Royal College of Physicians

2nd edition

Complex regional pain syndrome in adults

UK guidelines for diagnosis, referral and management in primary and secondary care

2018

Complex regional pain syndrome in adults

These guidelines were developed by a panel of experts with support from, representation and endorsement by the Royal College of General Practitioners, the Royal College of Physicians, the Faculty of Pain Medicine of the Royal College of Anaesthetists, the Royal College of Occupational Therapists, the British Orthopaedic Association, the British Pain Society, the British Psychological Society, the British Society of Rehabilitation Medicine, the Chartered Society of Physiotherapy, the Directorate of Defence Rehabilitation, the Physiotherapy Pain Association, the Society of British Neurological Surgeons, the Royal College of Emergency Medicine, the British Association of Plastic, Reconstructive and Aesthetic Surgeons, the Faculty of Occupational Medicine, the British Society for Surgery of the Hand, the British Association of Hand Therapists and the Pain Relief Foundation.

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Please see the Guideline Development Panel for the full list of authors.

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Royal College of Physicians
11 St Andrews Place
Regent's Park
London NW1 4LE

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Contents

Membership of the Guideline Development Panel for 2018

Chair: Dr Andreas Goebel PhD FRCA FFPMRCA
Reader in pain medicine, University of Liverpool, and honorary consultant, The Walton Centre NHS Foundation Trust, Liverpool

Professor Roger M Atkins MA MB BS DM FRCS
Consultant orthopaedic surgeon, Bristol Royal Infirmary

Dr Chris Barker DRCOG MRCGP
Specialist in pain medicine, clinical director, NHS Sefton Community Pain Service, Liverpool

Dr Heather Cameron PhD MCSP
Chief AHP Regional Services and physiotherapy professional lead, NHS Greater Glasgow and Clyde

Dr Helen Cohen PhD FRCP
Consultant rheumatologist and chronic pain, Royal National Orthopaedic Hospital, London

Fiona Cowell MCSP Grad Dip Phys MSc
Extended scope physiotherapist in trauma management, Royal Liverpool and Broadgreen NHS Trust, Liverpool

Paul Eldridge MA MB MChir FRCS
Consultant neurosurgeon, The Walton Centre NHS Foundation Trust, Liverpool

Sue Fullilove MBBS MA FRCS(Orth)
Consultant orthopaedic hand surgeon, Plymouth Hospitals NHS Trust, Plymouth

Sharon Gillespie MCSP Grad Dip Phys MSc
Clinical physiotherapy specialist in hands (member of BAHT), Royal Liverpool and Broadgreen NHS Trust, Liverpool

Dr Henry Guly
Consultant in emergency medicine

Mr James Henderson MA MD EurDipHandSurg FRCS(Plas)
Consultant plastic, reconstructive and hand surgeon, North Bristol NHS Healthcare Trust

Professor George Ikkos Hon FRCPsych FRSA
Consultant psychiatrist in liaison psychiatry, Royal National Orthopaedic Hospital NHS Trust

Dr Fergus Jepson
Consultant in amputee rehabilitation medicine, Lancashire Teaching Hospitals NHS Foundation Trust

Dr Martin Johnson DRCOG DCH MRCGP
RCGP Clinical lead for chronic pain and Co-chair Chronic Pain Policy Coalition

Dr Natalie Lane
Consultant clinical psychologist, The Walton Centre NHS Foundation Trust, Liverpool

Dr Jenny Lewis PhD MSc Dip COT
Senior clinical research occupational therapist, The Royal National Hospital for Rheumatic Diseases, Royal United Hospitals NHS Foundation Trust, Bath; Senior lecturer, University of the West of England, Bristol

Sarah Lewis
Clinical nurse specialist in pain management, Defence Medical Rehabilitation Centre Headley Court

Dr Siva Mani-Babu
Consultant in sport and exercise medicine, Centre for Spinal Rehabilitation, Defence Medical Rehabilitation Centre Headley Court

Professor Candida S McCabe PhD RGN
Florence Nightingale Foundation clinical professor in nursing, University of the West of England, Bristol; RNHRD, Royal United Hospitals NHS Foundation Trust, Bath

Miriam Parkinson BSc(Hons)OT
Extended scope practitioner occupational therapist (member of BAHT), East Lancashire Hospitals NHS Trust

Col Rhodri D Phillip OBE, FRCP
Clinical director, Defence Medical Rehabilitation Centre Headley Court

Dr Helen Poole PhD CPsychol
Reader in applied health psychology, Liverpool John Moores University

Professor Karen Rodham PhD CPsychol FBPsS
Professor of health psychology, Staffordshire University

Dr Mick Serpell FRCA FFPMRCA
Consultant and senior lecturer in anaesthesia and pain medicine, University Dept of Anaesthesia, Gartnavel General Hospital, Glasgow

Dr Nicholas Shenker PhD FRCP
Consultant rheumatologist, Addenbrookes Hospital, Cambridge

Dr Mark Taylor FRCA FFPMRCA
Consultant in Pain Medicine, University Hospitals Plymouth NHS Trust

Professor Lynne Turner-Stokes DM FRCP
Consultant in rehabilitation medicine, Regional Hyperacute Rehabilitation Unit, London North West University Healthcare NHS Trust; Northwick Park Professor of Rehabilitation Medicine, King's College London

Dr Charlie Vivian MSc DMS MFOM
Consultant occupational physician, Icarus Health

Dr Paul Wilkinson MB BS BMedSci MClinEd MRCGP FRCA FFPMRCA
Consultant in pain medicine, Royal Victoria Infirmary, Newcastle

Dr Ben Yates MSc, FCPodS, FACPS
Consultant podiatric surgeon, Great Western Hospitals NHS Foundation Trust

The revised text in the section on Long-term support was informed by patients with complex regional pain syndrome (CRPS). We sought patient views via the charities CRPS UK (charity no. 1165597) and Burning Nights (charity no. 1166522) on a draft of this section between April and August 2017. We wish to acknowledge and thank all contributors for their input into the final text.

Additional members of the original Guideline Development Panel for 2012

Mrs Linda Cossins MSc MCLIP
Information scientist, Pain Relief Foundation, Liverpool

Dr David J Eedy MD FRCP
Consultant dermatologist, Southern Health and Social Care Trust, Craigavon, Northern Ireland; British Association of Dermatologists

Louise Haynes BScOT MRes
Pain specialist occupational therapist, The Walton Centre NHS Foundation Trust, Liverpool

Professor Turo J Nurmikko PhD
Professor of pain science, Pain Research Institute, University of Liverpool; Pain Relief Foundation

Dr Roger Okell FRCA FRCP FFPMRCA
Consultant in anaesthesia and pain medicine, Leighton Hospital, Crewe

Mr Brian Simpson MD FRCS
Consultant neurosurgeon, Cardiff, Wales

Professor Blair H Smith MD MEd FRCGP FRCPEdin
Professor of primary care medicine, University of Aberdeen

Patient representatives

Ms Suzie Almond Patient representative, Stroud

Mr Terrence Carney Patient representative, Liverpool

Mrs Wendy Hall Patient representative, Chester

Mrs Penelope Halliday Patient representative, Liverpool

Mr Alan Pendleton MBE Chairman, Smile Pain Support Group, The Walton Centre NHS Foundation Trust, Liverpool

Mr John Sanders Patient representative, Birmingham

Ms Angeleça Silversides Patient representative, London

Ms Catherine Taylor Patient representative, Sheffield

Abbreviations

Colleges and professional institutions

ABN Association of British Neurologists
AOP Association of Orthopaedic Practitioners UK
BAD British Association of Dermatologists
BAHT British Association of Hand Therapists
BAPRAS British Association of Plastic, Reconstructive and Aesthetic Surgeons
BOA British Orthopaedic Association
BPS British Pain Society
BPS (Psychology) – British Psychological Society
BSCN British Society of Clinical Neurophysiology
BSRM British Society of Rehabilitation Medicine
BSR British Society for Rheumatology
BSSH British Society for Surgery of the Hand
COP The College of Podiatry
CSP Chartered Society of Physiotherapy
DDR Directorate of Defence Rehabilitation
FPM Faculty of Pain Medicine of the Royal College of Anaesthetists
FOM Faculty of Occupational Medicine
FSEM Faculty of Sport and Exercise Medicine
PPA Physiotherapy Pain Association
PRF Pain Relief Foundation
RCEM Royal College of Emergency Medicine
RCGP Royal College of General Practitioners
RCOT Royal College of Occupational Therapists
RCP Royal College of Physicians
RCR Royal College of Radiologists
SBNS Society of British Neurological Surgeons
VSGBI The Vascular Society

About the guidelines

These guidelines concern the diagnosis and management of patients with complex regional pain syndrome (CRPS). They provide recommendations for diagnosis, treatment and referral in a variety of clinical settings (primary care, occupational therapy and physiotherapy, surgical practice, rheumatology, neurology and neurosurgery, sport and exercise medicine (SEM), dermatology, pain medicine, rehabilitation medicine, emergency medicine and long-term care). Their purpose is to provide coherent guidance for professionals working in the different health specialties who care for these patients (see Fig 1, page 2). The document starts with an introduction for all interested parties, followed by specialty-specific sections. Supporting documents are appended.

Clinicians will find relevant information in both the introduction and respective specialty-specific sections. Recommendations are in framed boxes and are generally based on panel consensus and expert opinion; grading is not provided. A concise summary of the 2012 guideline is available as a separate document.[1] Grading of recommendations using the typology developed for the National Service Framework for Long-term Conditions[2] is given there.

Methodology of guideline development

Both the 2012 guidelines, and this 2018 revision of the guidelines were initiated by Dr Andreas Goebel and Dr Chris Barker in association with the Pain Relief Foundation and were developed by a UK panel of experts representing a variety of healthcare specialties and professions. In addition, various professional associations and colleges were represented on the panel. Patient representatives were invited to formulate the long-term care section. Expenses for attending meetings were funded by commercial sponsors (see Appendix 1). The guidelines are intended for use throughout the UK.

Systematic review methodology for the 2018 guidelines

See Appendix 2 for the detailed methodology used in the 2012 guideline and 2018 revision.

A previous systematic review considered the treatment of complex regional pain syndrome in adults, and included papers published from July 2000 to February 2012.[3] This 2013 Cossins *et al* review built on a previous review (Forouzanfar *et al* 2002,[4] which considered the treatment and prevention of reflex sympathetic dystrophy and CRPS from 1966 to June 2000). A further review was conducted in 2017, to identify the published evidence relating to the treatment of CRPS since 2012, and to consider if reviewing this recent evidence enables the drawing of any more definitive conclusions about the clinical utility of interventions for CRPS.

Recommendations

The recommendations were developed on the basis of panel consensus and expert opinion, with reference to the existing literature. Where possible, recommendations were informed by evidence from the reviews of randomised controlled trials (RCTs). (See summary of results of two reviews of RCTs in Appendix 16). No formal grading of recommendations was undertaken. At each stage of development the draft guidelines were circulated to members of the group for peer review prior to production of the final draft. Drafts of the 2012 guidelines were also sent for comments to additional expert patients, who had not otherwise participated in the guideline group; drafts of the 2018 revision were also reviewed by several UK CRPS patient groups (see page v).

Consultation process

The final draft of the guidelines was circulated to each of the bodies endorsing or supporting the guidelines (see page i). Comments were invited to be sent directly to the chair and were implemented in consultation with the committee members.

Review

This guidance will be reviewed 5 years from the revision date.

Introduction

Complex regional pain syndrome (CRPS) is a debilitating, painful condition in a limb, associated with sensory, motor, autonomic, skin and bone abnormalities.[5] CRPS commonly arises after injury to that limb. However, there is no relationship to the severity of trauma, and in some cases there is no precipitating trauma at all (9%). CRPS usually affects one limb, but in 7% of cases later spreads to involve additional limbs.[5–7] The European incidence rate of CRPS is 20–26/100,000 person-years.[8] The cause of CRPS is unknown.[9] Characteristically, there is interplay between peripheral and central pathophysiologies. The earlier concepts that the predominant problem is sympathetic dysfunction and that CRPS occurs in (stereotyped) stages are now obsolete. It is also now clear that CRPS is not associated with a history of pain-preceding psychological problems, or with somatisation or malingering.[10–12] If a patient presents with such problems, these should be addressed where appropriate, as would be good practice in other medical situations. Patients still report suffering from interactions with health professionals who do not believe that their condition is 'real'.[13] Independently, it is recognised that some people self-induce signs with the aim of making their limb appear as though they have CRPS.[14]

Limb signs (such as swelling/sweating and colour/temperature changes) usually reduce with time, even where pain, and motor symptoms persist.[15,16] However, such reduction of limb signs is in itself not 'recovery'. Where pain persists, the condition is best considered to be active. It is noted that, without limb signs, a diagnosis of CRPS according to the 'Budapest criteria' can sometimes not be made (see Table 1). These patients (who have fulfilled the criteria in the past, but now have lost some or all limb signs, yet have ongoing pain) may be diagnosed with 'CRPS-NOS' (not otherwise specified, see also footnote [†]).[17]

Table 1 Diagnostic criteria for CRPS (Budapest criteria)[17] (A–D must apply) [†]

A) The patient has continuing pain which is disproportionate to any inciting event			☐
B) The patient has at least one sign in two or more of the categories			☐
C) The patient reports at least one symptom in three or more of the categories			☐
D) No other diagnosis can better explain the signs and symptoms			☐
Category		**Sign (you can see or feel a problem)**	**Symptom (the patient reports a problem)**
1 'Sensory'	*Allodynia* (to light touch and/or temperature sensation and/or deep somatic pressure and/or *hyperalgesia* (to pinprick)	☐	Hyperesthesia does also qualify as a symptom ☐
2 'Vasomotor'	Temperature asymmetry and/or skin colour changes and/or skin colour asymmetry	If you notice temperature asymmetry: must be >1°C ☐	☐
3 'Sudomotor/oedema'	Oedema and/or sweating changes and/or sweating asymmetry	☐	☐
4 'Motor/trophic'	Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair/nail/skin)	☐	☐

[†] A third diagnostic subtype called CRPS-NOS (not otherwise specified) can be considered for patients who have abnormalities in fewer than three Budapest symptom categories, or two sign categories, including those who had more documented signs and symptoms in the past, if current 'signs and symptoms' are still felt to be best explained by CRPS.

The onset of symptoms for the majority occurs within 1 month of the trauma or immobilisation of the limb.[18] There is no proven cure for CRPS. Approximately 15% of sufferers will have unrelenting pain and physical impairment 2 years after CRPS onset and are considered to have a long-term condition, although more patients will have a lesser degree of ongoing pain and dysfunction.[19–21] Prompt diagnosis and early treatment are considered best practice in order to avoid secondary physical problems associated with disuse of the affected limb and the psychological consequences of living with an undiagnosed chronic pain.[22] However, this standard of care has yet to achieve widespread practice in the UK. Since the condition is uncommon, and the range of symptoms can mimic many other possible conditions seen by practitioners from various professional backgrounds (Fig 1), patients commonly experience a delay in diagnosis and the start of appropriate therapies.[8,23] The aim of these guidelines is to aid diagnosis in a range of primary and secondary care settings. This document will also provide guidance on how to manage CRPS with appropriate treatment or referral to other practitioners.

Fig 1 Range of services used by patients with CRPS

Diagnostic criteria

CRPS is the term given to a group of painful conditions formerly termed as listed in Table 2. The diagnosis of CRPS is based on clinical examination and is given when patients meet the 'New IASP* diagnostic criteria' (or Budapest criteria) described in Table 1. CRPS is a diagnosis of exclusion, and differentials are listed in Box 1 below.

* International Association for the Study of Pain

Box 1: Differential diagnoses*

- infection (bone, soft tissue, joint or skin)
- orthopaedic mal-fixation
- joint instability
- arthritis or arthrosis
- bone or soft tissue injury (including stress fracture, instability or ligament damage)
- compartment syndrome
- neural injury (peripheral nerve damage, including compression or entrapment, or central nervous system or spinal lesions), or neuropathy (such as from diabetes, alcohol misuse)
- thoracic outlet syndrome (due to nerve or vascular compression)
- arterial insufficiency (usually after preceding trauma, atherosclerosis in older people or thrombangiitis obliterans (Burger's disease))
- Raynaud's disease
- lymphatic or venous obstruction
- Gardner–Diamond syndrome (see the list of differential diagnoses in the Rheumatology, neurology, neurosurgery and SEM section)
- brachial neuritis or plexitis (Parsonage–Turner syndrome or neuralgic amyotrophy)
- erythromelalgia (may include all limbs)
- self-harm

Table 2 Earlier names for CRPS

Algodystrophy	Causalgia
Algoneurodystrophy	Reflex sympathetic dystrophy
Sudeck's atrophy	Shoulder–hand syndrome
Reflex neurovascular dystrophy	Fracture disease

CRPS can be divided into two types based on the absence (type 1, much more common) or presence (type 2) of a lesion to a major nerve. Currently this distinction has no relevance for management,‡ but it can have importance in some medico-legal cases. CRPS type 1 is accompanied by minimal distal small nerve fibre injury in some cases.[24]

Treatment approach

Pain is typically the leading symptom of CRPS and is often associated with limb dysfunction and psychological distress. For those in whom pain persists, psychological symptoms (anxiety, depression), and loss of sleep are likely to develop, even if they are not prominent at the outset. Therefore, an integrated interdisciplinary treatment approach is recommended, tailored to the individual patient. The primary aims are to reduce pain, preserve or restore function, and enable patients to manage their condition and improve their quality of life.

The four 'pillars' of care (education, pain relief, physical rehabilitation and psychological intervention – see Fig 2), which address these aims have equal importance. However, full recovery can be difficult to achieve in some patients, even with early appropriate treatment. Practitioners can support patients by providing a clear diagnosis, information and education about the disease, helping to set realistic goals and, where possible, involving the patient's partner and/or other family members.

* This list is not exhaustive.

‡ As an exception, in neurosurgical and surgical practice, in CRPS type 2, a nerve lesion can sometimes be directly treated (see 'Surgical management' in the section on surgical practice).

This document provides guidance on how best to meet treatment aims in a variety of clinical settings, for both acute and chronic CRPS.

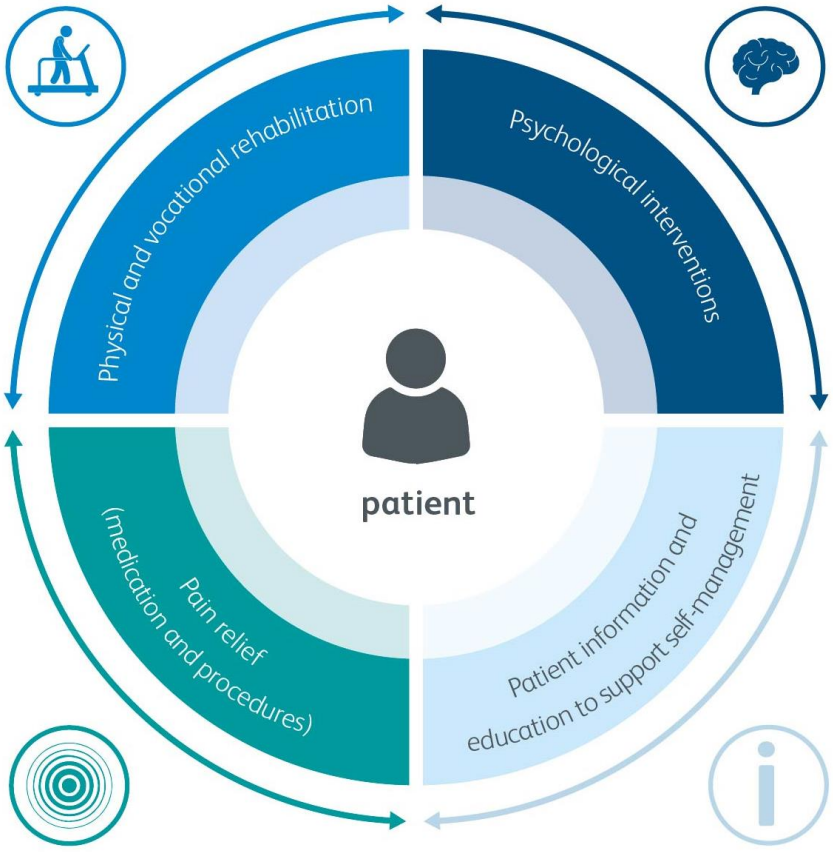

Fig 2 Four pillars of treatment for CRPS – an integrated interdisciplinary approach

Specialty guidelines

Primary care

Suspected or confirmed CRPS – diagnosis, management and referral in primary care in the UK: guidance for GPs and other primary care clinicians

Unilateral limb pain in patients presenting to the GP surgery has many potential causes. This section of the guideline aims to add clarity to the diagnosis and management (including immediate, short-term and long-term management) of CRPS in primary care. The starting point of the guideline assumes a degree of suspicion of the presence of CRPS; an exhaustive differential diagnostic list is beyond the scope of this document (see the list of differential diagnoses in the Rheumatology, neurology, neurosurgery and SEM section).

To improve the chance of a favourable outcome, three principal areas require attention:

- pain intensity
- limb dysfunction
- distress.

Diagnosis of CRPS

Recommendations

For best practice, GPs would:

- be aware of CRPS and recognise the clinical signs (see Appendix 3)
- have access to a CRPS diagnostic checklist (see Appendix 4)
- apply knowledge of the 'bio-psychosocial' assessment of pain.[25]

Referral

The main reasons to refer patients with CRPS are:

- to confirm diagnosis (pain services, neurology or rheumatology)
- to exclude ongoing pathology (eg surgical, rheumatology or neurology*services)
- when symptoms are difficult to control (pain services)
- to enable functional rehabilitation (pain and/or rehabilitation services).

It may be appropriate to manage confirmed CRPS in the primary care setting alone if the symptoms are mild.

Pragmatically, to categorise CRPS as 'mild', a patient would have few signs of significant pain-related disability or distress and either conventional or neuropathic drugs would manage pain intensity adequately. Patients who exhibit high levels of pain, disability or distress should be referred for specialist advice; in the meantime, active rehabilitation should be initiated as early as possible (see Occupational therapy and physiotherapy section, phase 3).

Recommendations

Referral of *suspected* CRPS is indicated in the following instances:

- For confirmation of the CRPS diagnosis.
- When pain treatment (see 'Management of suspected or confirmed CRPS' later in this section) is unsuccessful. In such cases, the patient should be referred to a pain specialist (in community or secondary care). This is essential even if other management is ongoing (eg by physiotherapy,

* In CRPS type 2 (defined as CRPS with associated damage to a major nerve), the cause for nerve damage, if unclear, should be assessed by a neurologist. CRPS can be triggered by nerve damage but does not cause nerve damage by itself.

orthopaedics or rheumatology). The GP should not rely on non-pain clinicians to manage the persistent pain.

- Even when the patient's pain is mild and controlled if there are concomitant signs of pain-related distress or disability. In such cases, the patient should be referred to a multidisciplinary pain clinic (in community or secondary care). Information about pain clinics is available through NHS Choices.

After trauma or surgery

- When a patient is already discharged from the trauma or surgical team, the GP should consider re-referral – for example, to the attending orthopaedic specialist/surgeon or trauma service – to allow for definite exclusion of ongoing pathology.

Without trauma (or after minor trauma)

- Patients with suspected CRPS without preceding trauma should be referred to secondary care (eg rheumatology) to exclude or address specific pathology.
- Isolated referral to physiotherapy/occupational therapy should be arranged with caution and only if the referrer is certain that there is no identifiable underlying cause (eg infection or other causes) (see Rheumatology, neurology, neurosurgery and SEM and Surgical practice sections for other causes).

