nutrients* 2020;**12**(8):2221. [DOI: [10.3390/nu12082221](https://doi.org/10.3390/nu12082221)]

**Jupudi 2021**

Jupudi R, Meeker TJ, Guduru A, Fleetwood MN, Tulloch IK, Lenz FA, et al. Systematic review and quantitative meta-analysis demonstrates analgesic effect of excitatory motor cortex non-invasive brain stimulation, which is inflated by small study and publication bias. *The Journal of Pain* 2021;**22**(5):587. [DOI: [10.1016/j.jpain.2021.03.039](https://doi.org/10.1016/j.jpain.2021.03.039)]

**Kapustin 2020**

Kapustin D, Bhatia A, McParland A, Trivedi A, Davidson A, Brull R, et al. Evaluating the impact of gabapentinoids on sleep health in patients with chronic neuropathic pain: a systematic review and meta-analysis. *Pain* 2020;**161**(3):476-90. [DOI: [10.1097/j.pain.0000000000001743](https://doi.org/10.1097/j.pain.0000000000001743)]

**Knezevic 2020**

Knezevic NN, Jovanovic F, Candido KD, Knezevic I. Oral pharmacotherapeutics for the management of peripheral neuropathic pain conditions - a review of clinical trials. *Expert*

*Opinion on Pharmacotherapy* 2020;**21**(18):2231-48. [DOI: [10.1080/14656566.2020.1801635](https://doi.org/10.1080/14656566.2020.1801635)]

#### Li 2015b

Li S, Li Q, Li Y, Li L, Tian H, Sun X. Acetyl-L-carnitine in the treatment of peripheral neuropathic pain: a systematic review and meta-analysis of randomized controlled trials. *PLoS One* 2015;**10**(3):e0119479. [DOI: [10.1371/journal.pone.0119479](https://doi.org/10.1371/journal.pone.0119479)]

#### Liao 2017

Liao CD, Tsao JY, Chen HC, Liou TH. Efficacy of stellate ganglion blockade applied with light irradiation: a systemic review and meta-analysis. *American Journal of Physical Medicine & Rehabilitation* 2017;**96**(6):e97-110. [DOI: [10.1097/PHM.0000000000000675](https://doi.org/10.1097/PHM.0000000000000675)]

#### Lin 2012

Lin H, Ma, TM. A meta analysis on acupuncture treatment of shoulder-hand syndrome [针灸疗法治疗肩手综合征疗效的]. *Acupuncture Research* 2012;**37**(1):77-82. [DOI: [10.13702/j.1000-0607.2012.01.003](https://doi.org/10.13702/j.1000-0607.2012.01.003)]

#### Lu 2009

Lu Y-M Fu L-X Mu J Xu H-J Qi Y. Acupuncture for post stroke shoulder hand syndrome: A systematic review. *Chinese Journal of Evidence-Based Medicine* 2009;**9**(9):976-8.

#### Lunn 2014

Lunn MP, Hughes RA, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. *Cochrane Database of Systematic Reviews* 2014, Issue 1. Art. No: CD007115. [DOI: [10.1002/14651858.CD007115.pub3](https://doi.org/10.1002/14651858.CD007115.pub3)]

#### Mailis-Gagnon 2004

Mailis-Gagnon A, Furlan AD, Sandoval JA, Taylor R. Spinal cord stimulation for chronic pain. *Cochrane Database of Systematic Reviews* 2004, Issue 3. Art. No: CD003783. [DOI: [10.1002/14651858.CD003783.pub2](https://doi.org/10.1002/14651858.CD003783.pub2)]

#### Markman 2017

Markman JD, Jensen TS, Semel D, Li C, Parsons B, Behar R, et al. Effects of pregabalin in patients with neuropathic pain previously treated with gabapentin: a pooled analysis of parallel-group, randomized, placebo-controlled clinical trials. *Pain Practice* 2017;**17**(6):718-28. [DOI: [10.1111/papr.12516](https://doi.org/10.1111/papr.12516)]

#### Martins de Andrade 2016

Martins de Andrade AL, Bossini PS, Parizotto NA. Use of low level laser therapy to control neuropathic pain: a systematic review. *Journal of Photochemistry and Photobiology* 2016;**164**:36-42. [DOI: [10.1016/j.jphotobiol.2016.08.025](https://doi.org/10.1016/j.jphotobiol.2016.08.025)]

#### Matuschek 2017

Matuschek K, Faißt A. The effectiveness of mirror therapy in reducing pain in clients with complex regional pain syndrome (CRPS) type I - a systematic review. [Die wirksamkeit der spiegeltherapie in bezug auf die schmerzreduktion bei klienten mit komplexem regionalem schmerzsyndrom (CRPS) typ I - ein systematischer review]. *Ergoscience* 2017;**12**(1):11-21. [DOI: [10.2443/skv-s-2017-54020170102](https://doi.org/10.2443/skv-s-2017-54020170102)]

#### McNicol 2013

McNicol ED, Midbari A, Eisenberg E. Opioids for neuropathic pain. *Cochrane Database of Systematic Reviews* 2013, Issue 8. Art. No: CD006146. [DOI: [10.1002/14651858.CD006146.pub2](https://doi.org/10.1002/14651858.CD006146.pub2)]

#### McNicol 2017

McNicol ED, Ferguson MC, Schumann R. Methadone for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2017, Issue 5. Art. No: CD012499. [DOI: [10.1002/14651858.CD012499.pub2](https://doi.org/10.1002/14651858.CD012499.pub2)]

#### McParland 2021

McParland A, Daniel K, Bhatia A, Clarke H, Aditya T, Brull R, et al. Cannabinoids and sleep health in patients with chronic neuropathic pain: A systematic review and meta-analysis. *Sleep* 2021;**44**(Supplement 2):A271-72. [DOI: [10.1093/sleep/zsab072.693](https://doi.org/10.1093/sleep/zsab072.693)]

#### Meng 2017

Meng H, Johnston B, Englesakis M, Moulin DE, Bhatia A. Selective cannabinoids for chronic neuropathic pain: a systematic review and meta-analysis. *Anesthesia & Analgesia* 2017;**125**(5):1638-52. [DOI: [10.1213/ANE.0000000000002110](https://doi.org/10.1213/ANE.0000000000002110)]

#### Mohiuddin 2021

Mohiuddin M, Pivetta B, Gilron I, Khan JS. Efficacy and safety of N-acetylcysteine for the management of chronic pain in adults: a systematic review & meta-analysis. *Pain Medicine* 2021;**22**(12):2896-907. [DOI: [10.1093/pm/pnab042](https://doi.org/10.1093/pm/pnab042)]

#### Moisset 2020

Moisset X, Bouhassira D, Couturier JA, Alchaar H, Conradi S, Delmotte MH, et al. Pharmacological and non-pharmacological treatments for neuropathic pain: systematic review and French recommendations. *Revue Neurologique* 2020;**176**(5):325-52. [DOI: [10.1016/j.neurol.2020.01.361](https://doi.org/10.1016/j.neurol.2020.01.361)]

#### Moore 2011

Moore RA, Wiffen PJ, Derry S, McQuay HJ. Gabapentin for chronic neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2011, Issue 3. Art. No: CD009183. [DOI: [10.1002/14651858.CD009183.pub2](https://doi.org/10.1002/14651858.CD009183.pub2)]

#### Moore 2012

Moore RA, Derry S, Aldington D, Cole P. Amitriptyline for neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 12. Art. No: CD008242. [DOI: [10.1002/14651858.CD008242.pub2](https://doi.org/10.1002/14651858.CD008242.pub2)]

#### Moore 2015a

Moore RA, Chi CC, Wiffen PJ, Derry S, Rice ASC. Oral nonsteroidal anti-inflammatory drugs for neuropathic pain. *Cochrane Database of Systematic Reviews* 2015, Issue 10. Art. No: CD010902. [DOI: [10.1002/14651858.CD010902.pub2](https://doi.org/10.1002/14651858.CD010902.pub2)]

#### Moore 2015b

Moore RA, Wiffen PJ, Derry S, Lunn MP. Zonisamide for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2015, Issue 1. Art. No: CD011241. [DOI: [10.1002/14651858.CD011241.pub2](https://doi.org/10.1002/14651858.CD011241.pub2)]

**Moore 2015c**

Moore RA, Derry S, Aldington D, Cole P, Wiffen PJ. Amitriptyline for neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2015, Issue 7. Art. No: CD008242. [DOI: [10.1002/14651858.CD008242.pub3](https://doi.org/10.1002/14651858.CD008242.pub3)]

**Mu 2017**

Mu A, Weinberg E, Moulin DE, Clarke H. Pharmacologic management of chronic neuropathic pain: review of the Canadian Pain Society consensus statement. *Canadian Family Physician* 2017;**63**(11):844-52.

**Méndez-Rebolledo 2017**

Méndez-Rebolledo G, Gatica-Rojas V, Torres-Cueco R, Albornoz-Verdugo M, Guzmán-Muñoz E. Update on the effects of graded motor imagery and mirror therapy on complex regional pain syndrome type 1: a systematic review. *Journal of Back and Musculoskeletal Rehabilitation* 2017;**30**(3):441-9. [DOI: [10.3233/BMR-150500](https://doi.org/10.3233/BMR-150500)]

**Mücke 2018**

Mücke M, Phillips T, Radbruch L, Petzke F, Häuser W. Cannabis-based medicines for chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2018, Issue 3. Art. No: CD012182. [DOI: [10.1002/14651858.CD012182.pub2](https://doi.org/10.1002/14651858.CD012182.pub2)]

**Nagpal 2021**

Nagpal A, Clements N, Duszynski B, Boies B. The effectiveness of dorsal root ganglion neurostimulation for the treatment of chronic pelvic pain and chronic neuropathic pain of the lower extremity: a comprehensive review of the published data. *Pain Medicine* 2021;**22**(1):49-59. [DOI: [10.1093/pm/pnaa369](https://doi.org/10.1093/pm/pnaa369)]

**Nardone 2018**

Nardone R, Brigo F, Höller Y, Sebastianelli L, Versace V, Saltuari L, et al. Transcranial magnetic stimulation studies in complex regional pain syndrome type I: a review. *Acta Neurologica Scandinavica* 2018;**137**(2):158-64. [DOI: [10.1111/ane.12852](https://doi.org/10.1111/ane.12852)]

**Ney 2013**

Ney JP, Devine EB, Watanabe JH, Sullivan SD. Comparative efficacy of oral pharmaceuticals for the treatment of chronic peripheral neuropathic pain: meta-analysis and indirect treatment comparisons. *Pain Medicine* 2013;**14**(5):706-19. [DOI: [10.1111/pme.12091](https://doi.org/10.1111/pme.12091)]

**O'Connell 2010**

O'Connell NE, Wand BM, Marston L, Spencer S, DeSouza LH. Non-invasive brain stimulation techniques for chronic pain. *Cochrane Database of Systematic Reviews* 2010, Issue 9. Art. No: CD008208. [DOI: [10.1002/14651858.CD008208.pub2](https://doi.org/10.1002/14651858.CD008208.pub2)]

**Oh 2015**

Oh HM, Chung ME. Botulinum toxin for neuropathic pain: a review of the literature. *Toxins* 2015;**7**(8):3127-54. [DOI: [10.3390/toxins7083127](https://doi.org/10.3390/toxins7083127)]

**Packham 2018**

Packham T, Holly J. Mechanism-specific rehabilitation management of complex regional pain syndrome: proposed

recommendations from evidence synthesis. *Journal of Hand Therapy* 2018;**31**(2):238-49. [DOI: [10.1016/j.jht.2018.01.007](https://doi.org/10.1016/j.jht.2018.01.007)]

**Pearl 2020**

Pearl K, Hadas O. Effectiveness of sensory therapy in reducing symptoms of complex regional pain syndrome: systematic review [עילות של טיפול תחושת בהפחתת סימפטומים של סקירה] שיטתית: Complex Regional Pain Syndrome]. *Journal of the Israeli Physical Therapy Society* 2020;**22**(1):48-64.

**Perez 2001**

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. *Journal of Pain and Symptom Management* 2001;**21**(6):511-26. [DOI: [10.1016/S0885-3924\(01\)00282-2](https://doi.org/10.1016/S0885-3924(01)00282-2)]

**Petzke 2016**

Petzke F, Enax-Krumova EK, Häuser W. Efficacy, tolerability and safety of cannabinoids for chronic neuropathic pain: a systematic review of randomized controlled studies [Wirksamkeit, verträglichkeit und sicherheit von cannabinoiden bei neuropathischen schmerzsyndromen]. *Der Schmerz* 2016;**30**(1):62-88. [DOI: [10.1007/s00482-015-0089-y](https://doi.org/10.1007/s00482-015-0089-y)]

**Roche Bueno 2020**

Roche Bueno JC. Meta-analysis and P-curve analysis of the efficacy of venlafaxine versus placebo in the treatment of neuropathic pain [Meta-análisis y análisis de curva- p sobre la eficacia de venlafaxina frente a placebo en el tratamiento del dolor neuropático]. *Neurología* 2020;**35**(8):597-8. [DOI: [10.1016/j.nrl.2019.03.015](https://doi.org/10.1016/j.nrl.2019.03.015)]

**Rothgangel 2011**

Rothgangel AS, Braun SM, Beurskens AJ, Seitz RJ, Wade DT. The clinical aspects of mirror therapy in rehabilitation: a systematic review of the literature. *International Journal of Rehabilitation Research* 2011;**34**(1):1-13. [DOI: [10.1097/MRR.0b013e3283441e98](https://doi.org/10.1097/MRR.0b013e3283441e98)]

**Selph 2011**

Selph S, Carson S, Fu R, Thakurta S, Low A, McDonagh M. Drug class review: neuropathic pain. Drug Effectiveness Review Project; Oregon Health & Science University; Final Update 1 Report, 2011 2011.

**Shi 2016**

Shi Y, Wu W. Treatment of neuropathic pain using pulsed radiofrequency: a meta-analysis. *Pain Physician* 2016;**19**(7):429-44.

**Shin 2021**

Shin DA, Kim TU, Chang MC. Minocycline for controlling neuropathic pain: a systematic narrative review of studies in humans. *Journal of Pain Research* 2021;**14**:139-145. [DOI: [10.2147/JPR.S292824](https://doi.org/10.2147/JPR.S292824)]

**Silvinato 2020**

Silvinato A, Floriano I, Bernardo WM. Multiple lidocaine infusions for relief of neuropathic pain: systematic review

and meta-analysis. *Revista da Associação Médica Brasileira* 2020;**66**(5):583-8. [DOI: [10.1590/1806-9282.66.5.583](https://doi.org/10.1590/1806-9282.66.5.583)]

#### Simpson 2009

Simpson E, Duenas A, Holmes M, Papaioannou D, Chilcott J. Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin: systematic review and economic evaluation. *Health Technology Assessment* 2009;**13**(17):1-179. [DOI: [10.3310/hta13170](https://doi.org/10.3310/hta13170)]

#### Singh 2017

Singh H, Bhushan S, Arora R, Buttar HS, Arora S, Singh B. Alternative treatment strategies for neuropathic pain: role of Indian medicinal plants and compounds of plant origin—a review. *Biomedicine & Pharmacotherapy* 2017;**92**:634-50. [DOI: [10.1016/j.biopha.2017.05.079](https://doi.org/10.1016/j.biopha.2017.05.079)]

#### Smart 2016

Smart KM, Wand BM, O'Connell NE. Physiotherapy for pain and disability in adults with complex regional pain syndrome (CRPS) types I and II. *Cochrane Database of Systematic Reviews* 2016, Issue 2. Art. No: CD010853. [DOI: [10.1002/14651858.CD010853.pub2](https://doi.org/10.1002/14651858.CD010853.pub2)]

#### Sommer 2020

Sommer C, Klose P, Welsch P, Petzke F, Häuser W. Opioids for chronic non-cancer neuropathic pain. An updated systematic review and meta-analysis of efficacy, tolerability and safety in randomized placebo-controlled studies of at least 4 weeks duration. *European Journal of Pain* 2020;**24**:3-18. [DOI: [10.1002/ejp.1494](https://doi.org/10.1002/ejp.1494)]

#### Stannard 2016

Stannard C, Gaskell H, Derry S, Aldington D, Cole P, Cooper TE, et al. Hydromorphone for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2016, Issue 5. Art. No: CD011604. [DOI: [10.1002/14651858.CD011604.pub2](https://doi.org/10.1002/14651858.CD011604.pub2)]

#### Stanton 2013

Stanton TR, Wand BM, Carr DB, Birklein F, Wasner GL, O'Connell NE. Local anaesthetic sympathetic blockade for complex regional pain syndrome. *Cochrane Database of Systematic Reviews* 2013, Issue 8. Art. No: CD004598. [DOI: [10.1002/14651858.CD004598.pub3](https://doi.org/10.1002/14651858.CD004598.pub3)]

#### Straube 2010

Straube S, Derry S, Moore RA, McQuay HJ. Cervico-thoracic or lumbar sympathectomy for neuropathic pain and complex regional pain syndrome. *Cochrane Database of Systematic Reviews* 2010, Issue 7. Art. No: CD002918. [DOI: [10.1002/14651858.CD002918.pub2](https://doi.org/10.1002/14651858.CD002918.pub2)]

#### Thieme 2016

Thieme H, Morkisch N, Rietz C, Dohle C, Borgetto B. The efficacy of movement representation techniques for treatment of limb pain—a systematic review and meta-analysis. *The Journal of Pain* 2016;**17**(2):167-80. [DOI: [10.1016/j.jpain.2015.10.015](https://doi.org/10.1016/j.jpain.2015.10.015)]

#### Tremont-Lukats 2005

Tremont-Lukats IW, Challapalli V, McNicol ED, Lau J, Carr DB. Systemic administration of local anesthetics to

relieve neuropathic pain: a systematic review and meta-analysis. *Anesthesia & Analgesia* 2005;**101**(6):1738-49. [DOI: [10.1213/01.ANE.0000186348.86792.38](https://doi.org/10.1213/01.ANE.0000186348.86792.38)]

#### Turner 2004

Turner JA, Loeser JD, Deyo RA, Sanders SB. Spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome: a systematic review of effectiveness and complications. *Pain* 2004;**108**(1-2):137-47. [DOI: [10.1016/j.pain.2003.12.016](https://doi.org/10.1016/j.pain.2003.12.016)]

#### Vargas-Espinosa 2012

Vargas-Espinosa ML, Sanmartí-García G, Vázquez-Delgado E, Gay-Escoda C. Antiepileptic drugs for the treatment of neuropathic pain: a systematic review. *Medicina Oral, Patología Oral, Cirugía Bucal* 2012;**17**(5):e786-93. [DOI: [10.4317/medoral.18001](https://doi.org/10.4317/medoral.18001)]

#### Visnjevac 2017

Visnjevac O, Costandi S, Patel BA, Azer G, Agarwal P, Bolash R, et al. A comprehensive outcome-specific review of the use of spinal cord stimulation for complex regional pain syndrome. *Pain Practice* 2017;**17**(4):533-45. [DOI: <https://dx.doi.org/10.1111/papr.12513>]

#### Wang 2017b

Wang D, Bao JB, Zhang K, Ju LF, Yu LZ. Pregabalin for the treatment of neuropathic pain in adults: a systematic review of randomized controlled trials. *International Journal of Clinical and Experimental Medicine* 2017;**10**(1):16-29.

#### Wang 2021

Wang RQ, Wu QZ, Huang CH, Rao WF. Network meta-analysis of 4 acupuncture therapies for shoulder hand syndrome after stroke [4种针刺疗法治疗中风后肩手综合征的网状Meta分析]. *Zhongguo Zhen Jiu [Chinese Acupuncture & Moxibustion]* 2021;**41**(5):563-9. [DOI: [10.13703/j.0255-2930.20200325-k0011](https://doi.org/10.13703/j.0255-2930.20200325-k0011)]

#### Wei 2019

Wei J, Zhu X, Yang G, Shen J, Xie P, Zuo X, et al. The efficacy and safety of botulinum toxin type A in treatment of trigeminal neuralgia and peripheral neuropathic pain: a meta-analysis of randomized controlled trials. *Brain and Behavior* 2019;**9**:e01409. [DOI: [10.1002/brb3.1409](https://doi.org/10.1002/brb3.1409)]

#### Wertli 2014

Wertli MM, Kessels AG, Perez RS, Bachmann LM, Brunner F. Rational pain management in complex regional pain syndrome 1 (CRPS 1)—a network meta-analysis. *Pain Medicine* 2014;**159**(9):1575-89. [DOI: [10.1111/pme.12466](https://doi.org/10.1111/pme.12466)]

#### Wiffen 2013a

Wiffen PJ, Derry S, Lunn MP, Moore RA. Topiramate for neuropathic pain and fibromyalgia in adults.. *Cochrane Database of Systematic Reviews* 2013, Issue 8. Art. No: CD008314. [DOI: [10.1002/14651858.CD008314.pub3](https://doi.org/10.1002/14651858.CD008314.pub3)]

#### Wiffen 2013b

Wiffen PJ, Derry S, Moore RA. Lamotrigine for chronic neuropathic pain and fibromyalgia in adults. *Cochrane*

Database of Systematic Reviews 2013, Issue 12. Art. No: CD006044. [DOI: [10.1002/14651858.CD006044.pub4](https://doi.org/10.1002/14651858.CD006044.pub4)]

#### Wiffen 2014a

Wiffen PJ, Derry S, Moore RA, Kalso EA. Carbamazepine for chronic neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2014, Issue 4. Art. No: CD005451. [DOI: [10.1002/14651858.CD005451.pub3](https://doi.org/10.1002/14651858.CD005451.pub3)]

#### Wiffen 2014b

Wiffen PJ, Derry S, Moore RA, Lunn MP. Levetiracetam for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2014, Issue 7. Art. No: CD010943. [DOI: [10.1002/14651858.CD010943.pub2](https://doi.org/10.1002/14651858.CD010943.pub2)]

#### Wiffen 2015

Wiffen PJ, Derry S, Moore RA, Stannard C, Aldington D, Cole P, et al. Buprenorphine for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2015, Issue 9. Art. No: CD011603. [DOI: [10.1002/14651858.CD011603.pub2](https://doi.org/10.1002/14651858.CD011603.pub2)]

#### Wiffen 2016

Wiffen PJ, Knaggs R, Derry S, Cole P, Phillips T, Moore RA. Paracetamol (acetaminophen) with or without codeine or dihydrocodeine for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2016, Issue 12. Art. No: CD012227. [DOI: [10.1002/14651858.CD012227.pub2](https://doi.org/10.1002/14651858.CD012227.pub2)]

#### Wiffen 2017

Wiffen PJ, Derry S, Bell RF, Rice AS, Toelle TR, Phillips T, et al. Gabapentin for chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2017, Issue 6. Art. No: CD007938. [DOI: [10.1002/14651858.CD007938.pub4](https://doi.org/10.1002/14651858.CD007938.pub4)]

#### Wrzosek 2015

Wrzosek A, Woron J, Dobrogowski J, Jakowicka-Wordliczek J, Wordliczek J. Topical clonidine for neuropathic pain. *Cochrane Database of Systematic Reviews* 2015, Issue 8. Art. No: CD010967. [DOI: [10.1002/14651858.CD010967.pub2](https://doi.org/10.1002/14651858.CD010967.pub2)]

#### Zhao 2018

Zhao J, Wang Y, Wang D. The effect of ketamine infusion in the treatment of complex regional pain syndrome: a systemic review and meta-analysis. *Current Pain and Headache Reports* 2018;**22**(12):1-8. [DOI: [10.1007/s11916-018-0664-x](https://doi.org/10.1007/s11916-018-0664-x)]

#### Zhou 2017

Zhou M, Chen N, He L, Yang M, Zhu C, Wu F. Oxcarbazepine for neuropathic pain. *Cochrane Database of Systematic Reviews* 2017, Issue 12. Art. No: CD007963. [DOI: [10.1002/14651858.CD007963.pub3](https://doi.org/10.1002/14651858.CD007963.pub3)]

#### Żyluk 2018

Żyluk A, Puchalski P. Effectiveness of complex regional pain syndrome treatment: a systematic review. *Neurochirurgia Polska* 2018;**52**(3):326-33. [DOI: [10.1016/j.pjnns.2018.03.001](https://doi.org/10.1016/j.pjnns.2018.03.001)]

## Additional references

#### Askin 2014

Askin A, Savas S, Koyuncuoglu HR, Baloglu HH, Inci MF. Low dose high frequency ultrasound therapy for stellate ganglion blockade in complex regional pain syndrome type I: a randomised placebo controlled trial. *International Journal of Clinical and Experimental Medicine* 2014;**7**(12):5603-11.

#### Aydemir 2006

Aydemir K, Taskaynatan MA, Yaziciloglu K, Ozgul A. The effects of stellate ganglion block with lidocaine and ultrasound in complex regional pain syndrome: a randomized, double blind, placebo controlled study [Kompleks bölgesel ağrı sendromunda lidokain ve ultrason ile yapılan stellat ganglyon blokajinin etkinliği: çift kör randomize plasebo kontrollü çalışma]. *Journal of Rheumatology and Medical Rehabilitation* 2006;**17**(3):193-200.

#### Azqueta-Gavaldon 2020

Azqueta-Gavaldon M, Youssef AM, Storz C, Lemme J, Schulte-Göcking H, Becerra L, et al. Implications of the putamen in pain and motor deficits in complex regional pain syndrome. *Pain* 2020;**161**(3):595-608. [DOI: [10.1097/j.pain.0000000000001745](https://doi.org/10.1097/j.pain.0000000000001745)]

#### Balanaser 2022

Balanaser M, Carley M, Baron R, Finnerup NB, Moore RA, Rowbotham MC, et al. Combination pharmacotherapy for the treatment of neuropathic pain in adults: systematic review and meta-analysis. *Pain* 2022 [Epub ahead of print]. [DOI: [10.1097/j.pain.0000000000002688](https://doi.org/10.1097/j.pain.0000000000002688)]

#### Balshem 2011

Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J et al. GRADE guidelines: 3. Rating the quality of evidence. *Journal of Clinical Epidemiology* 2011;**64**(4):401-6. [DOI: [10.1016/j.jclinepi.2010.07.015](https://doi.org/10.1016/j.jclinepi.2010.07.015)]

#### Barnhoorn 2015

Barnhoorn KJ, van de Meent H, van Dongen RTM, Klomp FP, Groenewoud H, Samwel H, et al. Pain exposure physical therapy (PEPT) compared to conventional treatment in complex regional pain syndrome type 1: a randomised controlled trial. *BMJ Open* 2015;**5**(12):e008283. [DOI: [10.1136/bmjopen-2015-008283](https://doi.org/10.1136/bmjopen-2015-008283)]

#### Benedetti 2018

Benedetti MG, Cavazzuti L, Mosca M, Fusaro I, Zati A. Bio-Electro-Magnetic-Energy-Regulation (BEMER) for the treatment of type I complex regional pain syndrome: a pilot study. *Physiotherapy Theory and Practice* 2018;**36**(4):498-506. [DOI: [10.1080/09593985.2018.1491661](https://doi.org/10.1080/09593985.2018.1491661)]

#### Bickerstaff 1991

Bickerstaff DR, Kanis JA. The use of nasal calcitonin in the treatment of post-traumatic algodystrophy. *British Journal of Rheumatology* 1991;**30**(4):291-4. [DOI: [10.1093/rheumatology/30.4.291](https://doi.org/10.1093/rheumatology/30.4.291)]

**Bies 2022**

Bies M, Ashmore Z, Qu W, Hunt C. Injectable biologics for neuropathic pain: a systematic review. *Pain Medicine* 2022;**23**(10):1733–49. [DOI: [10.1093/pm/pnac066](https://doi.org/10.1093/pm/pnac066)]

**Bilgili 2016**

Bilgili A, Çakır T, Dogan SK, Erçalık T, Filiz MB, Toraman F. The effectiveness of transcutaneous electrical nerve stimulation in the management of patients with complex regional pain syndrome: a randomized, double-blinded, placebo-controlled prospective study. *Journal of Back and Musculoskeletal Rehabilitation* 2016;**29**(4):661–71. [DOI: [10.3233/BMR-160667](https://doi.org/10.3233/BMR-160667)]

**Birklein 2014**

Birklein F, Drummond PD, Li W, Schlereth T, Albrecht N, Finch PM, et al. Activation of cutaneous immune responses in complex regional pain syndrome. *The Journal of Pain* 2014;**15**(5):485–95. [DOI: [10.1016/j.jpain.2014.01.490](https://doi.org/10.1016/j.jpain.2014.01.490)]

**Birklein 2015**

Birklein F, Schlereth T. Complex regional pain syndrome—significant progress in understanding. *Pain* 2015;**156**:S94–S103. [DOI: [10.1097/01.j.pain.0000460344.54470.20](https://doi.org/10.1097/01.j.pain.0000460344.54470.20)]

**Birklein 2017**

Birklein F, Dimova V. Complex regional pain syndrome—up-to-date. *Pain Reports* 2017;**2**(6):e624. [DOI: [10.1097/PR9.0000000000000624](https://doi.org/10.1097/PR9.0000000000000624)]

**Blanchard 1990**

Blanchard J, Ramamurthy S, Walsh N, Hoffman J, Schoenfeld L. Intravenous regional sympathectomy: a double-blind comparison of guanethidine, reserpine, and normal saline. *Journal of Pain and Symptom Management* 1990;**5**(6):357–61. [DOI: [10.1016/0885-3924\(90\)90030-n](https://doi.org/10.1016/0885-3924(90)90030-n)]

**BMJ Clinical Evidence**

BMJ Best Practice. Study design search filters. <https://bestpractice.bmj.com/info/toolkit/learn-ebm/study-design-search-filters/> (last accessed 11 October 2021).

**Bonelli 1983**

Bonelli S, Conoscente F, Movilia PG. Regional intravenous guanethidine vs. stellate ganglion block in reflex sympathetic dystrophies: a randomized trial. *Pain* 1983;**16**(3):297–307. [DOI: [10.1016/0304-3959\(83\)90118-5](https://doi.org/10.1016/0304-3959(83)90118-5)]

**Bounameaux 1984**

Bounameaux HM, Hellemans H, Verhaeghe R. Ketanserin in chronic sympathetic dystrophy. An acute controlled trial. *Clinical Rheumatology* 1984;**3**(4):556–7.

**Breuer 2014**

Breuer AJ, Mainka T, Hansel N, Maier C, Krumova EK. Short-term treatment with parecoxib for complex regional pain syndrome: a randomized, placebo-controlled double-blind trial. *Pain Physician* 2014;**17**:127–37.

**Bruehl 1999**

Bruehl S, Harden RN, Galer BS, Saltz S, Bertram M, Backonja M, et al. External validation of IASP diagnostic criteria for Complex

Regional Pain Syndrome and proposed research diagnostic criteria. International Association for the Study of Pain. *Pain* 1999;**81**(1–2):147–54. [DOI: [10.1016/s0304-3959\(99\)00011-1](https://doi.org/10.1016/s0304-3959(99)00011-1)]

**Bruehl 2010**

Bruehl S. An update on the pathophysiology of complex regional pain syndrome. *Anesthesiology* 2010;**113**(3):713–25. [DOI: [10.1097/ALN.0b013e3181e3db38](https://doi.org/10.1097/ALN.0b013e3181e3db38)]

**Bruehl 2015**

Bruehl S. Complex regional pain syndrome. *BMJ* 2015;**351**:h2730. [PMID: [10.1136/bmj.h2730](https://pubmed.ncbi.nlm.nih.gov/2611136/)]

**Bruehl 2022**

Bruehl S, Billings IV FT, Anderson S, Polkowski G, Shinar A, Schildcrout J, et al. Preoperative predictors of complex regional pain syndrome outcomes in the 6 months following total knee arthroplasty. *The Journal of Pain* (in press). [DOI: [10.1016/j.jpain.2022.04.005](https://doi.org/10.1016/j.jpain.2022.04.005)]

**Busse 2015**

Busse JW, Bartlett SJ, Dougados M, Johnston BC, Guyatt GH, Kirwan JR, et al. Optimal strategies for reporting pain in clinical trials and systematic reviews: recommendations from an OMERACT 12 Workshop. *The Journal of Rheumatology* 2015;**42**(10):1962–70. [DOI: [10.3899/jrheum.141440](https://doi.org/10.3899/jrheum.141440)]

**Büyükturan 2018**

Büyükturan O, Büyükturan B, Kurt EE. Effectiveness of electromagnetic field therapy in upper extremity complex regional pain syndrome type I: a randomized controlled study. *Journal of Exercise Therapy and Rehabilitation* 2018;**5**(1):9–18.

**Cacchio 2009a**

Cacchio A, De Blasis E, Necozone S, Di Orio F, Santilli V. Mirror therapy for chronic complex regional pain syndrome type 1 and stroke. *New England Journal of Medicine* 2009;**361**(6):634–6. [DOI: [10.1056/NEJMc0902799](https://doi.org/10.1056/NEJMc0902799)]

**Cacchio 2009b**

Cacchio A, De Blasis E, De Blasis V, Santilli V, Spacca G. Mirror therapy in complex regional pain syndrome type 1 of the upper limb in stroke patients. *Neurorehabilitation and Neural Repair* 2009;**23**(8):792–9. [DOI: [10.1177/1545968309335977](https://doi.org/10.1177/1545968309335977)]

**Carroll 2009**

Carroll I, Clark JD, Mackey S. Sympathetic block with botulinum toxin to treat complex regional pain syndrome. *Annals of Neurology* 2009;**65**(3):348–51. [DOI: [10.1002/ana.21601](https://doi.org/10.1002/ana.21601)]

**Cashin 2021**

Cashin AG, Richards GC, DeVito NJ, Mellor DT, Lee H. Registration of health and medical research. *BMJ Evidence-Based Medicine* 2021 Dec 21 [Epub ahead of print]. [DOI: [10.1136/bmjebm-2021-111836](https://doi.org/10.1136/bmjebm-2021-111836)]

**Chai 2016**

Chai GH. Acupuncture combined with rehabilitation training for 59 patients with shoulder hand syndrome. *China Nat* 2016;**24**:35–6.

**Chang 2005**

Chang N, Liu S. Therapeutic effect of acupuncture combined with rehabilitation exercise in patients with shoulder hand syndrome. *Journal of the Fourth Military Medical University* 2005;**26**:2295-2297.

**Chen 2015**

Chen Y, Huang TS, Liu KC. Clinical research of using acupuncture and rehabilitation training in the treatment of post-stroke shoulder hand syndrome. *Journal of Sichuan Traditional Chinese Medicine* 2015;**33**:150-2.

**Chitneni 2021**

Chitneni A, Patil A, Dalal S, Ghorayeb JH, Pham YN, Grigoropoulos G. Use of ketamine infusions for treatment of complex regional pain syndrome: a systematic review. *Cureus* 2021;**13**(10):e18910. [DOI: [10.7759/cureus.18910](https://doi.org/10.7759/cureus.18910)]

**Cohen 1998**

Cohen P, Uebelhart D. Indications of Pamidronate disodique(Aredia\*) in the treatment of post traumatic or post surgical of the distal upper limb algodystrophies [Indications du Pamidronate disodique(Aredia\*) dans le traitement des algodystrophies post-traumatiques ou post-chirurgicales de l'extrémité distale du membre supérieur]. In: Simon L, Pélissier J, Hérissou C, editors(s). *Progrès en MPR*. Paris: Masson, 1998:510-4.

**Cucherat 1997**

Cucherat M. Evaluation of the methodological quality of trials [Évaluation de la qualité méthodologique des essais]. In: Bouvenot G, editors(s). *Méta-analyse des essais thérapeutiques*. Paris: Masson, 1997:105-11.

**Datta Gupta 2022**

Datta Gupta A, Edwards S, Smith J, Snow J, Visvanathan R, Tucker G, et al. A systematic review and meta-analysis of efficacy of botulinum toxin A for neuropathic pain. *Toxins* 2022;**14**(36):1-14. [DOI: [10.3390/toxins14010036](https://doi.org/10.3390/toxins14010036)]

**de Mos 2007**

de Mos M, De Bruijn AGJ, Huygen FJPM, Dieleman JP, Stricker BHC, Sturkenboom MCJM. The incidence of complex regional pain syndrome: a population-based study. *Pain* 2007;**129**(1-2):12-20. [DOI: [10.1016/j.pain.2006.09.008](https://doi.org/10.1016/j.pain.2006.09.008)]

**de Mos 2008**

de Mos M, Huygen FJPM, Dieleman JP, Koopman JSHA, Stricker BHC, Sturkenboom MCJM. Medical history and the onset of complex regional pain syndrome (CRPS). *Pain* 2008;**139**(2):458-66. [DOI: [10.1016/j.pain.2008.07.002](https://doi.org/10.1016/j.pain.2008.07.002)]

**de Mos 2009**

de Mos, Sturkenboom MCJM, Huygen FJPM. Current understandings on complex regional pain syndrome. *Pain Practice* 2009;**9**(2):86-99. [DOI: [10.1111/j.1533-2500.2009.00262.x](https://doi.org/10.1111/j.1533-2500.2009.00262.x)]

**de Vet 1997**

de Vet HC, De Bie RA, Van Der Heijden GJ, Verhagen AP, Sijpkens P, Knipschild PG. Systematic reviews on the basis of

methodological criteria. *Physiotherapy* 1997;**83**(6):284-9. [DOI: [10.1016/S0031-9406\(05\)66175-5](https://doi.org/10.1016/S0031-9406(05)66175-5)]

**Deer 2017**

Deer TR, Levy RM, Kramer J, Poree L, Amirdelfan K, Grigsby E, et al. Dorsal root ganglion stimulation yielded higher treatment success rate for CRPS and causalgia at 3 and 12 months: randomized comparative trial. *Pain* 2017;**158**(4):669-81. [DOI: [10.1097/j.pain.0000000000000814](https://doi.org/10.1097/j.pain.0000000000000814)]

**den Hollander 2016**

den Hollander M, Goossens M, De Jong J, Ruijgrok J, Oosterhof J, Onghena P, et al. A randomized controlled trial of exposure in vivo vs pain-contingent treatment as usual in patients with complex regional pain syndrome type 1. *Pain* 2016;**157**(10):2318-29. [DOI: [10.1097/j.pain.0000000000000651](https://doi.org/10.1097/j.pain.0000000000000651)]

**den Hollander 2022**

den Hollander M, Smeets RJ, Van Meulenbroek T, Van Laake-Geelen CC, Baadjou VA, Timmers I. Exposure in vivo as a treatment approach to target pain-related fear: theory and new insights from research and clinical practice. *Physical Therapy*. 2022;**102**(2):1-9. [DOI: [10.1093/ptj/pzab270](https://doi.org/10.1093/ptj/pzab270)]

**Derry 2017a**

Derry S, Wiffen PJ, Kalso EA, Bell RF, Aldington D, Phillips T, et al. Topical analgesics for acute and chronic pain in adults- an overview of Cochrane Reviews. *Cochrane Database of Systematic Reviews* 2017, Issue 5. Art. No: CD008609. [DOI: [10.1002/14651858.CD008609.pub2](https://doi.org/10.1002/14651858.CD008609.pub2)]

**Devrimsel 2015**

Devrimsel G, Turkyilmaz AK, Yildirim M, Beyazal MS. The effects of whirlpool bath and neuromuscular electrical stimulation on complex regional pain syndrome. *Journal of Physical Therapy Science* 2015;**27**(1):27-30. [DOI: [10.1589/jpts.27.27](https://doi.org/10.1589/jpts.27.27)]

**Dimitrijevic 2014**

Dimitrijevic IM, Lazovic MP, Kocic MN, Dimitrijevic LR, Mantic DD, Stankovic AM. Effects of low-level laser therapy and interferential current therapy in the treatment of complex regional pain syndrome. *Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi [Turkish Journal of Physical Medicine and Rehabilitation]* 2014;**60**(2):98-105. [DOI: [10.5152/tftrd.2014.08466](https://doi.org/10.5152/tftrd.2014.08466)]

**Dirckx 2013**

Dirckx M, Groeneweg G, Wesseldijk F, Stronks DL, Huygen FJ. Report of a preliminary discontinued double-blind, randomized, placebo-controlled trial of the anti-TNF- $\alpha$  chimeric monoclonal antibody infliximab in complex regional pain syndrome. *Pain Practice* 2013;**13**(8):633-40. [DOI: [10.1111/papr.12078](https://doi.org/10.1111/papr.12078)]

**Dosenovic 2018**

Dosenovic S, Jelacic Kadic A, Vucic K, Markovina N, Pieper D, Puljak L. Comparison of methodological quality rating of systematic reviews on neuropathic pain using AMSTAR and R-AMSTAR. *BMC Medical Research Methodology* 2018;**18**(37):1-13. [DOI: [10.1186/s12874-018-0493-y](https://doi.org/10.1186/s12874-018-0493-y)]

**Duman 2009**

Duman I, Ozdemir A, Tan AK, Dincer K. The efficacy of manual lymphatic drainage therapy in the management of limb edema secondary to reflex sympathetic dystrophy. *Rheumatology International* 2009;**29**(7):759-63. [DOI: [10.1007/s00296-008-0767-5](https://doi.org/10.1007/s00296-008-0767-5)]

**Durmus 2004**

Durmus A, Cakmak A, Disci R, Muslumanoglu L. The efficiency of electromagnetic field treatment in complex regional pain syndrome type I. *Disability and Rehabilitation* 2004;**26**(9):537-45. [DOI: [10.1080/09638280410001683155](https://doi.org/10.1080/09638280410001683155)]

**Dworkin 2008**

Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *The Journal of Pain* 2008;**9**(2):105-21. [DOI: [10.1016/j.jpain.2007.09.005](https://doi.org/10.1016/j.jpain.2007.09.005)]

**Eckmann 2011**

Eckmann MS, Ramamurthy S, Griffin JG. Intravenous regional ketorolac and lidocaine in the treatment of complex regional pain syndrome of the lower extremity: a randomized, double-blinded, crossover study. *Clinical Journal of Pain* 2011;**27**(3):203-6. [DOI: [10.1097/AJP.0b013e3181fd5150](https://doi.org/10.1097/AJP.0b013e3181fd5150)]

**Eisenberg 2005**

Eisenberg E, Chistyakov AV, Yudashkin M, Kaplan B, Hafner H, Feinsod M. Evidence for cortical hyperexcitability of the affected limb representation area in CRPS: a psychophysical and transcranial magnetic stimulation study. *Pain* 2005;**113**(1-2):99-105. [DOI: [10.1016/j.pain.2004.09.030](https://doi.org/10.1016/j.pain.2004.09.030)]

**Elsamadicy 2018**

Elsamadicy AA, Yang S, Sergesketter AR, Ashraf B, Charalambous L, Kemeny H, et al. Prevalence and cost analysis of complex regional pain syndrome (CRPS): a role for neuromodulation. *Neuromodulation: Technology at the Neural Interface* 2018;**21**(5):423-30. [DOI: [10.1111/ner.12691](https://doi.org/10.1111/ner.12691)]

**Ernst 1995**

Ernst E, Resch KL, Fialka V, Ritter-Dittrich D, Alcamiloglu Y, Chen O, et al. Traditional acupuncture for reflex sympathetic dystrophy: A randomised, sham-controlled, double-blind trial. *Acupuncture in Medicine* 1995;**13**(2):78-80. [DOI: [10.1136/aim.13.2.78](https://doi.org/10.1136/aim.13.2.78)]

**Eun Young 2016**

Young H, Hyeyun K, Sang Hee I. Pamidronate effect compared with a steroid on complex regional pain syndrome type I: pilot randomised trial. *The Netherlands Journal of Medicine* 2016;**74**(1):30-35.

**Fialka 1993**

Fialka V, Resch KL, Ritter-Dietrich D, Alacamioglu Y, Chen O, Leitha T, et al. Acupuncture for reflex sympathetic dystrophy. *Archives of Internal Medicine* 1993;**153**(5):661-5. [DOI: [10.1001/archinte.1993.00410050089013](https://doi.org/10.1001/archinte.1993.00410050089013)]

**Fialka 1996**

Fialka V, Korpan M, Saradeth T, Paternostro-Slugo T, Hexel O, Frischenschlager O, et al. Autogenic training for reflex sympathetic dystrophy: a pilot study. *Complementary Therapies in Medicine* 1996;**4**(2):103-5. [DOI: [10.1016/S0965-2299\(96\)80026-4](https://doi.org/10.1016/S0965-2299(96)80026-4)]

**Fischer 2008**

Fischer MJ, Reiners A, Kohnen R, Bernateck M, Gutenbrunner C, Fink M, et al. Do occlusal splints have an effect on complex regional pain syndrome? A randomized, controlled proof-of-concept trial. *Clinical Journal of Pain* 2008;**24**(9):776-83. [DOI: [10.1097/AJP.0b013e3181790355](https://doi.org/10.1097/AJP.0b013e3181790355)]

**Fischer 2013**

Fischer SG, Collins S, Boogaard S, Loer SA, Zuurmond WW, Perez RSGM. Intravenous magnesium for chronic complex regional pain syndrome type I (CRPS-1). *Pain Medicine* 2013;**14**(9):1388-99. [DOI: [10.1111/pme.12211](https://doi.org/10.1111/pme.12211)]

**Frade 2005**

Frade LC, Lauretti GR, Lima IC, Pereira NL. The antinociceptive effect of local or systemic parecoxib combined with lidocaine/clonidine intravenous regional analgesia for complex regional pain syndrome type I in the arm. *Anesthesia and Analgesia* 2005;**101**(3):807-11. [DOI: [10.1213/01.ane.0000166980.45162.1c](https://doi.org/10.1213/01.ane.0000166980.45162.1c)]

**Freitas 2013**

Freitas TS, Deusdara R, Kessler I. Pulsed radiofrequency of sympathetic lumbar plexus versus sympathetic block in the management of lower limb complex regional pain syndrome type. *Stereotactic and Functional Neurosurgery* 2013;**91**(107).

**Friend 2022**

Friend G, Walsh N, Llewellyn A. Allied healthcare professional interventions for complex regional pain syndrome-which work? A systematic review of the literature. *Rheumatology* 2022;**61**(Suppl1):i156. [DOI: [10.1093/rheumatology/keac133.285](https://doi.org/10.1093/rheumatology/keac133.285)]

**Galer 1998**

Galer BS, Bruehl S, Harden RN. IASP diagnostic criteria for complex regional pain syndrome: a preliminary empirical validation study. *Clinical Journal of Pain* 1998;**14**(1):48-54.

**Gao 2016**

Gao Y. Effectiveness evaluation of acupuncture combined with rehabilitation exercise for shoulder hand syndrome. *Guide of Chinese Medicine* 2016;**14**:198.