Referral of confirmed CRPS

Other than in mild cases of CRPS (see Referral earlier in this section), patients should be referred to a pain specialist for further management.

It may also be appropriate instead to refer cases of confirmed CRPS to specialist rehabilitation or vocational rehabilitation services if:

- CRPS presents in the context of another existing disabling condition (eg stroke or severe multiple trauma)
- specialist facilities, equipment or adaptations are required or need review
- the patient needs specialist vocational rehabilitation or support to return to work (this service is sometimes also provided by pain management services)
- litigation is ongoing, requiring support to facilitate an early conclusion.

Management of suspected or confirmed CRPS

Both pain, and CRPS-associated *body perception disturbances*[23] can cause distress, and additional suffering may be caused, as patients struggle to explain these symptoms.[†] Advising that such feelings are normal, and reinforcing pain management principles, such as pacing, goal setting and relaxation, is helpful.

Recommendations

For best practice, GPs:

- would aim to confirm the diagnosis – this may require further diagnostic opinion (see Referral earlier in this section)
- would have access to evidence-based information to share with patients (see 'Online sources of information for patients' in Appendix 12).

[†] Patients may describe their limb with negative emotions such as hate, anger, disgust and repulsion; they often have a strong desire for amputation of the affected limb, perceive changes in limb size and structure, or dissociation from the limb. These perceptions may influence patients' engagement with therapy.

Management of pain is important to minimise suffering. This should be done in parallel with any ongoing investigation and management of potentially relevant pathology that may be contributing to the pain.

- The aim of medication is to minimise pain and support physical rehabilitation. If the patient is waiting for an appointment with a pain specialist, they should be seen regularly and be advised about the use and titration of simple analgesics.
- If simple medication does not reduce the patient's pain to a mild level after 3–4 weeks, consider using medication for neuropathic pain according to neuropathic pain guidelines.* [26] Earlier use may be appropriate.
- Other specialists may also initiate neuropathic pain drugs, but the GP is usually best placed to arrange the follow-up required for drug titration (see also section on Surgical practice).

There is currently a lack of evidence to inform the best functional advice to offer patients with suspected CRPS, or CRPS for which concomitant pathology has not yet been ruled out. Pragmatically, encouragement of gentle limb use and active lifestyle is recommended for all patients.♦ This should include:

- gentle limb movement (unless contraindicated for surgical reasons) (see section on Surgical practice)
- frequent attention to the affected limb
- normalising the sensation of the affected limb, 'desensitisation', following appropriate guidance (see Appendix 5)
- progressing to more active use (eg weight bearing and stretching) when tolerated.

If there is any doubt about the safety of movement, the advice of an orthopaedic surgeon or rheumatologist should be sought.

Mild cases of CRPS may be managed with simple and/or neuropathic pain medications and general advice regarding exercise.

Good communication between primary and secondary care is essential:

- GPs and other primary care clinicians should be involved in the care initiated by the secondary care service/pain specialist. The treatment plan should be clear in all cases.
- The long-term management of treatment-resistant CRPS should be shared between the primary care clinician and chronic pain service and, where appropriate, specialist rehabilitation services (see recommendations on 'Referral' earlier in this section).
- Where multiple clinicians are involved, there is an increased risk of fragmentation of care or conflicting advice; this is well understood by the GP. Often part of the GP's role will be to ensure that the patient has a clear and consistent view of the problem. The GP can minimise any inconsistencies through objective interpretation of opinions and clear communication with the patient. The GP will often decide whether further clarification is required from the specialists involved.

* For further information regarding neuropathic pain, see the national guidance documents for the UK published by the National Institute for Health and Care Excellence (NICE) (this document was not developed for CRPS; however, it is considered appropriate to use these medications in the treatment of CRPS). https://www.nice.org.uk/guidance/cg173[26]

♦ Some GPs choose to refer to physiotherapy to enhance the encouragement for patients to stay active and move the limb etc

Occupational therapy and physiotherapy

Settings

Occupational therapists and physiotherapists provide rehabilitation to those with CRPS in diverse settings, as categorised below:

- outpatient rehabilitation: either in the community or in hospital units
- inpatient rehabilitation: multidisciplinary inpatient rehabilitation is described in the section on Rehabilitation medicine
- pain management programmes (PMPs): these are multidisciplinary programmes, normally (although not always) carried out in an outpatient group setting and often attached to pain medicine departments; a more detailed description is available in the British Pain Society's leaflet *Guidelines for pain management programmes for adults.*

CRPS rehabilitation algorithm for occupational therapists and physiotherapists

Figure 3 illustrates the recommended algorithm for rehabilitation of patients with CRPS, and is based on expert opinion. The algorithm is suitable for both acute and more established CRPS. Decisions are based on the degree of symptom severity and treatment response. Patients referred to physiotherapy/occupational therapy with an already confirmed diagnosis of CRPS enter phase 3 of the algorithm.

Phase 1: undiagnosed CRPS

A therapist* in any rehabilitation setting may identify a patient presenting with signs and symptoms of CRPS without prior diagnosis by a medical doctor.

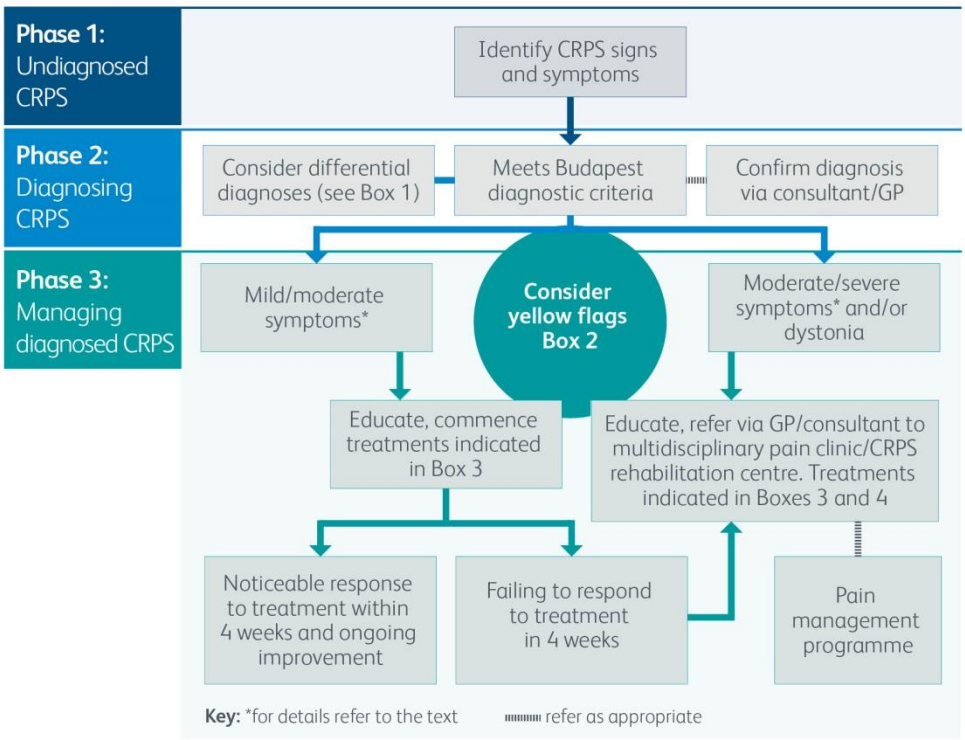

Fig 3 CRPS rehabilitation algorithm for occupational therapists and physiotherapists

* Occupational therapist and physiotherapist are referred to as therapist.

Phase 2: diagnosing CRPS

Confirmation of diagnosis is based on presenting signs and symptoms in accordance with the Budapest criteria[17,27] (see Table 1 in the Introduction, and Appendix 4). Although experienced therapists may make a diagnosis of CRPS, this generally should be confirmed by a doctor* (eg the patient's consultant or GP).

It is important to consider other possible pathologies (differential diagnoses) during diagnostic assessment (for guidance see Introduction Box 1).

Phase 3: managing diagnosed CRPS

There is no standardised battery of assessments for CRPS. It is not within the scope of these guidelines to be prescriptive about these measures, yet validated measures should be used as far as possible.

The degree of symptom severity is assessed to determine which of the two arms within phase 3 of the algorithm to follow.

Treatment should be initiated as early as possible. Patients presenting with mild to moderate disease and some patients with recent onset severe disease that is quickly resolving (eg shortly after trauma), can be treated using approaches such as those outlined in Box 3. If there is no response to treatment within 4 weeks, refer (see Fig 3). If at any stage during treatment the therapist is unsure whether to continue with single-handed therapy or to refer for multidisciplinary rehabilitation, further advice should be sought from an experienced colleague.

Mild CRPS signs and symptoms

To categorise CRPS as 'mild', a patient would have few signs of significant pain-related disability or distress, and either conventional or neuropathic drugs would manage pain intensity adequately. Patients who exhibit high levels of pain, disability or distress should be referred to a multidisciplinary pain clinic (ie two or more disciplines) or a rehabilitation CRPS unit.

Moderate to severe presentation/poor treatment response

If one or more of the following features that indicate moderate or severe disease and/or poor recovery are present, an early referral to a multidisciplinary pain clinic or specialist unit is recommended:

- presentation with moderate to severe signs and symptoms (except if of very recent onset after trauma and quickly resolving)
- presence of dystonia
- no positive treatment response within 4 weeks
- condition deteriorates or improvements are not sustained despite ongoing treatment.

In addition to providing CRPS-specific rehabilitation techniques, specialist units may treat patients with advanced drug and interventional techniques, including spinal cord stimulation. A GP or consultant referral to a multidisciplinary pain clinic or CRPS specialist unit can usually be initiated by the therapist (see Appendix 8 for a list of centres specialising in CRPS). Some regions have direct therapy referral agreements with the local multidisciplinary pain clinic.

Descriptions of the rehabilitation provided by pain clinics and rehabilitation medicine are presented in the sections on Pain medicine and Management of patients with CRPS and complex disability in

* It is recognised that patients with early CRPS are often diagnosed, treated with physiotherapy/occupational therapy and discharged without formal confirmation of the diagnosis by a doctor; however, patients should in general be seen by a doctor for medication management.

rehabilitation services, respectively. Examples of CRPS-specific rehabilitation techniques are outlined in Box 4.

After referral, it is important to continue treatment until the patient has been assessed by the pain clinic or CRPS specialist unit.

In circumstances where the therapist works within a multidisciplinary team, referral back to the team member who originally referred the patient for additional or alternative input may be appropriate.

Parallel referral to a multidisciplinary, psychology-led pain management programme should be discussed in accordance with the therapist unit's referral criteria.

Yellow flags

Recognition of psychosocial risk factors, referred to as yellow flags (Box 2),[28] can support therapists in understanding contributing causes for suboptimal treatment response and should be considered within the context of phase 3 of the algorithm. The presence of these factors has been used in other pain conditions to predict chronicity.[29]

Yellow flags may be present at initial assessment or may develop and become apparent during treatment. Recognition of these flags may guide referral to multidisciplinary pain clinics and psychology-led PMPs.

Box 2: Yellow flags (adapted from Main and Williams, 2002[30])

- iatrogenic factors, ie previous negative experiences with health professionals
- poor coping strategies, eg ongoing 'guarding' of the limb despite education
- involved in litigation/securing benefits (note that this may affect progress with treatment in some patients, but there must be no assumption that this applies in every patient)
- overuse of appliances
- distress
- anxiety/depression
- lack of willingness to set goals
- passive in treatment sessions
- inaccurate beliefs despite education
- fear avoidance
- negative family influences

Treatment approaches

When using the below-listed approaches, treating therapists must be familiar with their application specifically for people with CRPS, as even routine therapies may need to be delivered in an adapted way for this group.

Successive use of multiple approaches may lead to prolonged treatment. Therapists should refer as appropriate if there is no improvement after 4 weeks (see Fig 3).

Box 3: Therapeutic approaches[31*♦]

- patient education and support[32]
- self-administered tactile and thermal desensitisation with the aim of normalising touch perception (see Appendix 5)[33]
- general exercises and strengthening[34]
- functional activities
- mirror visual feedback[35–38]
- gait re-education[39]
- transcutaneous electrical nerve stimulation (TENS)[40]
- postural control
- pacing, prioritising and planning activities[41]
- goal setting[42–44]
- relaxation techniques[45]
- coping skills[46]
- hydrotherapy[47]
- sleep hygiene[48]
- oedema control strategies[49]
- vocational support[50]
- facilitating self-management of condition[51]
- splinting (generally short term, in acute CRPS)[‡52,53]

Box 4: Examples of CRPS-specific rehabilitation techniques

- graded motor imagery[54,55]
- tactile discrimination[56]
- strategies to correct body perception disturbance,[†] involving looking, touching and thinking about the affected body part[57,33]
- mental visualisation to normalise altered size and form perception of affected body part[58]
- functional movement techniques to improve motor control and awareness of affected limb position[58]
- principles of stress loading[59,60]
- conflict allodynia re-education to reduce fear of physical contact with others in community settings[61]
- management of CRPS-related dystonia

Recommendations

For best practice, therapists would:

- be aware of CRPS and recognise the clinical signs
- be aware of the Budapest criteria for diagnosing CRPS (see Introduction, and Appendix 4)
- initiate treatment as early as possible
- provide patient education about the condition
- know of the nearest multidisciplinary pain clinic or CRPS specialist rehabilitation centre
- recognise non-resolving moderate or severe symptoms and, where appropriate, initiate referral to a multidisciplinary pain clinic or CRPS specialist centre for rehabilitation.

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[*] This list is not exhaustive.

[♦] None of these techniques have been assessed in randomised controlled trials; however, a combination of some techniques was more successful than social work in one trial.[31]

[‡] Limited use where clinically appropriate; avoid prolonged periods of immobilisation or covering up of the limb.

[†] Body perception disturbance (BPD) concerns emotional feelings towards, and self-ownership of the affected limb. It can be assessed and reviewed using the Bath CRPS BPD scale.[23]

Surgical practice

Diagnosis, prevention, management and referral of patients with CRPS in surgical practice in the UK

The available evidence suggests that transient CRPS is common after limb fractures and limb surgery (1%–25% of cases).[62–64] The pain improves in most cases and CRPS lasting longer than a few months is an uncommon condition, with a prevalence of less than one in 1,500, although even a transient episode of CRPS may give rise to long-term disability due to functional[65] and/or structural changes.*

Diagnosis

CRPS is a diagnosis of exclusion. In a surgical context, alternative causes of persistent limb pain include infection, orthopaedic mal-fixation, instability, arthritis or arthrosis, and neuropathic pain from nerve entrapment or nerve damage.[66] 'Scalding' pain in the distribution of a peripheral nerve in an orthopaedic setting should be urgently reviewed by the surgeon because of the possibility of nerve damage related to surgery or injury.

Both the new IASP (Budapest) criteria, which were developed in a pain medicine context (see Table 1), and 'Atkins criteria', which were developed in an orthopaedic context† (Appendix 6) provide similar results in the diagnosis of CRPS in orthopaedic practice.[67]

The Budapest criteria have been adopted by the International Association for the Study of Pain, and should generally be used in surgical practice. Concerns remain about these criteria in a judicial context, because of their patient-response-related features such as hyperalgesia and motor-weakness.

Plaster and dressing tightness, or a perception of tightness, and disproportionate pain while in plaster, or when the plaster is removed may be early warning signs for CRPS.[68]

Sensory and motor 'neglect-like symptoms' (sensory: 'my hand does not feel as if it belongs to me'; motor: 'I cannot move my limb the way I want to, and this is not due to my pain') are features of CRPS that may be common after trauma, even in the absence of CRPS.[69,70] These signs are unlikely to indicate a primary psychological dysfunction.[71]

Recommendations

- Surgeons should be aware that there are diagnostic criteria for CRPS, including the 'New IASP' (Budapest) criteria, and Atkins criteria. They should be able to use one of these sets of criteria in their clinical practice. Use of the New IASP (Budapest) criteria is recommended.
- Surgeons should be aware that CRPS may never fully resolve and that it often severely reduces patients' quality of life and may be associated with increased psychological distress.[72,19]
- Surgeons should be aware that the diagnosis of CRPS can be made in patients who have only had minor soft tissue injury. It may even occur without a traumatic event.
- A CRPS diagnostic checklist should be available in orthopaedic and plastic surgery departments, including outpatient departments and plaster rooms.

* Such as contracture and ankylosis, such changes are rare.

† In this guidance, use of the Atkins criteria is considered or recommended only in an orthopaedic context and not in other contexts, such as pain medicine or general practice.

- Classic descriptions emphasise that bone involvement is universal in CRPS after trauma. At an early stage, there will be increased uptake on the delayed part of the technetium-99m-methylene diphosphonate (Tc-99m MDP) bone scan and at a later stage there will be osteoporosis. However, CRPS is a clinical diagnosis that does not depend on the results of a bone scan. The routine use of three-phase bone scans is not necessary and may delay the start of treatment,[73] and is therefore not recommended.
- General post-fracture/operation patient information leaflets should include advice to observe and report warning signs for CRPS. A sample leaflet is available (see Appendix 7).

Management

The development of CRPS should not be considered evidence of suboptimal surgical management.[66]

Recommendations

- Healthcare professionals in plastic and orthopaedic surgery practice involved in the care of patients with CRPS should be aware of the basic principles of CRPS therapy (refer to the four pillars of care described in the Introduction).
- Management should include provision of general information about CRPS, including reassurance that the pain will improve in at least 80% of cases, although lesser ongoing pain and motor dysfunction may be common.[65]
- The surgeon should reassure the patient that CRPS is a recognised condition, although its causes are poorly understood.
- Physiotherapy and/or occupational therapy,[†] unless contraindicated, should be initiated immediately when CRPS is suspected. General advice should include focusing on the affected limb, gentle movement, light functional activity, and desensitisation. Temporary splinting in a position of safety may relieve pain and be an adjunct to mobilisation, but the treatment of early CRPS is generally by gentle mobilisation. Immobilisation of a joint in a patient with CRPS carries a risk of long-term stiffness. Early functional weight-bearing is to be encouraged to accelerate rehabilitation. Orthotic devices such as insoles can support weight-bearing but require a physiotherapist's supervision. Excessive mobilisation that strongly exacerbates pain is contraindicated.
- The surgical team should initiate early treatment with simple analgesic drugs. These may include codeine, dihydrocodeine, tramadol,[*] non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol, as appropriate.[♦] These drugs do not necessarily affect the specific pain of CRPS but may reduce ongoing trauma-related pains and assist in the process of mobilisation.
- Surgeons may initiate treatment with other drugs useful for neuropathic pain, such as tricyclic antidepressants (nortriptyline, imipramine or amitriptyline)[74] and anticonvulsants (gabapentin[75] or pregabalin, see Fig 4), but the GP or pain specialist is usually best placed to arrange the follow up required for drug titration (see Primary care section). If a patient requires anticonvulsive or antidepressant drugs or strong opioids for the control of neuropathic pain or the treatment of CRPS, serious consideration should be given to urgent referral to a pain consultant.

[†] Referral to a specialist hand therapy service, where available, is preferable for upper limb CRPS. In the UK, hand therapists are specialised physiotherapists or occupational therapists.
[*] Note, tramadol is a controlled drug.
[♦] Note, long-term opioid treatment is rarely appropriate.

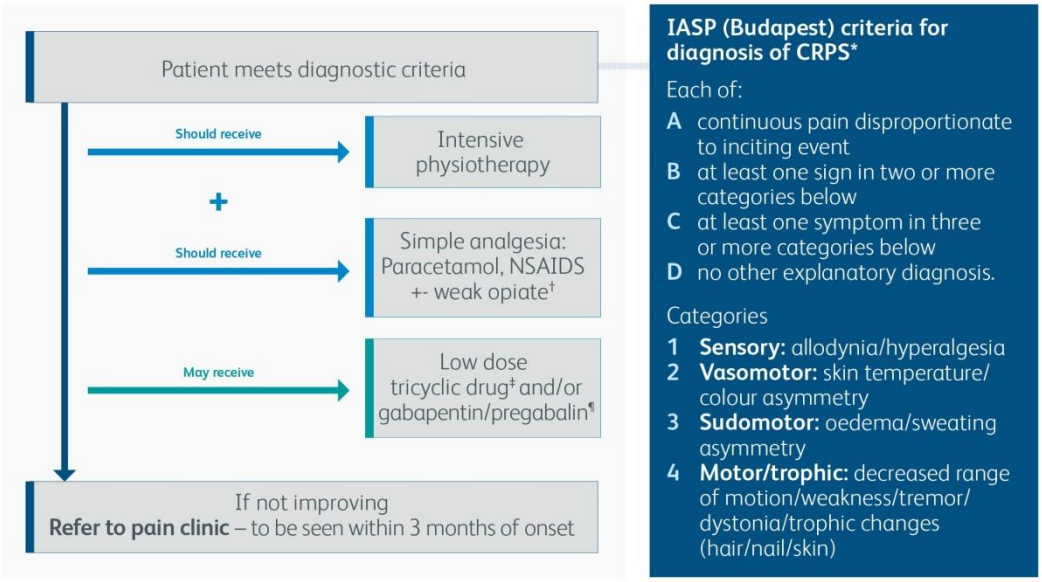


Fig 4 Management of CRPS in surgical outpatients

Guanethidine blocks should not be used in orthopaedic-/ plastic surgery practice (see Pain medicine section for clarification).[4,76]

Orthopaedic and plastic surgeons should be aware of specific treatments for chronic CRPS, such as specialist physiotherapy and occupational therapy, multidisciplinary pain management programmes, spinal cord stimulation and specialist rehabilitation programmes.

Ideally, surgical departments should have an in-house pathway for CRPS in place. A senior member of the surgical department acting as 'CRPS champion' (or 'Pain champion') may be best placed to achieve this.[77]

Prevention

There is no recommendation for any prophylaxis for CRPS because of insufficient evidence. There is however mounting evidence that a dedicated pathway instituted in the very early phase after trauma, featuring high vigilance for abnormal pain responses, combined with early rehabilitative treatment can reduce the incidence of CRPS after trauma.[77]

Risk of surgery in patients with CRPS

If elective surgery on a limb previously affected by CRPS is delayed until acute signs of CRPS have clearly improved, the rate of operation-triggered recurrence of CRPS is <15%, with most recurrent cases being mild.[78,79]

Expert opinion suggests that complications following surgery in patients with CRPS may be common. Reasons may include the adverse reaction of patients with CRPS to surgical pain and the adverse impact of body perception disturbances[23] and poor motor control[80] on rehabilitation; however, this field needs further study.

Recommendations

- Surgery should be avoided on a CRPS-affected limb where possible, and be deferred where it cannot be avoided until 1 year after the active process has resolved.[78]
- Surgery may be indicated in CRPS type 2 when there is an identifiable remediable nerve lesion (eg certain cases of neuropathic pain due to either nerve compression by scar tissue, neuroma formation or perioperative nerve injury, such as through a needle stitch) but should be undertaken only when, on balance, the expected benefit from pain reduction outweighs the risk of exacerbation.
- Where surgery on an affected limb is necessary, this ideally should be performed by a surgeon with experience in operating on patients with CRPS with an anaesthetist who is also a pain specialist (see the section on Pain medicine).

Surgery to amputate the CRPS-affected limb[†]

Clinical teams are increasingly being approached by patients with requests for amputation of affected limbs. News reports of patients cutting off their own limbs have placed additional pressure on clinical teams to provide or seek surgical solutions, including amputation.