**Gatzinsky 2021**

Gatzinsky K, Bergh C, Liljegren A, Silander H, Samuelsson J, Svanberg T, et al. Repetitive transcranial magnetic stimulation of the primary motor cortex in management of chronic neuropathic pain: a systematic review. *Scandinavian Journal of Pain* 2021;**21**(1):8-21. [DOI: [10.1515/sjpain-2020-0054](https://doi.org/10.1515/sjpain-2020-0054)]

**Glynn 1993**

Glynn CJ, Stannard S, Collins PA, Casale R. The role of peripheral sudomotor blockade in the treatment of patients with

sympathetically maintained pain. *Pain* 1993;**53**(1):39-42. [DOI: [10.1016/0304-3959\(93\)90053-R](https://doi.org/10.1016/0304-3959(93)90053-R)]

#### Gobelet 1986

Gobelet C, Meier JL, Schaffner W. Calcitonin and reflex sympathetic dystrophy syndrome. *Clinical Rheumatology* 1986;**5**(3):382-8.

#### Gobelet 1992

Gobelet C, Waldburger M, Meier JL. The effect of adding calcitonin to physical treatment on reflex sympathetic dystrophy. *Pain* 1992;**48**(2):171-5. [DOI: [10.1016/0304-3959\(92\)90055-G](https://doi.org/10.1016/0304-3959(92)90055-G)]

#### Goebel 2010

Goebel A, Baranowski A, Maurer K, Ghai A, McCabe C, Ambler G. Intravenous immunoglobulin treatment of the complex regional pain syndrome: a randomized trial. *Annals of Internal Medicine* 2010;**152**(3):152-8. [DOI: [10.7326/0003-4819-152-3-201002020-00006](https://doi.org/10.7326/0003-4819-152-3-201002020-00006)]

#### Goebel 2013

Goebel A, Blaes F. Complex regional pain syndrome, prototype of a novel kind of autoimmune disease. *Autoimmunity Reviews* 2013;**12**(6):682-6. [DOI: [10.1016/j.autrev.2012.10.015](https://doi.org/10.1016/j.autrev.2012.10.015)]

#### Goebel 2017

Goebel A, Bisla J, Carganillo R, Frank B, Gupta R, Kelly J, et al. Low-dose intravenous immunoglobulin treatment for long-standing complex regional pain syndrome: a randomized trial. *Annals of Internal Medicine* 2017;**167**:476-83. [DOI: [10.7326/M17-0509](https://doi.org/10.7326/M17-0509)]

#### Goebel 2018

Goebel A, Barker CH, Turner-Stokes L. Complex regional pain syndrome in adults: UK guidelines for diagnosis, referral and management in primary and secondary care 2nd edition. Royal College of Physicians 2018.

#### Goebel 2019

Goebel A, Barker C, Birklein F, Brunner F, Casale R, Eccleston C, et al. Standards for the diagnosis and management of complex regional pain syndrome: results of a European Pain Federation task force. *European Journal of Pain* 2019;**23**(4):641-51. [DOI: [10.1002/ejp.1362](https://doi.org/10.1002/ejp.1362)]

#### Goebel 2021

Goebel A, Birklein F, Brunner F, Clark JD, Gierthmühlen J, Harden N, et al. The Valencia consensus-based adaptation of the IASP complex regional pain syndrome diagnostic criteria. *Pain* 2021;**162**(9):2346-8. [DOI: [10.1097/j.pain.0000000000002245](https://doi.org/10.1097/j.pain.0000000000002245)]

#### Goldkuhle 2018

Goldkuhle M, Narayan VM, Weigl A, Dahm P, Skoetz N. A systematic assessment of Cochrane reviews and systematic reviews published in high-impact medical journals related to cancer. *BMJ Open* 2018;**8**:e020869. [DOI: [10.1136/bmjopen-2017-020869](https://doi.org/10.1136/bmjopen-2017-020869)]

#### Goris 1987

Goris RJA, Dongen LMV, Winters HAH. Are toxic oxygen radicals involved in the pathogenesis of reflex sympathetic dystrophy? *Free Radical Research Communications* 1987;**3**(1-5):13-8. [DOI: [10.3109/10715768709069764](https://doi.org/10.3109/10715768709069764)]

#### Grieve 2017

Grieve S, Perez RSGM, Birklein F, Brunner F, Bruehl S, Harden N. Recommendations for a first core outcome measurement set for complex regional pain syndrome clinical studies (COMPACT). *Pain* 2017;**158**(6):1083-90. [DOI: [10.1097/j.pain.0000000000000866](https://doi.org/10.1097/j.pain.0000000000000866)]

#### Grieve 2019

Grieve S, Llewellyn A, Jones L, Manns S, Glanville V, McCabe CS. Complex regional pain syndrome: an international survey of clinical practice. *European Journal of Pain* 2019;**23**(10):1890-903. [DOI: [10.1002/ejp.1463](https://doi.org/10.1002/ejp.1463)]

#### Groeneweg 2008

Groeneweg G, Huygen FJPM, Niehof SP, Wesseldijk F, Bussmann JBJ, Schasfoort FC, et al. Effect of tadalafil on blood flow, pain, and function in chronic cold complex regional pain syndrome: a randomized controlled trial. *BMC Musculoskeletal Disorders* 2008;**9**(143). [DOI: [10.1186/1471-2474-9-143](https://doi.org/10.1186/1471-2474-9-143)]

#### Groeneweg 2009

Groeneweg JG, Huygen FJ, Niehof SP, Wesseldijk F, Bussmann JB, Schasfoort FC, et al. No recovery of cold complex regional pain syndrome after transdermal isosorbide dinitrate: a small controlled trial. *Journal of Pain and Symptom Management* 2009;**38**(3):401-8. [DOI: [10.1016/j.jpainsymman.2008.10.006](https://doi.org/10.1016/j.jpainsymman.2008.10.006)]

#### Gustin 2010

Gustin SM, Schwarz A, Birbaumer N, Sines N, Schmidt AC, Veit R, et al. NMDA-receptor antagonist and morphine decrease CRPS-pain and cerebral pain representation. *Pain* 2010;**151**(1):69-76. [DOI: [10.1016/j.pain.2010.06.022](https://doi.org/10.1016/j.pain.2010.06.022)]

#### Guyatt 2006

Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, 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**(1):174-81. [DOI: [10.1378/chest.129.1.174](https://doi.org/10.1378/chest.129.1.174)]

#### Halicka 2021

Halicka M, Vittersø AD, McCullough H, Goebel A, Heelas L, Proulx MJ, et al. Prism adaptation treatment for upper-limb complex regional pain syndrome: a double-blind randomized controlled trial. *Pain* 2021;**162**(2):471-89. [DOI: [10.1097/j.pain.0000000000002053](https://doi.org/10.1097/j.pain.0000000000002053)]

#### Hanna 1989

Hanna MH, Peat SJ. Ketanserin in reflex sympathetic dystrophy. A double-blind placebo controlled cross-over trial. *Pain* 1989;**38**(2):145-50. [DOI: [10.1016/0304-3959\(89\)90232-7](https://doi.org/10.1016/0304-3959(89)90232-7)]

**Harden 2005**

Harden RN, Bruehl SP. Diagnostic criteria: the statistical derivation of the four criterion factors. In: Wilson P, Stanton-Hicks M, Harden RN, editors(s). CRPS: Current Diagnosis and Therapy. Progress in Pain Research and Management. Vol. **32**. Seattle: IASP Press, 2005:45-58.

**Harden 2007**

Harden RN, Bruehl S, Stanton-Hicks M, Wilson PR. Proposed new diagnostic criteria for complex regional pain syndrome. *Pain Medicine* 2007;**8**(4):326-31. [DOI: [10.1111/j.1526-4637.2006.00169.x](https://doi.org/10.1111/j.1526-4637.2006.00169.x)]

**Harden 2010**

Harden RN, Bruehl S, Perez RS, Birklein F, Marinus J, Maihofner C, et al. Validation of proposed diagnostic criteria (the "Budapest Criteria") for complex regional pain syndrome. *Pain* 2010;**150**(2):268-74. [DOI: [10.1016/j.pain.2010.04.030](https://doi.org/10.1016/j.pain.2010.04.030)]

**Harden 2022**

Harden RN, McCabe CS, Goebel A, Massey M, Suvar T, Grieve S, et al. Complex regional pain Syndrome: practical diagnostic and treatment guidelines. *Pain Medicine* 2022;**23**(1):S1-S53. [DOI: [10.1093/pm/pnac046](https://doi.org/10.1093/pm/pnac046)]

**Harris 2009**

Harris RE, Zubieta JK, Scott DJ, Napadow V, Gracely RH, Clauw DJ. Traditional Chinese acupuncture and placebo (sham) acupuncture are differentiated by their effects on  $\mu$ -opioid receptors (MORs). *Neuroimage* 2009;**47**(3):1077-1085. [DOI: [10.1016/j.neuroimage.2009.05.083](https://doi.org/10.1016/j.neuroimage.2009.05.083)]

**Hary 2022**

Hary V, Schitter S, Martinez V. Efficacy and safety of botulinum A toxin for the treatment of chronic peripheral neuropathic pain: a systematic review of randomized controlled trials and meta-analysis. *European Journal of Pain* 2022;**26**(5):980-90. [DOI: [10.1002/ejp.1941](https://doi.org/10.1002/ejp.1941)]

**Hazneci 2005**

Hazneci B, Tan AK, Özdem T, Dinçer K, Kalyon TA. The effects of transcutaneous electroneurostimulation and ultrasound in the treatment of reflex sympathetic dystrophy syndrome [Refleks sempatik distrofi sendromu tedavisinde transkutanöz elektronöstimülasyon ve ultrasonun etkileri]. *Türkiye Fiziksel Tıp ve Rehabilitasyon Dergisi [Turkish Journal of Physical Medicine and Rehabilitation]* 2005;**51**(3):83-9.

**Herlyn 2010**

Herlyn P, Müller-Hilke B, Wendt M, Hecker M, Mittlmeier T, Gradl G. Frequencies of polymorphisms in cytokines, neurotransmitters and adrenergic receptors in patients with complex regional pain syndrome type I after distal radial fracture. *The Clinical Journal of Pain* 2010;**26**(3):175-81. [DOI: [10.1097/AJP.0b013e3181bfff8b9](https://doi.org/10.1097/AJP.0b013e3181bfff8b9)]

**Higgins 2011**

Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;**343**:d5928. [DOI: [10.1136/bmj.d5928](https://doi.org/10.1136/bmj.d5928)]

**Higgins 2021**

Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 6.2 (updated February 2021). Cochrane, 2021. Available from [training.cochrane.org/handbook](https://training.cochrane.org/handbook).

**Hoffmann 2014**

Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;**348**:g1687. [DOI: [10.1136/bmj.g1687](https://doi.org/10.1136/bmj.g1687)]

**Hoffmann 2017**

Hoffmann TC, Oxman AD, Ioannidis JP, Moher D, Lasserson TJ, Tovey DI, et al. Enhancing the usability of systematic reviews by improving the consideration and description of interventions. *BMJ* 2017;**358**:j2998. [DOI: [10.1136/bmj.j2998](https://doi.org/10.1136/bmj.j2998)]

**Hwang 2014**

Hwang H, Cho S, Lee JH. The effect of virtual body swapping with mental rehearsal on pain intensity and body perception disturbance in complex regional pain syndrome. *Journal of Rehabilitation Research* 2014;**37**(2):167-72. [DOI: [10.1097/MRR.000000000000053](https://doi.org/10.1097/MRR.000000000000053)]

**Jadad 1996**

Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Controlled Clinical Trials* 1996;**17**(1):1-12. [DOI: [10.1016/0197-2456\(95\)00134-4](https://doi.org/10.1016/0197-2456(95)00134-4)]

**Jeon 2014**

Jeon B, Cho S, Lee JH. Application of virtual body swapping to patients with complex regional pain syndrome: a pilot study. *Cyberpsychology, Behavior, and Social Networking* 2014;**17**(6):366-70. [DOI: [10.1089/cyber.2014.0046](https://doi.org/10.1089/cyber.2014.0046)]

**Jia 2022**

Jia Y, Wang Z, Ma Y, Wang T, Feng K, Feng G, et al. Efficacy and safety of high-voltage versus standard-voltage pulsed radiofrequency ablation for patients with neuropathic pain: protocol for a systematic review and meta-analysis. *BMJ Open* 2022;**12**(7):e063385. [PMID: [10.1136/bmjopen-2022-063385](https://pubmed.ncbi.nlm.nih.gov/363385/)]

**Jiang 2022**

Jiang X, Yan W, Wan R, Lin Y, Zhu X, Song G, et al. Effects of repetitive transcranial magnetic stimulation on neuropathic pain: a systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews* 2022;**132**:130-41. [DOI: [10.1016/j.neubiorev.2021.11.037](https://doi.org/10.1016/j.neubiorev.2021.11.037)]

**Johnson 2022**

Johnson S, Cowell F, Gillespie S, Goebel A. Complex regional pain syndrome what is the outcome? A systematic review of the course and impact of CRPS at 12 months from symptom onset and beyond. *European Journal of Pain* 2022;**26**(6):1203-20. [DOI: [10.1002/ejp.1953](https://doi.org/10.1002/ejp.1953)]

**Kahan 2022**

Kahan BC, Morris TP, Goulão B, Carpenter J. Estimands for factorial trials. *Statistics in Medicine* 25 June 2022 [Epub ahead of print]. [DOI: [10.1002/sim.9510](https://doi.org/10.1002/sim.9510)]

**Kalita 2006**

Kalita J, Vajpayee A, Misra UK. Comparison of prednisolone with piroxicam in complex regional pain syndrome following stroke: a randomized controlled trial. *QJM: An International Journal of Medicine* 2006;**99**(2):89-95. [DOI: [10.1093/qjmed/hcl004](https://doi.org/10.1093/qjmed/hcl004)]

**Kalita 2016**

Kalita J, Misra U, Kumar A, Bhoi SK. Long-term prednisolone in post-stroke complex regional pain syndrome. *Pain Physician* 2016;**19**(8):565-74.

**Kemler 2000**

Kemler MA, Barendse GAM, Van Kleef M, De Vet HCW, Rijkers CPM, Furnée CA, et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *New England Journal of Medicine* 2000;**343**(9):618-24. [DOI: [10.1056/NEJM200008313430904](https://doi.org/10.1056/NEJM200008313430904)]

**Kemler 2004**

Kemler MA, De Vet HCW, Barendse GAM, Van Den Wildenberg FAJM, Van Kleef M. The effect of spinal cord stimulation in patients with chronic reflex sympathetic dystrophy: two years' follow-up of the randomized controlled trial. *Annals of Neurology* 2004;**55**(1):13-8. [DOI: [10.1002/ana.10996](https://doi.org/10.1002/ana.10996)]

**Kemler 2008**

Kemler MA, de Vet HC, Barendse GA, van den Wildenberg FA, van Kleef M. Effect of spinal cord stimulation for chronic complex regional pain syndrome type I: five-year final follow-up of patients in a randomized controlled trial. *Journal of Neurosurgery* 2008;**108**(2):292-8. [DOI: [10.3171/JNS/2008/108/2/0292](https://doi.org/10.3171/JNS/2008/108/2/0292)]

**Kettler 1988**

Kettler RE, Abram SE. Intravenous regional droperidol in the management of reflex sympathetic dystrophy: a double-blind, placebo-controlled, crossover study. *Anesthesiology* 1988;**69**(6):933-6. [DOI: [10.1097/0000542-198812000-00020](https://doi.org/10.1097/0000542-198812000-00020)]

**Kho 1995**

Kho KH. The impact of acupuncture on pain in patients with reflex sympathetic dystrophy. *The Pain Clinic* 1995;**8**(1):59-61.

**Knotkova 2021**

Knotkova H, Hamani C, Sivanesan E, Le Beuffe MF, Moon JY, Cohen SP, et al. Neuromodulation for chronic pain. *The Lancet* 2021;**397**(10289):2111-24. [DOI: [10.1016/S0140-6736\(21\)00794-7](https://doi.org/10.1016/S0140-6736(21)00794-7)]

**Knudsen 2019**

Knudsen LF, Terkelsen AJ, Drummond PD, Birklein F. Complex regional pain syndrome: a focus on the autonomic nervous system. *Clinical Autonomic Research* 2019;**29**(4):457-67. [DOI: [10.1007/s10286-019-00612-0](https://doi.org/10.1007/s10286-019-00612-0)]

**Kong 2016**

Kong LJ, Lauche R, Klose P, Bu JH, Yang XC, Guo CQ, et al. Tai Chi for chronic pain conditions: a systematic review and meta-analysis of randomized controlled trials. *Scientific Reports* 2016;**6**. [DOI: [10.1038/srep25325](https://doi.org/10.1038/srep25325)]

**Korpan 1999**

Korpan MI, Dezu Y, Scneider B, Leitha T, Fialka-Moser V. Acupuncture in the treatment of posttraumatic pain syndrome. *Acta Orthopaedica Belgica* 1999;**65**(2):197-201.

**Kozin 1981**

Kozin F, Ryan LM, Carrera GF, Soin JS, Wortmann RL. The reflex sympathetic dystrophy syndrome (RSDS): III. Scintigraphic studies, further evidence for the therapeutic efficacy of systemic corticosteroids, and proposed diagnostic criteria. *American Journal of Medicine* 1981;**70**(1):23-30. [DOI: [10.1016/0002-9343\(81\)90407-1](https://doi.org/10.1016/0002-9343(81)90407-1)]

**Kozin 1992**

Kozin F. Reflex sympathetic dystrophy syndrome: a review. *Clinical and Experimental Rheumatology* 1992;**10**(4):401-9.

**Kriek 2017**

Kriek N, Groeneweg JG, Stronks DL, De Ridder D, Huygen FJ. Preferred frequencies and waveforms for spinal cord stimulation in patients with complex regional pain syndrome: a multicentre, double-blind, randomized and placebo-controlled crossover trial. *European Journal of Pain* 2017;**21**(3):507-19. [DOI: [10.1002/ejp.944](https://doi.org/10.1002/ejp.944)]

**Krämer 2014**

Krämer HH, Hofbauer LC, Szalay G, Breimhorst M, Eberle T, Zieschang K, et al. Osteoprotegerin: a new biomarker for impaired bone metabolism in complex regional pain syndrome? *Pain* 2014;**155**(5):889-95. [DOI: [10.1016/j.pain.2014.01.014](https://doi.org/10.1016/j.pain.2014.01.014)]

**Lee 2022**

Lee B, Di Pietro F, Henderson LA, Austin PJ. Altered basal ganglia infraslow oscillation and resting functional connectivity in complex regional pain syndrome. *Journal of Neuroscience Research* 2022;**100**(7):1487-505. [DOI: [10.1002/jnr.25057](https://doi.org/10.1002/jnr.25057)]

**Lewis 2007**

Lewis JS, Kersten P, McCabe CS, McPherson KM, Blake DR. Body perception disturbance: a contribution to pain in complex regional pain syndrome (CRPS). *Pain* 2007;**133**(1-3):111-9. [DOI: [10.1016/j.pain.2007.03.013](https://doi.org/10.1016/j.pain.2007.03.013)]

**Lewis 2021**

Lewis JS, Newport R, Taylor G, Smith M, McCabe CS. Visual illusions modulate body perception disturbance and pain in complex regional pain syndrome: a randomized trial. *European Journal of Pain* 2021;**25**(7):1551-63. [DOI: [10.1002/ejp.1766](https://doi.org/10.1002/ejp.1766)]

**Li 2012a**

Li N, Tian F, Wang C, Yu P, Zhou X, Wen Q, et al. Therapeutic effect of acupuncture and massage for shoulder hand syndrome in hemiplegia patients: a clinical two-centre randomized controlled trial. *Journal of Traditional Chinese Medicine* 2012;**32**(3):343-9. [DOI: [10.1016/s0254-6272\(13\)60035-7](https://doi.org/10.1016/s0254-6272(13)60035-7)]

**Li 2012b**

Li SZ, Wang WY, Liu J. Acupuncture combined with rehabilitation training for shoulder hand syndrome after apoplexy. *Chinese Journal of Traditional Medical Science and Technology* 2012;**19**:552-3.

**Li 2015a**

Li ZF, Gu JH, Hu M. Clinical observation of acupuncture for 46 patients with shoulder hand syndrome after stroke. *Chinese Journal of Ethnomedicine and Ethnopharmacy* 2015;**24**:78-79.

**Liang 2016**

Liang LN, Zhang YJ, Liu YH. Acupuncture combined rehabilitation training for 30 patients with post stroke should hand. *Laboratory Medicine* 2016;**31**:203.

**Liao 2006**

Liao HW. Clinical observations on the efficacy of occupational therapy plus acupuncture for treating reflex sympathetic dystrophy. *Shanghai Journal of Acupuncture and Moxibustion* 2006;**25**:9-10.

**Lim 2007**

Lim KB, Lee HJ, Joo SJ, Kim JY, Lim SS. The comparison of effects between stellate ganglion block and oral corticosteroid therapy in post-stroke complex regional pain syndrome. *Journal of the Korean Academy of Rehabilitation Medicine* 2007;**31**(4):417-22.

**Livingstone 2002**

Livingstone JA, Atkins RM. Intravenous regional guanethidine blockade in the treatment of post-traumatic complex regional pain syndrome type 1 (algodystrophy) of the hand. *The Journal of Bone and Joint Surgery* 2002;**84**(3):380-6. [DOI: [10.1302/0301-620x.84b3.11901](https://doi.org/10.1302/0301-620x.84b3.11901)]

**Lotze 2007**

Lotze M, Moseley GL. Role of distorted body image in pain. *Current Rheumatology Reports* 2007;**9**(6):488-96. [DOI: [10.1007/s11926-007-0079-x](https://doi.org/10.1007/s11926-007-0079-x)]

**Lukovic 2006**

Lukovic TZ, Ilic KP, Jevtic M, Toncev G. Corticosteroids and physical agents in treatment of complex regional pain syndrome type I. *Medicus* 2006;**7**(2):70-2.

**Mangnus 2022a**

Mangnus TJ, Bharwani KD, Dirckx M, Huygen FJ. From a symptom-based to a mechanism-based pharmacotherapeutic treatment in complex regional pain syndrome. *Drugs* 2022;**82**:511-531. [DOI: [10.1007/s40265-022-01685-4](https://doi.org/10.1007/s40265-022-01685-4)]

**Mangnus 2022b**

Mangnus TJ, Bharwani KD, Stronks DL, Dirckx M, Huygen FJ. Ketamine therapy for chronic pain in The Netherlands: a nationwide survey. *Scandinavian Journal of Pain* 2022;**22**(1):97-105. [DOI: [10.1515/sjpain-2021-0079](https://doi.org/10.1515/sjpain-2021-0079)]

**Manicourt 2004**

Manicourt DH, Brasseur JP, Boutsen Y, Depreseux G, Devogelaer JP. Role of alendronate in therapy for posttraumatic

complex regional pain syndrome type I of the lower extremity. *Arthritis and Rheumatism* 2004;**50**(11):3690-7. [DOI: [10.1002/art.20591](https://doi.org/10.1002/art.20591)]

**Manjunath 2008**

Manjunath PS, Jayalakshmi TS, Dureja GP, Prevost AT. Management of lower limb complex regional pain syndrome type 1: an evaluation of percutaneous radiofrequency thermal lumbar sympathectomy versus phenol lumbar sympathetic neurolysis - a pilot study. *Anesthesia and Analgesia* 2008;**106**(2):647-9. [DOI: [10.1213/01.ane.0000298285.39480.28](https://doi.org/10.1213/01.ane.0000298285.39480.28)]

**Manning 2014**

Manning DC, Alexander G, Arezzo JC, Cooper A, Harden RN, Oaklander AL, et al. Lenalidomide for complex regional pain syndrome type 1: lack of efficacy in a phase II randomized study. *The Journal of Pain* 2014;**15**(12):1366-76. [DOI: [10.1016/j.jpain.2014.09.013](https://doi.org/10.1016/j.jpain.2014.09.013)]

**Marinus 2011**

Marinus J, Moseley GL, Bircklein F, Baron R, Maihöfner C, Kingery WS, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurology* 2011;**10**(7):637-48. [DOI: [10.1016/S1474-4422\(11\)70106-5](https://doi.org/10.1016/S1474-4422(11)70106-5)]

**Merskey 1994**

Merskey H, Bogduk N. Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms. 2nd edition. Seattle: IASP Press, 1994.

**Miao 1996**

Miao HS, Zhu LL. Rehabilitation Evaluation and Treatment for Stroke. Beijing: Huaxia Publishing House, 1996.

**Miller 2019**

Miller C, Williams M, Heine P, Williamson E, O'Connell N. Current practice in the rehabilitation of complex regional pain syndrome: a survey of practitioners. *Disability and Rehabilitation* 2019;**41**(7):847-53. [DOI: [10.1080/09638288.2017.1407968](https://doi.org/10.1080/09638288.2017.1407968)]

**Moore 2010**

Moore RS, Eccleston C, Derry S, Wiffen P, Bell RF, Straube S, et al on behalf of the ACTINPAIN writing group of the IASP Special Interest Group (SIG) on Systematic Reviews in Pain Relief. "Evidence" in chronic pain - establishing best practice in the reporting of systematic reviews. *Pain* 2010;**150**(3):386-9. [DOI: [10.1016/j.pain.2010.05.011](https://doi.org/10.1016/j.pain.2010.05.011)]

**Moseley 2004**

Moseley GL. Graded motor imagery is effective for long-standing complex regional pain syndrome: a randomised controlled trial. *Pain* 2004;**108**(1):192-8. [DOI: [10.1016/j.pain.2004.01.006](https://doi.org/10.1016/j.pain.2004.01.006)]

**Moseley 2006**

Moseley GL. Graded motor imagery for pathologic pain: a randomized controlled trial. *Neurology* 2006;**67**(12):2129-34. [DOI: [10.1212/01.wnl.0000249112.56935.32](https://doi.org/10.1212/01.wnl.0000249112.56935.32)]

**Moseley 2009**

Moseley GL, Wiech K. The effect of tactile discrimination training is enhanced when patients watch the reflected image of their unaffected limb during training. *Pain* 2009;**144**(3):314-9. [DOI: [10.1016/j.pain.2009.04.030](https://doi.org/10.1016/j.pain.2009.04.030)]

**Moseley 2012**

Moseley GL, Flor H. Targeting cortical representations in the treatment of chronic pain: a review. *Neurorehabilitation and Neural Repair* 2012;**26**(6):646-52. [DOI: [10.1177/1545968311433209](https://doi.org/10.1177/1545968311433209)]

**Moseley 2014**

Moseley GL, Herbert RD, Parsons T, Lucas S, Van Hilten JJ, Marinus J. Intense pain soon after wrist fracture strongly predicts who will develop complex regional pain syndrome: prospective cohort study. *The Journal of Pain* 2014;**15**(1):16-23. [DOI: [10.1016/j.jpain.2013.08.009](https://doi.org/10.1016/j.jpain.2013.08.009)]

**Mucha 1992**

Mucha C. Effects of CO<sub>2</sub>-baths in the combined concept of the early functional therapy in cases of algodystrophy [Einflub von CO<sub>2</sub>-Badern im fruhfunktionellen Therapiekonzept der Algodystrophie]. *Physikalische Medizin und Kur Medizin* 1992;**2**:173-8.

**Munts 2009**

Munts AG, van der Plas AA, Voormolen JH, Marinus J, Teepe-Twiss IM, Onkenhout W, et al. Intrathecal glycine for pain and dystonia in complex regional pain syndrome. *Pain* 2009;**146**(1-2):199-204. [DOI: [10.1016/j.pain.2009.07.030](https://doi.org/10.1016/j.pain.2009.07.030)]

**Munts 2010**

Munts AG, van der Plas AA, Ferrari MD, Teepe-Twiss IM, Marinus J, van Hilten JJ. Efficacy and safety of a single intrathecal methylprednisolone bolus in chronic complex regional pain syndrome. *European Journal of Pain* 2010;**14**(5):523-8. [DOI: [10.1016/j.ejpain.2009.11.004](https://doi.org/10.1016/j.ejpain.2009.11.004)]

**Nascimento 2010**

Nascimento MS, Klamt JG, Prado WA. Intravenous regional block is similar to sympathetic ganglion block for pain management in patients with complex regional pain syndrome type I. *Brazilian Journal of Medical and Biological Research* 2010;**43**:1239-44. [DOI: [10.1590/S0100-879X2010007500123](https://doi.org/10.1590/S0100-879X2010007500123)]

**Nelson 2006**

Nelson DV, Stacey BR. Interventional therapies in the management of complex regional pain syndrome. *Clinical Journal of Pain* 2006;**22**(5):438-42. [DOI: [10.1097/01.ajp.0000192515.50955.9f](https://doi.org/10.1097/01.ajp.0000192515.50955.9f)]

**Niu 2015**

Niu GP. Clinical study of acupuncture combined with rehabilitation training for shoulder hand syndrome. *Henan Traditional Chinese Medicine* 2015;**35**:2846-7.

**Nüesch 2010**

Nüesch E, Trelle S, Reichenbach S, Rutjes AW, Tschannen B, Altman DG, et al. Small study effects in meta-analyses

of osteoarthritis trials: meta-epidemiological study. *BMJ* 2010;**341**:c3515. [DOI: [10.1136/bmj.c3515](https://doi.org/10.1136/bmj.c3515)]

**O'Connell 2018**

O'Connell NE, Marston L, Spencer S, DeSouza LH, Wand BM. Non-invasive brain stimulation techniques for chronic pain. *Cochrane Database of Systematic Reviews* 2018;**4**:CD008208. [DOI: [10.1002/14651858.CD008208.pub5](https://doi.org/10.1002/14651858.CD008208.pub5)]

**O'Connell 2021**

O'Connell NE, Ferraro MC, Gibson W, Rice AS, Vase L, Coyle D, et al. Implanted spinal neuromodulation interventions for chronic pain in adults. *Cochrane Database of Systematic Reviews* 2021, Issue 12. Art. No: CD013756. [DOI: [10.1002/14651858.CD013756.pub2](https://doi.org/10.1002/14651858.CD013756.pub2)]

**O'Neill 2014**

O'Neill J, Tabish H, Welch V, Petticrew M, Pottie K, Clarke M, et al. Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health. *Journal of Clinical Epidemiology* 2014;**67**:56-64. [DOI: [10.1016/j.jclinepi.2013.08.005](https://doi.org/10.1016/j.jclinepi.2013.08.005)]

**Oerlemans 1999**

Oerlemans HM, Oostendorp RAB, De Boo T, Goris RJA. Pain and reduced mobility in complex regional pain syndrome I: outcome of a prospective randomised controlled clinical trial of adjuvant physical therapy versus occupational therapy. *Pain* 1999;**83**(1):77-83. [DOI: [10.1016/s0304-3959\(99\)00080-9](https://doi.org/10.1016/s0304-3959(99)00080-9)]

**Ogawa 1998**

Ogawa S, Suzuki H, Shiotani MI, Ooseto K, Masuda Y, Kawachi S, et al. A randomized clinical trial of sarpogrelate hydrochloride for neuropathic pain in patients with post-herpetic neuralgia and reflex sympathetic dystrophy. *Pain Clinic* 1998;**11**(2):125-32.

**Ott 2018**

Ott S, Maihöfner C. Signs and symptoms in 1,043 patients with complex regional pain syndrome. *The Journal of Pain* 2018;**19**(6):599-611. [DOI: [10.1016/j.jpain.2018.01.004](https://doi.org/10.1016/j.jpain.2018.01.004)]

**Ozcan 2019**

Ozcan DS, Tatli HU, Polat CS, Oken O, Koseoglu BF. The effectiveness of fluidotherapy in poststroke complex regional pain syndrome: a randomized controlled study. *Journal of Stroke and Cerebrovascular Diseases* 2019;**28**(6):1578-85. [DOI: [10.1016/j.jstrokecerebrovasdis.2019.03.002](https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.03.002)]

**Page 2016**

Page MJ, Shamseer L, Altman DG, Tetzlaff J, Sampson M, Tricco AC, et al. Epidemiology and reporting characteristics of systematic reviews of biomedical research: a cross-sectional study. *PLoS Medicine* 2016;**13**(5):e1002028. [DOI: [10.1371/journal.pmed.1002028](https://doi.org/10.1371/journal.pmed.1002028)]

**Page 2021**

Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;**372**:n71. [DOI: [10.1136/bmj.n71](https://doi.org/10.1136/bmj.n71)]

**Parkitny 2013**

Parkitny L, McAuley JH, Di Pietro F, Stanton TR, O'Connell NE, Marinus J, et al. Inflammation in complex regional pain syndrome: a systematic review and meta-analysis. *Neurology* 2013;**80**(1):106-17. [DOI: [10.1212/WNL.0b013e31827b1aa1](https://doi.org/10.1212/WNL.0b013e31827b1aa1)]

**Parmar 2016**

Parmar MK, Sydes MR, Morris TP. How do you design randomised trials for smaller populations? A framework. *BMC Medicine* 2016;**14**:183. [DOI: [10.1186/s12916-016-0722-3](https://doi.org/10.1186/s12916-016-0722-3)]

**Partington 2022**

Partington G, Cro S, Mason A, Phillips R, Cornelius V. Design and analysis features used in small population and rare disease trials: a targeted review. *Journal of Clinical Epidemiology* 2022;**144**:93-101. [DOI: [10.1016/j.jclinepi.2021.12.009](https://doi.org/10.1016/j.jclinepi.2021.12.009)]

**Perez 2003**

Perez RSGM, Zuurmond WWA, Bezemer PD, Kuik DJ, Van Loenen AC, De Lange JJ, et al. The treatment of complex regional pain syndrome type I with free radical scavengers: a randomized controlled study. *Pain* 2003;**102**(3):297-307. [DOI: [10.1016/S0304-3959\(02\)00414-1](https://doi.org/10.1016/S0304-3959(02)00414-1)]

**Perez 2008**

Perez RS, Pragt E, Geurts J, Zuurmond WW, Patijn J, van Kleef M. Treatment of patients with complex regional pain syndrome type I with mannitol: a prospective, randomized, placebo-controlled, double-blinded study. *The Journal of Pain* 2008;**9**(8):678-86. [DOI: [10.1016/j.jpain.2008.02.005](https://doi.org/10.1016/j.jpain.2008.02.005)]

**Perez 2014**

Perez RS, Geertzen JH, Dijkstra PU, Dirckx M, Van Eijs F, Frölke JP, et al. Updated guidelines complex regional pain syndrome type I. Netherlands Society of Anaesthesiologists/ Netherlands Society of Rehabilitation Specialists 2014;**2014**.

**Picarelli 2010**

Picarelli H, Teixeira MJ, de Andrade DC, Myczkowski ML, Luvisotto TB, Yeng LT, et al. Repetitive transcranial magnetic stimulation is efficacious as an add-on to pharmacological therapy in complex regional pain syndrome (CRPS) type I. *The Journal of Pain* 2010;**11**(11):1203-10. [DOI: [10.1016/j.jpain.2010.02.006](https://doi.org/10.1016/j.jpain.2010.02.006)]

**Pieper 2014**

Pieper D, Antoine SL, Mathes T, Neugebauer EA, Eikermann M. Systematic review finds overlapping reviews were not mentioned in every other overview. *Journal of Clinical Epidemiology* 2014;**67**(4):368-75. [DOI: [10.1016/j.jclinepi.2013.11.007](https://doi.org/10.1016/j.jclinepi.2013.11.007)]

**Pleger 2004**

Pleger B, Janssen F, Schwenkreis P, Völker B, Maier C, Tegenthoff M. Repetitive transcranial magnetic stimulation of the motor cortex attenuates pain perception in complex regional pain syndrome type I. *Pain* 2004;**356**(2):87-90. [DOI: [10.1016/j.neulet.2003.11.037](https://doi.org/10.1016/j.neulet.2003.11.037)]

**Pollock 2022**

Pollock M, Fernandes RM, Becker LA, Pieper D, Hartling L. Chapter V: Overviews of Reviews. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.3 (updated February 2022). Cochrane, 2022. Available from [www.training.cochrane.org/handbook](http://www.training.cochrane.org/handbook).

**Price 1998**

Price DD, Long S, Wilsey B, Rafii A. Analysis of peak magnitude and duration of analgesia produced by local anesthetics injected into sympathetic ganglia of complex regional pain syndrome patients. *Clinical Journal of Pain* 1998;**14**(3):216-26.

**PROSPERO**

National Institute for Health Research. PROSPERO: international prospective register of systematic reviews. [www.crd.york.ac.uk/prospéro](http://www.crd.york.ac.uk/prospéro) (accessed 11 July 2022).

**Raja 2021**

Raja SN, Buvanendran A, Marcondes L. Complex regional pain syndrome: a comprehensive qualitative research study on unmet needs in the "patient journey". *Journal of Pain Research* 2021;**14**:2391-2401. [DOI: [10.2147/JPR.S317648](https://doi.org/10.2147/JPR.S317648)]

**Ramamurthy 1995**

Ramamurthy S, Hoffman J. Intravenous regional guanethidine in the treatment of reflex sympathetic dystrophy/causalgia: a randomized, double-blind study. *Anesthesia and Analgesia* 1995;**81**(4):718-23. [DOI: [10.1097/0000539-199510000-00011](https://doi.org/10.1097/0000539-199510000-00011)]

**Rauck 1993**

Rauck RL, Eisenach JC, Jackson K, Young LD, Southern J. Epidural clonidine treatment for refractory reflex sympathetic dystrophy. *Anesthesiology* 1993;**79**(6):1163-9.

**Rauck 2015**

Rauck RL, North J, Eisenach JC. Intrathecal clonidine and adenosine: effects on pain and sensory processing in patients with chronic regional pain syndrome. *Pain* 2015;**156**(1):88-95. [DOI: [10.1016/j.pain.000000000000007](https://doi.org/10.1016/j.pain.000000000000007)]

**Reinders 2002**

Reinders MF, Geertzen JHB, Dijkstra PU. Complex regional pain syndrome type I: use of the international association for the study of pain diagnostic criteria defined in 1994. *Clinical Journal of Pain* 2002;**18**(4):207-15. [DOI: [10.1097/00002508-200207000-00001](https://doi.org/10.1097/00002508-200207000-00001)]

**Robinson 2004**

Robinson JN, Sandom J, Chapman PT. Efficacy of pamidronate in complex regional pain syndrome type I. *Pain Medicine* 2004;**5**(3):276-80. [DOI: [10.1111/j.1526-4637.2004.04038.x](https://doi.org/10.1111/j.1526-4637.2004.04038.x)]

**Rocco 1989**

Rocco AG, Kaul AF, Reisman RM, Gallo JP, Lief PA. A comparison of regional intravenous guanethidine and reserpine in reflex sympathetic dystrophy a controlled, randomized, double-blind crossover study. *Clinical Journal of Pain* 1989;**5**(3):205-9. [DOI: [10.1097/00002508-198909000-00002](https://doi.org/10.1097/00002508-198909000-00002)]

**Rocha 2014**

Rocha RDO, Teixeira MJ, Yeng LT, Cantara MG, Faria VG, Liggieri V, et al. Thoracic sympathetic block for the treatment of complex regional pain syndrome type I: a double-blind randomized controlled study. *Pain* 2014;**155**(11):2274-81. [DOI: [10.1016/j.pain.2014.08.015](https://doi.org/10.1016/j.pain.2014.08.015)]

**Rodriguez 2005**

Rodriguez RF, Bravo LE, Tovar MA, Castro F, Ramos GE, Mendez F. Determination of the analgesic efficacy of the stellate ganglion blockade in the alleviation of pain mediated by the sympathetic nervous system in patients with Complex Regional Pain Syndrome [Determinacion de la eficacia analgesica de los bloqueos del ganglio estrellado en el alivio del dolor mediado por el sistema nervioso simpatico, en pacientes con sindrome doloroso regional complejo del miembro superior]. *Revista Colombiana de Anestesiología* 2005;**33**(3):153-9.

**Rolls 2020**

Rolls C, McCabe C, Llewellyn A, Jones GT. What is the incidence of complex regional pain syndrome (CRPS) Type I within four months of a wrist fracture in the adult population? A systematic review. *Hand Therapy* 2020;**25**(2):45-55. [DOI: [10.1177/1758998320910179](https://doi.org/10.1177/1758998320910179)]

**Safarpour**

Safarpour D, Salardini A, Richardson D, Jabbari B. Botulinum toxin A for treatment of allodynia of complex regional pain syndrome: a pilot study. *Pain Medicine* 2010;**11**(9):1411-4. [DOI: [10.1111/j.1526-4637.2010.00929.x](https://doi.org/10.1111/j.1526-4637.2010.00929.x)]

**Saha 2021**

Saha S, Sur M, Ray Chaudhuri G, Agarwal S. Effects of mirror therapy on oedema, pain and functional activities in patients with poststroke shoulder-hand syndrome: a randomized controlled trial. *Physiotherapy Research International* 2021;**26**(3):e1902. [DOI: [10.1002/pri.1902](https://doi.org/10.1002/pri.1902)]

**Sahin 2006**

Sahin F, Yilmaz F, Kotevoglou N, Kuran B. Efficacy of salmon calcitonin in complex regional pain syndrome (type 1) in addition to physical therapy. *Clinical Rheumatology* 2006;**25**(2):143-8. [DOI: [10.1007/s10067-005-1153-2](https://doi.org/10.1007/s10067-005-1153-2)]

**Sandroni 2003**

Sandroni P, Benrud-Larson LM, McClelland RL, Low PA. Complex regional pain syndrome type I: incidence and prevalence in Olmsted county, a population-based study. *Pain* 2003;**103**(1-2):199-207. [DOI: [10.1016/s0304-3959\(03\)00065-4](https://doi.org/10.1016/s0304-3959(03)00065-4)]

**Sarkar 2017**

Sarkar B, Goswami S, Mukherjee D, Basu S. Efficacy of motor imagery through mirror visual feedback therapy in complex regional pain syndrome: a comparative study. *Indian Journal of Pain* 2017;**31**(3):164-69. [DOI: [10.4103/ijpn.ijpn\\_51\\_17](https://doi.org/10.4103/ijpn.ijpn_51_17)]

**Savaş 2018**

Savaş S, İnal EE, Yavuz DD, Uslusoy F, Altuntaş SH, Aydın MA. Risk factors for complex regional pain syndrome in patients with surgically treated traumatic injuries attending hand therapy.

*Journal of Hand Therapy* 2018;**31**(2):250-4. [PMID: 10.1016/j.jht.2017.03.007]

**Scheffold 2015**

Scheffold BE, Hsieh CL, Litscher G. Neuroimaging and neuromonitoring effects of electro and manual acupuncture on the central nervous system: a literature review and analysis. *Evidence-Based Complementary and Alternative Medicine* 2015;**2015**:1-29. [DOI: [10.1155/2015/641742](https://doi.org/10.1155/2015/641742)]

**Schreuders 2014**

Schreuders TAR, Tichelaar R, Huygen FJPM, Hitters MWMGC, Stam HJ, Selles RW. Effects of a graded motor imagery program in patients with longstanding complex regional pain syndrome I (as supplied 29 May 2014). Data on file.

**Schulz 2010**

Schulz KF, Altman DG, Moher D, on behalf of the CONSORT group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;**340**:c332. [DOI: [10.1136/bmj.c332](https://doi.org/10.1136/bmj.c332)]

**Schwartzman 2009**

Schwartzman RJ, Alexander GM, Grothusen JR, Paylor T, Reichenberger E, Perreault M. Outpatient intravenous ketamine for the treatment of complex regional pain syndrome: a double-blind placebo controlled study. *Pain* 2009;**147**(1-3):107-15. [DOI: [10.1016/j.pain.2009.08.015](https://doi.org/10.1016/j.pain.2009.08.015)]

**Schünemann 2020**

Schünemann HJ, Higgins JPT, Vist GE, Glasziou P, Akl EA, Skoetz N, Guyatt GH. Chapter 14: Summary of findings' tables and grading the certainty of the evidence. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.3 (updated February 2022). Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.2 (updated February 2021) 2021.

**Shang 2008**

Shang YJ, Ma CC, Cai YY. Clinical study on acupuncture combined with rehabilitation therapy for treatment of post stroke shoulder-hand syndrome. *Chinese Journal of Acupuncture and Moxibustion* 2008;**28**:331-3.

**Shea 2007**

Shea BJ, Grimshaw JM, Wells G, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Medical Research Methodology* 2007;**7**(10):1-7. [DOI: [10.1186/1471-2288-7-10](https://doi.org/10.1186/1471-2288-7-10)]

**Shea 2017**

Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017;**358**:j4008. [DOI: [10.1136/bmj.j4008](https://doi.org/10.1136/bmj.j4008)]

**Shen 2014**

Shen ZH. Clinical observation of acupuncture combined with rehabilitation training for shoulder hand syndrome. *Shenzhen Journal of Integrated Traditional Chinese and Western Medicine* 2014;**24**:56-8.

**Shipton 2009**

Shipton EA. Complex regional pain syndrome: mechanisms, diagnosis, and management. *Current Anaesthesia and Critical Care* 2009;**20**:209-14. [DOI: [10.1016/j.cacc.2009.07.012](https://doi.org/10.1016/j.cacc.2009.07.012)]

**Short 2018**

Short B, Fong J, Galvez V, Shelker W, Loo CK. Side-effects associated with ketamine use in depression: a systematic review. *The Lancet Psychiatry* 2018;**5**(1):65-78. [DOI: [10.1016/S2215-0366\(17\)30272-9](https://doi.org/10.1016/S2215-0366(17)30272-9)]

**Sigtermans 2009**

Sigtermans MJ, van Hilten JJ, Bauer MCR, Arbous MS, Marinus J, Sarton EY, et al. Ketamine produces effective and long-term pain relief in patients with complex regional pain syndrome type I. *Pain* 2009;**145**:304-11. [DOI: [10.1016/j.pain.2009.06.023](https://doi.org/10.1016/j.pain.2009.06.023)]

**Siongco 2020**

Siongco PR, Rosales RL, Moore AP, Freynhagen R, Arimura K, Kanovsky P, et al. Botulinum neurotoxin injections for muscle-based (dystonia and spasticity) and non-muscle-based (neuropathic pain) pain disorders: a meta-analytic study. *Journal of Neural Transmission* 2020;**127**(6):935-951. [DOI: [10.1007/s00702-020-02163-5](https://doi.org/10.1007/s00702-020-02163-5)]

**Soin 2021**

Soin A, Soin Y, Dann T, Buenaventura R, Ferguson K, Atluri S, et al. Low-dose naltrexone use for patients with chronic regional pain syndrome: a systematic literature review. *Pain Physician* 2021;**24**(4):E393-E406.

**Steinbrocker 1948**

Steinbrocker O, Spitzer N, Friedman HH. The shoulder-hand syndrome in reflex dystrophy of the upper extremity. *Annals of Internal Medicine* 1948;**29**(1):22-52.