There is insufficient robust literature to predict outcome from amputation, with just two small series publishing comprehensive results:

Deliessen *et al* (1995) reported disappointing results in their series of 28 patients, with recurrent symptoms at some level in all cases, and only two patients successfully wearing a prosthesis although the majority (24/28) reported overall satisfaction with the results.[81]

A more recent series of n=36 from Jan Geertzen's team in the Netherlands[82,83] reported somewhat more positive results, although over 77% reported phantom limb pain more than 1 year after amputation, and 27% had recurrent CRPS in the stump; 22/36 (61%) used a prosthesis. Nevertheless, the majority of patients reported that they would choose to undergo amputation again in the same circumstances.

Based on these two small series, we offer the following guidance.[♦]

Recommendations: A) Referral for amputation

Both in cases where a surgeon considers referral for amputation, or where such a referral is considered by other specialties, a multidisciplinary team including, as a minimum, a consultant in pain medicine, a pain specialised psychologist (or a specialist liaison psychiatrist), and a specialised physiotherapist or occupational therapist all experienced in chronic pain management and CRPS, must be involved before such referral is made. Where a non-surgical specialist considers initiation of such referral for amputation, an orthopaedic surgeon must also have clarified any requirements for non-amputation orthopaedic management as appropriate. This will allow the multidisciplinary team to:

- appropriately explore and trial those treatments advocated within these guidelines including specialist pain coping/management therapies, and neuromodulation treatments
- contribute to the decision-making process about amputation; factors to be weighted include unrealistic expectations, psychological disorders and negative coping mechanisms, which may be yellow flags for negative outcomes,[83] whereas resilience may be a positive predictor.[85]

[†] In addition to orthopaedic surgeons and plastic surgeons, vascular surgeons are sometimes involved in performing amputation for CRPS.

[♦] More recently, a small retrospective case series has reported improvements following – mostly lower limb – amputation, with little pain relief; the demographics of this Israeli cohort do not correspond to the UK patient population: patients were mostly male, and the average CRPS onset was around or below 30 years of age.[84]

- identify CRPS-specific caveats (Box 5).
- A full explanation of the risks associated with amputation must be given and documented in those exceptional cases, where a referral for consideration of amputation is made. This includes those issues listed in Box 5. Patients and their families should be made aware that the amputation is unlikely to resolve their pain, and the CRPS may recur in the stump or in another limb, and prosthesis use may not be possible.

A list of general amputation complications is provided in Appendix 9.

Recommendations: B) Assessment and planning for amputation*

- Amputee rehabilitation is complex in this situation, and must be carefully considered as part of pre-operative planning, including the level of amputation, stump fashioning and post-operative rehabilitation. Therefore, a consultant in rehabilitation medicine who is also specialised in amputee rehabilitation should be involved in the preoperative assessment and planning, and a tertiary amputee rehabilitation service must be involved, preferably where staff have specific experience of treating this CRPS patient group.
- Where referral to the amputee rehabilitation service is received without prior involvement of specialised pain services detailed above, involvement of such services should generally now first be sought, prior to further management within the amputee rehabilitation service.
- Natural recovery from CRPS is frequent within 18–24 months after CRPS onset,[19] and can occur even in very longstanding cases. Amputation is rarely justified within 24 months after CRPS onset excepting cases listed in the next paragraph.
- Amputation may be considered in very rare cases of intractable infection of the affected limb that cannot be controlled with antibiotics. Except in immediate emergencies, involvement of the outlined multidisciplinary teams is essential. Patients should be made aware that ulceration might recur in the stump after amputation.

A UK-wide registry of amputations performed in patients with CRPS should be established.

Box 5: CRPS-specific caveats and risks with limb amputation

Caveats

- A strong desire to have the CRPS-affected limb amputated can occur from early after CRPS onset. This desire may in some cases be part of the CRPS-related, regional body-dysmorphia, which may be caused by a CRPS-associated shift in cortical limb-representation.[23,57] This desire may confound the validity of a patient's wish to pursue amputation to reduce pain or improve function.
- CRPS will spread to other limbs in 7% of cases; this risk is unlikely to be reduced with amputation[5]

Risks

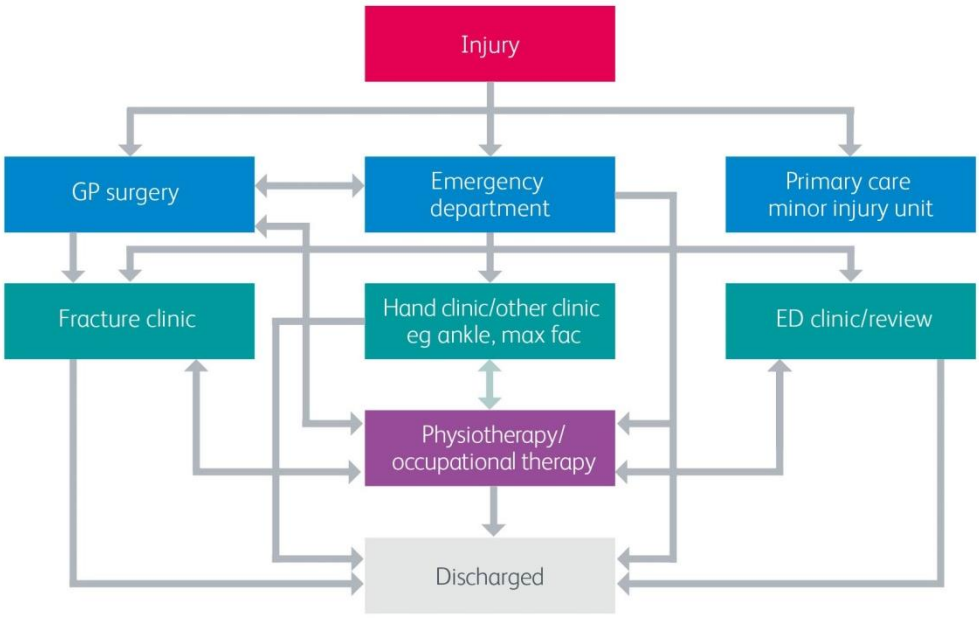
- Development of phantom limb pain
- Development of stump pain preventing use of the prosthesis
- Occurrence of CRPS in the remaining part of the limb
- Triggering of CRPS by surgery required for stump neuroma treatment[86]
- Development of CRPS in other limbs
- Recurrence of ulceration and infection in the stump
- Delayed/problematic wound healing

* At some centres, specialists in amputee rehabilitation work closely with the patient's multidisciplinary pain team; such a joint assessment process can effectively support decision making.

Emergency medicine

Limb injury is a very common presentation in emergency departments (ED) and a small proportion of these patients will develop CRPS.

After attendance at the ED, patients with limb fractures and significant soft tissue injuries will usually be referred to a fracture clinic or hand clinic; other patients with lesser injuries may be discharged, referred for physiotherapy or referred to their GP for follow-up (see Fig 5 Flowchart).



Note: referral pathways from the primary care minor injury unit are not shown
ED = Emergency department

Fig 5 Flowchart: EM care pathway for patients with limb injury

Thus, most patients with limb pain are seen in the ED once. However, a number of EDs run follow-up clinics for patients with soft tissue injuries, where patients with continuing limb pain may be seen, and independently patients will frequently re-present to the ED with continuing limb pain.

There are many potential causes for limb pain; CRPS should be considered in the differential diagnosis. This emergency medicine (EM) CRPS guideline aims to clarify the diagnosis and management of suspected or confirmed CRPS within the ED.

Appropriate training of all ED-associated professionals about CRPS management within the ED is key to achieving best care. A senior member of the ED acting as 'CRPS champion' (or 'Pain Champion') may be best placed to achieve this.[77]

Diagnosis of CRPS should be made using the new 'IASP criteria' (also termed Budapest criteria, Appendix 4). CRPS is a clinical diagnosis and there are no specific investigations to confirm it, but investigations may be required to rule out other causes of limb pain.

The investigation and management of a painful limb may be considered at four stages after the injury: i) initial attendance early after injury, ii) repeat visit <4 weeks, iii) repeat visit >4 weeks, and iv) known CRPS flare up.

i) Initial attendance early after injury

Diagnosis

The CRPS diagnosis within the first few weeks after injury is difficult to secure, because signs and symptoms are often indistinguishable from normal variations to the post-injury or post-operative response. It is common for patients to have pain out of proportion to that expected for their injury, and the vast majority of these responses resolve.[16]

Patients with disproportionate pain (both CRPS and non-CRPS) often have a grossly distorted perception of the painful limb.[87]

Management

ED physicians should provide reassurance that enhanced symptoms are common after injury but usually resolve.

Appropriate analgesia should be prescribed as per standard ED practice. The aim is to minimise pain and support physical rehabilitation.

Where not contraindicated, advice should be given to touch/stroke the skin of the painful parts and to gently use the limb, even where this appears counterintuitive to the patient (see Appendix 5: Desensitisation).

Patients with excessive, disproportionate pain who are not being followed up elsewhere should be considered for ED review 4–6 weeks after trauma; alternatively review should be recommended to the GP; in either case ED physicians should consider highlighting the risk of future development of CRPS.[88]

Where follow-up will be arranged through fracture clinic or hand clinic (see Fig 5 Flowchart), ED physicians should highlight any concerns about future CRPS development.

ii) Repeat attendance for pain in the acute phase (<4 weeks) after injury

Diagnosis

Repeat attendance is common for exaggerated pains, sensitivity, non-specific pins and needles sensations, swelling, tightness in the plaster cast, sweating, temperature and color changes, or movement problems. The ED clinician will exclude differentials per normal practice. Although CRPS can often not be reliably diagnosed before 4 weeks after injury, continuation of these symptoms may indicate that the patient is at risk to develop CRPS. ED physicians may consider arranging for the patient to be seen for follow-up > 4 weeks after injury to allow a definite diagnosis.

Management

i) If a patient returns with severe, unexplained limb pain and/or tight plaster cast within 4 weeks after trauma having tried simple analgesia, and where significant pathology has been excluded, ED physicians should consider rapid referral to physiotherapy or occupational therapy in addition to analgesia only if there is access to PT/OT with experience in treating exaggerated pain after injury. Alternatively, recommendation of rapid referral should be made in the GP letter.

ii) The patient's normal care provider, eg orthopaedics, plastics or fracture clinic teams should be informed about this repeat visit.

iii) Any concerns about future CRPS development should be communicated in the referral/letter, making reference to the UK CRPS guidelines document if necessary.
iv) If the patient can be reviewed in an ED clinic, medication for neuropathic pain according to neuropathic pain guidelines[26] should be considered and an up-titration protocol provided. Otherwise consideration of neuropathic drug initiation should be highlighted in the GP letter.
v) The importance of the GP as coordinator of care should be emphasised to the patient to support holistic, multidisciplinary care as well as reduce the potential reliance upon the ED.

iii) Late (>4 weeks) after injury

Diagnosis – undiagnosed CRPS

CRPS should be considered in the differential diagnosis of a patient who continues to complain of limb pain post-injury.

If CRPS is suspected the ED clinician should:

- exclude alternative diagnoses
- make a diagnosis of CRPS using new IASP (Budapest) criteria (Appendix 4)
- be aware that communication of this diagnosis can be distressing to the patient, and should be undertaken with caution, and reassurance (see below)
- document the CRPS diagnosis within the ED note-keeping system
- communicate the CRPS diagnosis to both the GP, and the patient's normal care provider, eg orthopaedics/plastics/plaster team
- if there is diagnostic uncertainty (eg where CRPS is suspected and concomitant pathology is also present), refer the patient to either pain medicine services, neurology, rheumatology, or orthopaedic services for clarification, as appropriate; communicate the suspected CRPS diagnosis in the referral letter.

Management

Patients should be reassured: most people will get better quickly.[19]
Simple advice on avoidance of overactivity, encouragement of both steady, light function (see orthopaedic section), and attending to/touching the limb (see Appendix 5). This will be further developed by the treating PT/OT.

- Where the patient is followed up in an ED/review clinic, management with neuropathic pain drugs should be initiated where appropriate, and the up-titration regimen included with the prescription.[26]
- refer the patient urgently to a therapist (PT or OT) with appropriate experience.
- the letter to the GP should:
    - include the CRPS diagnosis and information on management initiated (including referral to PT/OT)
    - provide the UK Guidance CRPS GP information leaflet, or a comparable electronic link
    - suggest initiation of neuropathic pain drugs if this is not done in the ED
    - suggest referral to the local chronic pain clinic
- where direct referral from the ED to the pain clinic is possible, this should be initiated, except in mild cases.

iv) Patients with a known diagnosis of CRPS attending ED with a flare-up of pain (this is uncommon)

The management of established CRPS in emergency medicine (EM) parallels that of exacerbations/unsatisfactory management of pain in other chronic pain conditions. The usual reason for attendance will be inadequate analgesia, but there are other potential causes, such as a new injury, or overwhelming distress. Patients should already have a management plan in place, and visits may represent failure of their community/specialist management plan.

The ED physician should:

- be aware that manipulation of a limb for diagnostic purposes in patients with established CRPS can be very painful and should be avoided; asking for permission to touch/manipulate may reduce patient distress
- provide reassurance. Explain that pain flares are expected and will settle over few days or weeks
- consider giving advice to reduce intensity (but not frequency) of physical therapy during flare-up, and in all cases to continue with regular exercises where not contraindicated; recommend that the patient contacts their PT/OT where applicable
- generally not initiate changes to drug treatment, assuming that the patient is being treated appropriately, eg by a pain specialist, or for mild cases by the GP
- not treat with strong opioids, or benzodiazepines, even as a one-off treatment. However, the avoidance of such treatment may be challenging, where appropriate multidisciplinary treatment has not yet been initiated
- where not already done, consider recommending to the GP initiation of neuropathic pain treatment, and referral to pain clinic
- where applicable, outline appropriate treatment options. Consider signposting to CRPS UK guidance
- ensure multidisciplinary pain management has been considered (if it is clear that current care is not adequate this will require liaison with other clinicians, eg GP or pain physician).

Recommendations: Diagnosis of CRPS in emergency medicine

- CRPS should not be diagnosed before 2–4 weeks following the triggering trauma.
- ED physicians should know to diagnose CRPS using new IASP (Budapest) criteria.
- In case of diagnostic uncertainty, the patient should be referred as appropriate, and the suspected CRPS diagnosis should be communicated in the referral letter.
- In case of concern about future development of CRPS early (<4 weeks) after a triggering trauma, eg in patients with disproportionately high pain intensity, or plaster tightness consider inviting the patient for a follow-up visit in ED review clinic, or recommend GP review >4 weeks after the trauma, to establish a definite diagnosis.
- ED physicians should gain a good understanding of why a flare in symptoms of established CRPS requiring an ED visit has occurred, or refer onwards to establish this. Potential reasons for flare include worsening of CRPS pathology, tolerance to medication, reduced functionality or failure of the agreed management plan.

Recommendations: Management and referral of CRPS in emergency medicine

- Patients with enhanced pain early after limb injury should be reassured that enhanced symptoms after injury resolve in a large majority of cases.
- Functional rehabilitation of these patients is no different with, or without a diagnosis of CRPS
- Where not contraindicated, these patients should be advised to gently touch, move and use their limbs.
- Consider rapid referral to PT/OT of early (<4 weeks after injury) repeat attenders.
- Simple analgesics should be initiated, as per standard ED practice. In undiagnosed patients with enhanced pain unresponsive to simple analgesics neuropathic pain medication can be considered depending on local protocol.
- Concerns about future development of CRPS should be communicated in clinic and referral letters.
- Any communication about CRPS to the patient should be done with care to avoid unnecessary distress.
- CRPS first diagnosed in ED should either be referred directly to a pain service, or referral to pain services should be recommended to the GP. Neuropathic pain drugs[26] should be initiated in parallel.
- The management plan of patients with already established CRPS should be reviewed to ensure it is appropriate, and has been agreed between all involved. Discordance between clinician and patient can risk compromising the effectiveness of the plan and lead to further ED attendances. Emergency treatment of established CRPS with strong opioids or benzodiazepines is discouraged.

Rheumatology, neurology, neurosurgery and SEM*

Management of suspected and confirmed CRPS in rheumatology, neurology, neurosurgery and sport and exercise medicine (SEM)

Diagnosis

Earlier (now superseded) terms for CRPS are given in Table 2 in the Introduction. In patients with an established diagnosis of CRPS, neurologists are sometimes asked to determine whether there is accompanying nerve damage and, if there is, to determine whether the same injury that caused the nerve damage had caused CRPS (ie CRPS type 2) or whether the nerve damage is concomitant or preceded the CRPS.

Box 6: Selected differential diagnoses for CRPS in rheumatology, neurology, neurosurgery and SEM*, although not necessarily in all four disciplines

- bone or soft tissue injury (including stress fracture, ligament damage and instability)
- compartment syndrome
- neuropathic pain (eg due to peripheral nerve damage including compression or entrapment neuropathy or due to central nervous system or spinal lesions)
- arthritis or arthrosis
- thoracic outlet syndrome (due to nerve or vascular compression)
- infection (bone, soft tissue, joint or skin)
- arterial insufficiency (usually due to atherosclerosis in older people, trauma or thrombangiitis obliterans (Burger's disease))
- lymphatic or venous obstruction
- Raynaud's disease
- Gardner–Diamond syndrome†
- brachial neuritis or plexitis (Parsonage–Turner syndrome or neuralgic amyotrophy)
- erythromelalgia (may include all limbs)
- self-harm[14]

Recommendations

- Rheumatologists, neurologists, neurosurgeons and SEM physicians should be familiar with the Budapest criteria for the diagnosis of CRPS (see Appendix 4).
- In persistent limb pain, in the absence of a neurological or neurosurgical explanation, a diagnosis of CRPS should be considered (see Appendix 4). This also applies if a lesion of the somatosensory nervous system is identified but the pain is disproportionate and there are associated features of CRPS.

* Neurology and neurosurgery here relates to general neurology and neurosurgery. Pain-related neurosurgery and guidance for neurologists working in pain clinics can be found in the section on Pain medicine.

† Psychogenic purpura (Gardner–Diamond syndrome, autoerythrocyte sensitisation or painful bruising syndrome) is a rare and poorly understood clinical presentation of unexplained painful ecchymotic lesions, mostly on the extremities and/or face.

Management and referral

For surgical management, refer to the Surgical practice section.

Recommendations

Rheumatologists, neurologists and neurosurgeons should be aware of advanced treatments for CRPS, including specialist physiotherapy and occupational therapy, multidisciplinary pain management programmes, spinal cord stimulation and specialist rehabilitation programmes.

In neurological and neurosurgical practice, when a diagnosis has been made patients with CRPS should generally be referred to a pain unit for comprehensive assessment and/or specialist treatments (information about pain services is available on the NHS Choices website).

However, if individual specialists with a special interest in CRPS wish to manage the condition, the four 'pillars' of treatment (pain relief, physical and vocational rehabilitation, psychological intervention, and patient education and self-management), as described in the Introduction, have equal importance and should be delivered with an integrated interdisciplinary approach.

To facilitate this, the following aspects of care should be available to patients:

- expertise in the physical rehabilitation of patients with chronic pain conditions
- management of pain (see section on Pain medicine)
- psychological intervention specific to pain in the form of a multidisciplinary, usually cognitive behavioural therapy (CBT)-oriented, pain management programme (PMP)[89] (see the British Pain Society's guidance on PMPs); most PMPs integrate the physical rehabilitation aspect with CBT*
- patient education as an important part of treatment; patient information resources are available (see Appendix 12)
- specialists being aware that there are also centres with a special interest in CRPS for referral (see Appendix 8).

* Cognitive behavioural therapy (CBT) is not a single therapy or even a single set of standardised interventions. Rather, CBT is a broad category of different treatment regimens. However, CBT regimens almost always include cognitive therapy (the 'C' of CBT) as a core component. Usually CBT also includes interventions designed to alter behaviours (the 'B' of CBT) and some combination of operant treatment, coping skills training, relaxation strategies, pacing or activity–rest cycling, exercise and activity management, and pleasant activity scheduling.[90]

Dermatology

Diagnosis

In dermatology, CRPS has previously been known by a number of other, now superseded, terms, which are listed in Table 2. Higher awareness of CRPS is required by dermatologists, as early diagnosis helps management and recovery.

In addition to the typical trauma, antecedent factors that may lead to presentation to dermatologists include stroke, myocardial infarction, tuberculosis and herpes zoster, as well as more distinct dermatological events such as vasculitis, Weber–Christian syndrome, nail biopsy, excisional skin biopsy and epitheloid haemangioma. Although it is not clear how some conditions lead to CRPS, the common unifying factor in most instances is trauma. In leg ulcers, the injury from the ulcers themselves is probably involved.

The skin presentation of CRPS seems to take distinct forms that are sometimes sequential. There can be vasodilation and sudomotor dysfunction (hot, red and dry skin) or signs of vasoconstriction and hyperhidrosis (cold, blue and sweaty skin). These signs and symptoms can interchange.

Recognition of changes in skin may help in the diagnosis. The skin in CRPS may become either thin and glossy or thickened. Nails may show decreased or increased growth or thickening, become brittle or develop striations. In addition, hair growth can be increased or decreased. These changes may be due to vasoconstriction (resulting in skin hypoxia) or decreased range in motion of the skin from inactivity of underlying joints, tendons or ligaments. In chronic cases, skin sometimes becomes thin, atrophic and dry. Fingertips may diminish in volume, and deeper structures, including fascia, may become thickened, resulting in contractures. However, many patients have no trophic skin changes.

Box 7: Dermatological manifestations of CRPS[†]

- erythema
- skin atrophy
- oedema
- hypohydrosis
- warmth
- hyperhydrosis
- pallor
- Beau's lines in nails
- cyanosis
- factious ulcers
- hypertrichosis
- vesicles or bullae
- hypotrichosis
- leukonychia
- nail ridging
- onychodystrophy

Recommendations

- The diagnosis should be based on the Budapest criteria.[17,27]
- The Budapest criteria (Appendix 4) achieve 80–90% accuracy. Given that no objective tests have been validated, the diagnosis is clinical.

[†] Source: Phelps RG, Wilentz S. Reflex sympathetic dystrophy. *Int J Dermatol* 2000;39:481–6

Referral

Recommendations

- Patients who are first diagnosed in dermatology should be referred to a pain management team.
- Dermatologists may also receive referrals for dermatological input in the management of severe skin manifestations in patients with CRPS.

Management

Treatment principles should be those outlined in the Introduction.

Recommendations

- A multiprofessional approach is essential.
- Dermatologists should be aware that in patients with problematic oedema, spinal cord stimulation treatment initiated by a pain specialist or neurosurgeon may reduce oedema.
- Recommendations for the treatment of skin ulcers, skin infection and problematic oedema are described in Appendix 10.

Pain medicine

Diagnosis and management of CRPS in pain clinics in the UK. Guidance for pain physicians* and neurosurgeons with a special interest in the management of pain

Diagnosis

Recommendations

- Pain specialists and neurosurgeons with a special interest in the management of pain should be aware of the Budapest criteria for the diagnosis of CRPS[17,27] (see Introduction and Appendix 4).
- These criteria rely on a clinical examination to diagnose CRPS. The use of additional tests is not recommended. However, in some instances, certain tests such as magnetic resonance imaging (MRI) and nerve conduction measurements may be appropriate to exclude other diagnoses.

Management

Recommendations

- Patient information and education is an important part of the management of CRPS.
- Template information leaflets are included in Appendix 12, with additional links to other sources of patient information on the web.
- Management should include reassurance that the pain will resolve, either completely or partially, in up to 80% of cases, although ongoing lesser pain and motor dysfunction with limited limb disability may be more common.[16,19]
- Patient and doctor should agree on a treatment plan.
- If there is a lack of progress, the treatment plan should be re-evaluated.

Drug treatment**

- No drugs are licensed to treat CRPS in the UK.
- Drugs with efficacy in neuropathic pain should be used according to the National Institute for Health and Care Excellence (NICE) guidelines for neuropathic pain[26] (developed for a non-specialist setting) and the 'strong recommendations' of the Neuropathic Pain Special Interest Group of the International Association for the Study of Pain (IASP). †91
- Where drugs with efficacy in neuropathic pain are not sufficiently effective, drug reduction or drug cessation may improve the balance between effects and side effects.
- Pamidronate (single 60 mg intravenous dose) should be considered for suitable patients with CRPS less than 6 months in duration as a one-off treatment.††
- Intravenous regional sympathetic blocks (IVRSB) with guanethidine should not be used routinely in the treatment of CRPS, as four randomised controlled trials have not demonstrated any benefit.[4]
- Low-dose immunoglobulin treatment, or treatment with lenalidomide should not be offered as there is definite evidence for a lack of effect.[92,93]

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* In pain centres, pain physicians may have various backgrounds, including anaesthetics, rheumatology and neurology.
** The diagnosis of CRPS type 1 or 2 has no consequence for drug management. As an exception, in orthopaedic practice, in CRPS type 2, a nerve lesion can sometimes be directly treated (see 'Surgical management' in 'Surgical practice' section).
† These documents were not developed for CRPS. However, it is considered appropriate to use this medication in the treatment of CRPS.
†† The Guideline Development Panel recognises that there may be other, newer types of bisphosphonates that may be appropriate/available in equivalent doses. Several trials of newer bisphosphonates for the treatment of CRPS had been completed awaiting publication at the time of publication of this revision (2018).

- Some additional drugs demonstrate efficacy to treat pain in CRPS. For information only, a summary of the results from two systematic reviews is given in Appendix 16. However, no treatment recommendations are given due to combinations of the following factors:
  - The evidence is only preliminary.
  - Some drug treatments are not feasible for use in a clinical setting.
  - Other drugs are unavailable or restricted in the UK.

Physical and vocational rehabilitation

Both early and late CRPS should be treated with physiotherapy and/or occupational therapy[31,94] delivered by therapists competent in treating patients with chronic pain and/or CRPS.

Physiotherapists and/or occupational therapists should be involved in the management of patients as early as is possible in the treatment pathway.

The therapists associated with the pain service should:

- address functional needs (sleep hygiene, self-care, leisure and work)
- teach pacing/activity modification and relaxation/mindfulness strategies to support self-management of the condition
- be aware of regional support services for return to work or to maintain existing employment; in some pain services therapists liaise directly with employers.

This list is not exhaustive.

Where such physiotherapy and/or occupational therapy services are not available within the pain management setting, a member of the pain team should be aware of regional support services such as specialised rehabilitation/vocational rehabilitation programmes (see Rehabilitation medicine section).

Qigong (Tai chi) exercises should be considered.[95]

Interventions

Neuromodulation* should be considered in patients with CRPS who have not responded to appropriate integrated management, including pain physiotherapy (see Occupational therapy and physiotherapy section). This treatment can be carried out only in secondary or tertiary centres (see BPS patient information** and NICE guidance† for further information). Pain specialists should be aware that there is some evidence that the efficacy of spinal cord stimulation generally declines over time.[96–97]

Psychological interventions

The treatment of chronic pain should include provision of psychological interventions specific to pain in the form of a group-based multidisciplinary pain management programme, for those who require it, based on an appropriate assessment method.††[99] In a minority of cases, 1:1 psychological support may be more appropriate. Psychological interventions often follow principles of CBT (see footnote on page 24); however, alternative methods have also shown efficacy.[100]

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* 'Neuromodulation' refers to both 'spinal cord stimulation', and 'dorsal ganglion stimulation'. The long-term evidence for the latter, newer technology has not yet been established.[98]

** https://www.britishpainsociety.org/static/uploads/resources/files/book_scs_patient.pdf

† www.nice.org.uk/nicemedia/pdf/TA159Guidance.pdf

†† As in other chronic pain situations, some patients with significant distress may need individual therapy as a precursor to group-based treatment.

In some centres, interventions (including injection of local anaesthetic solution to the sympathetic chain, epidural catheters delivering a local anaesthetic and clonidine, or interscalene indwelling catheters) are used with an aim of 'breaking the cycle' of pain or aiding physiotherapy. Although there is currently no conclusive evidence for this practice from randomised controlled trials, considerable anecdotal evidence suggests that pain levels can remain low after such intervention in CRPS of relatively short duration (<6/12).

More research is needed before these methods can be formally recommended. We also note that some pain centres have historically provided IVRSB with guanethidine in subsets of patients with CRPS who show positive responses to such treatment. Current evidence suggests that guanethidine itself is not active,[4] but that the other components of the treatment, including the tourniquet, may be active.[101]

Surgery (including amputation)

If surgery is considered necessary on limbs currently or previously affected with CRPS, or in patients in whom other limbs are currently or have previously been affected, clinicians should note that there is no evidence that any particular anaesthetic technique is superior in preventing recurrence of CRPS, postoperative pain exacerbation or new CRPS in a previously unaffected limb. (Please refer to the section on Surgical practice for a discussion of i) the risks of operations in either suspected, or diagnosed CRPS; ii) amputation as a treatment).

Treatment for symptoms and/or signs other than pain

For CRPS-related limb dystonia, intrathecal baclofen treatment can be considered only if all other options, including oral medications, have failed.[102] Intrathecal treatment should be delivered only in specialised centres; its adverse event profile is poor. In some cases, no effective tolerable treatment can be established. The overall efficacy of regional botulinum toxin for CRPS-related dystonia is poor; some patients might experience improvement.[103] Serial splinting by experienced physiotherapists may symptomatically improve some cases of dystonia, but care should be taken to give time to exposing the limb for the conduct of desensitisation therapies (see Appendix 5).

In cases of refractory, disabling limb swelling, advice from a lymphoedema nurse should be sought (see Appendix 10). Spinal cord stimulation may reduce limb swelling in some cases.

In patients with CRPS and skin ulcers with or without infection, tissue viability and/or dermatological opinion should be sought as early as possible (see Appendix 10). Where ulcers occur in parallel with limb oedema, reduction of the oedema with spinal cord stimulation may promote ulcer healing in some cases.

Prevention

There is no recommendation for any prophylaxis for CRPS because of insufficient evidence. There is however mounting evidence that a dedicated pathway, instituted in the very early phase after trauma and featuring high vigilance for abnormal pain responses, combined with early rehabilitative treatment, can dramatically reduce the incidence of CRPS after trauma.[77]

Experimental treatments

Although the systematic review, which underpins the guidelines, included only RCTs, many other treatments for CRPS have been studied. A list of these treatments, with references, is provided in Appendix 15. However, these treatments should generally not be used outside a research setting.

Referral

Recommendations

- Patients should be referred in a timely manner based on individual assessment
- Complex regional pain syndrome that developed in the context of surgical practice, eg fracture, should be considered for referral for a further surgical opinion to exclude the contribution of mechanical causes such as instability, mal-fixation, arthrosis, infection and neuropathic pain from nerve entrapment.
- Practitioners should consider referral of patients to specialised secondary pain management care or specialist tertiary care for the following reasons:
  - specialised treatment eg spinal cord stimulation or a pain management programme
  - management for non-resolving (eg after 6–12 months), worsening or highly distressing CRPS; CRPS with dystonia; blistering skin changes; ulceration; lymphoedema or myoclonus; and children/adolescents.
  - further consultation and assessment or if the patient requests a second opinion.
- Patients with blistering skin changes, ulceration, skin infection or disabling limb swelling should be referred to a dermatologist and those with isolated disabling limb swelling to a lymphoedema nurse. Pain specialists should be aware that spinal cord stimulation may reduce limb swelling in some cases.[104]
- Pain specialists should be aware of centres with a special interest in CRPS treatment (see Appendix 8) and of the nearest centre with a neuromodulation service. Pain specialists should also be aware of the role of specialist rehabilitation services in supporting patients with severe complex disability and those requiring vocational support (see section on Rehabilitation medicine).
- At discharge, information about CRPS (see Appendix 3) and its management should be sent to the patient's GP with the clinic letter.

Competence

Recommendations

- Pain specialists, including GPs and neurosurgeons with an interest in neuromodulation, and all allied health professionals involved in treating these patients should be aware of available treatments for CRPS and their effectiveness.

Rehabilitation medicine

Management of patients with CRPS and complex disability in rehabilitation services

Specialist rehabilitation

A proportion of patients with CRPS will have complex combined physical, emotional, psychological and behavioural disability, and may require the support of a specialist rehabilitation service. The provision of specialist rehabilitation services for musculoskeletal conditions is currently patchy across the UK, and even where these services exist, they are often poorly integrated into the CRPS care pathway. The aims of this section are to highlight the availability of this resource to pain management specialists, to detail its strengths, and to confirm for the benefit of the rehabilitation team those requirements specific to CRPS.

Definitions of 'specialist rehabilitation' are given in Box 8.

Box 8: Definitions of rehabilitation

Rehabilitation medicine is the medical specialty concerned with the prevention, diagnosis, treatment and rehabilitation management of people with disabling medical conditions.

Rehabilitation is a process of assessment, treatment and management by which the individual (and their family/carers) are supported to achieve their maximum potential for physical, cognitive, social and psychological function, participation in society, and quality of life. It is divided into two main approaches:

- restorative: a goal-orientated process by which the individual is supported to achieve optimal function and independence
- disability management: a collaborative approach in which the team works with the patient and their family to support adjustment to change, prevent avoidable complications and minimise the effects of a disabling condition.

Specialist rehabilitation teams are interdisciplinary and led or supported by a consultant trained and accredited in rehabilitation medicine. They work closely with other specialties (eg neurology, rheumatology, orthopaedics, pain specialists, neuropsychiatry, etc) to support patients and their families with complex medical, physical, emotional, behavioural and psychological needs arising from long-term disabling conditions.

Some patients with CRPS and complex disability can develop 'learned disuse' and marked disability behaviour in their attempts to avoid pain, which may be compounded by well-meaning but inappropriate support from local disability services and, in some cases, family. For these patients, early engagement of specialist rehabilitation services with the patient, their family and their local services may break this cycle. Close liaison between pain management and specialist rehabilitation teams can enhance independence and participation,[22,105] mitigate effects from perverse incentives,[†] and ensure long-term care and support.

Diagnosis

The diagnosis of CRPS is made on the basis of the Budapest criteria (see Table 1 in Introduction and Appendix 4 for more details). Some patients will progress to develop long-standing CRPS. Over time, the typical vasomotor changes may become less prominent. Patients can therefore no longer fulfil the Budapest criteria but nevertheless have ongoing significant pain and/or motor and trophic dysfunction. The Budapest criteria suggest the use of the diagnostic subtype 'CRPS not otherwise

[†] A perverse incentive is an incentive that is likely to be withdrawn if the patient makes functional improvement.

specified' (CRPS-NOS) for patients who do not fully meet the criteria but whose signs and symptoms could not be explained better by another diagnosis. For patients who fulfilled the Budapest criteria in the past but no longer do so, the term CRPS-NOS may also be used. Where patients present later in the course of their condition (as is often the case in rehabilitation medicine), careful history-taking is required to establish whether autonomic changes were present earlier on. Because painful symptoms will have persisted for a while, it is expected that there will often be some features of psychological distress. In the remainder of this section, the term 'CRPS' is used as shorthand for both CRPS and CRPS-NOS.

Patient selection and referral

Examples of patients who may benefit from input from specialist rehabilitation include those:

- with CRPS-related severe complex disability with CRPS presenting in the context of another existing disabling condition (eg stroke or severe multiple trauma) with complex psychological or psychiatric comorbidities – either predating or postdating the onset of CRPS
- who require specialist facilities, equipment or adaptations or review
- who are unable to work and require specialist vocational rehabilitation or support
- who have ongoing litigation and require support to facilitate an early conclusion.

Whether a patient with complex disability is primarily under the care of the interdisciplinary pain team with input from specialist rehabilitation, or vice versa, will depend on the required key elements of the treatment programme and the expertise and resources within the respective teams (Table 3). In general, most ambulant patients are best managed primarily by the pain team, with support, where needed, from specialist rehabilitation. However, some patients will have conditions that render them unsuitable for treatment in a pain management programme and are better managed primarily by the rehabilitation team. This includes, for example, patients with severe concomitant physical or psychiatric disability (including some cases in which either the team or the patient feel that group treatment is not appropriate); in addition, patients in whom the consistency and structure of a 24-hour rehabilitative milieu is required to retain and carry over gains, may require management in an inpatient rehabilitation setting. Simultaneous support from the pain team is essential when the rehabilitation team infrequently sees patients with CRPS, or does not have the resources to provide cognitive behavioural therapy.

Table 3 Key elements of expertise for the treatment of patients with CRPS and complex disability that may be provided by specialist rehabilitation and pain teams

Specialist rehabilitation team	Specialist pain team
• complex disability self-management	• Specialist pain psychologists working in pain management delivering support for the emotional impact of CRPS, and recommendations for treatment options and their timing, including SCS and PMP
• assessment and provision of special facilities and equipment	• pain relief strategies (summarised in the section on Pain medicine)
• vocational rehabilitation	• specialist physiotherapy and occupational therapy techniques, including novel therapies for CRPS (see the section on Occupational therapy and physiotherapy), such as mirror training[37] or graded motor imagery,[54] desensitisation (see Appendix 5), pacing and relaxation[†]
• support for litigation (to facilitate an early conclusion)	• Provision of PMP

[†] These therapies may also be provided by some specialist rehabilitation teams.

Management

A coordinated multidimensional programme is required,[106] which should be delivered in the context of a cognitive behavioural approach. Key elements include:

- engagement – education and information for the patient and their family
- medical management
- psychosocial and behavioural management
- physical management
- activities of daily living and societal participation.

(Further details are given in Appendix 13, which is adapted from the British Society of Rehabilitation Medicine (BSRM) report on musculoskeletal rehabilitation.)[106]

Vocational and litigation support may be provided by specialist rehabilitation teams and, in other cases, these services are integrated into the regional pain management programme.

Vocational rehabilitation*

Inactivity can compound the pain experience and the physical consequences of disuse. The loss of employment and its financial consequences serve to compound the psychosocial disadvantage experienced by patients and their families.

Referral to the disability employment adviser may be required to access the various work support programmes available from the Department of Work and Pensions (DWP). However, because staff at the DWP may lack understanding of CRPS, liaison may be required through specialist vocational support programmes. Occupational health information is provided in Appendix 11.

Litigation

Because of the association between CRPS and injury or minor surgery, claims for compensation are not uncommon.

Litigation tends to fuel stress, which may adversely affect outcomes and ability to engage in rehabilitation.[107]

Consultants in rehabilitation medicine may have a useful role in this context, as medicolegal training is a standard part of the curriculum for rehabilitation medicine.

* The BSRM has published guidelines to vocational rehabilitation in long-term neurological conditions, which provide detailed guidance on specialist vocational rehabilitation. (British Society of Rehabilitation Medicine. *Vocational assessment and rehabilitation for people with long-term neurological conditions: Recommendations for best practice.* BSRM: London, 2010; http://www.bsrm.org.uk/downloads/vr4ltncv45fl-websecure.pdf)

Recommendations

In the management of patients with CRPS and complex needs:

- Patients with complex disabling CRPS should have access to specialist interdisciplinary rehabilitation programmes led or supported by a consultant in rehabilitation, as described in Appendix 13 (examples of referral criteria are listed under Selection and referral).
- Specialist rehabilitation teams and pain management services should work together in close liaison to share their expertise and resources for the management of patients with CRPS and complex needs.
- Whether the patient is primarily under the care of the interdisciplinary pain team with input from specialist rehabilitation, or vice versa, management should depend on the key elements of the programme that are required and on the expertise and resources within the respective teams (see Table 3 earlier in this section).
- In either situation, care should be delivered in the context of a cognitive behavioural approach involving both the patient and their family.
- The rehabilitation programme should be goal orientated, with active engagement of the patient and their family in setting goals so that the patient remains in control and responsible for the rate of progress.
- Patients should have access to vocational assessment at an early stage in the condition to support them to stay in work if possible.
- Ongoing specialist vocational support should be provided in conjunction with the disability employment adviser to access the various work support programmes available from the DWP.
- If productive work is impossible, patients should have appropriate support to withdraw from work, and vocational rehabilitation efforts should focus on leisure and social activities instead.
- If the patient is engaged in litigation with respect to their CRPS, the rehabilitation team should provide support to facilitate its conclusion as soon as possible.

Long-term support in CRPS

A proportion of patients with CRPS will have ongoing symptoms requiring long-term support. Patients report the following with respect to long-term management:

- They are concerned that many doctors and therapists have little understanding of CRPS and its management (see Online sources of information for patients in Appendix 12). They are therefore worried about being discharged from specialist pain and other services, as it is often difficult to re-access specialist expertise when required after discharge.[13]
- They are afraid of relinquishing social benefits and financial support as their condition improves in case they are unable to manage back at work, especially if their condition fluctuates from day to day.
- They want to be in control of their own condition and to remain as active and independent as possible. The following would enable them to do this:[108]
    - better information and advice to help them manage their own condition, particularly about the forms of support that may be available to help them return to or remain in work
    - flexible support (eg through personalised budgets) to allow them to make their own choice about the types of support that will work best for them at any given stage in their disease.

As long as the lifeline to the specialist service remains in place, patients are generally happy to accept fairly low levels of contact. Feasible models of support include:

- a named single point of contact within the pain team (eg nurse, doctor or physiotherapist) who they could contact if needed, without requirement to wait for a new referral
- being included in a register or flagged in some way on the GP records, so that they could get rapid access if needed in case of a flare of their symptoms
- access to self-help and peer support groups – possibly run by the voluntary sector, with occasional professional support from the specialist team
- access to facilities such as hydrotherapy and adapted gym facilities, where they could continue their own self-exercise programmes.

The aim of this guidance is to support self-management by empowering patients to manage their own condition, but with the knowledge that help and advice is available when needed. Although formal health economic evaluation is currently lacking, experience suggests that providing a relatively low-cost lifeline does not produce dependence on or excessive use of specialist services but can be effective in avoiding more expensive crisis management.

The longer-term management of people with CRPS can be based around the framework provided by the National Service Framework (NSF) for Long-term Conditions (Appendix 14).

Recommendations for long-term care and support may be mapped broadly onto the NSF's quality requirements, including:

- person-centred integrated information and care planning (QR1)[†]
- ongoing access to specialist care (QR2)
- community rehabilitation and support (QR5 and QR8)
- vocational support (QR6)
- support for families and carers (QR10).

[†] QR numbers refer to NSF mapping (Appendix 14)

Recommendations

Person-centred integrated information and care planning (QR1)

People with CRPS should have access to appropriate information about their condition.
Those who have complex long-term needs for care and support should have:

- a named single point of contact for advice and information
- integrated care planning, involving all of the agencies involved in their care, at a frequency agreed between the patient and their support team (usually no less than once a year).

The named point of contact may change over time according to the individual's needs, but professionals, or teams taking on this role must have appropriate understanding of the long-term management of CRPS and should also have access to expert support and advice from specialist pain and rehabilitation services when this is required.

Ongoing access to specialist care (QR2)

People with CRPS who require continued contact with specialist pain or rehabilitation services should have access to these through an appropriate route, which may include telephone or email access to a named team member and/or access by self-referral, within 1 year of treatment completion, subject to funding agreements.

At the treatment centre, provisions should be made for rapid processing of repeat GP referrals, eg by triaging upon receipt to physiotherapy/occupational therapy, a pain management programme and/or outpatient doctor appointment.

Community rehabilitation and support (QR5 and QR8)

People with CRPS should have access to a range of facilities to maintain their levels of activity and societal participation, which may include:

- self-help and peer support groups[109]
- facilities for self-directed exercise (eg adapted gym and swimming/hydrotherapy pool)
- support for social and leisure activities
- psychological intervention and counselling regarding the psychological consequences of living with the condition.

These services are often appropriately run by voluntary organisations, with input from professionals as required. Recruitment and training of volunteers who have CRPS to help with these services should be considered.

People with CRPS should have access to flexible support systems (eg personalised health and social care budgets) to maximise autonomy and choice of the most suitable forms of activities as their needs change over time.

Vocational support (QR6)

People with CRPS should have ongoing access to vocational support to help them remain in or return to work (see Appendix 11). Support may include:

- various work support schemes provided through the Department of Work and Pensions (DWP) (eg the 'Access to work' scheme, which provides support for special equipment or the cost of getting to work for those unable to use public transport; see section on Rehabilitation medicine for more details)

- education for employers, occupational health doctors and advisers from the DWP about the specific requirements of people with CRPS.

Support for families and carers (QR10)

Families and carers of people with CRPS should have access to advice, support and information, including:

- support to manage their own needs
- support to maintain relationships.

Vocational support, and family and carer support services can often appropriately be run by voluntary organisations.

Appendices

Appendix 1 Commercial sponsors

Abbott
Elder House
Blythe Valley Park
Solihull
B90 8AJ

Astellas Pharma Ltd
Lovett House
Lovett Road
Staines
Middlesex TW18 3AZ

Axsome Therapeutics Inc
25 Broadway
9th Floor
New York, NY 10004

Boston Scientific
Breakspear Park
Breakspear Way
Hemel Hempstead
Herts HP2 4TZ

Grünenthal Ltd
Aston Court
Kingmead Business Park
Frederick Place
High Wycombe
Bucks HP11 1LA

Medtronic Ltd
Suite 1, Building 5
Croxley Green Business Park
Watford
Herts WD18 8WW

NAPP Pharmaceuticals Ltd
Cambridge Science Park
Milton Road
Cambridge CB4 0AB

Nevro Medical Ltd
Carrick House
Lypiatt Road
Cheltenham
Gloucestershire GL50 2QJ

Pfizer Ltd
Walton Oaks
Dorking Road, Walton-on-the-Hill
Tadworth
Surrey KT20 7NS

Appendix 2 Systematic review methodology 2010/12 and 2016/17

Methodology 2010/12

We reviewed randomised controlled trials (RCTs) published on the treatment and prevention of CRPS from July 2000 through to April 2010. A previous systematic review published in 2002,[3] which reviewed RCTs on the treatment and prevention of reflex sympathetic dystrophy (RSD) and CRPS from 1966 through to June 2000, formed the basis of the methodology for this review.

MEDLINE (PubMed), Scopus, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Allied and Complementary Medicine Database (AMED) bibliographic databases and the Cochrane Central Register of Controlled Trials were searched electronically using combinations of the following search terms: complex regional pain syndromes; causalgia; reflex sympathetic dystrophy with therapy; drug therapy; rehabilitation; randomised controlled trial; clinical trial; prevention and control. All foreign language papers were included.

Three reviewers filtered the resulting studies. Trials were included at this stage only if they were appropriately randomised,[110] ie if the randomisation was described and deemed appropriate. If the randomisation was described but deemed inappropriate, then the study was excluded. However, if the study was described as randomised but the method of randomisation was not described, these papers were allowed to remain in the review.

A study was regarded as relevant to this review if either pain intensity or prevention of CRPS was given as an outcome measure. Studies were excluded if they compared two active interventions and there was no significant difference in outcome between the two intervention groups with no control group. Paediatric studies were excluded and also studies with composite outcomes, eg 'CRPS score' compiled using various parameters, if pain intensity was not also given separately.