**Stewart 2012**

Stewart L, Moher D, Shekelle P. Why prospective registration of systematic reviews makes sense. *Systematic Reviews* 2012;**1**(7):1-4. [DOI: [10.1186/2046-4053-1-7](https://doi.org/10.1186/2046-4053-1-7)]

**Strauss 2021**

Strauss S, Barby S, Härtner J, Neumann N, Moseley GL, Lotze M. Modifications in fMRI representation of mental rotation following a 6 week graded motor imagery training in chronic CRPS patients. *The Journal of Pain* 2021;**22**(6):680-91. [DOI: [10.1016/j.jpain.2020.12.003](https://doi.org/10.1016/j.jpain.2020.12.003)]

**Sun 2012**

Sun YZ, Wang YJ, Wang W. Effect of acupuncture plus rehabilitation training on shoulder-hand syndrome due to ischemic stroke. *Journal of Acupuncture and Tuina Science* 2012;**10**:109-13.

**Taskaynatan 2004**

Taskaynatan AM, Ozgul A, Kenan Tan A, Dincer K, Alp Kalyon T. Bier block with methylprednisolone and lidocaine in CRPS type I: a randomized, double-blinded, placebo-controlled study. *Regional Anesthesia and Pain Medicine* 2004;**29**(5):408-12. [DOI: [10.1016/j.rapm.2004.05.007](https://doi.org/10.1016/j.rapm.2004.05.007)]

**Tie 2016**

Tie M. Effectiveness of rehabilitation training for shoulder hand syndrome after stroke. *Contemp Med Symp* 2016;**14**:144-5.

**Topcuoglu 2015**

Topcuoglu A, Gokkaya NKO, Ucan H, Karakuş D. The effect of upper-extremity aerobic exercise on complex regional pain syndrome type I: a randomized controlled study on subacute stroke. *Topics in Stroke Rehabilitation* 2015;**22**(4):253-61. [DOI: [10.1179/1074935714Z.00000000025](https://doi.org/10.1179/1074935714Z.00000000025)]

**Toshniwal 2012**

Toshniwal G, Sunder R, Thomas R, Dureja GP. Management of complex regional pain syndrome type I in upper extremity —evaluation of continuous stellate ganglion block and continuous infraclavicular brachial plexus block: a pilot study. *Pain Medicine* 2012;**13**(1):96-106. [DOI: [10.1111/j.1526-4637.2011.01285.x](https://doi.org/10.1111/j.1526-4637.2011.01285.x)]

**Treede 2019**

Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *Pain* 2019;**160**(1):19-27. [DOI: [10.1097/j.pain.0000000000001384](https://doi.org/10.1097/j.pain.0000000000001384)]

**Uher 2000**

Uher EM, Vacariu G, Schneider B, Fialka V. Comparison of manual lymph drainage with physical therapy in complex regional pain syndrome type I. A comparative randomized controlled therapy study. *Wiener klinische Wochenschrift [The Central European Journal of Medicine]* 2000;**112**:133-7.

**Urits 2021**

Urits I, Schwartz RH, Orhurhu V, Maganty NV, Reilly BT, Patel PM, et al. A comprehensive review of alternative therapies for the management of chronic pain patients: acupuncture, tai chi, osteopathic manipulative medicine, and chiropractic care. *Advances in Therapy* 2021;**38**:76-89. [DOI: [10.1007/s12325-020-01554-0](https://doi.org/10.1007/s12325-020-01554-0)]

**UTHealth CINAHL Filter**

University of Texas School of Public Health. Search filters for systematic reviews and meta-analyses. [https://libguides.sph.uth.tmc.edu/search\\_filters/cinahl\\_filters](https://libguides.sph.uth.tmc.edu/search_filters/cinahl_filters) (accessed 11 October 2021).

**Van de Vusse 2004**

Van de Vusse AC, Stomp-van den Berg SGM, Kessels AHF, Weber WE. Randomised controlled trial of gabapentin in complex regional pain syndrome type I. *BMC Neurology* 2004;**4**(13). [DOI: [10.1186/1471-2377-4-13](https://doi.org/10.1186/1471-2377-4-13)]

**Van den Berg 2022**

Van den Berg C, De Bree PN, Huygen FJ, Tiemensma J. Glucocorticoid treatment in patients with complex regional pain syndrome: systematic review. *European Journal of Pain* 2022 [Epub ahead of print].. [DOI: [10.1002/ejp.2025](https://doi.org/10.1002/ejp.2025)]

**Van der Plas 2011**

Van der Plas AA, Marinus J, Eldabe S, Buchser E, Van Hilten JJ. The lack of efficacy of different infusion rates of intrathecal baclofen in complex regional pain syndrome: a randomized, double-blind, crossover study. *Pain Medicine* 2011;**1**(12):459-65. [DOI: [10.1111/j.1526-4637.2011.01065.x](https://doi.org/10.1111/j.1526-4637.2011.01065.x)]

**Van der Plas 2013**

Van der Plas AA, Schilder JC, Marinus J, Van Hilten JJ. An explanatory study evaluating the muscle relaxant effects of intramuscular magnesium sulphate for dystonia in complex regional pain syndrome. *The Journal of Pain* 2013;**14**(11):1341-8. [DOI: [10.1016/j.jpain.2013.05.013](https://doi.org/10.1016/j.jpain.2013.05.013)]

**Van Kleef 2009**

Van Kleef M, Mekhail N, Van Zundert J. Evidence-based guidelines for interventional pain medicine according to clinical diagnoses. *Pain Practice* 2009;**9**(4):247-51. [DOI: [10.1111/j.1533-2500.2009.00297.x](https://doi.org/10.1111/j.1533-2500.2009.00297.x)]

**Van Rooijen 2012**

Van Rooijen DE, Roelen DL, Verduijn W, Haasnoot GW, Huygen FJ, Perez RS, et al. Genetic HLA associations in complex regional pain syndrome with and without dystonia. *Journal of Pain* 2012;**13**(8):784-9. [DOI: [10.1016/j.jpain.2012.05.003](https://doi.org/10.1016/j.jpain.2012.05.003)]

**Van Tulder 1997**

Van Tulder MW, Koes BW, Bouter LM. Conservative treatment of acute and chronic nonspecific low back pain: a systematic review of randomized controlled trials of the most common interventions. *Spine* 1997;**22**(18):2128-56.

**Varena 2000**

Varena M, Zucchi F, Ghiringhelli D, Binelli L, Bevilacqua M, Bettica P, et al. Intravenous clodronate in the treatment of reflex sympathetic dystrophy syndrome. A randomized, double blind, placebo controlled study. *Journal of Rheumatology* 2000;**27**(6):1477-83.

**Varena 2013**

Varena M, Adami S, Rossini M, Gatti D, Idolazzi L, Zucchi F, et al. Treatment of complex regional pain syndrome type I with neridronate: a randomized, double-blind, placebo-controlled study. *Rheumatology* 2013;**52**(3):534-42. [DOI: [10.1093/rheumatology/kes312](https://doi.org/10.1093/rheumatology/kes312)]

**Varena 2021**

Varena M, Braga V, Gatti D, Iolascon G, Frediani B, Zucchi F, et al. Intramuscular neridronate for the treatment of complex regional pain syndrome type 1: a randomized, double-blind, placebo-controlled study. *Therapeutic Advances in Musculoskeletal Disease* 2021;**13**:1-12. [DOI: [10.1177/1759720X211014020](https://doi.org/10.1177/1759720X211014020)]

**Veldman 1993**

Veldman PH, Reynen HM, Arntz IE, Goris RJ. Signs and symptoms of reflex sympathetic dystrophy: prospective study of 829 patients. *Lancet* 1993;**342**(8878):1012-6. [DOI: [10.1016/0140-6736\(93\)92877-V](https://doi.org/10.1016/0140-6736(93)92877-V)]

**Verhagen 1998**

Verhagen AP, De Vet HC, De Bie RA, Kessels AG, Boers M, Bouter LM, et al. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *Journal of Clinical Epidemiology* 1998;**51**(12):1235-41.

**Vlaeyen 2012**

Vlaeyen JWS, Morley SJ, Linton SJ, Boersma K, de Jong, J. Pain-related fear exposure-based treatments for chronic pain. Washington DC: IASP Press, 2012.

**Vural 2016**

Vural SP, Yuzer GF, Ozcan DS, Ozbudak SD, Ozgirgin N. Effects of mirror therapy in stroke patients with complex regional pain syndrome type 1: a randomized controlled study. *Archives of Physical Medicine and Rehabilitation* 2016;**97**(4):575-81. [DOI: [10.1016/j.apmr.2015.12.008](https://doi.org/10.1016/j.apmr.2015.12.008)]

**Wallace 2000**

Wallace MS, Ridgeway BM, Leung AY, Gerayli A, Yaksh TL. Concentration-effect relationship of intravenous lidocaine on the allodynia of complex regional pain syndrome types I and II. *Anesthesiology* 2000;**92**(1):75-83. [DOI: [10.1097/0000542-200001000-00017](https://doi.org/10.1097/0000542-200001000-00017)]

**Wan 2013**

Wan WR, Wang TL, Cheng SL. Post stroke shoulder hand syndrome treated with acupuncture and rehabilitation: a randomized controlled trial. *Chinese Acupuncture & Moxibustion* 2013;**33**(11):970-4.

**Wang 2017a**

Wang XQ, Gao Y, Gao S. Acupuncture combined with rehabilitation on the influence of PRI, FMA and MBI in patients with shoulder hand syndrome with stroke. *Global Traditional Chinese Medicine* 2017;**10**:361-3.

**WHO 2023**

World Health Organization. Traditional, complementary and integrative medicine . [www.who.int/health-topics/traditional-complementary-and-integrative-medicine](http://www.who.int/health-topics/traditional-complementary-and-integrative-medicine) (accessed 2 May 2023).

**Wie 2021**

Wie C, Gupta R, Maloney J, Pew S, Freeman J, Strand N. Interventional modalities to treat complex regional pain syndrome. *Current Pain and Headache Reports* 2021;**25**(2):1-6. [DOI: [10.1007/s11916-020-00904-5](https://doi.org/10.1007/s11916-020-00904-5)]

**Williams 2020**

Williams AC, Fisher E, Hearn L, Eccleston C. Psychological therapies for the management of chronic pain (excluding headache) in adults. *Cochrane Database of Systematic*

Reviews 2020, Issue 8. Art. No: CD007407. [DOI: [10.1002/14651858.CD007407.pub4](https://doi.org/10.1002/14651858.CD007407.pub4)]

#### Wu 1999

Wu W, Bandilla E, Ciccone DS, Yang J, Cheng SCS, Carner N, et al. Effects of qigong on late-stage complex regional pain syndrome. *Alternative Therapies in Health and Medicine* 1999;**5**(1):45-54.

#### Wu 2014

Wu ZG. Acupuncture combined with rehabilitation training for 100 patients with shoulder-hand syndrome after stroke. *Chinese Medicine Modern Distance Education of China* 2014;**12**:81-2.

#### Xu 2015

Xu F, Li HL, Zhang Q. Acupuncture combined with rehabilitation training for shoulder hand syndrome after ischemic stroke Chinese: a randomized controlled trial. *Chinese Journal of Trauma and Disability Medicine* 2017;**23**:141-2.

#### Yoo 2012

Yoo SD, Jung SS, Kim HS, Yun DH, Kim DH, Chon J, et al. Efficacy of ultrasonography guided stellate ganglion blockade in the stroke patients with complex regional pain syndrome. *Annals of Rehabilitation Medicine* 2012;**36**(5):633-9. [DOI: [10.5535/arm.2012.36.5.633](https://doi.org/10.5535/arm.2012.36.5.633)]

#### Zeng 2003

Zeng X, Chen S, Guan C, Jiang L, Wang L. Block of ganglion stellatum on improving edema and range of movement in shoulder-hand syndrome. *Chinese Journal of Clinical Rehabilitation* 2003;**7**(7):1194-5.

#### Zhang 2015

Zhang XR. Clinical effectiveness analyses of acupuncture combined with rehabilitation training for shoulder hand syndrome after stroke. *China Medical Engineering* 2015;**23**:200.

#### Zhao 2004

Zhao XF, Song H. Acupuncture for 30 patients with shoulder hand syndrome after stroke. *Chinese Journal of Information on Traditional Chinese Medicine* 2004;**11**:535-3.

#### Zhong 2011

Zhong Q, Feng QH, Yi G. Synthetic rehabilitation therapy for shoulder hand syndrome after stroke. *Practical Journal of Clinical Medicine* 2011;**8**:115-6.

#### Zuurmond 1996

Zuurmond WWA, Langendijk PNJ, Bezemer PD, Brink HEJ, De Lange JJ, Van Loenen AC. Treatment of acute reflex sympathetic dystrophy with DMSO 50% in a fatty cream. *Acta Anaesthesiologica Scandinavica* 1996;**40**(3):364-7. [DOI: [10.1111/j.1399-6576.1996.tb04446.x](https://doi.org/10.1111/j.1399-6576.1996.tb04446.x)]

### References to other published versions of this review

#### O'Connell 2011

O'Connell NE, Wand BM, McAuley J, Marston L, Moseley GL. Interventions for treating pain and disability in adults with complex regional pain syndrome. *Cochrane Database of Systematic Reviews* 2011, Issue 11. Art. No: CD009416. [DOI: [10.1002/14651858.CD009416](https://doi.org/10.1002/14651858.CD009416)]

#### O'Connell 2013

O'Connell NE, Wand BM, McAuley J, Marston L, Moseley GL. Interventions for treating pain and disability in adults with complex regional pain syndrome: an overview of systematic reviews. *Cochrane Database of Systematic Reviews* 2013, Issue 4. Art. No: CD009416. [DOI: [10.1002/14651858.CD009416.pub2](https://doi.org/10.1002/14651858.CD009416.pub2)]

## ADDITIONAL TABLES

**Table 1. The Budapest diagnostic criteria for CRPS**

- 
1. Continuing pain, which is disproportionate to any inciting event
- 
2. Must report at least one symptom in three of the four following categories\*
    - *Sensory*: reports of hyperaesthesia and/or allodynia
    - *Vasomotor*: reports of temperature asymmetry and/or skin colour changes and/or skin colour asymmetry
    - *Sudomotor/oedema*: reports of oedema and/or sweating changes and/or sweating asymmetry
    - *Motor/trophic*: reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
- 
3. Must display at least one sign at time of evaluation in two or more of the following categories\*
    - *Sensory*: evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)
    - *Vasomotor*: evidence of temperature asymmetry and/or skin colour changes and/or asymmetry
    - *Sudomotor/oedema*: evidence of oedema and/or sweating changes and/or sweating asymmetry
    - *Motor/trophic*: evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
-

**Table 1. The Budapest diagnostic criteria for CRPS** (Continued)

4. There is no other diagnosis that better explains the signs and symptoms

\*The Budapest research criteria increases specificity for research settings by requiring the presence of all four symptom categories and at least two sign categories

**Table 2. Reasons for review exclusion**

Reason for exclusion	Papers excluded
Ineligible study design	<a href="#">Aiyer 2018*</a> ; <a href="#">Bussa 2015*</a> ; <a href="#">De Souza 2015*</a> ; <a href="#">Dirckx 2012*</a> ; <a href="#">Dworkin 2013*</a> ; <a href="#">Friend 2022*</a> ; <a href="#">Galafassi 2021*</a> ; <a href="#">Jadad 1995*</a> ; <a href="#">Nagpal 2021*</a> ; <a href="#">Roche Bueno 2020*</a> ; <a href="#">Soin 2021*</a> ; <a href="#">Wang 2021**</a> ; <a href="#">Wertli 2014**</a> ; <a href="#">Żyluk 2018*</a>
Insufficient CRPS exclusivity	<a href="#">Aamir 2020</a> ; <a href="#">Aiyer 2016</a> ; <a href="#">Andreae 2015</a> ; <a href="#">Balanaser 2022</a> ; <a href="#">Bies 2022</a> ; <a href="#">Birse 2012</a> ; <a href="#">Boychuk 2015</a> ; <a href="#">Boyd 2019</a> ; <a href="#">Brookes 2017</a> ; <a href="#">Buksnys 2020</a> ; <a href="#">Casale 2021</a> ; <a href="#">Chaparro 2012</a> ; <a href="#">Cooper 2017</a> ; <a href="#">Corrigan 2012</a> ; <a href="#">Datta Gupta 2022</a> ; <a href="#">David 2018</a> ; <a href="#">Deer 2020</a> ; <a href="#">Derry 2012a</a> ; <a href="#">Derry 2012b</a> ; <a href="#">Derry 2013</a> ; <a href="#">Derry 2014</a> ; <a href="#">Derry 2015a</a> ; <a href="#">Derry 2015b</a> ; <a href="#">Derry 2016</a> ; <a href="#">Derry 2017b</a> ; <a href="#">Derry 2019</a> ; <a href="#">Di Stefano 2021</a> ; <a href="#">Duarte 2020</a> ; <a href="#">Duehmke 2017</a> ; <a href="#">Dykukha 2021</a> ; <a href="#">Eccleston 2015</a> ; <a href="#">Finnerup 2015</a> ; <a href="#">Gallagher 2015</a> ; <a href="#">Gaskell 2014</a> ; <a href="#">Gaskell 2016</a> ; <a href="#">Gibson 2017</a> ; <a href="#">Hary 2022</a> ; <a href="#">Hearn 2012</a> ; <a href="#">Hearn 2014a</a> ; <a href="#">Hearn 2014b</a> ; <a href="#">Hoydonckx 2019</a> ; <a href="#">Iskedjian 2007</a> ; <a href="#">Jia 2022</a> ; <a href="#">Jiang 2022</a> ; <a href="#">Jin 2015</a> ; <a href="#">Ju 2017</a> ; <a href="#">Julian 2020</a> ; <a href="#">Jupudi 2021</a> ; <a href="#">Kapustin 2020</a> ; <a href="#">Knezevic 2020</a> ; <a href="#">Li 2015b</a> ; <a href="#">Liao 2017</a> ; <a href="#">Lunn 2014</a> ; <a href="#">Mailis-Gagnon 2004</a> ; <a href="#">Markman 2017</a> ; <a href="#">Martins de Andrade 2016</a> ; <a href="#">McNicol 2013</a> ; <a href="#">McNicol 2017</a> ; <a href="#">McParland 2021</a> ; <a href="#">Meng 2017</a> ; <a href="#">Mohiuddin 2021</a> ; <a href="#">Moisset 2020</a> ; <a href="#">Moore 2012</a> ; <a href="#">Moore 2015a</a> ; <a href="#">Moore 2015b</a> ; <a href="#">Moore 2015c</a> ; <a href="#">Mu 2017</a> ; <a href="#">Mücke 2018</a> ; <a href="#">Ney 2013</a> ; <a href="#">O'Connell 2010</a> ; <a href="#">Petzke 2016</a> ; <a href="#">Shi 2016</a> ; <a href="#">Shin 2021</a> ; <a href="#">Silvinato 2020</a> ; <a href="#">Singh 2017</a> ; <a href="#">Sommer 2020</a> ; <a href="#">Stannard 2016</a> ; <a href="#">Thieme 2016</a> ; <a href="#">Tremont-Lukats 2005</a> ; <a href="#">Vargas-Espinosa 2012</a> ; <a href="#">Wang 2017b</a> ; <a href="#">Wei 2019</a> ; <a href="#">Wiffen 2013a</a> ; <a href="#">Wiffen 2013b</a> ; <a href="#">Wiffen 2014a</a> ; <a href="#">Wiffen 2014b</a> ; <a href="#">Wiffen 2015</a> ; <a href="#">Wiffen 2016</a> ; <a href="#">Wiffen 2017</a> ; <a href="#">Zhou 2017</a> ; <a href="#">Wrzosek 2015</a>
No novel coverage in addition to existing Cochrane reviews or other included reviews	<a href="#">Azari 2012</a> ; <a href="#">Brunner 2009</a> ; <a href="#">Chitneni 2021</a> ; <a href="#">Collins 2010</a> ; <a href="#">Connolly 2015</a> ; <a href="#">Daly 2009</a> ; <a href="#">Fabregat 2013</a> ; <a href="#">Gatzinsky 2021</a> ; <a href="#">Grabow 2003</a> ; <a href="#">Lu 2009</a> ; <a href="#">Matuschek 2017</a> ; <a href="#">Méndez-Rebolledo 2017</a> ; <a href="#">Nardone 2018</a> ; <a href="#">Oh 2015</a> ; <a href="#">Pearl 2020</a> ; <a href="#">Perez 2001</a> ; <a href="#">Rothgangel 2011</a> ; <a href="#">Selph 2011</a> ; <a href="#">Siongco 2020</a> ; <a href="#">Simpson 2009</a> ; <a href="#">Turner 2004</a> ; <a href="#">Van den Berg 2022</a> ; <a href="#">Visnjevac 2017</a>
Previous version of already included review	<a href="#">Cepeda 2005</a> ; <a href="#">Moore 2011</a> ; <a href="#">Stanton 2013</a> ; <a href="#">Smart 2016</a> ; <a href="#">Straube 2010</a>
Did not report outcomes relevant to this overview	<a href="#">Lin 2012</a> ; <a href="#">Packham 2018</a>
Included randomised and non-randomised studies but did not report separately	<a href="#">Zhao 2018</a>

\*Not a systematic review that satisfied a judgement of 'Yes' on third AMSTAR criterion ([Shea 2007](#))

\*\*Excluded due to unclear network meta-analysis methodology and uninterpretable effect estimates

**Table 3. List of interventions, reviews and trials included in the overview**

Intervention	Review	Trials contributed and sample size (n)
<b>Oral, intravenous and topical pharmacotherapy</b>		
Bisphosphonates	<a href="#">Chauvineau 2005</a>	<a href="#">Cohen 1998</a> (n = 14)
	<a href="#">Chevreau 2017</a>	<a href="#">Manicourt 2004</a> (n = 40)

**Interventions for treating pain and disability in adults with complex regional pain syndrome- an overview of systematic reviews (Review)**

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**Table 3. List of interventions, reviews and trials included in the overview** (Continued)

		Robinson 2004 (n = 27)
		Varenna 2000 (n = 32)
		Varenna 2013 (n = 82)
	Duong 2018	Eun Young 2016 (n = 21)
	Fassio 2022	Varenna 2021 (n = 78)
Botulinum toxin A	Duong 2018	Safarpour (n = 8)
Calcitonin	Tran 2010	Gobelet 1992 (n = 66)
		Gobelet 1986 (n = 24)
		Sahin 2006 (n = 35)
Corticosteroids	Duong 2018	Kalita 2016 (n = 58)
	Fischer 2010	Kalita 2006 (n = 60)
		Lukovic 2006 (n = 60)
Free radical scavengers	Fischer 2010	Goris 1987 (n = 20)
		Zuurmond 1996 (n = 30)
		Perez 2003 (n = 146)
	Fischer 2010	Perez 2008 (n = 41)
Gabapentin	Moore 2014 (Cochrane)	Van de Vusse 2004 (n = 58)
Immunoglobulin	Duong 2018	Goebel 2010 (n = 12)
Infliximab	Xu 2016	Dirckx 2013 (n = 13)
Isosorbide dinitrate	Duong 2018	Groeneweg 2009 (n = 24)
Lenalidomide	Duong 2018	Manning 2014 (n = 147)
NMDA receptor antagonists	Orhurhu 2019	Schwartzman 2009 (n = 60)
		Sigtermans 2009 (n = 19)
	Duong 2018	Fischer 2013 (n = 56)
		Van der Plas 2013 (n = 22)
	Cossins 2013	Gustin 2010 (n = NR)
NSAIDs	Duong 2018	Breuer 2014 (n = 20)
Sarpogrelate hydrochloride	Tran 2010	Ogawa 1998 (n = 30)
Tadalafil	Tran 2010	Groeneweg 2008 (n = 24)