In a second step, the filtered studies were evaluated for their methodological quality using a 15-item checklist,[111] identical to that used in the 2002 Forouzanfar review. Six reviewers, in three groups of two each scored a third of the identified papers, such that each paper was scored by two people. Scores were then agreed between reviewers and any disagreement was settled by a third reviewer. A trial was considered to be of good quality if the methodological score was 50 or greater and of low quality if the score was less than 50.

Studies were considered to be positive if pain intensity was significantly reduced by the intervention described when compared with placebo or a control group. Studies were classed as negative if there was no difference in pain intensity after the intervention when compared to placebo. A similar classification was used for prevention studies.

Four levels of evidence of effectiveness were defined using the Van Tulder method (Table 4),[112] based on the methodological quality and outcome of the studies.

Table 4 Levels of evidence of effectiveness of treatments for CRPS

Level of effectiveness	Evidence required
Strong	Multiple good-quality RCTs
Moderate	One good-quality RCT and one or more low-quality RCTs
Limited	One good-quality RCT OR multiple low-quality RCTs
No evidence	One low-quality RCT OR no relevant RCTs OR contradictory outcomes

Methodology 2016/17

In June 2016 PubMed and CENTRAL (Cochrane library) were searched. The search terms used were those used in the previous systematic reviews.[3] Search terms included those to identify randomised controlled trials AND complex regional pain syndrome OR the older terms used for CRPS: causalgia OR reflex sympathetic dystrophy. An additional search was completed in Scopus in September 2016; this search did not find any additional papers that had not been identified in the previous search.

RCTs were the only study design included, no language restriction was applied. This review excluded studies in children and those with other neuropathic pain conditions that were not CRPS. CRPS diagnosis is based on clinical signs and symptoms, to be included in this review studies had to report the clinical diagnostic criteria used. Studies that did not report the diagnostic criteria were excluded.

The interventions included in this review included any drug treatment (via any route of administration), medical procedures, physiotherapy, occupational therapy or pain management programmes.

Outcome measures included in this review were: pain intensity, pain duration, frequency of pain, sensory symptoms, allodynia, motor symptoms, quality of life, and adverse effects.

Included studies

There were 17 identified studies in total: nine drug therapy (seven vs placebo, two vs comparator), eight non-drug (four vs control, four vs comparator).

There were 11 studies identified that met the inclusion criteria for this review that included an intervention compared with a placebo. Of these, seven were of drug treatments,[92,113–18] one study each of sympathetic block,[119] virtual body swapping,[120]mirror therapy,[38] and aerobic exercise.[34] Six studies had been undertaken in Europe, two in Turkey and one each in South Korea, USA and Brazil.

There were six studies that included interventions compared with each other. Of these, two were of drug treatments,[121,122] one was of blocks,[123] one was of aspects of virtual body swapping,[124] and two were of differing physical therapy treatments.[125,126]

All of the included studies had CRPS diagnosed by established criteria; four studies used the Budapest criteria,[92,117,118,122] ten studies used the 'old' International Association for the Study of Pain (IASP) criteria,[34,113–6,119,120,123,124,126] two studies used the Harden criteria, 2007,[121,125] and one study used the Veldman criteria, 1993.[38]

Six studies included CRPS of the upper limb,[34,38,115,118,119,123] three studies included CRPS of the hand or foot,[92,113,117] one study included CRPS of the lower limb,[121] four studies included 1 extremity,[114,124–6] one study included ≥1 extremity[116] and one study included CRPS with no further specifications given.[123] Three studies considered CRPS in the affected limb of those who had had a stroke.[34,38,122]

There were single centre site studies[34,38,113,114,116,118–26] and two multicentre studies.[92,117] One study[115] was an upper limb subgroup of a larger CRPS study,[127] the original study had been included in the Cossins *et al* (2013) systematic review.[3]

Drug treatment studies

There were two studies that considered magnesium compared with placebo in people with CRPS of the upper or lower extremities. One study each included parecoxib, infliximab, lenalidomide,

ketamine and neridronate compared with placebo. One study compared intrathecal adenosine and clonidine and one study compared pamidronate and prednisolone.

Duration of CRPS

For a large proportion of people with CRPS the condition appears to improve or even resolve spontaneously.[19] CRPS that continues for >1 year can be considered chronic or long-standing and provides a considerable treatment challenge. This review included studies with participants with diagnosed CRPS of any duration.

For the studies included in this review:

- two specified in the inclusion criteria durations of CRPS ≤1 year[113,117] and a further two studies only had participants with CRPS of ≤1 year[115,123]
- two specified in the inclusion criteria durations of CRPS ≥1 year[92,116] and a further three studies only had participants with CRPS of ≥1 year[120,121,124]
- six studies included participants with ranges of duration of the condition, of these two specified in the inclusion criteria durations of CRPS ≥6 months,[114,119] and four did not specify duration for inclusion[34,118,125,126]
- two studies did not report the disease duration of CRPS[38,122]
- there were no long-term follow-up outcome data reported in the drug-based studies, with no outcomes measured beyond 12 weeks in any of the studies.

Quality

The quality of the identified evidence was considered for the pain outcomes in the included studies. As the review was undertaken to inform guideline development the GRADE system was applied (http://www.gradeworkinggroup.org/). GRADE aims to provide a transparent, structured process for presenting evidence summaries. In this system RCTs are automatically initially considered to be high-quality evidence prior to the assessment. The GRADE factors are then assessed and when appropriate may lead to the up or downgrading of the quality of the evidence.

Additional review September 2016–April 2018

Just before the manuscript was sent for final formatting, PubMed was searched using the same search terms for very recent publications. Two identified RCTs were analysed in more detail.[93,98] Both were multi-centre studies using Budapest diagnostic criteria. One study was of a drug therapy compared with placebo, which included patients with CRPS in both upper and lower limbs with a minimal duration of ≥1 year;[93] the other study compared an intervention with another intervention in patients with lower limb CRPS of at least 6 months' duration.[98]

Appendix 3 Sample information leaflet for GPs

Complex regional pain syndrome (CRPS)

CRPS is a chronic condition characterised by limb pain, and dysfunction within the motor, sensory and autonomic nervous systems.

A CRPS limb has some of the following features:

- pain disproportionate to that expected after the relevant trauma
- abnormal swelling
- abnormal colour (may appear red, mottled or cyanosed, or all at different times)
- abnormal temperature
- abnormal sweating
- motor dysfunction
- abnormal skin or nail appearance.

Often patients describe the limb as feeling like it doesn't belong to them, and express a hypothetical desire for amputation of the limb. The pain can be very severe. There is usually difficulty in moving the CRPS limb, which can be related to pain but also motor dyspraxia.

Epidemiology and impact

CRPS is usually post-traumatic (eg following radial fracture), although 10% cases have no obvious causal event. CRPS is also usually, unilateral although in approximately 7% of cases there is later involvement of additional limbs. The incidence of CRPS is similar to that of multiple sclerosis, but up to 80% of CRPS cases improve or resolve within 18 months. Half of these cases continue with long-term functional problems, and nearly half of patients do not return to work as a result of their chronic functional disability and residual pain.

Aetiology

Exact mechanisms for the pathogenesis of CRPS are not understood. A combination of elements including inflammation, dysfunction within sympathetic and somatosensory nervous system, and cortical (not psychological) factors are thought to contribute to the generation and perpetuation of symptoms.

Diagnosis

A combination of the presenting features will be seen. See Appendix 4 for a diagnostic checklist.

Management in primary care

What to tell patients

It is important for the CRPS sufferer to understand the role of physiotherapy in rehabilitation. This may appear counter-intuitive, as even with gentle physiotherapy the pain may worsen, and reassurance may be necessary.

There is no cure for CRPS, but the majority of patients will get better. As CRPS can cause high intensity pain and body perception disturbances, clinicians should be aware that patients with CRPS may struggle to understand and rationalise what they are feeling; this situation may add to their distress. Explaining that their feelings are normal, and reinforcing pain management principles, such as pacing, goal setting and relaxation, is helpful. A purely biomedical focus (cure seeking or solely reducing pain intensity) is unlikely to be of sufficient help and may impede progress. Improving disability and distress from CRPS is helpful in long-term recovery.

Crisis management
Pain flares in CRPS are normal and should not be considered as a worsening of the condition. Usually a flare will settle over days or a few weeks. Continuing treatment, possibly with reducing the intensity of physical therapy (not the frequency) is important to maintain recovery and speed the resolution of flare. If the situation becomes difficult to control, it is important to involve a multidisciplinary pain clinic with access to specialised pain psychology support where needed, in the first instance. This will avoid referral to other specialists for additional assessment, and prevent further escalation of suffering.

Spread
Patients are often scared that their CRPS spreads. These patients can be reassured that true CRPS spread is rather rare, occurring in about 7% of all cases, although transient pains in other limbs may be more common.

Appendix 4 CRPS diagnostic checklist

A) The patient has continuing pain which is disproportionate to any inciting event ☐ B) The patient has at least one sign in two or more of the categories ☐ C) The patient reports at least one symptom in three or more of the categories ☐ D) No other diagnosis can better explain the signs and symptoms ☐			
Category		**Sign (you can see or feel a problem)**	**Symptom (the patient reports a problem)**
1 'Sensory'	*Allodynia* (to light touch and/or temperature sensation and/or deep somatic pressure and/or *hyperalgesia* (to pinprick)	☐	Hyperesthesia does also qualify as a symptom ☐
2 'Vasomotor'	Temperature asymmetry and/or skin colour changes and/or skin colour asymmetry	If you notice temperature asymmetry: must be >1°C ☐	☐
3 'Sudomotor/oedema'	Oedema and/or sweating changes and/or sweating asymmetry	☐	☐
4 'Motor/trophic'	Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair/nail/skin)	☐	☐

Please note:

- Distinction between CRPS type 1 (no nerve injury) and CRPS type 2 (major nerve injury) is possible, but has no relevance for treatment. As an exception, in surgical practice, in CRPS type 2, a nerve lesion can sometimes be directly treated (see Surgical management in Surgical practice section).
- If the patient has a lower number of signs or symptoms, or no signs, but signs and/or symptoms cannot be explained by another diagnosis, 'CRPS-NOS' (not otherwise specified), can be diagnosed. CRPS-NOS can also apply to patients with documented CRPS signs/symptoms in the past.

If A, B, C *and* D above are all ticked, please diagnose CRPS. If in doubt, or for confirmation, please refer to your local specialist.

Explanation of terms

'Hyperalgesia' is when a normally painful sensation (eg from a pinprick) is more painful than normal; 'allodynia' is when a normally not painful sensation (eg from touching the skin) is now painful; 'hyperesthesia' is when the skin is more sensitive to a sensation than normal.

A special feature in CRPS

In category 4, the decreased range of motion/weakness is not due to pain. It is also not due to nerve damage or a joint or skin problem. This is a special feature in CRPS and is due to a poorly understood disturbed communication between the brain and the limb. A helpful question to assess this feature

is: ‘If I had a magic wand to take your pain away, could you then move your ... (eg fingers)?’. Many patients will answer with ‘no’ to that question.

Unusual CRPS

Around 10% of patients with CRPS cannot recall a specific trauma or may report that their CRPS developed with an everyday activity such as walking or typewriting. In some people CRPS can have a bilateral onset. In about 7% CRPS can spread to involve other limbs. Around 15% of CRPS patients do not improve after 2 years. It is appropriate to make the diagnosis of CRPS in these unusual cases.

Note: psychological findings, such as anxiety, depression or psychosis do not preclude the diagnosis of CRPS.

Appendix 5 Desensitisation

General patient information on therapy to help sensations to the skin feel more normal*

This is a therapy known as desensitisation.

The goal of these activities is to make sensations to the skin of the body area affected by complex regional pain syndrome (CRPS) feel more normal. The aim is to re-educate the sensory system, part of which involves areas of the brain.

General instructions

Many of these activities involve touch, and are suitable for the upper limbs (arms and hands) and lower limbs (legs and feet), although some are specific to one limb as indicated. These activities can be done on a daily basis and incorporated into your normal routine. Where possible, feel the sensation on a part of your body not affected by CRPS first, and remember how that normal sensation felt when then applying to the affected area.

Regular practice: little and often

Regular practice of these activities will increase the benefit. A short period of desensitisation (even 1–2 minutes) as many times as possible throughout the day is recommended. It might be helpful to set aside particular times during the day to perform them. A quiet, relaxed environment with few distractions will help you to concentrate on the task.

As you progress you may find other activities within your daily routine in which to incorporate these principles.

Discomfort

It is usual for these activities to be uncomfortable and somewhat painful while doing them and shortly afterwards. You may find that there are certain activities that you are unable to tolerate. Choose one that you feel comfortable with and gradually progress to others as you are able to do so. If you experience intolerable pain and discomfort, then stop that activity and find one that is more tolerable.

Concentration is important

To help normalise the system, it is important that you concentrate on the quality of the sensation. This can be done by first undertaking the activity on a limb unaffected by CRPS. Concentrate on how this sensation feels, remember it and then undertake the activity on the affected area, while looking at it and thinking about it.

* Adapted from a leaflet provided by experts at the Royal National Hospital for Rheumatic Diseases, with permission.

Suggested activities

1. Activities of daily living

Desensitisation therapy can be incorporated into activities of daily living as part of your normal routine.

While in bed
Feel the bed sheet against your unaffected limb. Close your eyes and concentrate on the quality of that sensation. Now feel the bed sheet against your affected area and recall how that normal sensation felt while thinking about the area you are touching.

While dressing
Concentrate on your affected limb by looking at it and thinking about it as you get dressed. Feel the texture of the garment against your skin both on the unaffected and the affected areas.

While having a bath or shower
Select a water temperature that you can tolerate. Feel the water on your unaffected body and now on your affected limb whilst looking at it and thinking about it. Recall how that normal sensation of the water felt against your skin.

Gently rub either a soft flannel, sponge or 'scrunchy' on the unaffected areas of your body. Use various movements such as circular actions, rubbing, patting and stroking. Concentrate on how these normal sensations felt while applying the movements to the affected areas of your body.

Activities for the upper limb only

While washing up
Feel the temperature of the water on both the affected and unaffected areas of your hands. Think about how the normal sensation of the water feels while concentrating on your affected hand. Focus on the action of your affected hand in the water. Where tolerable, use different water temperatures such as tepid, hot and cold. Immerse your unaffected hand first, then your affected hand for short periods. These periods can be lengthened over time.

While cooking
When you are making pastry or bread, mix it with both hands. Concentrate on the texture of the mixture and action as you are doing so.

2. Use of different textures

Applying different textures to the skin is another way to re-educate the sensory system.

Gather a variety of rough and smooth textures that you can tolerate. Here are some suggestions:
Smooth – felt, satin, silk, velvet, make-up or soft paint brushes
Rough – towelling, netting, scourers, flannel, wool, hook velcro.

Place them on your unaffected limb and apply movements such as light stroking, firm stroking, tapping and circular actions. Note the various normal sensations that you feel. Now on the affected limb, apply the texture in similar movements working from an area that you can tolerate towards the more uncomfortable skin areas, for example from the top of the arm towards the hand. Concentrate on the area by looking at it and thinking about it. Recall the normal sensations that you felt on the unaffected limb.

3. Massage

Massaging the affected limb can also be beneficial. This can either be done by yourself or someone else. Moisturisers or massage oils can be used. Be sure not to use anything which may irritate the skin. Use different pressures such as soft touch and firm massage where tolerable. Apply various movements such as patting, stroking and circular actions. Concentrate on the area being touched by looking at and thinking about it. Massage from your fingers and toes towards the centre of your body.

Appendix 6 Atkins diagnostic criteria for CRPS in an orthopaedic setting

Atkins criteria[62,128]

The diagnosis is made clinically by finding the following associated sets of abnormalities:

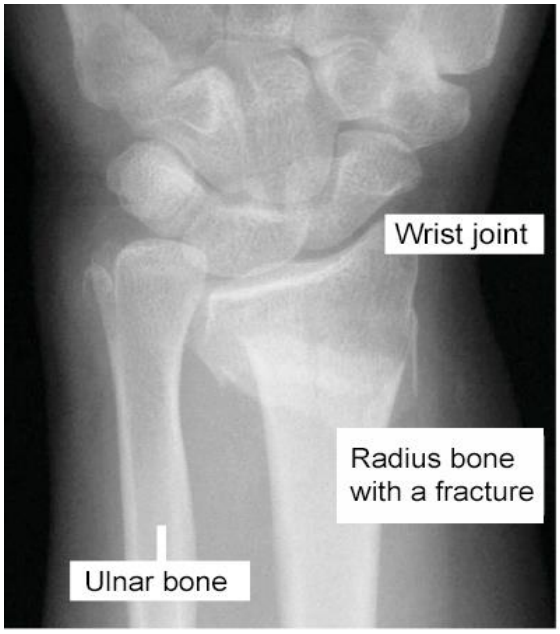
1 neuropathic pain; nondermatomal, without cause, burning, with associated allodynia and hyperpathia
2 vasomotor instability and abnormalities of sweating; warm red and dry, cool blue and clammy or an increase in temperature sensitivity; associated with an abnormal temperature difference between the limbs
3 swelling
4 loss of joint mobility with associated joint and soft-tissue contracture, including skin thinning and hair and nail dystrophy.

The diagnosis is excluded by the existence of conditions that would otherwise account for the degree of dysfunction.

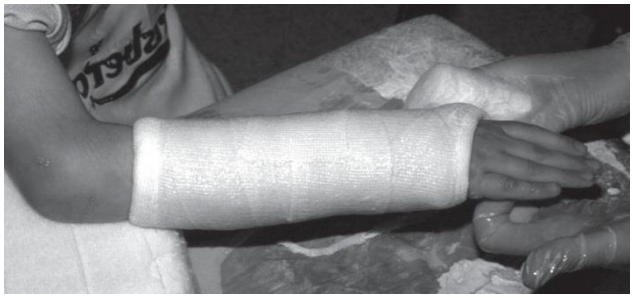
Appendix 7 Post-fracture/operation patient information leaflet

This sample leaflet has been kindly provided by professionals at the Royal Liverpool Hospital, Liverpool, and has been adapted for this guidance.

A fracture is a break of the bone. Most wrist fractures are caused by a fall onto an outstretched hand, but a direct blow to the forearm can also cause a fracture.



Following a fracture the wrist is often immobilised in plaster cast or splint, usually for up to 6 weeks. This assists in stabilising the bones to help ensure they heal in a good position. In most simple fracture cases this is sufficient support. The plaster cast can also help to control your pain.

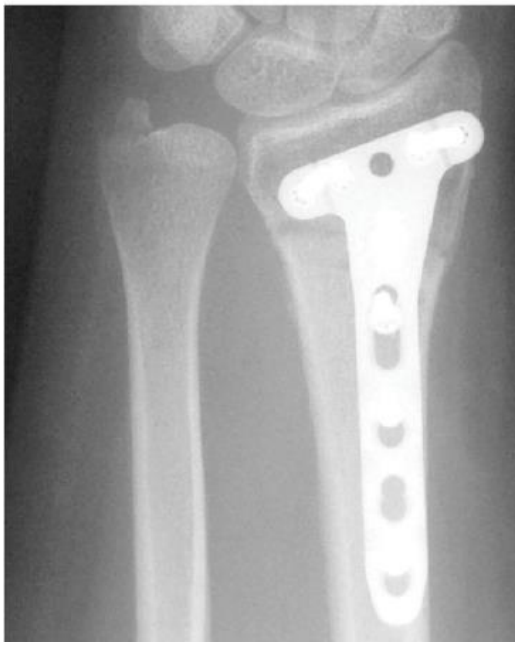


In some cases an operation may be suggested to improve the position of the bones so they heal in a more natural position and the soft tissues (muscles, tendons, ligaments and skin) are supported. Sometimes the support from a plaster is not enough to keep the bones in the best position.

If this is the case you may have the option of treating this with an operation using pins and/or plates to hold the bone firmly while it heals. This option will be discussed with you in clinic if it is relevant to you.

It is not always a clear case of an operation is the best treatment or a plaster is the best treatment and the pros and cons will be discussed with you on an individual basis (if appropriate) to help you decide which way you would prefer to be treated.

Radius bone with a fracture treated with screws and a plate to hold the bones in position while they heal.



What can I do now?

Do control your pain

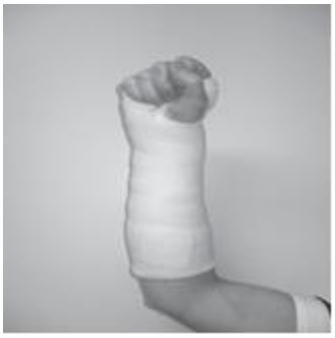
It is important that your pain is minimal to allow the uninjured parts to be kept moving and allow you to sleep well. Ask in clinic or your family doctor (GP) for a prescription if necessary. Your pharmacist may also be able to advise you.

Do reduce the swelling

Your hand and arm may swell because of your injury. This swelling may also increase your pain as it puts increased pressure on the injured parts. If the swelling continues it can cause your joints to become stiff. Any stiffness of the unaffected joints may delay your return to work or affect your ability to perform activities of daily living. A sling may be helpful in the first few days but should not be used for longer as this may result in stiffness.

Swelling can be reduced by raising your arm:

- Keep your hand raised above the level of your heart as much as possible.
- If resting/watching television, rest your arm out straight, raised on several pillows.
- Every 15 minutes within the hour, raise your hand right up above your head and ‘pump’ the fingers.



Do keep fingers, thumb, elbow and shoulder moving
In order to keep your uninjured joints healthy it is important they are kept moving. This will also encourage the blood supply to your soft tissues and reduce the swelling, as the muscle action helps squeeze the extra fluid away from the injury. Studies have shown that keeping the uninjured parts moving helps speed up your recovery once the plaster has been removed.

Do make sure your plaster fits comfortably
A well-fitting plaster will not stop you getting full finger movements, ie making a fist.

Do try to use your hand normally for all light activities
(Except in water) eg brushing hair, dressing, buttons, zips, feeding yourself; use your good hand to help if necessary. Try not to ignore your injured hand. This will help to prevent muscle weakness and abnormal pain responses.

Eat healthily and avoid smoking
Try to eat a healthy varied diet, as poor nutrition and smoking are known to slow healing. Vitamin C 500mg daily for the first 6 weeks may help to reduce the risk of complications.

What should I do if I have a problem with my plaster?
Any problems with your cast need to be reviewed by the medical team. Tightness, increase in pain while in cast, or loosening of the cast may cause further complications. (The cast should not move against your skin but also should not feel tight or cause swelling of your fingers or thumb, or cause pressure on your skin). If your new cast does not feel right we will always be happy to check it.

Possible complications
All risks of complications can be reduced if you follow the guidance in this leaflet.

Stiffness is a common complication in the short term and may take months to resolve but rarely affects function long term.

Reduced function is a common complication in the short term but only occasionally remains a long-term problem.

Persistent pain is uncommon in the long term but can occur.

If you have any of these problems contact the plaster room Monday to Friday between 9am and 12.30pm or attend the Emergency Department (A&E) as soon as possible between 9am and 4pm.

Return to the Emergency Department immediately if any of the following happens:

- increased swelling
- pins and needles/numbness
- inability to move fingers
- unusual colouring, eg blue/purple
- increased pain.

A very small group of patients can develop complications after wrist fracture, including a condition called complex regional pain syndrome (CRPS), which requires treatment with early physiotherapy. By following the advice given above, you help us to monitor you to ensure that if you are developing a rare complication we can act promptly to treat it.

Further information
Fracture clinic and plaster room Tel:
Physiotherapy/Occupational Therapy Department Tel:
Emergency Department Tel:
A website you may find useful: www.nhs.uk

Appendix 8 Centres with a special interest in CRPS

England

Addenbrooke's Hospital
Cambridge University Hospitals NHS Foundation Trust
Hills Road
Cambridge CB2 0QQ
Tel: 01223 245 151

Contact: Dr Nick Shenker

Central Manchester NHS Foundation Trust
The Kellgren Centre for Rheumatology
Oxford Road
Manchester M13 9WL
Tel: 0161 276 1234

Contact: Dr Rachel Gorodkin

Derriford Hospital
Derriford Road
Crownhill
Plymouth
Devon PL6 8DH
Tel: 0845 155 8155 / 01752 202082

Contact: Dr Somnath Bagchi

Manchester and Salford Pain Centre
Stott Lane
Salford
Manchester M6 8HD
Tel: 0161 206 4103

Contact: Mrs Alison Dwyer

Royal Devon and Exeter Hospital NHS Foundation Trust
Rheumatology Department
Barrack Road
Exeter EX2 5DW
Tel: 01392 411611

Contact: Dr Richard Haigh

Royal Liverpool and Broadgreen NHS Foundation Trust
Contact (for early CRPS treatment)
Royal Liverpool and Broadgreen Hospitals NHS Trust
Therapies Department/ Aanaesthetics and Pain
Prescot Street
Liverpool L7 8XP
Tel: 0151 706 2760/2614

Contact: Sharon Gillespie,
Fiona Cowell,
HooKee Tsang

The Royal National Hospital for Rheumatic Diseases
Royal United Hospitals NHS Foundation Trust
Upper Borough Walls
Bath BA1 1RL
Telephone: 01225 465941

Contact: Professor Candy McCabe

Royal National Orthopaedic Hospital (Stanmore)
Rheumatology
Brockley Hill
Stanmore HA7 4LP Tel: 020 8954 2300

Contact: Dr Helen Cohen

St Thomas' Hospital
Pain Clinic
Lambeth Palace Road London SE1 7EH
Tel: 020 7188 7188

Contact: Dr Nick Padfield,
Dr David Pang

University College London Hospitals
The National Hospital for Neurology and Neurosurgery @ Cleveland Street
25 Cleveland Street
London W1T 4AJ
Tel: 020 3448 4776

Contact: Dr Paul Nandi or
Mr Diarmuid Dennery

The Walton Centre NHS Foundation Trust
Lower Lane
Fazakerley
Liverpool L9 7LJ
Tel: 0151 525 3611

Contact: Dr Andreas Goebel

Scotland

New Stobhill Hospital
Stobhill ACH Chronic Pain Service
133 Balornock Road
Town Centre
Glasgow G21 3UW
Tel: 0141 355 1490

Contact: Dr Mick Serpell

Please note that this list is not exhaustive. There are likely to be additional UK centres and clinicians with an interest and appropriate expertise in the treatment of CRPS.

Appendix 9 General risks and potential complications from limb amputation

Phantom limb pain is described as pain experienced in the part of the limb that has been amputated as opposed to phantom limb sensation which is a non-painful sensation that the limb is still present. In the general amputee population, it has a high prevalence of over 80% of patients [129] with an average pain score 3–4/10 but range 0–10. High levels of pain pre-amputation are associated with higher pain post-amputation and this would include CRPS. Phantom limb pain can be extremely difficult to treat and can be a severely debilitating condition that in rare cases can be unresponsive to treatment.

- Stump pain is described as pain within the amputation stump itself.
- Allodynia is a condition where pain is felt when a non-painful stimulus is applied (such as touch). Sometimes this can be alleviated with medicated plasters or other technologies.
- Bone pain may be experienced in the cut end of the bone, and this may radiate proximally. This can lead to difficulties with prosthetic fitting and pain management, occasionally necessitating revision surgery. Bone spur formation occasionally occurs with spicules of bone growing from the cut end of the bone that can impinge on soft tissues and may require revision surgery.
- Infection in the bone (osteomyelitis) or in the soft tissue can give rise to pain and requires management with antibiotics and sometimes surgery.
- Sinus formation can occur where there has been a collection in the amputation stump that externalises through an opening in the skin. This can be a result of haematoma or infection and may require surgery.
- Muscle spasm or stump jactitation can be a very painful occurrence where the muscles that are surgically sutured in the stump can develop painful spasms that may require management with antispasmodics or muscle relaxants such as baclofen, diazepam or botox.
- Neuroma formation can occur in an amputation stump wherever a nerve is transected. This is painful and can cause problems with prosthetic fitting and occasionally need radiofrequency nerve ablation treatment, or surgery.
- Fixed flexion deformity can occur where the joints do not have full extension and usually results from inactivity.
- Psychological issues can occur due to an adjustment reaction to being an amputee whereby the patient may struggle with the loss of the limb in terms of the physicality and form of the body, and also the loss of the limb akin to a grieving process. This can be very difficult to manage, requiring mental health assessment and management.

Coming to terms with being an amputee with the resultant loss of perceived identity, changes in independence, mobility, perception of the future, and the necessity for new routines can increase stress levels and lead to mental health disorders such as anxiety and depression. Careful regular review is essential post-amputation and patients should only be seen in centres where psychology is part of the MDT.

Appendix 10 Recommendations for the treatment of skin ulcers, skin infection and problematic oedema

Changes in skin innervation, blood flow, interstitial fluid (oedema), the trophic constitution of the skin, and skin temperature can increase the risk of skin ulceration.[130] Some of these changes are often present in complex regional pain syndrome (CRPS). When ulceration occurs, this allows the entry and multiplication of microorganisms, so that patients are at risk of developing cellulitis and deeper tissue infections.

Assessment

In a patient with CRPS and skin ulceration in the affected limb, non-invasive Doppler studies should be used to exclude peripheral ischaemia.[130] For the lower limb, assessment of the ankle/brachial pressure index (ABPI) is essential to identify any ischaemic element, and should be carried out by someone trained in this technique, usually a nurse in tissue viability. Application of compression without taking into account the ABPI can result in gangrene.

Because all skin ulcers harbour skin microorganisms, swab cultures taken from patients with skin ulceration are usually positive. Positive swab cultures should not be treated unless there are signs of clinical infection.[131,132] Indication of infection includes systemic symptoms (eg fever and leucocytosis) or local signs such as spreading redness, warmth, induration, pain or tenderness. Erythema may be well demarcated or more diffuse. In severe cases, blistering/bullae, superficial haemorrhage into blisters, dermal necrosis, lymphangitis and lymphadenopathy may occur.[131,132]

Deep infection (eg necrotising fasciitis or osteomyelitis) has the risk of threatening a limb, and if suspected should be treated aggressively (see 'Management' below).

There is often a need to exclude underlying osteomyelitis, which may be suggested by bone destruction or periosteal reaction on plain X-rays, or if probing the wound using a blunt, sterile, stainless-steel probe one encounters bone,[133] but magnetic resonance imaging (MRI) is considered the imaging test of choice when osteomyelitis is suspected.[134] If osteomyelitis is suspected, the early intervention of an orthopaedic surgeon is essential.

Management

General measures such as adequate diet, ensuring adequate haemoglobin level, diabetic control and cessation of smoking should be emphasised where appropriate.[135]

The management of skin ulceration in CRPS follows general principles established for the management of diabetic foot ulcers. Removal of necrotic tissue, callus, infected or foreign material should be achieved by sharp debridement.[136] For deep or sloughy ulceration, weekly sharp debridement should be considered.[136] Pressure should be relieved using felted foam dressings and low-pressure garments (eg Alcast Walkers boots®, casts, or open shoes).

If infection is diagnosed on clinical grounds, then the choice of antibiotic should be based on the pathogens isolated from swabs, and if possible, tissue culture. The commonly useful broad-spectrum antibiotics are flucloxacillin in mild cases, with clindamycin, cephalexin, ciprofloxacin and amoxicillin-clavulanic acid (Augmentin) useful in more severe infection.[137] Soft-tissue infections require 10 days' therapy, while osteomyelitis may require more than 6 weeks of therapy.[130] Antimicrobial therapy in patients who do not improve can be guided by both skin biopsy,[138] which is more reliable than superficial swabs, and early advice from a bacteriologist/microbiologist.

In patients who have had at least two episodes of infection at the same site, prophylaxis with low-dose penicillin V or erythromycin (both typically 250mg bd) for a year should be considered.[139,140] Dressings that promote a moist wound environment should be the focus of care of chronic wounds.[140] Typically such dressings may include hydrocolloid dressings, or for wounds producing exudate, silver or iodine impregnated dressings, especially when infection is present.[141] Rarely platelet-derived growth factor[142] (Regranex®, Becaplerin gel®) or allogeneic cultured dermis (Dermograft®, Apligraf®) can be used in the wound dressing. While these have been shown in randomised controlled trials to promote wound healing in clean wounds, they are relatively expensive.

Where oedema is present in a patient with skin ulcerations, after full vascular investigation and since the oedema present in CRPS can foster both poor nutrition with consequent ulceration and superinfections when infection has been treated or excluded, appropriate compression bandaging should be used to disperse tissue fluid. The inclusion of the tissue viability and/or lymphoedema teams is crucial. Compression is usually achieved using wool (to even pressure and absorb exudate) and compression bandaging (eg Profore lite®, Profore®, Elset®) in spiral or figure of eight configuration, or graded compression hosiery, depending on vascular status. Other treatment for lymphoedema includes the use of intermittent pump compression (eg Flowpac® pump). Dermatologists should be aware that treatment with spinal cord stimulation (SCS) by pain specialists or neurosurgeons may reduce limb swelling in some cases.[104]

Appendix 11 Occupational health

About a third of patients with CRPS will report no remaining symptoms by 6 years after the triggering event. Most patients diagnosed with CRPS will experience substantial improvements over time. Nevertheless, individuals with CRPS will often be affected by symptoms that have a substantial (defined as 'not trivial') and long-term (defined as 12 months or longer) impact on their ability to undertake normal daily activities. Thus, a comment along the lines of 'I suggest you proceed as though the Equality Act applies' is reasonable.

The likelihood of the employee having a qualifying disability under the Act obliges the employer to consider the adjustments that have been recommended by occupational health (OH) practitioners, and determine whether or not these are reasonable. But the employer is not obliged to implement adjustments it deems to be unreasonable.

The prognosis for CRPS is uncertain, and it is counterproductive for OH practitioners to suggest otherwise. It is better to highlight the uncertainty, and advise management to identify targets for attendance and performance that are reasonable from their perspective. Employers should be encouraged to proceed with as much empathy and compassion as possible if they deem the adjustments to be unreasonable.

Appendix 12 Patient information

Information leaflet for patients: complex regional pain syndrome

What is complex regional pain syndrome (CRPS)?

CRPS pain usually develops in an arm or leg after an injury. Only rarely are other areas affected. It can affect people of all ages, including children. There are two types of CRPS:

- CRPS type 1 follows an injury to a limb, such as a broken bone or even a minor sprain.
- CRPS type 2 follows partial damage to a nerve in the limb. The symptoms are very similar. This form is very rare.

Previous names: complex regional pain syndrome type 1 (CRPS 1) was known as 'reflex sympathetic dystrophy (RSD)' or 'Sudeck's syndrome', and complex regional pain syndrome type 2 (CRPS 2) was known as 'causalgia'.

What is it like to have CRPS?

CRPS pain continues after the original injury has healed. It is often severe. The main symptom is pain in the arm or leg. The pain is often burning, sharp, stabbing or stinging, with tingling and numbness. There are a range of other symptoms which can change over time. The skin may become oversensitive to light touch. Clothes brushing the skin or even air blowing on the skin may be felt as severe pain. This unusual sensitivity is called 'allodynia' and is common in CRPS.

Other symptoms include skin colour change, swelling, stiffness, feelings of hot or cold, less or more sweating and changes to the hair, skin or nails. The pain and other symptoms often spread beyond the site of the original injury. For example, if you hurt a finger, the whole of the hand or forearm can be affected.

Often there is difficulty in moving the limb, together with weakness and sometimes shaking or jerking. Sometimes the muscles in the area can waste and the hand or foot can become twisted. Many patients say that their limb 'feels strange'. It can feel as if it does not belong to the rest of the body and as if it is not your own limb. Sometimes the limb feels bigger or smaller than the opposite, normal limb.

Although both the pain and abnormal feelings about your limb can cause distress, additional distress may be caused as these feelings may be new to you, and very difficult to explain. Some patients have frequent thoughts about wishing to cut off the limb. Unfortunately, even surgical amputation does not help the pain (actually, it may make it worse). In extreme pain, some people may consider suicide. If you do feel like this, please see your doctor.

What causes CRPS?

CRPS is a stronger-than-normal reaction of the body to injury. We don't know what causes CRPS. What we do know is that the abnormal reaction to injury happens both in the affected limb and in the brain. The nerves in the affected limb are much more sensitive than other nerves and this causes some of the tenderness to touch and pressure. The brain is also involved. The way the brain communicates with the affected limb often changes and this can cause some of the problems with movement.

CRPS is not in your mind. We also know that your mindset cannot cause CRPS, but that some psychological factors such as fear or worry can make the pain worse than it already is.

Does CRPS run in families?

It may be that genes have something to do with who develops CRPS pain after injury, but they are certainly not the only factor in deciding who gets it. It is also very unlikely that anyone else in your family will ever develop CRPS pain.

Could it have been prevented?

It is very unlikely that CRPS pain after your injury could have been prevented. The right diagnosis and treatment can reduce suffering from CRPS pain.

Will it get better?

CRPS gets better by itself or with treatment in the vast majority of patients (up to 80% or more). In some people, CRPS does not get better. We have no way of predicting whether your CRPS will get better and when. Unlike cancer or rheumatoid arthritis, CRPS does not destroy body tissues. Even if you have CRPS for several years, the rest of your body will continue to work as normal.

Does treatment help?

Treatment aims to improve your quality of life, functioning and reduce pain. It is likely that you can get some pain relief with treatment. The success of some treatments depends on the amount of effort you put into them. There is a range of treatments and your consultant or therapist will discuss these with you.

Exercise treatment

Most patients see physiotherapists (PTs) or occupational therapists (OTs). These therapists will work with you in a way which is specially geared towards your CRPS. For example, they may not even touch your limb. It is very important to exercise the limb gently following advice by a PT or OT.

Medication treatment

Drugs can sometimes reduce CRPS pain and may also help you to sleep. Your consultant will discuss the correct drug treatment with you. If appropriate, your consultant may also decide to offer you an injection treatment. In this case, you will receive more special information about that.

Psychological intervention

Sometimes psychological intervention can be helpful to reduce distress (this does not mean that the pain is all in your mind; it is not). Your consultant will be happy to discuss this with you.

Information leaflet for patients: specialised treatments for CRPS

What are specialised treatments for CRPS?

Specialised treatments either require a special team of healthcare professionals to deliver them, or these are new treatments, which need to be followed closely to make sure they work.

Should I be treated with a specialised treatment for CRPS?

The right treatment for CRPS varies from patient to patient. There are two specialised CRPS treatments which need to be given by teams of clinicians with experience in CRPS. These are: pain management programme/rehabilitation (PMP) and neuromodulation (spinal cord stimulation (SCS), and dorsal root ganglion stimulation (DRG)). Research shows that in some patients these treatments can work very well. Your consultant will discuss these treatments with you if he or she thinks you may need either of them. You may also receive a PMP and/or SCS/DRG information leaflet.

The PMP is a programme designed to help you to improve your quality of life and manage your pain better. It is group-based, and lasts between a few days and a few weeks. This is a 'multidisciplinary treatment', which means therapists from different professions work together (eg physiotherapists, doctors, nurses, occupational therapists and psychologists). The PMP is suitable for patients with CRPS, and also for people with other chronic pains. It is designed to improve your quality of life. It is important to understand it is not designed to take your pain away.

The second treatment, neuromodulation, is a fine wire which is placed close to the nerves in your back and connected to a 'stimulator'. The doctor puts the wire in the right place by using a similar technique to putting in an epidural for pain relief during pregnancy. The wire is usually kept in place like this for a short time, and if it works well, an operation is later performed to make it permanent. The neuromodulation device can be taken out in the future when it is not needed anymore.

Are there any other treatments?

There may be other treatments, but these are not as well researched as the treatments mentioned in your patient information leaflets. Your consultant will discuss with you whether or not other treatments would be suitable in your case.

Online sources of information for patients

Arthritis Research UK
www.arthritisresearchuk.org/arthritis-information/conditions/complex-regional-pain-syndrome.aspx

Reflex Sympathetic Dystrophy Association (RSDSA)
https://rsds.org/

CRPS Network UK
www.crpsnetworkuk.org

Information leaflets for employers, friends and family and healthcare professionals

https://sites.google.com/site/profkarenrodham/crps/crps-downloadable-docs

UK charities specific to CRPS

This list is not exhaustive – there may be additional charities, and the inclusion of these two charities must not be taken as an endorsement of any content posted on their websites:

CRPS UK
https://crps-uk.org/

Burning nights
http://www.burningnightscrps.org/

Explaining your condition to your doctor

The following information has been compiled and produced by the CRPS Patients Forum at the Royal National Hospital for Rheumatic Diseases (RNHRD) after adaptation from a version produced by the Reflex Sympathetic Dystrophy Syndrome Association in America.

The following information may be useful if you need to explain your condition to your doctor:

I have CRPS (complex regional pain syndrome)

CRPS is a nerve disorder that usually occurs after an injury or period of immobilisation. The principal symptom is pain, which can lead to disability.

I may look healthy but I often suffer from severe, unrelenting, nerve pain. My skin may swell, change colour or temperature, sweat or hurt to the lightest touch.

Often it is difficult for me to sleep, which affects my attention and concentration, or I may be on drugs, which do the same.

Chronic pain often leads to depression. Stress increases pain. I have good or bad days, or even hours. There is no cure at present.

Please help me by...

- believing that the pain is real even though it is invisible and may not be readily apparent by my demeanour or activities
- remembering that it can even hurt to be touched
- remaining positive.

Appendix 13 Key contents of an interdisciplinary specialist rehabilitation programme

Engagement: Education and information for the patient and his/her family

- Active engagement of the patient/family in goal setting, goal review
- Control – the patient remains responsible for their own rate of progress
- Understanding and insight:
  - how emotional stress, muscle tension and de-conditioning can increase pain experience
  - how their own behaviours may serve to exacerbate pain experience
- Learning:
  - self-management approach, including goal setting and pacing
  - the right balance between doing too much and too little
  - relaxation techniques, breathing exercises etc to reverse sympathetic arousal
- Empowering the family:
  - encouraging the individual to keep active and to do more for themselves

Medical management

- Investigation and confirmation of diagnosis
- Pharmacological intervention (in conjunction with pain team wherever appropriate) to provide a window of pain relief
- Reassurance that physical and occupational therapy are safe and appropriate
- Provide medical follow-up to prevent iatrogenic damage through inappropriate referral
- Support any litigation/compensation claim to its resolution and conclusion

Psychosocial and behavioural management

- Identify any psychological factors contributing to pain and disability
- Treat anxiety and depression
- Identify, explore and proactively address any internal factors (eg counter-productive behaviour patterns) or external influences (eg perverse incentives, family dynamics etc) which may perpetuate disability/dependency
- Consider needs of family/carers – provide psychological intervention/counselling where appropriate
- Provide a practical problem-solving, goal-orientated approach (involving both the patient and their family) to reduce barriers and promote healthy functioning

Physical management

- Retrain normal body posture
- Desensitisation – handling the affected part followed by passive stretching/isometric exercise
- Progression to active isotonic exercise and then strength training
- General body re-conditioning – cardiovascular fitness
- Encourage recreational physical exercise and functional goals
- Techniques to address altered perception and awareness of the limb, eg mirror visual feedback training or graded motor imagery

Activities of daily living and societal participation

- Support graded return to independence in activities of daily living with clear functional goals
- Assessment and provision of appropriate specialist equipment/adaptations to support independence[143]
- Removal of inappropriate/unnecessary equipment
- Adaptation of environment
- Extend social and recreational activities in and outside the home
- Workplace assessment/vocational re-training

Adapted from the BSRM report on musculoskeletal rehabilitation[106]

Appendix 14 The National Service Framework for Long-term Conditions

The National Service Framework (NSF) for Long-term Conditions (2005) provides a useful framework on which to underpin the longer-term management of patients and their families with long-term CRPS.[144] Although originally developed around six exemplar neurological conditions, the NSF standards (or 'quality requirements') were designed to be applicable across the broader spectrum of long-term conditions.

The NSF emphasises the need for lifelong care and integrated service provision. It therefore covers care at all stages along the pathway from diagnosis throughout an individual's life span, and encompasses both health and social care needs across primary secondary and tertiary services. It also emphasises the need to provide flexible support that maximises personal choice and empowers patients to manage their own condition.

Patients with CRPS form a diverse group and their needs will vary over time. The fish diagram (Fig A6) illustrates the 11 quality requirements (QRs) of the NSF, and the type of services that may need to be coordinated during integrated care planning for long-term care in CRPS patients.

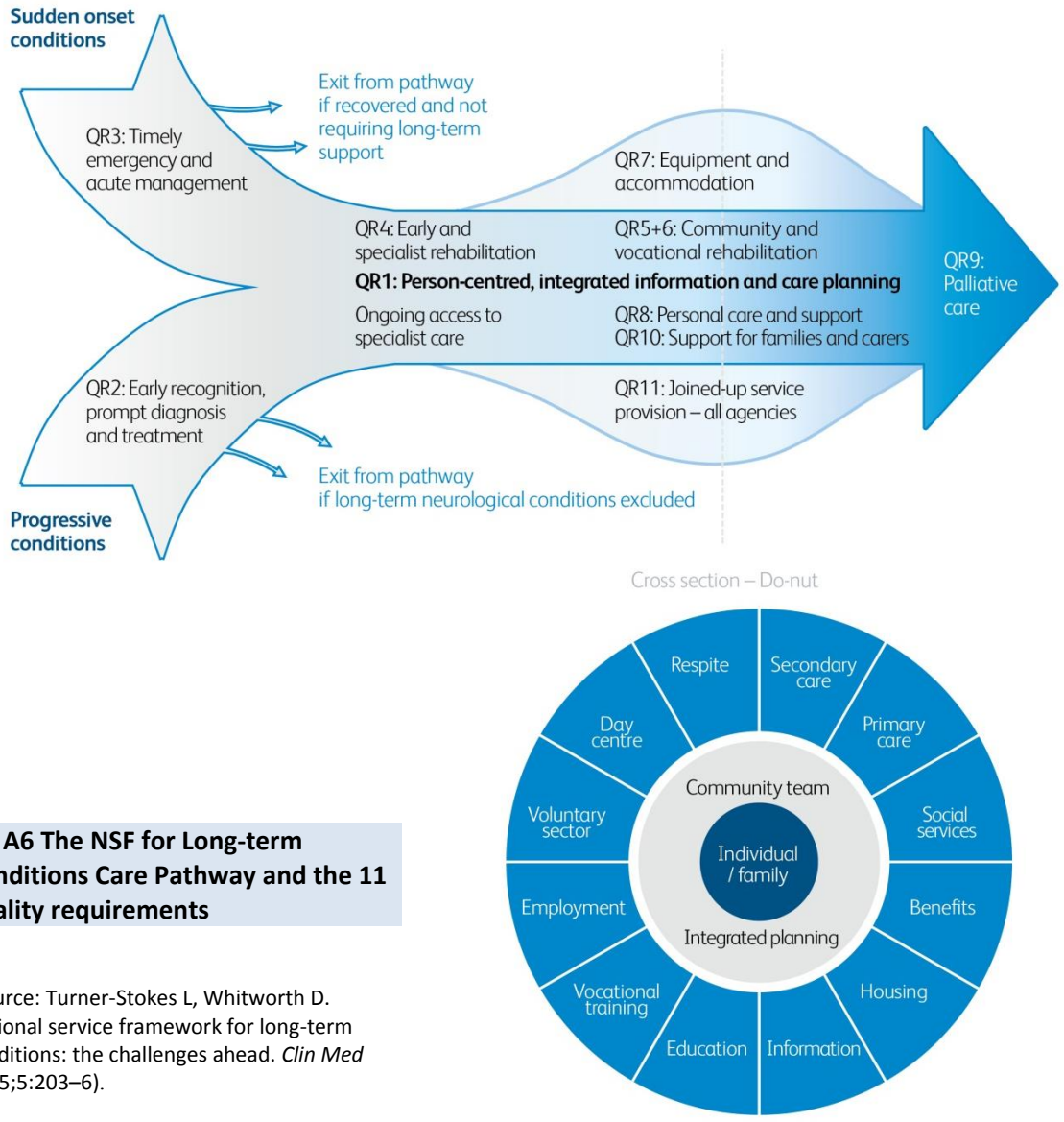


Fig A6 The NSF for Long-term Conditions Care Pathway and the 11 quality requirements

(Source: Turner-Stokes L, Whitworth D. National service framework for long-term conditions: the challenges ahead. *Clin Med* 2005;5:203–6).