**Interventional procedures**

**Table 3. List of interventions, reviews and trials included in the overview** (Continued)

Neuraxial therapy		
Epidural clonidine	<a href="#">Tran 2010</a>	<a href="#">Rauck 1993</a> (n = 26)
Intrathecal baclofen	<a href="#">Duong 2018</a>	<a href="#">Van der Plas 2011</a> (n = 14)
Intrathecal clonidine	<a href="#">Duong 2018</a>	<a href="#">Rauck 2015</a> (n = 20)
Intrathecal glycine	<a href="#">Duong 2018</a>	<a href="#">Munts 2009</a> (n = 18)
Intrathecal methylpred-nisolone	<a href="#">Duong 2018</a>	<a href="#">Munts 2010</a> (n = 10)
Intravenous regional blockade (IVRB)		
IVRB atropine	<a href="#">Tran 2010</a>	<a href="#">Glynn 1993</a> (n = 30)
IVRB droperidol	<a href="#">Xu 2016</a>	<a href="#">Kettler 1988</a> (n = 6)
IVRB guanethidine	<a href="#">Xu 2016</a>	<a href="#">Blanchard 1990</a> (n = 21) <a href="#">Livingstone 2002</a> (n = 57) <a href="#">Ramamurthy 1995</a> (n = 60)
IVRB guanethidine/lidocaine/reserpine	<a href="#">Xu 2016</a>	<a href="#">Rocco 1989</a> (n = 12)
IVRB ketanserin	<a href="#">Xu 2016</a>	<a href="#">Bounameaux 1984</a> (n = 9) <a href="#">Hanna 1989</a> (n = 9)
IVRB lidocaine	<a href="#">Challapalli 2005</a> (Cochrane)	<a href="#">Wallace 2000</a> (n = 16)
IVRB lidocaine/ketorolac	<a href="#">Xu 2016</a>	<a href="#">Eckmann 2011</a> (n = 12)
IVRB lidocaine/methylpred-nisolone	<a href="#">Fischer 2010</a>	<a href="#">Taskaynatan 2004</a> (n = 22)
IVRB parecoxib/lidocaine/clonidine	<a href="#">Fassio 2022</a>	<a href="#">Frade 2005</a> (n = 30)
Local anaesthetic sympathetic blockade (LASB)		
LASB	<a href="#">O'Connell 2016</a> (Cochrane)	<a href="#">Zeng 2003</a> (n = 60)
LASB lidocaine	<a href="#">O'Connell 2016</a> (Cochrane)	<a href="#">Aydemir 2006</a> (n = 25) <a href="#">Price 1998</a> (n = 7) <a href="#">Lim 2007</a> (n = 38) <a href="#">Nascimento 2010</a> (n = 43) <a href="#">Yoo 2012</a> (n = 42)

**Table 3. List of interventions, reviews and trials included in the overview** (Continued)

LASB botulinum toxin A/ bupivacaine	O'Connell 2016 (Cochrane)	Carroll 2009 (n = 9)
LASB bupivacaine	O'Connell 2016 (Cochrane)	Bonelli 1983 (n = 19) Toshniwal 2012 (n = 33)
LASB lidocaine/bupivacaine	O'Connell 2016 (Cochrane)	Rodriguez 2005 (n = 82)
LASB lidocaine/clonidine	O'Connell 2016 (Cochrane)	Freitas 2013 (n = 40)
LASB ropivacaine/triamci- nolone	O'Connell 2016 (Cochrane)	Rocha 2014 (n = 36)
Sympathectomy	Straube 2013 (Cochrane)	Manjunath 2008 (n = 20)
<b>Neuromodulation</b>		
Repetitive transcranial magnetic stimulation	Cossins 2013	Pleger 2004 (n = NR) Picarelli 2010 (n = NR)
Spinal cord stimulation	Duong 2018	Deer 2017 (n = 146) Kriek 2017 (n = 40)
	Tran 2010	Kemler 2000 (n = 54) Kemler 2004 (n = NR) Kemler 2008 (n = NR)
<b>Rehabilitation</b>		
CO <sub>2</sub> and whirlpool baths	Smart 2022 (Cochrane)	Mucha 1992 (n = 40) Devrimsel 2015 (n = 60)
Electrophysical agents	Smart 2022 (Cochrane)	Askin 2014 (n = 45) Benedetti 2018 (n = 30) Bilgili 2016 (n = 30) Büyükturan 2018 (n = 42) Dimitrijevic 2014 (n = 50) Durmus 2004 (n = 40) Hazneci 2005 (n = 30)
Electro-acupuncture and massage	Smart 2022 (Cochrane)	Li 2012a (n = 120)
Exposure-based interven- tions	Smart 2022 (Cochrane)	Barnhoorn 2015 (n = 56)

**Table 3. List of interventions, reviews and trials included in the overview** *(Continued)*  
[den Hollander 2016](#) (n = 46)

Fluidotherapy	<a href="#">Smart 2022</a> (Cochrane)	<a href="#">Ozcan 2019</a> (n = 32)
Graded motor imagery and mirror therapy	<a href="#">Smart 2022</a> (Cochrane)	<a href="#">Cacchio 2009a</a> (n = 24) <a href="#">Cacchio 2009b</a> (n = 48) <a href="#">Moseley 2004</a> (n = 13) <a href="#">Moseley 2006</a> (n = 37) <a href="#">Saha 2021</a> (n = 38) <a href="#">Sarkar 2017</a> (n = 30) <a href="#">Schreuders 2014</a> (n = 18) <a href="#">Strauss 2021</a> (n = 22) <a href="#">Vural 2016</a> (n = 30)
Manual lymphatic drainage	<a href="#">Smart 2022</a> (Cochrane)	<a href="#">Duman 2009</a> (n = 34) <a href="#">Uher 2000</a> (n = 40)
Multimodal physiotherapy	<a href="#">Smart 2022</a> (Cochrane)	<a href="#">Oerlemans 1999</a> (n = 135) <a href="#">Topcuoglu 2015</a> (n = 40)
Prism adaptation	<a href="#">Smart 2022</a> (Cochrane)	<a href="#">Halicka 2021</a> (n = 49)
Tactile discrimination	<a href="#">Smart 2022</a> (Cochrane)	<a href="#">Moseley 2009</a> (n = 10)
Virtual reality	<a href="#">Smart 2022</a> (Cochrane)	<a href="#">Hwang 2014</a> (n = 39) <a href="#">Jeon 2014</a> (n = 10) <a href="#">Lewis 2021</a> (n = 45)
<b>Complementary and alternative therapies</b>		
Acupuncture	<a href="#">Forouzanfar 2002</a>	<a href="#">Fialka 1993</a> (n = 14) <a href="#">Kho 1995</a> (n = 28) <a href="#">Korpan 1999</a> (n = 14)
	<a href="#">Smith 2005</a>	<a href="#">Ernst 1995</a> (n = 14)
	<a href="#">Peng 2018</a>	<a href="#">Chai 2016</a> (n = 118) <a href="#">Chang 2005</a> (n = 80) <a href="#">Chen 2015</a> (n = 94) <a href="#">Gao 2016</a> (n = 100) <a href="#">Li 2012b</a> (n = 60) <a href="#">Li 2015a</a> (n = 92) <a href="#">Liang 2016</a> (n = 32)

**Table 3. List of interventions, reviews and trials included in the overview** (Continued)

		Liao 2006 (n = 90)
		Niu 2015 (n = 108)
		Shang 2008 (n = 80)
		Shen 2014 (n = 60)
		Sun 2012 (n = 60)
		Tie 2016 (n = 100)
		Wan 2013 (n = 120)
		Wang 2017a (n = 142)
		Wu 2014 (n = 200)
		Xu 2015 (n = 80)
		Zhao 2004 (n = 54)
		Zhang 2015 (n = 92)
		Zhong 2011 (n = 158)
	Forouzanfar 2002	Korpan 1999 (n = 14)
Qigong	Smith 2005	Wu 1999 (n = 26)
Relaxation therapy	Smith 2005	Fialka 1996 (n = 18)
<b>Other interventions</b>		
Occlusal splints	Cossins 2013	Fischer 2008 (n = NR)

 CO<sub>2</sub>: carbon dioxide

IVRB: intravenous regional blockade

LASB: local anaesthetic sympathetic blockade

NMDA: N-methyl D-aspartate

NR: not reported

NSAIDs: non-steroidal anti-inflammatory drugs

**Table 4. Characteristics of included reviews**

Review	Date of last search	Population	Interventions	Comparisons	Outcomes of interest specified?	Reported outcomes relevant to this overview
<b>Cochrane reviews</b>						
Challapalli 2005	May 2004 (search stabilised in 2020)	Participants of any age with neuropathic pain	Lidocaine or its analogs given parenterally or orally	Placebo or any active treatment	Yes	Pain intensity; pain relief; adverse events
Moore 2014	March 2014	Adult participants ≥ 18 years of age and above with neuropathic pain	Gabapentin	Placebo, no intervention, or any other ac-	Yes	Pain intensity; adverse events; serious adverse events

**Table 4. Characteristics of included reviews** (Continued)

				Compara- tor		
<a href="#">O'Connell 2016</a>	September 2015	CRPS in children or adults (diagnostic criteria not specified)	Selective sympathetic blockade with local anaesthetics	Placebo, no treatment, or alternative intervention	Yes	Pain intensity, adverse events
<a href="#">Smart 2022</a>	July 2021	Adults ≥ 18 years of age, diagnosed with CRPS I or II using established or validated diagnostic criteria	Physiotherapy interventions employed either as stand-alone interventions or in combination	Placebo, no treatment, another intervention or usual care, or varying physiotherapy interventions compared with each other	Yes	Pain intensity; disability; health-related quality of life; patient global impression of change; adverse effects
<a href="#">Straube 2013</a>	June 2013 (search stabilised in 2020)	Participants of any age, with any duration of neuropathic pain or CRPS (diagnostic criteria not specified)	Destructive surgical or chemical sympathectomy	Placebo (sham) or other active treatment, provided both participants and outcome assessors were blind to treatment group allocation	Yes	Pain relief; adverse events
<b>non-Cochrane reviews</b>						
<a href="#">Chauvineau 2005</a>	2003	Participants with CRPS I or reflex sympathetic dystrophy (diagnostic criteria not specified)	Bisphosphonates	Not specified	No	Pain intensity; side effects
<a href="#">Chevreau 2017</a>	2014	Adult participants with CRPS I according to <a href="#">Harden 2007</a> and <a href="#">Harden 2010</a> criteria	Bisphosphonates	Placebo	Yes	Pain; function; adverse events
<a href="#">Cossins 2013</a>	February 2012	Adult participants with CRPS I or II (diagnostic criteria not specified)	Any intervention	Any comparison	Yes	Pain intensity
<a href="#">Duong 2018</a>	August 2017	Participants with CRPS (diagnostic criteria not specified)	Any intervention	Any comparison	No	Pain intensity; disability; adverse effects; patient-reported global assessment of effect
<a href="#">Fassio 2022</a>	June 2021	Adults with CRPS I according to <a href="#">Harden 2010</a> , <a href="#">Galer 1998</a> , <a href="#">Kozin 1981</a> or <a href="#">Veldman 1993</a> criteria	Pharmacological interventions	Placebo or other active treatments	Yes	Pain intensity; adverse events; serious adverse events

**Table 4. Characteristics of included reviews** (Continued)

Fischer 2010	December 2009	CRPS I (diagnostic criteria not specified)	Anti-inflammatory therapies	Any comparison	Yes	Pain, clinical improvement
Forouzanfar 2002	June 2000	RSD and CRPS I (diagnostic criteria not specified)	Any intervention	Any comparison	Yes	Pain intensity
Orhurhu 2019	December 2017	Subjects $\geq 18$ years of age with chronic pain for $\geq 3$ months	Ketamine	Placebo with or without conventional medical management	Yes	Pain intensity; adverse events
Peng 2018	July 2017	Participants aged $\geq 18$ years of age with clinically confirmed shoulder-hand syndrome after stroke without complications (diagnostic criteria not specified)	Traditional manual acupuncture combined with rehabilitation	Placebo/sham acupuncture plus rehabilitation therapy or rehabilitation therapy alone	Yes	Pain intensity; function; activities of daily living
Smith 2005	November 2004	CRPS I (diagnostic criteria not specified)	Physiotherapeutic modalities	Any comparison	No	Pain intensity, disability; participant ratings of improvement; activities of daily living
Tran 2010	April 2009	CRPS I and II (diagnostic criteria not specified)	Any intervention	Any comparison	No	Pain intensity; disability; quality of life; participant ratings of improvement; adverse events
Xu 2016	February 2015	CRPS (diagnostic criteria not specified)	Intravenous therapies	Any comparison	No	Pain intensity; function; quality of life; adverse effects

CRPS: complex regional pain syndrome

RSD: reflex sympathetic dystrophy

**Table 5. Results of AMSTAR 2 quality assessment**

Review ID	1	2*	3	4*	5	6	7*	8	9*	10	11*	12	13*	14	15*	16	Overall confidence
Challapalli 2005**	+	P	-	P	+	-	+	P	P	-	+	+	-	+	+	+	Low
Chauvineau 2005	-	-	-	P	-	-	-	P	-	-	NA	NA	-	-	NA	-	Critically low
Chevreau 2017	+	-	-	-	+	+	-	-	-	-	+	-	+	-	+	+	Critically low
Cossins 2013	+	-	+	P	+	+	+	P	P	-	NA	NA	+	+	NA	+	Low
Duong 2018	-	-	+	-	+	+	+	P	+	-	NA	NA	-	-	NA	+	Critically low
Fassio 2022	+	P	-	-	+	-	+	-	+	-	+	-	-	+	-	+	Critically low
Fischer 2010	-	-	-	P	-	-	-	P	P	-	NA	NA	-	-	NA	-	Critically low
Forouzanfar 2002	-	-	-	-	+	-	-	-	P	+	NA	NA	-	+	NA	+	Critically low
Moore 2014**	+	+	-	P	+	+	+	P	P	+	+	+	+	-	+	+	High
O'Connell 2016**	+	+	-	+	+	+	+	P	+	+	NA	NA	+	+	NA	+	High
Orhurhu 2019	+	+	-	P	+	-	-	+	+	-	+	-	+	+	+	+	Low
Peng 2018	+	-	-	-	+	+	-	-	+	-	+	-	+	-	+	+	Critically low
Smart 2022**	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	High

**Table 5. Results of AMSTAR 2 quality assessment** (Continued)

Smith 2005	-	-	-	-	-	-	-	-	P	-	-	NA	NA	-	-	NA	-	Critically low
Straube 2013**	+	+	+	+	+	+	+	+	+	+	-	NA	NA	+	+	NA	+	High
Tran 2010	-	-	+	-	-	-	+	P	-	-	NA	NA	-	-	NA	+	Critically low	
Xu 2016	-	-	-	-	+	+	-	P	-	-	NA	NA	-	-	NA	+	Critically low	

\*AMSTAR 2 critical domain; \*\*Cochrane review' += Yes; - = No; P = Partial yes; NA = No meta-analysis conducted

**AMSTAR Items**

1. Did the research questions and inclusion criteria for the review include the components of PICO?
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?\*
3. Did the review authors explain their selection of the study designs for inclusion in the review?
4. Did the review authors use a comprehensive literature search strategy?\*
5. Did the review authors perform study selection in duplicate?
6. Did the review authors perform data extraction in duplicate?
7. Did the review authors provide a list of excluded studies and justify the exclusions?\*
8. Did the review authors describe the included studies in adequate detail?
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?\*
10. Did the review authors report on the sources of funding for the studies included in the review?
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?\*
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
13. Did the review authors account for RoB in primary studies when interpreting/discussing the results of the review?\*
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?\*
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

**Table 6. Overview of reviews: Oral, intravenous and topical pharmacotherapy**

Intervention and comparison	Contributing reviews	Relative effect	Number of participants (trials)	GRADE certainty of evidence	Comments
<b>Anticonvulsants</b>					
Gabapentin					
Oral gabapentin vs placebo	<a href="#">Moore 2014</a> (Cochrane)	<p><b>Pain intensity</b></p> <p>GPE 'very much improved': RR 4.00, 95% CI 0.90 to 17.83; P = 0.07</p> <p><b>Adverse events</b></p> <p>Any adverse event: RR 1.64, 95% CI 1.15 to 2.32 (higher for gabapentin)</p> <p>Somnolence: RR 4.72, 95% CI 1.45 to 15.35 (higher for gabapentin)</p> <p>Peripheral oedema: RR 0.31, 95% CI 0.03 to 2.93</p> <p>Ataxia: RR 9.0, 95% CI 0.5 to 162.53</p>	58 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
<b>Anti-inflammatory therapies</b>					
Corticosteroids					
Oral prednisolone vs oral piroxicam	<a href="#">Fischer 2010</a>	<p><b>Disability</b></p> <p>Barthel index: no significant between-group difference</p>	60 (1)	Very low	Downgraded once for inconsistency and twice for imprecision
Continued oral prednisolone vs withdrawal of oral prednisolone	<a href="#">Duong 2018</a>	<p><b>Pain intensity</b></p> <p>VAS: mean (SD) 2.4 (1.0) vs 4.9 (2.1); P &lt; 0.01 (in favour of continued oral prednisolone)</p>	58 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and twice for imprecision

**Table 6. Overview of reviews: Oral, intravenous and topical pharmacotherapy** (Continued)

<b>Disability</b>					
					Bathel Index: no significant between-group difference
					Modified Rankin Scale: no significant between-group difference
Oral prednisone vs placebo	<a href="#">Fischer 2010</a>	<b>Pain intensity</b>	60 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and twice for imprecision
					VAS: no significant between-group difference
<b>NSAIDs</b>					
Intravenous parecoxib vs placebo	<a href="#">Duong 2018</a>	<b>Pain intensity</b>	20 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
					No between-group difference
<b>Free radical scavengers</b>					
<b>DMSO</b>					
Topical DMSO vs placebo	<a href="#">Fischer 2010</a>	<b>Pain intensity</b>	30 (1)	Very low	Downgraded once for inconsistency and twice for imprecision
					VAS: significant between-group difference (in favour of DMSO)
Topical DMSO vs oral N-acetylcysteine	<a href="#">Fischer 2010</a>	<b>Pain intensity</b>	146 (1)	Low	Downgraded once for inconsistency and once for imprecision
					No significant between-group difference
<b>Mannitol</b>					
Intravenous mannitol vs placebo	<a href="#">Fischer 2010</a>	<b>Pain intensity</b>	41 (1)	Very low	Downgraded once for inconsistency and twice for imprecision
					VAS: no significant between-group difference
<b>Bisphosphonates</b>					
Bisphosphonates vs placebo	<a href="#">Chevreau 2017</a>	<b>Pain intensity</b>	259 (5)	Low	Downgraded once for inconsistency and once for imprecision
	<a href="#">Fassio 2022</a>				SMD: -2.6, 95% CI -1.8 to -3.4; P = 0.001; I <sup>2</sup> = 81%; 4 trials; n = 181 (in favour of bisphosphonates)

**Table 6. Overview of reviews: Oral, intravenous and topical pharmacotherapy** (Continued)

			0 to 100 VAS: MD -21.80; 95% CI -30.28 to -13.32; 1 trial; n = 78 (in favour of bisphosphonates)		
	<a href="#">Chevreau 2017</a>	<b>Adverse events</b>	181 (4)	Moderate	Downgraded once for imprecision
			Any adverse event: RR 2.10, 95% CI 1.27 to 3.47 (higher for bisphosphonates)		
Intranasal pamidronate vs intranasal calcitonin	<a href="#">Chauvineau 2005</a>	<b>Pain intensity</b>	14 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
			VAS: no significant between-group differences at post-intervention, short-term & medium-term		
<b>Calcitonin</b>					
Intranasal calcitonin vs placebo	<a href="#">Tran 2010</a>	<b>Pain intensity</b>	38 (1)	Very	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
			No between-group difference		
Calcitonin + physiotherapy vs physiotherapy alone	<a href="#">Tran 2010</a>	<b>Pain intensity</b>	90 (2)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
			No between-group difference 1 trial		
			Four-point pain scale: significant between-group difference (in favour of calcitonin + physiotherapy; 1 trial)		
Intranasal calcitonin vs oral paracetamol	<a href="#">Tran 2010</a>	<b>Pain intensity</b>	35 (1)	Very low	Downgraded once serious study limitations, once for inconsistency and twice for imprecision
			No between-group difference		
<b>Immunomodulators</b>					
Infliximab					
Intravenous infliximab vs placebo	<a href="#">Xu 2016</a>	<b>Pain intensity</b>	13 (1)	Very low	Downgraded once serious study limitations, once for inconsistency and twice for imprecision
			No between-group difference		
Lenalidomide					

**Table 6. Overview of reviews: Oral, intravenous and topical pharmacotherapy** (Continued)

Oral lenalidomide vs placebo	Duong 2018	<b>Pain intensity</b>	147 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and once for imprecision
		≥ 30% responder rate: no between-group differences			
		<b>Disability</b>			
		Activity rating: no between-group difference			
<b>NMDA receptor antagonists</b>					
Ketamine					
Intravenous ketamine vs placebo	Orhurhu 2019	<b>Pain intensity</b>	79 (2)	Very low	Downgraded once for serious study limitations and twice for imprecision
		0 to 10 NRS: post-intervention MD -2.38, 95% CI -3.53 to -1.23; $I^2 = 34.9%$ ; $\text{Tau}^2 = 0.34$ ; 2 trials, n = 79 (in favour of ketamine); medium term MD -0.55, 95% CI -1.50 to 0.39; $I^2 = 0%$ ; 2 trials, n = 79			
Magnesium					
Intravenous magnesium vs placebo	Duong 2018	<b>Pain intensity</b>	56 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
		11-point NRS: no between-group differences at post-intervention, short-term & medium-term			
Memantine					
Memantine	Cossins 2013	<b>Pain intensity</b>	NR (1)	Very low	Downgraded once for inconsistency and twice for imprecision
		VAS: significant between-group difference (in favour of memantine)			
<b>Other pharmacological therapies</b>					
Botulinum toxin A					
Intradermal/subcutaneous botulinum toxin A vs placebo	Duong 2018	<b>Pain intensity</b>	8 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
		BPI: no between-group difference			

**Table 6. Overview of reviews: Oral, intravenous and topical pharmacotherapy** (Continued)

Isosorbide dinitrate					
Topical isosorbide dinitrate vs placebo	Duong 2018	<b>Pain intensity</b>  No between-group difference	24 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
		<b>Disability</b>  DASH: no between-group difference			
Sarpogrelate hydrochloride					
Oral sarpogrelate hydrochloride + conventional care vs conventional care alone	Tran 2010	<b>Pain intensity</b>  VAS: no between-group difference	30 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
Tadalafil					
Oral tadalafil vs placebo	Tran 2010	<b>Pain intensity</b>  VAS: 15% vs 0% reduction, P = 0.004, (in favour of tadalafil)	24 (1)	Very low	Downgraded once serious study limitations, once for inconsistency and twice for imprecision

Unless specifically stated, comparisons refer to outcomes measured at the end of the intervention period.

BPI = Brief Pain Inventory

DASH = Disabilities of the Arm, Shoulder and Hand questionnaire

DMSO = dimethyl sulfoxide

GPE = Global Perceived Effect

MD = mean difference

NR = not reported

NRS = numeric rating scale

SMD = standardised mean difference

RR = risk ratio

VAS = visual analogue scale

**Table 7. Overview of reviews: Interventional procedures**

Intervention and comparison	Contributing reviews	Relative effect	Number of participants (trials)	GRADE certainty of evidence	Comments
Neuraxial therapy					
Epidural pharmacological administration					

**Table 7. Overview of reviews: Interventional procedures** (Continued)

Epidural clonidine (300 µg and 700 µg) vs placebo	<a href="#">Tran 2010</a>	<b>Pain intensity</b>	26 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
		VAS: significant between-group difference (in favour of both clonidine doses)			
Epidural clonidine 300 µg vs epidural clonidine 700 µg	<a href="#">Tran 2010</a>	<b>Pain intensity</b>	26 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
		VAS: no significant difference			
		<b>Adverse events</b>			
		Sedation: significant between-group difference (higher for 700 µg clonidine)			
<b>Intrathecal pharmacological administration</b>					
Intrathecal bupivacaine 0.75 mg/mL vs 3 mg/mL infusions	<a href="#">Duong 2018</a>	<b>Pain intensity</b>	14 (1)	Very low	Downgraded once for inconsistency and twice for imprecision
		NRS: no between-group difference			
Intrathecal clonidine vs intrathecal adenosine	<a href="#">Duong 2018</a>	<b>Pain intensity</b>	20 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
		> 30% responder rate: no between-group difference			
Intrathecal glycine vs placebo	<a href="#">Duong 2018</a>	<b>Pain intensity</b>	18 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
		NRS: no between-group difference			
		<b>Disability</b>			
		Radboud Skills Questionnaire: no between-group difference			
		Walking Skills Questionnaire: no between-group difference			

**Table 7. Overview of reviews: Interventional procedures** (Continued)

<b>Adverse events</b>					
Any adverse event: no between-group difference					
Intrathecal methyl-prednisolone vs placebo	<a href="#">Duong 2018</a>	<b>Pain intensity</b>	10 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and twice for imprecision
NRS: no between-group difference					
<b>Intravenous regional blockade (IVRB)</b>					
Atropine IVRB vs placebo	<a href="#">Tran 2010</a>	<b>Pain intensity</b>	30 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and twice for imprecision
NRS: no between-group difference					
Droperidol IVRB vs placebo	<a href="#">Xu 2016</a>	<b>Pain intensity</b>	6 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and twice for imprecision
No between-group difference					
Guanethidine IVRB vs placebo	<a href="#">Xu 2016</a>	<b>Pain intensity</b>	138 (3)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
No between-group differences post-intervention (2 trials); increase in pain intensity in guanethidine group at medium-term (1 trial)					
<b>Adverse events</b>					
117 (2)					
Very low					
Downgraded once for serious study limitations, once for inconsistency, and once for imprecision					
Any adverse event: No between-group difference (1 trial)					
Vasomotor instability: significant between-group difference (higher for guanethidine IVRB; 1 trial)					
Ketanserin IVRB vs placebo	<a href="#">Forouzanfar 2002</a>	<b>Pain intensity</b>	18 (2)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision

**Table 7. Overview of reviews: Interventional procedures** (Continued)

			No significant between-group difference (1 trial)		
			VAS: significant between-group difference (in favour of ketanserin IVRB; 1 trial)		
Lidocaine IVRB vs placebo	<a href="#">Challapalli 2005</a> (Cochrane)	<b>Adverse events</b>	16 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and twice for imprecision
			Light-headedness: significant between-group difference (higher for lidocaine IVRB)		
Methylprednisolone + lidocaine Bier block vs placebo	<a href="#">Fischer 2010</a>	<b>Pain intensity</b>	22 (1)	Very low	Downgraded once for inconsistency, and twice for imprecision
			VAS: no significant between-group difference		
Guanethidine + lidocaine IVRB vs reserpine + lidocaine IVRB vs lidocaine IVRB alone	<a href="#">Xu 2016</a>	<b>Pain intensity</b>	12 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and twice for imprecision
			No between-group difference		
Parecoxib, lidocaine + clonidine IVRB vs lidocaine and clonidine IVRB vs intravenous parecoxib, lidocaine and clonidine	<a href="#">Xu 2016</a>	<b>Pain intensity</b>	30 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and twice for imprecision
			Significant between-group difference (in favour of parecoxib, lidocaine and clonidine IVRB)		
<b>Local anaesthetic sympathetic blockade</b>					
Lidocaine stellate ganglion block vs placebo	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	32 (2)	Moderate	Downgraded once for imprecision
			VAS: no significant between-group difference		
Lidocaine stellate ganglion block vs stellate ganglion ultrasound	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	25 (1)	Low	Downgraded once for inconsistency and once for imprecision
			VAS: no significant between-group difference		
Bupivacaine stellate ganglion block vs guanethidine IVRB	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	19 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and once for imprecision

**Table 7. Overview of reviews: Interventional procedures** (Continued)

					100 mm linear scale: no significant between-group difference
Lidocaine + clonidine lumbar plexus sympathetic block vs lumbar plexus pulsed radiofrequency	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	40 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and once for imprecision
		No significant between-group difference			
Lidocaine stellate ganglion block vs oral prednisone	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	38 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and once for imprecision
		0 to 3 scale hand pain: MD 0.00, 95% CI -0.35 to 0.35			
Lidocaine sympathetic block vs lidocaine + clonidine IVRB	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	43 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and once for imprecision
		0 to 10 VAS: no significant between-group difference			
Ropivacaine/triamcinolone thoracic sympathetic block vs subcutaneous ropivacaine/triamcinolone	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	36 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and once for imprecision
		0 to 10 BPI: post-intervention MD -1.25, 95% CI -3.20 to 0.70; long-term follow-up (MD -2.39, 95% CI -4.72 to -0.06 (in favour of sympathetic block))			
Continuous bupivacaine stellate ganglion block vs continuous bupivacaine brachial plexus block	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	33 (1)	Low	Downgraded once for inconsistency and once for imprecision
		0 to 10 scale: significant between-group difference in favour of continuous brachial plexus block			
Lidocaine image-guided vs lidocaine nonimage-guided stellate ganglion block	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	42 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, once for imprecision, and once for indirectness
		0 to 10 VAS: MD -0.58, 95% CI -1.51 to 0.35			
Stellate ganglion block + rehabilitation vs rehabilitation alone	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	60 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency and once for imprecision.
		0 to 10 VRS: MD 0.2, 95% CI -1.3 to 1.7			
Lidocaine and bupivacaine stellate ganglion block +	<a href="#">O'Connell 2016</a> (Cochrane)	<b>Pain intensity</b>	82 (1)	Very low	Downgraded once for serious study limitations,

**Table 7. Overview of reviews: Interventional procedures** (Continued)

conventional care vs conventional care alone			50% responder rate: ARR = 17%; NNTB = 6%		once for inconsistency and once for imprecision
<b>Sympathectomy</b>					
Percutaneous radiofrequency thermal lumbar sympathectomy vs phenol lumbar sympathetic neurolysis	<a href="#">Straube 2013</a>	<b>Pain intensity</b>	20 (1)	Very low	Reasons for downgrading NR
		No significant between-group difference post-intervention or medium-term			

Unless specifically stated comparisons refer to outcomes measured at the end of the intervention period.

ARR = absolute risk reduction

BPI = Brief Pain Inventory

IVRB = intravenous regional blockade

MD = mean difference

NNTB = number needed to treat for an additional beneficial outcome

NR = not reported

NRS = numeric rating scale

VAS = visual analogue scale

VRS = verbal rating scale

**Table 8. Overview of reviews: Neuromodulation**

Intervention and comparison	Contributing reviews	Relative effect	Number of participants (trials)	GRADE certainty of evidence	Comments
<b>Neuromodulation</b>					
Implanted spinal neuromodulation					
Standard, burst, 500 Hz and 1000 Hz SCS vs placebo	<a href="#">Duong 2018</a>	<b>Pain intensity</b>	40 (1)	Very low	Downgraded once for inconsistency and twice for imprecision
		Significant between-group differences (in favour of all SCS groups)			
SCS vs dorsal root ganglion stimulation	<a href="#">Duong 2018</a>	<b>Adverse events</b>	146 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
		No between-group differences at long-term			
SCS + physiotherapy vs physiotherapy alone	<a href="#">Tran 2010</a>	<b>Pain intensity</b>	52 (2)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision

**Table 8. Overview of reviews: Neuromodulation** *(Continued)*

		VAS: mean (SD) 2.4 (2.5) vs 0.2 (1.4); $P < 0.001$ at medium-term; significant between-group differences at long-term (both in favour of SCS)			sistency and twice for imprecision
<b>Disability</b>					
No between-group difference at medium-term					
Non-invasive brain stimulation					
Repetitive transcranial magnetic stimulation vs placebo	<a href="#">Cossins 2013</a>	<b>Pain intensity</b>	NR (2)	Very low	Downgraded once for inconsistency and twice for imprecision
		Significant between-group differences post-intervention (2 trials); no significant between-group difference at medium-term (1 trial)			

Unless specifically stated comparisons refer to outcomes measured at the end of the intervention period.

MD = mean difference

NR = not reported

SCS = spinal cord stimulation

VAS: visual analogue scale

**Table 9. Overview of reviews: Rehabilitation**

Intervention and comparison	Contributing reviews	Relative effect	Number of participants (trials)	GRADE certainty of evidence	Comments
<b>Sensory-motor training strategies</b>					
Graded motor imagery (GMI)					
GMI vs standard care	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	68 (3)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
		0 to 100 VAS: post-intervention MD -14.45, 95% CI -23.02 to -5.87, $P = 0.001$ ; $I^2 = 29\%$ ; two trials, $n = 49$ ; medium-term MD -21.00, 95% CI -31.17 to -10.83; 1 trial, $n = 37$ (both in favour of GMI)			
		No between-group difference short-term (1 trial)			
<b>Disability</b>					

**Table 9. Overview of reviews: Rehabilitation** (Continued)

			0 to 10 patient specific functional scale: post-intervention MD 1.87, 95% CI 1.03 to 2.71, $P < 0.001$ ; $I^2 = 41\%$ ; 2 trials, $n = 49$ ; medium-term MD 2.30, 95% CI 1.12 to 3.48, $P < 0.001$ ; 1 trial, $n = 37$		
GMI vs waiting-list control	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	22 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
					0 to 10 VAS: MD -0.58, 95% CI -1.94 to 0.78
		<b>Adverse events</b>			
					Increased swelling of the affected limb in 2 participants; increased pain in 12 participants (both occurring in GMI group)
Mirror therapy					
Mirror therapy vs placebo	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	24 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
					0- to 100 VAS: 7/8 participants experienced reduced pain with mirror therapy vs 1/8 with placebo
Mirror therapy + stroke rehabilitation vs placebo mirror therapy + stroke rehabilitation	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	48 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
					0 to 10 VAS: post-intervention MD -2.9, 95% CI -4.23 to -1.57, $P < 0.001$ ; medium-term MD -3.4, 95% CI -4.71 to -2.09; $P < 0.001$ (both in favour of mirror therapy)
		<b>Disability</b>			
					0 to 5 Wolf Motor Function: post-intervention 0-5 scale, MD -1.9, 95% CI -2.36 to -1.44; $P < 0.001$ ; medium-term MD -2.3, 95% CI -2.88 to -1.72; $P < 0.001$
Mirror therapy vs mental imagery	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	24 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and

**Table 9. Overview of reviews: Rehabilitation** (Continued)

		0 to 100 VAS: 7/8 participants experienced reduced pain with mirror therapy vs 2/8 with placebo			once for imprecision
Mirror therapy + stroke rehabilitation vs stroke rehabilitation alone	<a href="#">Smart 2022</a> (Cochrane)	<p><b>Pain intensity</b></p> <p>0 to 10 NRS: MD -1.40, 95% CI -2.26 to -0.54, P &lt; 0.001; 1 trial (in favour of mirror therapy)</p> <p>0 to 10 VAS: median within group change 0-10 VAS, 3 vs 1; 1 trial (in favour of mirror therapy)</p> <p><b>Disability</b></p> <p>18 to 126 FIM: MD 21.95, 95% CI 9.71 to 34.19; P &lt; 0.001; 1 study (in favour of mirror therapy)</p> <p>0 to 14 Fugl-Meyer Assessment: median within-group change 3 vs 0; 1 study (in favour of mirror therapy)</p>	68 (2)	Very low	Downgraded twice for serious study limitations, and once for imprecision.
Mirror visual feedback + medical management vs contrast baths + medical management	<a href="#">Smart 2022</a> (Cochrane)	<p><b>Pain intensity</b></p> <p>11-point NRS: MD -2.65, 95% CI -3.14 to -2.16; P &lt; 0.001 (in favour of mirror visual feedback)</p>	30 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
Mirror visual feedback + medical management vs contrast baths and exercise + medical management	<a href="#">Smart 2022</a> (Cochrane)	<p><b>Pain intensity</b></p> <p>11-point NRS: MD -2.60, 95% CI -3.08 to -2.12; P &lt; 0.001 (in favour of mirror visual feedback)</p>	30 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
Virtual reality					
Virtual body swapping with mental rehearsal vs 'watching movement only'	<a href="#">Smart 2022</a> (Cochrane)	<p><b>Pain intensity</b></p> <p>11-point pain scale: no between-group difference</p>	39 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision

**Table 9. Overview of reviews: Rehabilitation** (Continued)

Virtual body swapping with mental rehearsal vs mental rehearsal only	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  11-point pain scale: no between-group difference	39 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
Virtual body swapping with mental rehearsal vs virtual body swapping alone	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  No between-group difference	10 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
Virtual reality vs sham virtual reality	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  11-point NRS: MD 1.2; SMD 0.7 (measures of variance NR)	45 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
<b>Tactile discrimination</b>					
Four tactile discrimination training protocols compared with each other	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  100 mm VAS: no between-group differences	10 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
<b>Adverse events</b>					
Increased pain during training					
<b>Prism adaptation</b>					
Prism adaptation treatment vs placebo	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  11-point NRS: no between-group differences post-intervention and medium-term	49 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision.
<b>Electrophysical agents</b>					
Stellate ganglion ultrasound vs placebo	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  10 cm VAS: no between-group difference	45 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
<b>Disability</b>					

**Table 9. Overview of reviews: Rehabilitation** (Continued)

DASH: no between-group difference					
Stellate ganglion ultrasound vs TENS	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  0-10 VAS: MD 2.13, 95% CI 1.47 to 2.79; P < 0.001 (in favour of TENS)	30 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
Electromagnetic field therapy vs placebo	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  10 cm VAS: MD -2.2, 95% CI -1.99 to -2.41; P < 0.001; 1 trial; MD 1.6, 95% CI 0.83 to 2.37, P < 0.001; 1 trial (both in favour of electromagnetic field therapy); no between-group difference in 1 trial  <b>Disability</b>  0 to 100 Maryland Foot Score: MD 14.4, 95% CI 11.36 to 17.44; P < 0.001; one study, n = 18 (in favour of electromagnetic field therapy)  0 to 100 DASH: MD -14.0 95% CI -4.41 to -23.59; P < 0.004; 1 study, n = 12 (in favour of electromagnetic field therapy)  0 to 100 Quick-DASH: 0-100, MD 2, 95% CI -3.91 to 7.91; one study  <b>Adverse events</b>  No between-group difference (1 study)	112 (3)	Very low	Downgraded once for serious study limitations, once for inconsistency
TENS vs placebo	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  10 cm VAS: MD -9, 95% CI -18.5 to 0.5; P = 0.074 (in favour of TENS)  <b>Disability</b>	30 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision

**Table 9. Overview of reviews: Rehabilitation** (Continued)

Duruöz Hand Index: MD -3.6, 95% CI -13.38 to 6.18; P = 0.48					
Laser therapy vs interferential therapy	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  0 to 100 VAS: MD -8.6, 95% CI -16.27 to -0.93; P = 0.03 (in favour of laser therapy)	50 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
<b>Adverse events</b>					
No between-group difference					
CO <sub>2</sub> bath therapy and exercise vs exercise alone	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  Between-group difference in favour of CO <sub>2</sub> bath therapy	40 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
Whirlpool baths vs neuromuscular electrical stimulation	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  10 cm VAS: MD -0.65, 95% CI -1.03 to -0.27; P < 0.001 (in favour of whirlpool bath)	60 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
<b>Adverse events</b>					
No between-group difference					
Fluidotherapy + stroke rehabilitation vs stroke rehabilitation alone	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>  10 cm VAS: no between-group difference	32 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
<b>Disability</b>					
FIM: no between-group difference					
<b>Exposure-based interventions</b>					
Pain exposure physical therapy	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	56 (1)	Very low	Downgraded once for serious study limitations, once for

**Table 9. Overview of reviews: Rehabilitation** (Continued)

apy vs usual physiotherapy		1-10 VAS: MD 0.61, 95% CI -0.70 to 1.92 at long-term			inconsistency, and once for imprecision
		<b>Disability</b>			
		0 to 100 DASH: MD 6.47, 95% CI -5.97 to 18.90 at long-term			
		0 to 40 Lower Limb Tasks Questionnaire: MD 5.11, 95% CI -0.45 to 10.68 at long-term			
Exposure in vivo vs usual physiotherapy	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	46 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
		0 to 10 NPS: MD -2.04 95% CI -3.01 to -1.07; P = 0.001 post-intervention; MD -2.82, 95% CI -4.18 to -1.46; P = 0.001 at medium-term (both in favour of exposure in vivo)			
		<b>Disability</b>			
		0 to 5 Radboud Skills Questionnaire: MD -1.08, 95% CI -1.60 to -0.56; P = 0.001 post-intervention; MD -1.30, 95% CI -0.92 to -1.69; P = 0.001 medium-term (both in favour of exposure in vivo)			
		0 to 10 Walking Ability Questionnaire: no between-group difference post-intervention; MD -3.62, 95% CI -6.78 to -0.47; P = 0.02 at medium-term (in favour of exposure in vivo)			
<b>Multimodal physiotherapy</b>					
Physiotherapy vs minimal care	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	135 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
		Between-group difference post-intervention; no between-group difference at long-term			
		<b>Disability</b>			

**Table 9. Overview of reviews: Rehabilitation** (Continued)

		5 to 50 Impairment Level Sum Score: MD -3.7, 95% CI -7.13 to -0.27, P = 0.03; long-term follow-up (in favour of physiotherapy)			
		Radboud Skills Questionnaire: no between-group difference at long-term			
		Modified Greentest: no between-group difference at long-term			
		Radboud Dexterity Test: no between-group difference at long-term			
Physiotherapy vs occupational therapy	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	135 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
		No between-group difference at long-term			
		<b>Disability</b>			
		Impairment Level Sum Score: no between-group difference at long-term			
		Radboud Skills Questionnaire: no between-group difference at long-term			
		Modified Greentest: no between-group difference at long-term			
		Radboud Dexterity Test: no between-group difference at long-term			
Upper limb aerobic exercise + physiotherapy vs physiotherapy alone	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	40 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
		10 cm VAS: MD -1.9, 95% CI -3.23 to -0.57; P < 0.005			
<b>Other physiotherapy-based interventions</b>					
Manual lymphatic	<a href="#">Smart 2022</a> (Cochrane)	<b>Pain intensity</b>	74 (2)	Very low	Downgraded once for serious study

**Table 9. Overview of reviews: Rehabilitation** (Continued)

drainage therapy vs conventional care		No between-group difference			limitations, once for inconsistency, and once for imprecision
Electro-acupuncture and massage vs rehabilitation	Smart 2022 (Cochrane)	<b>Pain intensity</b>	120 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
		Pain on movement NRS: MD -1.70, 95% CI -2.09 to -1.31; P = 0.01 post-intervention; MD -1.40, 95% CI -1.78 to -1.02; P < 0.001 at short-term (both in favour of electro-acupuncture and massage)			
		<b>Disability</b>			
		Fugl-Meyer hand: no between-group difference post-intervention			
		Fugl-Meyer upper limb no between-group difference at short-term			
		<b>Adverse events</b>			
		No between-group difference			

Unless specifically stated, comparisons refer to outcomes measured at the end of the intervention period.

CO<sub>2</sub> = carbon dioxide

DASH = Disabilities of the Arm, Shoulder and Hand questionnaire

FIM = Functional Independence Measure

GMI = graded motor imagery

MD = mean difference

NR = not reported

NPS = neuropathic pain scale

NRS = numeric rating scale

TENS = transcutaneous electrical nerve stimulation

VAS = visual analogue scale

**Table 10. Overview of reviews: Complementary and alternative therapies and other interventions**

Intervention and comparison	Contributing reviews	Relative effect	Number of participants (trials)	GRADE certainty of evidence	Comments
<b>Complementary and alternative therapies</b>					
Acupuncture					

**Table 10. Overview of reviews: Complementary and alternative therapies and other interventions** (Continued)

Acupuncture vs sham acupuncture	<a href="#">Forouzanfar 2002</a>	<b>Pain intensity</b>  VAS: no between-group differences (2 trials); significant between-group difference (in favour of acupuncture; 1 trial)	56 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and once for imprecision
Traditional manual acupuncture + rehabilitation vs rehabilitation alone	<a href="#">Peng 2018</a>	<b>Pain intensity</b>  VAS: MD 1.49, 95% CI 1.15 to 1.82; $I^2 = 71%$ ; $\text{Tau}^2 = 0.17$ ; 9 trials, $n = 834$ (in favour of manual acupuncture)  <b>Disability</b>  Fugl-Meyer Assessment: MD 8.42, 95% CI 6.74 to 10.10; $I^2 = 94%$ ; $\text{Tau}^2 = 13.07$ ; 20 trials, $n = 1918$ (in favour of manual acupuncture)	1918 (20)	Very low	Downgraded once for serious study limitations, once for inconsistency, once for imprecision and once for indirectness
Qigong					
Qigong vs placebo	<a href="#">Smith 2005</a>	<b>Pain intensity</b>  VAS: significant difference in number of participants with decreased pain (91% vs 36%; in favour of qigong)	26 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and twice for imprecision
Relaxation therapy					
Autogenic relaxation training + home treatment vs home treatment alone	<a href="#">Smith 2005</a>	<b>Pain intensity</b>  VAS: no between-group difference	18 (1)	Very low	Downgraded once for serious study limitations, once for inconsistency, and twice for imprecision
<b>Other interventions</b>					
Occlusal splints					
Occlusal splint vs control	<a href="#">Cossins 2013</a>	<b>Pain intensity</b>  NRS: no between-group difference	NR (1)	Very low	Downgraded once for inconsistency and twice for imprecision.

Unless specifically stated comparisons refer to outcomes measured at the end of the intervention period.

NRS = numeric rating scale

VAS = visual analogue scale

## APPENDICES

### Appendix 1. Search strategy Ovid MEDLINE

1 exp Complex Regional Pain Syndromes/

2 exp Neuralgia/

3 regional pain syndrome\*.tw.

4 CRPS.tw.

5 (reflex and (sympathetic or neurovascular) and dystrophy).tw.

6 (RSD or RND).tw.

7 sudeck's atrophy.tw.

8 sudecks atrophy.tw.

9 algodystrophy.tw.

10 shoulder-hand syndrome\*.tw.

11 causalgia.tw.

12 algoneurodystrophy.tw.

13 (neuropathic pain or neuralgia).tw.

14 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13

15 (201110\* or 201111\* or 201112\* or 2012\* or 2013\* or 2014\* or 2015\* or 2016\* or 2017\* or 2018\* or 2019\* or 2020\* or 2021\* or 2022\*).ed.

16 review.pt.