Appendix 15 Experimental treatments for CRPS – published research

Treatments for CRPS based on publications from June 2000 to November 2016 of trials which were not RCTs. These treatments cannot currently be recommended because although there may be some evidence, there is not sufficient evidence available to support their efficacy.

Anaesthetic blockade with specific agents

Chen LC, Wong CS, Huh BK *et al.* Repeated lumbar sympathetic blockade with lidocaine and clonidine attenuates pain in complex regional pain syndrome type 1 patients – a report of two cases. *Acta Anaesthesiol Taiwan* 2006;44(2):113–7.

Hord ED, Stojanovic MP, Vallejo R *et al*. Multiple Bier blocks with labetalol for complex regional pain syndrome refractory to other treatments. *J Pain Symptom Manage* 2003;25(4):299–302.

Kastler A, Aubry S, Sailley N, Michalakis D, Siliman G, Gory G, Lajoie JL, Kastler B. CT-guided stellate ganglion blockade vs. radiofrequency neurolysis in the management of refractory type I complex regional pain syndrome of the upper limb. *Eur Radiol* 2013;23(5):1316–22.

Analgesic cream

Russo MA, Santarelli DM. A novel compound analgersic cream (Ketamine, Pentoxifylline, Clonidine, DMSO) for complex regional pain syndrome patients. *Pain Pract* 2016;16(1):E14–20.

Brachial plexus analgesia

Azad SC, Beyer A, Romer AW *et al.* Continuous axillary brachial plexus analgesia with low dose morphine in patients with complex regional pain syndromes. *Eur J Anaesthesiol* 2000;17(3):185–8.

Day M, Pasupuleti R, and Jacobs S. Infraclavicular brachial plexus block and infusion for treatment of long-standing complex regional syndrome type 1: A case report. *Pain Physician* 2004;7(2):265–8.

Combined spinal cord stimulation and intrathecal therapy

Goto S, Taira T, Horisawa S, Yokote A, Sasaki T, Okada Y. Spinal cord stimulation and intrathecal baclofen therapy: combined neuromodulation for treatment of advanced complex regional pain syndrome. *Stereotact Funct Neurosurg* 2013;91(6):386–91.

Dry needling

Vas LC, Pai R, Pattnaik M. Musculoskeletal ultrasonography in CRPS: assessment of muscles before and after motor function recovery with dry needling as the sole treatment. *Pain Physician* 2016;19(1):E163–79.

Electroconvulsive therapy (ECT)

Fukui S, Shigemori S, Nosaka S. Beneficial effects of electroconvulsive therapy on clinical features and thalamic blood flows in a CRPS type 1 patient. *Br J Anaesth* 2002;16(3):248–50.

McDaniel WW. Electroconvulsive therapy in complex regional pain syndromes. *J FCT* 2003;19(4):226–9.

Wolanin MW, Gulevski V, and Schwartzman RJ. Treatment of CRPS with ECT. *Pain Physician* 2007;10(4):573–8.

Hyperbaric oxygen therapy

Kiralp MZ, Yildiz S, Vural D *et al*. Effectiveness of hyperbaric oxygen therapy in the treatment of complex regional pain syndrome. *J Int Med Res* 2004;32:258–262.

Peach G. Hyperbaric oxygen and the reflex sympathetic dystrophy syndrome: a case report. *Undersea & hyperbaric medicine* 1995;22(4):407–8.

Ketamine – anaesthetic, high-dose treatment ('ketamine coma')

Kiefer RT, Rohr P, Ploppa A, Altemeyer KH, Schwartzman RJ. Complete recovery from intractable complex regional pain syndrome, CRPS-type I, following anesthetic ketamine and midazolam. *Pain Pract* 2007;7(2):147–50.

Kiefer RT, Rohr P, Ploppa A *et al.* Efficacy of ketamine in anesthetic dosage for the treatment of refractory complex regional pain syndrome: an open-label phase II study. *Pain Med* 2008;9(8):1173–201.

Koffler SP, Hampstead BM, Irani F *et al.* The neurocognitive effects of 5 day anesthetic ketamine for the treatment of refractory complex regional pain syndrome. *Arch Clin Neuropsychol* 2007;22(6):719–29.

Ketamine infusion combined with nerve block

Everett A, Mclean B, Plunkett A, Buckenmaier C. A unique presentation of complex regional pain syndrome type I treated with a continuous sciatic peripheral nerve block and parenteral ketamine infusion: A case report. *Pain Med* 2009;10(6):1136–9.

Ketamine – oral

Villanueva-Perez VL, Cerda-Olmedo G, Samper JM *et al.* Oral ketamine for the treatment of type I complex regional pain syndrome. *Pain Pract* 2007;7(1):39–43.

Local anaesthetic infusion with physiotherapy

Mak PH, Irwin MG, Tsui SL. Functional improvement after physiotherapy with a continuous infusion of local anaesthetics in patients with complex regional pain syndrome. *Acta Anaesthesiol Scand* 2003;47(1):94–7.

Lycra pressure garments (eg 'second skin' devices)

Ramsey L. Report of a focus group survey of current practice in the therapeutic treatment of Complex Regional Pain Syndrome in the United Kingdom. *Hand Therapy* 2008;13:45–53.

Memantine

Sinis N, Birbaumer N, Schwarz A et al. Memantine and Complex Regional Pain Syndrome (CRPS): effects of treatment and cortical reorganisation. *Handchir Mikrochir Plast Chir* 2006;38(3):164–71.

Sinis S, Birbaumer N, Gustin S et al. Memantine treatment of complex regional pain syndrome: a preliminary report of six cases. *Clin J Pain* 2007;23(3):237–43.

Vanden Daele E, Hans G, Vercauteren M. Memantine for the treatment of complex regional pain syndrome type I. *Acta Anaesthesiologica Belgica* 2007;58(2):157.

Goebel A. 2012 Morphine and memantine treatment of long-standing complex regional pain syndrome. *Pain Med* 2012;13(3):357–8.

Motor cortex stimulation

Son UC, Kim MC, Moon DE, Kang JK. Motor cortex stimulation in a patient with intractable complex regional pain syndrome type II with hemibody involvement. Case report. *J Neurosurg* 2003;98(1):175–9.

Velasco F, Carrillo-Ruiz JD, Castro G *et al*. Motor cortex electrical stimulation applied to patients with complex regional pain syndrome. *Pain* 2009;147(1–3):91–8.

Nerve decompression

Placzek JD, Boyer MI, Gelberman RH, Sopp B, Goldfarb CA. Nerve decompression for complex regional pain syndrome type II following upper extremity surgery. *J Hand Surg Am* 2005;30(1):69–74.

Neurofeedback

Jensen MP, Grierson C, Tracy-Smith V, Bacigalupi SC, Othmer SF. Neurofeedback treatment for pain associated with complex regional pain syndrome type I. *J Neurother* 2007;11(1):45–53.

Oral phenoxybenzamine

Inchiosa MA Jr, Kizelshteyn G. Treatment of complex regional pain syndrome type I with oral phenoxybenzamine: rationale and case reports. *Pain Pract* 2008;8(2):125–32.

Peripheral nerve stimulation

Mirone G, Natale M, Rotondo M. Peripheral median nerve stimulation for the treatment of iatrogenic complex regional pain syndrome (CRPS) type II after carpal tunnel surgery. *J Clin Neuroscience* 2009;16(6):825–7.

Johnson S, Ayling H, Sharma M, Goebel A. External noninvasive peripheral nerve stimulation treatment of neuropathic pain: A prospective audit. *Neuromodulation* 2015;18(5):384–91.

Plasma exchange

Aradillas E, Schwartzman RJ, Grothusen JR, Goebel A, Alexander GM. Plasma exchange therapy in patients with complex regional pain syndrome. *Pain Physician* 2015;18(4):383–94.

Goebel A, Jones S, Oomman S, Callaghan T, Sprotte G. Treatment of long-standing complex regional pain syndrome with therapeutic plasma exchange: a preliminary case series of patients treated in 2008-2014. *Pain Med* 2014;15(12):2163–4.

Blaes F, Dharmalingam B, Tschernatsch M *et al.* Improvement of complex regional pain syndrome after plasmapheresis *Eur J Pain* 2015;19:503–7.

Surgical sympathectomy

Bandyk DF, Johnson BL, Kirkpatrick AF et al. Surgical sympathectomy for reflex sympathetic dystrophy syndromes. *J Vasc Surg* 2002;35(2):269–77.

Bosco Vieira DJ, Kux P, Duarte DF. Endoscopic thoracic sympathicotomy for the treatment of complex regional pain syndrome. *Clin Auton Res* 2003;13(Suppl 1):I58–I62.

Golubev VG, Krupatkin AI, Zeinalov VT, Merkulov MV, Kuz'michev VA. New facilities in management of complex regional pain upper limb syndrome with thoracoscopic sympathectomy. *Vestn Ross Akad Med Nauk* 2008;(8):52–5.

Kargar S, Parizi FS. Thoracoscopic symp athectomy in causalgia. *Ann Chir Gynaecol* 2001;90(3):193–4.

Tactile discrimination

Moseley GL, Zalucki NM, Wiech K. Tactile discrimination, but not tactile stimulation alone, reduces chronic limb pain. *Pain* 2008;137(3):600–8.

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.

Topical capsaicin

Ribbers GM, Stam HJ. Complex regional pain syndrome type I treated with topical capsaicin: a case report. *Arch Phys Med Rehabil* 2001;82(6):851–2.

Topical lidocaine – patches

Vorobeychik Y, Giampetro D M. Topical lidocaine and epidural bupivacaine/hydromorphone in the treatment of complex regional pain syndrome type II. *Pain Physician* 2007;10:511–7 (Letter).

Kamarkar A, Lieberman I. Management of complex regional pain syndrome type II using Lidoderm 5% patches. *Br J Anaesth* 2007;98(2):261–2.

Ziconotide

Kapural L, Lokey K, Leong MS *et al.* Intrathecal ziconotide for complex regional pain syndrome: seven case reports. *Pain Pract* 2009;9(4):296–303.

Appendix 16 Systematic review update – RCTs published from April 2010 – December 2011

Further to the previous review period, we reviewed randomised controlled trials (RCTs) published on the treatment of CRPS from April 2010 to December 2011.

Medline (PubMed), SCOPUS, CINAHL, and AMED bibliographic databases and the Cochrane Central Register of Controlled Trials were searched electronically using combinations of the following search terms: complex regional pain syndromes; with therapy; drug therapy; rehabilitation; randomised controlled trial; clinical trial. All foreign language papers were included.

One reviewer filtered the resulting 16 studies. Four studies were found to be appropriately randomised and thus further assessed by another reviewer (see Appendix 2 for full description of methodology).

The filtered studies were not scored for their methodological quality as in the main review but were assessed as follows:

van der Plas 2011[145]

Randomisation	suitable, appropriate
Outcome measure	NRS pain, NRS dystonia
Early or late	late (Median 12.5 years)
Diagnosis	IASP criteria
Intervention	intrathecal baclofen for dystonia
Design	active v active in two concentrations/infusion rates double-blind cross-over
Outcome	increased infusion rate of more dilute solution does not improve control of dystonia
Population	14 patients already receiving ITB for dystonia with unsatisfactory response

Eckmann 2011[146]

Randomisation	suitable, appropriate
Outcome measure	NRS pain, short-term pain NRS, limb volume difference, joint pain score, ROM
Early or late	1 to 29 months
Diagnosis	IASP, lower limb
Intervention	intravenous regional block with lignocaine (50 mls 0.5%) and ketorolac (0, 30, 60, 120 mg)
Design	active v active – lignocaine plus various ketorolac dose double-blind cross-over
Outcome	negative (only 1 day of pain relief after ketorolac)
Population	10 patients with lower limb CRPS

Gustin 2010[147]

Randomisation	randomised, method not explained
Outcome measure	VAS rest pain, VAS movement pain, disability score, functional MRI
Early or late	6 to 36 months
Diagnosis	IASP, mixed type I and II
Intervention	morphine alone v morphine with memantine*

* These results were not replicated in a later study. Goebel A. Morphine and memantine treatment of long-standing complex regional pain syndrome. *Pain Med* 2012;13(3):357–8.

Design	active v active double-blind
Outcome	positive; combination was more effective than morphine alone, from 1 to at least 8 weeks into the intervention
Population	20 patients with CRPS

Picarelli 2010[148]

Randomisation	randomised, method not explained
Outcome measure	VAS pain, McGill questionnaire, depression and anxiety, disability
Early or late	10–180 months
Diagnosis	IASP CRPS type I upper limb
Intervention	repetitive transcranial magnetic stimulation v. sham (1x per day for 10 days)
Design	active v placebo/sham (best medical treatment was continued in both groups) double-blind
Outcome	repetitive transcranial magnetic stimulation relieves pain better than sham (greatest pain relief at day 10, not persisting after 1 week or 3 months)
Population	23 'refractory' patients completed the protocol
Comment	figure 2 incorrectly labelled? Shows sham better than active

Glossary of terms

Allodynia	Meaning ‘other pain’. This is a pain due to a stimulus that does not normally provoke pain, and which can be either thermal or mechanical.
Ankylosis	A stiffness of a joint due to abnormal adhesion and rigidity of the bones of the joint, which may be the result of injury or disease. The rigidity may be complete or partial and may be due to inflammation of the tendons or muscular structures outside the joint, or of the tissues of the joint itself.
Anticonvulsants	A diverse group of pharmaceuticals used in the treatment of epileptic seizures. Anticonvulsants are also increasingly being used in the treatment of bipolar disorder, since many seem to act as mood stabilisers. Anticonvulsants are more accurately called antiepileptic drugs (AEDs).
Antidepressants	Medication used to alleviate mood disorders, such as major depression and dysthymia, and anxiety disorders such as social anxiety disorder. Drugs including the monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), tetracyclic antidepressants (TeCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) are most commonly associated with the term.
Beau’s lines	Deep transverse grooves of nails. They can be on any or all nails. They may look like indentations or ridges in the nail plate.
Bullae	Large vesicles.
CBT	Cognitive behavioural therapy. This is not a single therapy or even a single set of standardised interventions. Rather CBT is a broad category of different treatment regimens. Almost always, however, CBT regimens include cognitive therapy (the ‘C’ of CBT) as a core component. Usually CBT also includes interventions designed to alter behaviours (the ‘B’ of CBT), and some combination of operant treatment, coping skills training, relaxation strategies, pacing/activity-rest cycling, exercise and activity management, and/or pleasant activity scheduling.
Compartment syndrome	The compression of nerves, blood vessels, and muscle inside a closed space (compartment) within the body. This leads to tissue death from lack of oxygenation due to the blood vessels being compressed by the raised pressure within the compartment. Compartment syndrome most often involves the forearm and lower leg.
Contracture	In a muscle or muscle fibre, usually refers to a continuous contraction in the absence of a stimulus, such as an action potential. A muscle contracture is a shortening of a muscle or joint.
Debridement	The medical removal of a patient’s dead, damaged, or infected tissue to improve the healing potential of the remaining healthy tissue. Removal may be surgical, mechanical, chemical, autolytic (self-digestion), or by larval (maggot) therapy, whereby certain species of live larvae selectively eat only necrotic tissue.
Dystonia	A neurological movement disorder, in which sustained muscle contractions cause twisting and repetitive movements or abnormal postures.

Epithelioid haemangioma	Angiolymphoid hyperplasia with eosinophilia (also known as epithelioid hemangioma), usually presents with pink to red-brown, dome-shaped, dermal papules or nodules of the head or neck, especially about the ears and on the scalp.
Erythromelalgia	Also known as Mitchell's disease (after Silas Weir Mitchell), acromelalgia, redneuralgia, or erythermalgia, is a rare neurovascular peripheral pain disorder. There is severe burning pain (in the small fibre sensory nerves) and skin redness. The attacks are periodic and are commonly triggered by heat, pressure, mild activity, exertion, insomnia or stress.
Erythema	Redness of the skin, caused by hyperemia of the capillaries in the lower layers of the skin. It occurs with any skin injury, infection, or inflammation.
Fascia	A layer of fibrous tissue that permeates the human body. A fascia is a connective tissue that surrounds muscles, groups of muscles, blood vessels, and nerves, binding those structures together. It consists of several layers: a superficial fascia, a deep fascia, and a subserous (or visceral) fascia and extends uninterrupted from the head to the tip of the toes.
Hyperaesthesia	A condition that involves an abnormal increase in sensitivity to stimuli of the senses. Stimuli of the senses can include sound that one hears, foods that one tastes, textures that one feels, and so forth.
Hyperalgesia	A condition where normally painful stimuli (eg a pinprick) are more painful than usual.
Hyperhidrosis	Condition characterised by abnormally increased perspiration, in excess of that required for regulation of body temperature.
Hypoxia	A pathological condition in which the body as a whole, or a region of the body is deprived of adequate oxygen supply.
Hypertrichosis	Hair growth on the body in an amount considered abnormal. There are two distinct types of hypertrichosis: generalised hypertrichosis, which occurs over the entire body, and localised hypertrichosis, which is restricted to a certain area.
Hypotrichosis	Condition of abnormal hair patterns – predominantly loss or reduction. It occurs, most frequently, by the growth of vellus hair in areas of the body that normally produce terminal hair.
Intrathecal	Something introduced into or occurring in the space under the arachnoid membrane of the brain or spinal cord.
Litigation	A lawsuit or a civil action brought in a court of law in which a plaintiff, a party who claims to have incurred damages as a result of a defendant's actions, demands a legal or equitable remedy.
Leukonychia	Increased whiteness and opacity of the nails.
Motor dyspraxia	Motor skills disorder (also known as motor coordination disorder or motor dyspraxia) is a human developmental disorder that impairs motor coordination in daily activities. It is neurological in origin.
Myoclonus	Brief, involuntary twitching of a muscle or a group of muscles. It is a medical

	sign. The myoclonic twitches are usually caused by sudden muscle contractions; they also can result from brief lapses of contraction.
Neuromodulation	In neuromodulation, several classes of neurotransmitters regulate diverse populations of central nervous system neurons (one neuron uses different neurotransmitters to connect to several neurons). This is in contrast to direct synaptic transmission, in which one presynaptic neuron directly influences a postsynaptic partner (one neuron reaching one other neuron), neuromodulatory transmitters secreted by a small group of neurons diffuse through large areas of the nervous system. Neuromodulation also refers to the effect of neurostimulation such as spinal cord stimulation.
Neuropathic pain	'Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system'. Neuropathic pain may have continuous and/or episodic (paroxysmal) components. Common qualities include burning or coldness, 'pins and needles' sensations, numbness and itching.
Osteoporosis	A disease of bones that leads to an increased risk of fracture. In osteoporosis, the bone mineral density (BMD) is reduced, bone microarchitecture is deteriorating, and the amount and variety of proteins in bone is altered.
Onychodystrophy	Nail disease. A deformation of the nails.
Pathophysiology	The study of the changes of normal mechanical, physical, and biochemical functions, either caused by a disease, or resulting from an abnormal syndrome.
Placebo	A placebo is a sham or simulated medical intervention that can produce a (perceived or actual) improvement, called a placebo effect.
Prophylaxis	Any medical or public health procedure whose purpose is to prevent, rather than treat or cure a disease.
Qigong (Tai Chi)	A set of exercises, originally a Chinese martial art. Qi and gong – the two words are combined to describe systems and methods of 'energy cultivation' and the manipulation of intrinsic energy within living organisms.
Randomisation	Randomisation is the process of making something random.
Somatisation	A tendency to experience and communicate somatic distress in response to psychosocial stress and to seek medical help for it.
Spinal cord stimulation	A device is used to send pulsed electrical signals to the spinal cord to control chronic pain. It consists of stimulating electrodes implanted in the epidural space (space within the spinal canal lying outside the dura mater), an electrical pulse generator implanted in the lower abdominal area or gluteal region, conducting wires connecting the electrodes to the generator internally, and the generator remote control. Spinal cord stimulation (SCS) has notable analgesic properties.
Sudomotor	A medical term used to describe something that stimulates the sweat glands.
Systematic review	A literature review focused on a research question that tries to identify, appraise, select and synthesise all high-quality research evidence relevant to that question. Systematic reviews of high-quality randomised controlled trials are crucial to evidence-based medicine.

Thoracic outlet syndrome	A syndrome involving compression at the superior thoracic outlet, of a neurovascular bundle passing between the anterior scalene and middle scalene muscles. It can affect the brachial plexus (nerves that pass into the arms from the neck), and/or the subclavian artery or vein (blood vessels that pass between the chest and upper extremity).
Vasculitis	A heterogeneous group of disorders that are characterised by inflammatory destruction of blood vessels. Both arteries and veins are affected. Lymphangitis is sometimes considered a type of vasculitis. Vasculitis is primarily due to leukocyte migration and resultant damage.
Vasoconstriction	Narrowing of the blood vessels resulting from contraction of the muscular wall of the vessels, particularly the large arteries, small arterioles and veins. The process is the opposite of vasodilation, the widening of blood vessels.
Vasodilation	Widening of blood vessels resulting from relaxation of smooth muscle cells within the vessel walls, particularly in the large arteries, smaller arterioles and large veins. The process is essentially the opposite of vasoconstriction, or the narrowing of blood vessels. When vessels dilate, the flow of blood is increased due to a decrease in vascular resistance. Therefore, dilation of arterial blood vessels (mainly arterioles) leads to a decrease in blood pressure.
Weber-Christian syndrome	Also known as relapsing febrile non-suppurative panniculitis. A cutaneous condition characterised by recurrent subcutaneous nodules that heal with depression of the overlying skin. It is a type of panniculitis.

References

1 Turner-Stokes L, Goebel A. Complex regional pain syndrome: concise guidance. *Clin Med* 2011;11(6):596–600.

2 Turner-Stokes L, Harding R, Sergeant J, Lupton C, McPherson K. Generating the evidence base for the National Service Framework for long-term conditions: a new research typology. *Clin Med* 2006;6(1):91–7.