17 (medline or medlars or embase or pubmed or cochrane).tw,sh.

18 (scisearch or psychinfo or psycinfo).tw,sh.

19 cinahl.tw,sh.

20 ((hand adj2 search\$) or (manual\$ adj2 search\$)).tw,sh.

21 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online database\$).tw,sh.

22 (pooling or pooled or mantel haenszel).tw,sh.

23 (peto or dersimonian or der simonian or fixed effect).tw,sh.

24 (retraction of publication or retracted publication).pt.

25 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24

26 16 and 25

27 meta-analysis.pt.

28 meta-analysis.sh.

29 (meta-analys\$ or meta analys\$ or metaanalys\$).tw,sh.

30 (systematic\$ adj5 review\$).tw,sh.

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- 31 (systematic\$ adj5 overview\$).tw,sh.  
 32 (quantitativ\$ adj5 review\$).tw,sh.  
 33 (quantitativ\$ adj5 synthesis\$).tw,sh.  
 34 (methodologic\$ adj5 review\$).tw,sh.  
 35 (methodologic\$ adj5 overview\$).tw,sh.  
 36 (integrative research review\$ or research integration).tw.  
 37 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36  
 38 26 or 37

[BMJ Clinical Evidence](#) search filter for MEDLINE used

## Appendix 2. Search strategy Ovid Embase

- 1 exp Complex Regional Pain Syndrome/  
 2 exp Neuralgia/  
 3 regional pain syndrome\*.tw.  
 4 CRPS.tw.  
 5 (reflex and (sympathetic or neurovascular) and dystrophy).tw.  
 6 (RSD or RND).tw.  
 7 sudeck's atrophy.tw.  
 8 sudecks atrophy.tw.  
 9 algodystrophy.tw.  
 10 shoulder-hand syndrome\*.tw.  
 11 causalgia.tw.  
 12 algoneurodystrophy.tw.  
 13 (neuropathic pain or neuralgia).tw.  
 14 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13  
 15 (201110\* or 201111\* or 201112\* or 2012\* or 2013\* or 2014\* or 2015\* or 2016\* or 2017\* or 2018\* or 2019\* or 2020\* or 2021\* or 2022\*).dd.  
 16 exp review/  
 17 (literature adj3 review\$).ti,ab.  
 18 exp meta analysis/  
 19 exp "Systematic Review"/  
 20 16 or 17 or 18 or 19  
 21 (medline or medlars or embase or pubmed or cinahl or amed or psychlit or psyclit or psychinfo or psycinfo or scisearch or cochrane).ti,ab.  
 22 RETRACTED ARTICLE/  
 23 21 or 22  
 24 20 and 23

25 (systematic\$ adj2 (review\$ or overview)).ti,ab.

26 (meta?anal\$ or meta anal\$ or meta-anal\$ or metaanal\$ or metanal\$).ti,ab.

27 24 or 25 or 26

28 14 and 15 and 27

[BMJ Clinical Evidence](#) search filter for Embase used

### Appendix 3. Search strategy Cochrane Database of Systematic Reviews/DARE

#1 MeSH descriptor Complex Regional Pain Syndromes explode all trees

#2 MeSH descriptor Neuralgia explode all trees

#3 regional pain syndrome\*

#4 CRPS

#5 (reflex and (sympathetic or neurovascular) and dystrophy)

#6 RSD or RND

#7 (sudeck's or sudecks) next atrophy

#8 algodystrophy

#9 shoulder-hand syndrome\*

#10 causalgia

#11 algoneurodystrophy

#12 (neuropathic pain or neuralgia)

#13 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12)

### Appendix 4. Search strategy CINAHL

S18 S16 AND S17

S17 (TI (systematic\* n3 review\*)) or (AB (systematic\* n3 review\*)) or (TI (systematic\* n3 bibliographic\*)) or (AB (systematic\* n3 bibliographic\*)) or (TI (systematic\* n3 literature)) or (AB (systematic\* n3 literature)) or (TI (comprehensive\* n3 literature)) or (AB (comprehensive\* n3 literature)) or (TI (comprehensive\* n3 bibliographic\*)) or (AB (comprehensive\* n3 bibliographic\*)) or (TI (integrative n3 review)) or (AB (integrative n3 review)) or (JN "Cochrane Database of Systematic Reviews") or (TI (information n2 synthesis)) or (TI (data n2 synthesis)) or (AB (information n2 synthesis)) or (AB (data n2 synthesis)) or (TI (data n2 extract\*)) or (AB (data n2 extract\*)) or (TI (medline or pubmed or psyclit or cinahl or (psycinfo not "psycinfo database") or "web of science" or scopus or embase)) or (AB (medline or pubmed or psyclit or cinahl or (psycinfo not "psycinfo database") or "web of science" or scopus or embase)) or (MH "Systematic Review") or (MH "Meta Analysis") or (TI (meta-analy\* or metaanaly\*)) or (AB (meta-analy\* or metaanaly\*))

S16 S14 AND S15

S15 EM 20111001-20221007

S14 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13

S13 neuropathic pain or neuralgia

S12 algoneurodystrophy

S11 causalgia

S10 shoulder-hand syndrome\*

S9 algodystrophy

S8 sudecks atrophy

S7 sudeck's atrophy

S6 RSD or RND

S5 (reflex and (sympathetic or neurovascular) and dystrophy)

S4 CRPS

S3 regional pain syndrome\*

S2 (MH "Neuralgia+")

S1 (MH "Complex Regional Pain Syndromes+")

[UTHealth CINAHL Filter](#) used

### Appendix 5. Search strategy PEDro

Abstract & Title: regional pain syndrome or CRPS or "reflex sympathetic dystrophy" or "reflex neurovascular dystrophy" or RSD or RND or "sudeck's atrophy" or "sudecks atrophy" or algodystrophy or shoulder-hand syndrome or causalgia or algoneurodystrophy or "neuropathic pain" or neuralgia

Problem: Pain

Topic: Chronic pain

Method: Systematic review

Published since: 2011

### Appendix 6. Search strategy LILACS (Birme)

regional pain syndrome\$ or CRPS or "reflex sympathetic dystrophy" or "reflex neurovascular dystrophy" or RSD or RND or "sudeck's atrophy" or "sudecks atrophy" or algodystrophy or shoulder-hand syndrome\$ or causalgia or algoneurodystrophy or "neuropathic pain" or neuralgia [Words] and 2011 or 2012 or 2013 or 2014 or 2015 or 2016 or 2017 or 2018 or 2019 or 2020 or 2021 [Country, year publication] and review or meta-analysis [Publication type]

### Appendix 7. Search strategy Epistemonikos

(title:((title:(regional pain syndrome\*) OR abstract:(regional pain syndrome\*)) OR (title:(CRPS OR RSD OR RND) OR abstract:(CRPS OR RSD OR RND)) OR (title:(algodystrophy) OR abstract:(algodystrophy)) OR (title:(shoulder-hand syndrome\*) OR abstract:(shoulder-hand syndrome\*)) OR (title:(causalgia OR algoneurodystrophy OR "neuropathic pain" OR neuralgia) OR abstract:(causalgia OR algoneurodystrophy OR "neuropathic pain" OR neuralgia)) OR (title:(reflex sympathetic dystrophy" OR "reflex neurovascular dystrophy")) OR abstract:(reflex sympathetic dystrophy" OR "reflex neurovascular dystrophy")))) OR abstract:((title:(regional pain syndrome\*) OR abstract:(regional pain syndrome\*)) OR (title:(CRPS OR RSD OR RND) OR abstract:(CRPS OR RSD OR RND)) OR (title:(algodystrophy) OR abstract:(algodystrophy)) OR (title:(shoulder-hand syndrome\*) OR abstract:(shoulder-hand syndrome\*)) OR (title:(causalgia OR algoneurodystrophy OR "neuropathic pain" OR neuralgia) OR abstract:(causalgia OR algoneurodystrophy OR "neuropathic pain" OR neuralgia)) OR (title:(reflex sympathetic dystrophy" OR "reflex neurovascular dystrophy")) OR abstract:(reflex sympathetic dystrophy" OR "reflex neurovascular dystrophy"))))

### Appendix 8. Search results by source

#### 2013 Version

DATABASE	Date of Search	Range of search	RESULTS
MEDLINE (OVID)	7 Oct 2011	Medline 1948 to Sep week 4 2011	417
Embase (OVID)	7 Oct 2011	1980 to 2011 week 39	1070
CDSR ( <i>The Cochrane Library</i> )	7 Oct 2011	Issue 10 2011	331
DARE	7 Oct 2011	Issue 4 2011	98

(Continued)

CINAHL (EBsco)	10 Oct 2011	1982 to date of search	152
PEDro	10 Oct 2011	1929 to date	21
LILACS	11 Oct 2011	All years	103
NCDDR			defunct
TOTAL			2192

## 2022 Version

DATABASE	Date of Search	Range of search	RESULTS
MEDLINE (OVID)	10 Oct 2022	Oct 2011 to 7 Oct 2022	1276
Embase (OVID)	10 Oct 2022	Oct 2011 to 7 Oct 2022	1732
CDSR ( <i>The Cochrane Library</i> )	10 Oct 2022	Issue 10 of 12, 2022	80
CINAHL (EBsco)	10 Oct 2022	Oct 2011 to Oct 2022	1065
PEDro	10 Oct 2022	Oct 2011 to Oct 2022	20
LILACS	10 Oct 2022	2011 to Oct 2022	64
Epistemonikos	10 Oct 2022	Oct 2011 to 10 Oct 2022	70
Citation alerts	2022		3
TOTAL			4310

## Appendix 9. AMSTAR 2 assessment criteria

AMSTAR 2 is a 16-item critical appraisal tool to assist in identifying high quality systematic reviews. AMSTAR 2 is not designed to generate a summary score, but an overall rating based on weaknesses in 7 critical domains\*.

1. Did the research questions and inclusion criteria for the review include the components of PICO?
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?\*
3. Did the review authors explain their selection of the study designs for inclusion in the review?
4. Did the review authors use a comprehensive literature search strategy?\*
5. Did the review authors perform study selection in duplicate?
6. Did the review authors perform data extraction in duplicate?
7. Did the review authors provide a list of excluded studies and justify the exclusions?\*
8. Did the review authors describe the included studies in adequate detail?
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?\*
10. Did the review authors report on the sources of funding for the studies included in the review?
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?\*

12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?\*
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?\*
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

#### **Ratings in overall confidence in the results of the review :**

High (zero or one non-critical weakness): the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.

Moderate (more than one non-critical weakness): the systematic review has more than one weakness, but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review.

Low (one critical flaw with or without non-critical weaknesses): the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest.

Critically low (more than one critical flaw with or without non-critical weaknesses): the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

### **Appendix 10. Summary of low- and very low-certainty evidence results**

#### **Oral, intravenous and topical pharmacotherapy**

##### **There is low-certainty evidence that:**

- Compared with placebo, bisphosphonates may reduce pain intensity
- Compared with oral N-acetylcysteine, topical DMSO may not reduce pain intensity

##### **There is very low-certainty evidence that:**

- Compared with placebo, oral prednisone, intravenous mannitol, botulinum toxin A, intranasal calcitonin, intravenous infliximab and intravenous parecoxib may not reduce pain intensity
- Compared with placebo, intradermal/subcutaneous botulinum toxin A may not reduce pain intensity or disability
- Compared with placebo, oral gabapentin may not reduce pain intensity and it may increase the risk of experiencing adverse events
- Compared with oral piroxicam, oral prednisone may not reduce disability
- Continuing treatment with oral prednisolone may reduce pain intensity more than discontinuing oral prednisolone
- Compared with placebo, oral prednisone may not reduce pain intensity
- Compared with intranasal calcitonin, intranasal pamidronate may not reduce pain intensity
- Compared with physiotherapy, calcitonin plus physiotherapy may have little to no effect on pain intensity
- Compared with oral paracetamol, intranasal calcitonin may not reduce pain intensity
- Compared with placebo, oral lenalidomide may not reduce pain intensity or disability
- Compared with placebo, topical isosorbide dinitrate may not reduce pain intensity or disability
- Compared with placebo, intravenous ketamine may reduce pain intensity
- Compared with placebo, intravenous magnesium may have no effect on pain intensity
- Compared with morphine plus placebo, memantine plus morphine may reduce pain intensity
- Compared with conventional care, oral sarpogrelate hydrochloride plus usual care may not reduce pain intensity
- Compared with placebo, oral tadalafil may reduce pain intensity

#### **Interventional procedures**

##### **There is low-certainty evidence that:**

- Compared with stellate ganglion ultrasound, lidocaine stellate ganglion may not reduce pain intensity
- Compared with continuous bupivacaine stellate ganglion block, continuous brachial plexus block may reduce pain intensity

##### **There is very low-certainty evidence that:**

- Compared with placebo, epidural clonidine may reduce pain intensity
- Compared with a slow intrathecal baclofen infusion, a fast intrathecal baclofen infusion may have no effect on pain intensity

- Compared with a 300µg epidural clonidine, 700µg epidural clonidine may have no effect on pain intensity and may increase the risk of sedation
- Compared with intrathecal clonidine, intrathecal adenosine may have no effect on pain intensity
- Compared with placebo, intrathecal glycine may have no effect on pain intensity, disability, or adverse events
- Compared with placebo, guanethidine IVRB may have no effect on pain intensity post-intervention but may reduce pain intensity at medium-term follow-up, and may have little to no effect on adverse events
- Compared with placebo, ketanserin IVRB may have little to no effect on pain intensity
- Compared with placebo, lidocaine IVRB may increase the incidence light-headedness
- Compared with each other, guantheidine plus lidocaine IVRB, reserpine plus lidocaine IVRB, and lidocaine IVRB protocols may have no effect on pain intensity
- Compared with IV parecoxib, lidocaine and clonidine, and IVRB with lidocaine and clonidine, IVRB with parecoxib, lidocaine and clonidine may reduce pain intensity
- Compared with guanethidine IVRB, bupivacaine stellate ganglion block may have no effect on pain intensity
- Compared with radiofrequency lumbar block, lidocaine and clonidine lumbar sympathetic block may have no effect on pain intensity
- Compared with oral prednisone, lidocaine stellate ganglion block may have no effect on pain intensity
- Compared with lidocaine and clonidine IVRB, lidocaine sympathetic block may have no effect on pain intensity
- Compared with subcutaneous ropivacaine and triamcinolone, thoracic sympathetic block using the same agents may have no effect on pain intensity
- Compared with lidocaine image-guided stellate ganglion block, lidocaine nonimage-guided stellate ganglion block may have no effect on pain intensity
- Compared with rehabilitation, stellate ganglion block plus rehabilitation may have no effect on pain intensity
- Compared with conventional care, lidocaine and bupivacaine stellate ganglion block plus conventional care may reduce pain intensity
- Compared with phenol lumbar sympathetic neurolysis, percutaneous radiofrequency thermal lumbar sympathectomy may not reduce pain intensity

## Neuromodulation

### There is very low-certainty evidence that:

- Compared with placebo, standard, burst and high frequency spinal cord stimulation may reduce pain intensity
- Compared with spinal cord stimulation, dorsal root ganglion stimulation may not increase the risk of adverse events
- Compared with physiotherapy, spinal cord stimulation plus physiotherapy may reduce pain intensity and may have no effect on disability at medium-term follow-up
- Compared with placebo, repetitive transcranial magnetic stimulation may reduce pain intensity post-intervention but may have no effect on pain intensity at medium-term follow-up

## Rehabilitation

### There is very low-certainty evidence that:

- Compared with placebo, mirror therapy and virtual reality may reduce pain intensity
- Compared with placebo, prism adaptation may have no effect on pain intensity
- Compared with standard care, graded motor imagery may reduce pain intensity and disability at post-intervention and medium-term follow-up, but may have no effect on pain intensity at short-term follow-up
- Compared with a waiting list control, graded motor imagery may have no effect on pain intensity
- Compared with mental imagery, mirror therapy may reduce pain intensity
- Compared with stroke rehabilitation, mirror therapy plus stroke rehabilitation may reduce pain intensity and improve function
- Compared with medical management plus contrast baths and medical management, contrast baths and exercise, mirror visual feedback plus medical management may improve pain intensity
- Compared with each other, four different tactile discrimination protocols may have no differential effects on pain intensity
- Compared with placebo, stellate ganglion ultrasound may not reduce pain intensity or disability
- Compared with TENS, stellate ganglion ultrasound may reduce pain intensity
- Compared with placebo, electromagnetic field therapy may reduce pain intensity and disability, but the evidence is conflicting
- Compared with placebo, TENS may have no effect on pain intensity and disability
- Compared with inferential therapy, laser therapy may reduce pain intensity
- Compared with exercise, CO<sub>2</sub> bath therapy may reduce pain intensity
- Compared with stroke rehabilitation, fluidotherapy plus stroke rehabilitation may have no effect on pain intensity or disability

- Compared with usual physiotherapy, pain exposure physical therapy may have no effect on pain intensity or disability
- Compared with usual physiotherapy, exposure in vivo may reduce pain intensity and disability
- Compared with minimal care, physiotherapy may reduce pain intensity post-intervention but may have no effect at long-term follow-up; and may reduce disability at long-term follow-up but the evidence is conflicting
- Compared with occupational therapy, physiotherapy may have no effect on pain intensity or disability
- Compared with physiotherapy, manual lymphatic drainage may have no effect on pain intensity
- Compared with rehabilitation, massage plus electro-acupuncture may reduce pain intensity, but may have no effect on disability

### Complementary and alternative therapies and other interventions

#### There is very low-certainty evidence that:

- Compared with placebo, acupuncture and qigong may reduce pain intensity
- Compared with home treatment, autogenic relaxation plus home treatment may have no effect on pain intensity
- Compared with placebo, occlusal splints may have no effect on pain intensity

For all of the comparisons with very low-certainty evidence, we suggest this represents insufficient evidence to either support or refute the use of these interventions. Comparisons with low-certainty evidence should be treated with substantial caution.

### WHAT'S NEW

Date	Event	Description
9 June 2023	New citation required but conclusions have not changed	Compared with the previous version of this overview, the current version included downgraded certainty in evidence for several interventions: ketamine, calcitonin, graded motor imagery, mirror therapy and multimodal physiotherapy. The current version also found moderate-certainty evidence that bisphosphonates are probably associated with an increased risk of adverse events of any nature.
9 June 2023	New search has been performed	This overview has been updated to include the results of a new search in October 2022. The overview now includes five Cochrane and 12 non-Cochrane systematic reviews, comprising data from 127 randomised controlled trials.

### HISTORY

Protocol first published: Issue 11, 2011

Review first published: Issue 4, 2013

Date	Event	Description
15 December 2016	Review declared as stable	See Published notes.
15 July 2016	Amended	See Published notes.
17 June 2015	Review declared as stable	This review will be assessed for further updating in 2016.

### CONTRIBUTIONS OF AUTHORS

MCF: conceived updates to methodology for the current version, collated the searches in collaboration with the PaPaS information specialist, applied eligibility criteria, assessed reviews, extracted and analysed data, judged the certainty in evidence using GRADE, interpreted the results, and led the write-up of the overview. MF will be responsible for identifying the need for a future update to this overview.

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AGC: applied eligibility criteria, assessed reviews, extracted and analysed data, interpreted the results and contributed to the write-up of the overview.

BMW: contributed to protocol design, interpreted the results, and contributed to the write-up of the overview.

KMS: applied eligibility criteria, assessed reviews, extracted and analysed data, interpreted the results, and contributed to the write-up of the overview.

CB: applied eligibility criteria, assessed reviews, extracted and analysed data, interpreted the results, and contributed to the write-up of the overview.

LM: contributed to protocol design, provided statistical advice, interpreted the results, and contributed to the write-up of the overview.

GLM: contributed to protocol design, advised as a content expert on CRPS, reviewed the final list of reviews for possible omissions, interpreted the results, and contributed to the write-up of the overview.

JHM: contributed to protocol design, provided methodological advice, acted as third reviewer, interpreted the results and contributed to the write-up of the overview.

NOC: conceived and designed the protocol, conceived updates to methodology for the current version, applied eligibility criteria, assessed reviews, extracted and analysed data, judged the certainty in evidence using GRADE, interpreted the results, and contributed to the write-up of the overview.

## DECLARATIONS OF INTEREST

NOC and BMW were authors of one included review ([O'Connell 2016](#)) and KMS, MCF, BM and NOC were authors of another included review ([Smart 2022](#)). Different authors (AGC, CB) conducted the AMSTAR 2 assessments for these reviews.

GLM was the lead author on three included studies ([Moseley 2004](#); [Moseley 2006](#); [Moseley 2009](#)) but was not involved in the data extraction process or writing of or interpretation of results for these trials. GLM has co-authored a textbook on the use of graded motor imagery in chronic pain, for which he receives author royalties.

MCF, AGC, BMW, GLM, JHM and NOC are involved in the conduct of a randomised controlled trial testing memantine and graded motor imagery for complex regional pain syndrome. At the time of writing this review, the trial is recruiting participants and is registered on the Australian New Zealand Clinical Trials Registry (ACTRN12621000175875).

CB has an annual contract (Independent Contractor) to provide 12 hours of pain education lectures to pain and spine fellows at Kaiser Permanente. This position is not relevant nor a conflict to this title.

NOC is an author and PaPaS Co-ordinating editor. NOC had no input into the editorial decisions or processes for this overview.

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Salary for AGC
- University of Notre Dame, Australia  
Salary for BW
- University College London, UK  
Salary for LM
- University of South Australia, Australia  
Salary for GLM

- Neuroscience Research Australia, Australia

Salary for JM

- Brunel University, UK

Salary for NOC

### External sources

- National Institute for Health Research (NIHR), UK

Cochrane Infrastructure funding to the Cochrane Pain, Palliative and Supportive Care Review Group (PaPaS)

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In this updated overview, we made a number of changes compared with the protocol ([O'Connell 2011](#)) and the original version of the overview ([O'Connell 2013](#)):

- Background: this section has been updated in the current version of the overview to include recent information on CRPS diagnosis, pathophysiology and incidence.
- Searches: in the current version of this overview, we searched Epistemonikos but did not search the Database of Abstracts of Reviews of Effects (DARE), as it is no longer updated.
- Outcomes: in the current version of this overview, we grouped outcomes into post-intervention, short-term, medium-term and long-term follow-up periods, reporting only a single effect for each period.
- Assessment of methodological quality of included reviews: in the current version of this overview, we used the revised AMSTAR 2 instead of the original AMSTAR tool to assess the methodological quality of both Cochrane and non-Cochrane reviews.
- Assessment of the certainty of the evidence in included reviews: where reviews did not use GRADE to assess the certainty in evidence, we conducted these assessments ourselves using updated criteria compared with the previous version of this overview and the protocol (for a full description see [Assessment of methodological quality of included reviews](#)). We applied these judgements to all outcomes rather than only the primary outcomes, as done in the previous version of this overview.
- Interpretation of effects: in the current version of this overview, we interpreted minimally important between-group differences for pain intensity using OMERACT 12 recommendations.

## INDEX TERMS

### Medical Subject Headings (MeSH)

Analgesics [administration & dosage]; Calcitonin [therapeutic use]; Complex Regional Pain Syndromes [\*therapy]; Diphosphonates [therapeutic use]; \*Disabled Persons; Guanethidine [therapeutic use]; Imagery, Psychotherapy [methods]; Ketamine [administration & dosage]; Nerve Block [methods]; Pain Management [\*methods]; Physical Therapy Modalities; Review Literature as Topic; Sympatholytics [therapeutic use]

### MeSH check words

Adult; Humans