3 Cossins L, Okell R, Simpson B *et al.* Treatment of complex regional pain syndrome: a systematic review of randomized controlled trials published from June 2000 to February 2012. *Eur J Pain* 2013; 17(2):158–73.

4 Forouzanfar T, Koke AJ, van Kleef KM, Weber WE. Treatment of complex regional pain syndrome type I. *Eur J Pain* 2002;6(2):105–22.

5 Veldman PH, Reynen HM, Arntz IE, Goris RJ. Signs and symptoms of reflex sympathetic dystrophy: prospective study of 829 patients. *Lancet* 1993;342(8878):1012–16.

6 van Rijn MA, Marinus J, Putter H *et al.* Spreading of complex regional pain syndrome: not a random process. *J Neural Transm* 2011;118(9):1301–9.

7 Maleki), LeBel AA, Bennett GJ, Schwartzman RJ. Patterns of spread in complex regional pain syndrome, type I (reflex sympathetic dystrophy). *Pain* 2000;88(3):259–66.

8 de Mos M, de Bruijn AG, Huygen FJ *et al.* The incidence of complex regional pain syndrome: a population-based study. *Pain* 2007;129(1–2):12–20.

9 Marinus J, Moseley GL, Birklein F *et al*. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol* 2011;10(7):637–48.

10 Beerthuizen A, van 't Spijker A, Huygen FJ, Klein J, de Witt WR. Is there an association between psychological factors and the Complex Regional Pain Syndrome type 1 (CRPS1) in adults? A systematic review. *Pain* 2009; 145(1–2):52–9.

11 de Mos M, Huygen FJ, Dieleman JP *et al.* Medical history and the onset of complex regional pain syndrome (CRPS). *Pain* 2008.

12 Beerthuizen A, Stronks DL, Huygen FJ *et al.* The association between psychological factors and thedevelopment of complex regional pain syndrome type 1 (CRPS1) – a prospective multicenter study. *Eur J Pain* 2011;15(9):971–5.

13 Rodham K, Boxell E, McCabe C, Cockburn M, Waller E. Transitioning from a hospital rehabilitation programme to home: exploring the experiences of people with complex regional pain syndrome. *Psychol Health* 2012;27(10):1150–65.

14 Mailis-Gagnon A, Nicholson K, Blumberger D, Zurowski M. Characteristics and period prevalence of self-induced disorder in patients referred to a pain clinic with the diagnosis of complex regional pain syndrome. *Clin J Pain* 2008;24(2):176–85.

15 Birklein F. Complex regional pain syndrome. *J Neurol* 2005;252(2):131–38.

16 Bean DJ, Johnson MH, Kydd RR. The outcome of complex regional pain syndrome type 1: a systematic review. *J Pain* 2014;15(7):677–90.

17 Harden RN, Bruehl S, Stanton-Hicks M, Wilson PR. Proposed new diagnostic criteria for complex regional pain syndrome. *Pain Med* 2007;8(4):326–31.

18 McBride A, Atkins B. Complex regional pain syndrome. *Current Orthopaedics* 2005;19:155–65.

19 de Mos M, Huygen FJ, Hoeven-Borgman M *et al.* Outcome of the Complex Regional Pain Syndrome. *Clin J Pain* 2009;25(7):590–7.

20 Field J, Warwick D, Bannister GC. Features of algodystrophy ten years after Colles' fracture. *J Hand Surg Br* 1992;17(3):318–20.

21 Schasfoort FC, Bussman)G, Stam H). Impairments and activity limitations in subjects with chronic upper limb complex regional pain syndrome type I. *Arch Phys Med Rehabil* 2004;85(4):557–66.

22 Harden RN, Swan M, King A, Costa B, Barthel J. Treatment of complex regional pain syndrome: functional restoration. *Clin J Pain* 2006;22(5):420–4.

23 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):111–19.

24 Oaklander AL, Fields HL. Is reflex sympathetic dystrophy/complex regional pain syndrome type I a small-fiber neuropathy? *Ann Neurol* 2009;65(6):629–38.

25 Breivik H, Borchgrevink PC, Allen SM *et al.* Assessment of pain. *Br J Anaesth* 2008;101(1):17–24.

26 NICE. *Neuropathic pain in adults: pharmacological management in non-specialist settings.* London: NICE, 2013.

27 Harden RN, Bruehl S, Perez RSGM *et al.* Validation of proposed diagnostic criteria (the 'Budapest Criteria') for complex regional pain syndrome. *Pain* 2010;150(2):268–74.

28 Geertzen JH, van Wilgen CP, Schrier E, Dijkstra PV. Chronic pain in rehabilitation medicine. *Disabil Rehabil* 2006;28(6):363–7.

29 Kendall NAS, Linton SJ, Main CJ. Guide to assessing psychosocial yellow flags in acute low back pain: Risk factors for long-term disability and work loss. Wellington, NZ: NACHO, 1997.

30 Main CJ, Williams ACC. Clinical review. ABC of psychological medicine: musculoskeletal pain. *Br Med J* 2002; 325(7363):534–7.

31 Oerlemans HM, Oostendorp RA, de BT, Goris RJ. 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.

32 Superio-Cabuslay E, Ward MM, Lorig KR. Patient education interventions in osteoarthritis and rheumatoid arthritis: A meta-analytic comparison with nonsteroidal antiinflammatory drug treatment. *Arthritis Rheum* 1996;9(4):292–301.

33 Lewis JS, Coales K, Hall J, McCabe CS. Now you see it, now you don't. Sensory re-education in Complex Regional Pain Syndrome. *Hand Ther* 2011;16(2):29–38.

34 Topcuoglu A, Gokkaya NK, 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. *Top Stroke Rehabil* 2015;22(4):253–61.

35 Sntbeyaz S, Yavuzer G, Sezer N, Koseoglu BF. Mirror Therapy Enhance s Lower-Extremity Motor Recovery and Motor Functioning After Stroke: A Randomized Controlled Trial. *Arch Phys Med* Rehabil 2007;88(5):555–9.

36 Ramachandran VS. Phantoms in the brain. London: Fourth Estate, 1999.

37 McCabe CS, Haigh RC, Ring EF *et al.* A controlled pilot study of the utility of mirror visual feedback in the treatment of complex regional pain syndrome (type 1). *Rheumatology* (Oxford) 2003;42(1):97–101.

38 Vural SP, Yuzer GFN, Ozcan DS *et al.* Effects of mirror therapy in stroke patients with complex regional pain syndrome type l: a randomized controlled study. *Archives of Physical Medicine and Rehabilitation* 2016;97:575–81.

39 Lennon S. Gait re-education based on the Bobath Concept in two patients with hemiplegia following stroke. *Phys Ther* 2001;81(3):924–35.

40 Brosseau L, Milne S, Robinson V *et al.* Efficacy of the transcutaneous electrical nerve stimulation for the treatment of chronic low back pain: A meta-analysis. *Spine* 2002;27(6):596–603.

41 Gill JR, Brown CA. A structured review of the evidence for pacing as a chronic pain intervention. *Eur J Pain* 2009;13(2):214–16.

42 Holliday RC, Ballinger C, Playford ED. Goal setting in neurological rehabilitation: Patients' perspectives. *Disabil Rehabil* 2007;29(5):389–94.

43 Holliday RC, Cano S, Freedman JA, Playford ED. Should patients participate in clinical decision making? An optimised balance block design controlled study in a rehabilitation unit. *J Neurol Neurosurg Psychiatry* 2007; 78(6):576–80.

44 O'Brien EM, Staud RM, Hassinger DA *et al.* Patient-centered perspective on treatment outcomes in chronic pain. *Pain Med* 2010;11(1):6–15.

45 Persson AL, Veenhuizen H, Zachrison L, Gard G. Relaxation as a treatment for chronic musculoskeletal pain – A systematic review of randomised controlled studies. *Phys Ther Rev* 2008;13(5):355–65.

46 Fernandez E, Turk DC. The utility of cognitive coping strategies for altering pain perception: a meta-analysis. *Pain* 1989;38(2):123–35.

47 Perraton L, Machotka Z, Kumar S. Components of effective randomized controlled trials of hydrotherapy programs for fibromyalgia syndrome: A systematic review. *J Pain Res* 2009;2:165–73.

48 Currie SR, Wilson KG, Pontefract AJ, deLaplante L. Cognitive-behavioral treatment of insomnia secondary to chronic pain. *J Consult Clin Psychol* 2000;68(3):407–16.

49 Vasudevan SV, Melvin JL. Upper extremity edema control: rationale of the techniques. *Am J Occup Ther* 1979;8:520–3.

50 Watson PJ, Booker CK, Moores L, Main CJ. Returning the chronically unemployed with low back pain to employment. *Eur J Pain* 2004;8(4):359–69.

51 Jensen MP, Turner JA, Romano JM. Self-efficacy and outcome expectancies: relationship to chronic pain coping strategies and adjustment. *Pain* 1991;44(3):263–9.

52 Atkins R. Aspects of current management: complex regional pain syndrome. *J Bone & Joint Surg* 2003;85b(8): 1100–06.

53 Bushnell TG, Cobo-Castro T. Complex regional pain syndrome: becoming more or less complex? *Man Ther* 1999;4(4):221–8.

54 Moseley GL. Graded motor imagery is effective for long-standing complex regional pain syndrome: a randomised controlled trial. *Pain* 2004;108(1–2):192–98.

55 Moseley GL. Graded motor imagery for pathologic pain. *Neurology* 2006;67(December):2129–34.

56 Moseley GL, Zalucki NM, Wiech K. Tactile discrimination, but not tactile stimulation alone, reduces chronic limb pain. *Pain* 2008;137(3):600–08.

57 Lewis J, McCabe CS. Body perception disturbance (BPD) in CRPS. *Practical Pain Management* 2010:60–66.

58 Lewis JS, Kersten P, McPherson KM *et al.* Wherever is my arm? Impaired upper limb position accuracy in Complex Regional Pain Syndrome. *Pain* 2010;149(3):463–9.

59 Carlson L, Watson H. Treatment of reflex sympathetic dystrophy using the stress loading program. *J Hand Ther* 1988;1:149–54.

60 Kirk Watson H, Carlson L. Treatment of reflex sympathetic dystrophy of the hand with an active 'stress loading' program. *J Hand Surg Eur* Vol 1987;12:779–85.

61 McCabe CS, Blake DR. An embarrassment of pain perceptions? Towards an understanding of and explanation for the clinical presentation of CRPS type 1. *Rheumatology* 2008;47(11):1612–16.

62 Atkins RM, Duckworth T, Kanis JA. Features of algodystrophy after Colles' fracture. *J Bone Joint Surg Br* 1990;72(1):105–10.

63 Dijkstra PU, Groothoff JW, ten Duis HJ, Geertzen JH. Incidence of complex regional pain syndrome type I after fractures of the distal radius. *Eur J Pain* 2003;7(5):457–62.

64 Stanos SP, Harden N, Wagner-Raphael L, Saltz SL. A prospective clinical model for investigating the development of CRPS. In: Harden N, Baron R, Janig W (eds). *Complex Regional Pain Syndrome*. Seattle: IASP press, 2001:151–64.

65 Bean DJ, Johnson MH, Heiss-Dunlop W, Kydd RR. Extent of recovery in the first 12 months of complex regional pain syndrome type-1: A prospective study. *Eur J Pain* 2016;20(6):884–94.

66 Atkins RM. Principles of Complex Regional Pain Syndrome. In: Bucholz R, Rockwood, Green (eds). *Fractures in Adults.* 7th edn. Philadelphia: Lippincott Williams & Wilkins, 2011.

67 Thomson McBride AR, Barnett AJ, Livingstone JA, Atkins RM. Complex regional pain syndrome (type 1): a comparison of 2 diagnostic criteria methods. *Clin J Pain* 2008;24(7):637–40.

68 Field J, Protheroe DL, Atkins RM. Algodystrophy after Colles fractures is associated with secondary tightness of casts. *J Bone Joint Surg Br* 1994;76(6):901–5.

69 Frettloh J, Huppe M, Maier C. Severity and specificity of neglect-like symptoms in patients with complex regional pain syndrome (CRPS) compared to chronic limb pain of other origins. *Pain* 2006;124(1–2):184–9.

70 McCabe CS, Cohen H, Hall J *et al.* Somatosensory conflicts in complex regional pain syndrome type 1 and fibromyalgia syndrome. *Curr Rheumatol Rep* 2009;11(6):461–5.

71 Wittayer M, Dimova V, Birklein F, Schlereth T. Correlates and importance of neglect-like symptoms in complex regional pain syndrome. *Pain* 2018;159(5):978–86.

72 Kemler MA, Furnee CA. Economic evaluation of spinal cord stimulation for chronic reflex sympathetic dystrophy. *Neurology* 2002;59(8):1203–9.

73 Atkins RM, Tindale W, Bickerstaff D, Kanis JA. Quantitative bone scintigraphy in reflex sympathetic dystrophy. *Br J Rheumatol* 1993;32(1):41–5.

74 Perez RS, Zollinger PE, Dijkstra PU *et al.* Clinical practice guideline 'Complex regional pain syndrome type I'. *Ned Tijdschr Geneeskd* 2007;151(30):1674–79.

75 van de Vusse AC, Stomp-van den Berg SG, Kessels AH, Weber WE. Randomised controlled trial of gabapentin in Complex Regional Pain Syndrome type 1 [ISRCTN84121379]. *BMC Neurol* 2004:4–13.

76 Livingstone JA, Atkins RM. Intravenous regional guanethidine blockade in the treatment of post-traumatic complex regional pain syndrome type 1 (algodystrophy) of the hand. *J Bone Joint Surg Br* 2002;84(3):380–6.

77 Gillespie S, Cowell F, Cheung G, Brown D. Can we reduce the incidence of complex regional pain syndrome type I in distal radial fractures? The Liverpool experience. *Hand Therapy* 2016;21:123–30.

78 Katz MM, Hungerford DS. Reflex sympathetic dystrophy affecting the knee. *J Bone Joint Surg Br* 1987;69(5):797–803.

79 Veldman PH, Goris RJ. Surgery on extremities with reflex sympathetic dystrophy. *Unfallchirurg* 1995;98(1):45–8.

80 Galer BS, Butler S, Jensen MP. Case reports and hypothesis: a neglect-like syndrome may be responsible for the motor disturbance in reflex sympathetic dystrophy (Complex Regional Pain Syndrome-1). *J Pain Symptom Manage* 1995;10(5):385–91.

81 Dielissen PW, Claassen AT, Veldman PH, Goris RJ. Amputation for reflex sympathetic dystrophy. *J Bone Joint Surg Br* 1995;77(2):270–3.

82 Krans-Schreuder HK, Bodde MI, Schrier E *et al*. Amputation for long-standing, therapy-resistant type-I complex regional pain syndrome. *J Bone Joint Surg Am* 2012;94(24):2263–8.

83 Bodde MI, Dijkstra PU, Schrier E *et al*. Informed decision-making regarding amputation for complex regional pain syndrome type I. *J Bone Joint Surg Am* 2014;96(11):930–4.

84 Midbari A, Suzan E, Adler T *et al*. Amputation in patients with complex regional pain syndrome: a comparative study between amputees and non-amputees with intractable disease. *Bone Joint J* 2016;98-B(4):548–54.

85 Bodde MI, Schrier E, Krans HK, Geertzen JH, Dijkstra PU. Resilience in patients with amputation because of complex regional pain syndrome type I. *Disabil Rehabil* 2014;36(10):838–43.

86 Goebel A, Lewis S, Phillip R, Sharma M. Dorsal root ganglion stimulation for complex regional pain syndrome (CRPS) recurrence after amputation for CRPS, and failure of conventional spinal cord stimulation. *Pain Pract* 2018;18(1):104–8.

87 McCabe CS, Haigh RC, Shenker NG, Lewis J, Blake DR. Phantoms in rheumatology. In: *Osteoarthritic joint pain* (Novartis Found Symp 260). Wiley, Chichester 2004:154–178

88 Lorimer Moseley G, Herbert RD, Parsons T et al. Intense pain soon after wrist fracture strongly predicts who will develop complex regional pain syndrome: prospective cohort study. *J Pain* 2014;15(1):16–23.

89 Morley S, Eccleston C, Williams A. Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour therapy and behaviour therapy for chronic pain in adults, excluding headache. *Pain* 1999; 80(1–2):1–13.

90 Jensen MP. Psychosocial approaches to pain management: an organizational framework. *Pain* 2011;152(4):717–25.

91 Finnerup NB, Attal N, Haroutounian S *et al*. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurol* 2015 Feb;14(2):162–73.

92 Manning DC, Alexander G, Arezzo JC *et al.* Lenalidomide for complex regional pain syndrome type 1: lack of efficacy in a phase II randomized study. *J Pain* 2014;15:1366–76.

93 Goebel A, Bisla J, Carganillo R *et al*. Low-dose intravenous immunoglobulin treatment for long-standing complex regional pain syndrome: a randomized trial. *Ann Intern Med* 2017;167(7):476–83.

94 Oerlemans HM, Oostendorp RAB, Severens JL *et al.* Favourable effect of adjuvant physical therapy (and to a lesser extent occupational therapy) compared with social work in reflex sympathetic dystrophy of one upper limb: A randomised controlled clinical trial. *Nederlands Tijdschrift voor Geneeskunde* 2002;146: 895–902.

95 Wu WH, Bandilla E, Ciccone DS *et al.* Effects of qigong on late-stage complex regional pain syndrome. *Altern Ther Health Med* 1999;5(1):45–54.

96 Kemler MA, de Vet HC, Barendse GA, van den Wildenberg FA, van Kleef KM. 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. *J Neurosurg* 2008;108(2):292–8.

97 Kemler MA, de Vet HC, Barendse HA, van den Wildenberg FA, van Kleef KM. Spinal cord stimulation for chronic reflex sympathetic dystrophy – five-year follow-up. *N Engl J Med* 2006;354(22):2394–6.

98 Deer TR, Levy RM, Kramer J *et al.* Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain syndrome and causalgis at 3 and 12 months: a randomized comparative trial. *Pain* 2017;158:669–81.

99 Eccleston C, Williams AC, Morley S. Psychological therapies for the management of chronic pain (excluding headache) in adults. *Cochrane Database Syst Rev* 2009;(2):CD007407.

100 Hann K, McCracken L. A systematic review of randomized controlled trials of Acceptance and Commitment Therapy for adults with chronic pain: Outcome domains, design quality, and efficacy. *Journal of Contextual Behavioral Science* 2014;3(4):217–27.

101 Mbizvo GK, Nolan SJ, Nurmikko TJ, Goebel A. Placebo responses in long-standing complex regional pain syndrome: a systematic review and meta-analysis. *J Pain* 2015 Feb;16(2):99–115.

102 van Rijn MA, Munts AG, Marinus J *et al.* Intrathecal baclofen for dystonia of complex regional pain syndrome. *Pain* 2009;143(1–2):41–7.

103 van Rooijen DE, Geraedts EJ, Marinus J, Jankovic J, Van Hilten JJ. Peripheral trauma and movement disorders: a systematic review of reported cases. *J Neurol Neurosurg Psychiatry* 2011;82:892–8.

104 Kemler MA, Barendse GA, van KM *et al.* Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *New Engl J Med* 2000;343:618–24.

105 Bruehl S, Chung OY. Psychological and behavioral aspects of complex regional pain syndrome management. *Clinical Journal of Pain* 2006;22(5):430–7.

106 British Society of Rehabilitation Medicine. *BSRM Musculoskeletal rehabilitation*. London: BSRM, 2004.

107 Bruehl S, Harden RN, Sorrell P. 'Complex regional pain syndromes. A fresh look at a difficult problem.' Conference proceedings. 62nd Annual Assembly of AAMPR, 2000.

108 Rodham K, McCabe C, Pilkington M, Regan L. Coping with chronic complex regional pain syndrome: advice from patients for patients. *Chronic Illn* 2013;9:29–42.

109 Funnell MM. Peer-based behavioural strategies to improve chronic disease self-management and clinical outcomes: evidence, logistics, evaluation considerations and needs for future research. *Fam Pract* 2010;27 Suppl 1:i17–i22.

110 Jadad AR, Moore RA, Carroll D *et al.* Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996;17(1):1–12.

111 de Vet HC, de Bie RA, van der Heijden GJ *et al.* Systematic Reviews on the Basis of Methodological Criteria. *Physiotherapy* 1997;83(6):284–9.

112 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* (Phila Pa 1976) 1997;22(18):2128–56.

113 Dirckx M, Groeneweg G, Wesseldijk F *et al.* Report of a preliminary discontinued double-blind, randomized, placebo-controlled trial of the anti-TNF-α chimeric monoclonal antibody infliximab in complex regional pain syndrome. *Pain Pract* 2013;13:633–40.

114 Fischer SGL, Collins S, Boogaard S *et al.* Intravenous magnesium for chronic complex regional pain syndrome type 1 (CRPS-1). *Pain Med* 2013;14:1388–99.

115 Schilder JCM, Sigtermans MJ, Schouten AC *et al.* Pain relief is associated with improvement in motor function in complex regional pain syndrome type 1: secondary analysis of a placebo-controlled study on the effects of ketamine. *J Pain* 2013;14:1514–21.

116 van der Plas AA, Schilder JCM, Marinus J, van Hilten JJ. An explanatory study evaluating the muscle relaxant effects of intramuscular magnesium sulphate for dystonia in complex regional pain syndrome. *J Pain* 2013;14:1341–48.

117 Varenna M, Adami S, Rossini M *et al.* Treatment of complex regional pain syndrome type 1 with neidronate: a randomized, double-blind, placebo-controlled study. *Rheumatology* 2013;52:534–42.

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

119 Rocha R dO, Teixeira MJ, Yeng LT *et al.* Thoracic sympathetic block for the treatment of complex regional pain syndrome type 1: a double-blind randomized controlled study. *Pain* 2014;155:2274–81.

120 Jeon B, Cho S, Lee J-H. Application of virtual body swapping to patients with complex regional pain syndrome: a pilot study. *Cyberpsychol Behav Soc Netw* 2014;17:366–70.

121 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.

122 Eun Young H, Hyeyun K, Sang Hee I. Pamidronate effect compared with a steroid on complex regional pain syndrome type I: Pilot randomised trial. *Neth J Med* 2016;74(1):30–5.

123 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 Med* 2012;13(1):96–106.

124 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. *Int J Rehabil Res* 2014;37(2):167–72.

125 Barnhoorn KJ, van de Meent H, van Dongen RT *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.

126 den Hollander M, Goossens M, de Jong J *et al*. Expose or protect? 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.

127 Sigtermans MJ, Hilten JJ, Bauer MCR *et al.* Ketamine produces effective and long-term pain relief in patients with Complex Regional Pain Syndrome Type 1. *Pain* 2009;06.023.

128 Atkins RM, Duckworth T, Kanis JA. Algodystrophy following Colles' fracture. *J Hand Surg Br* 1989;14(2):161–4.

129 Clark RL, Bowling FL, Jepson F, Rajbhandari S. Phantom limb pain after amputation in diabetic patients does differ from that after amputation in nondiabetic patients. *Pain* 2013;154:729–32.

130 Boulton AJ, Kirsner RS, Vileikyte L. Clinical practice. Neuropathic diabetic foot ulcers. *N Engl J Med* 2004; 351(1):48–55.

131 Eron LJ. Infections of skin and soft tissues: outcome of a classification scheme. *Clinical Infectious Diseases* 2000;31:287.

132 Lipsky BA. A report from the international consensus on diagnosing and treating the infected diabetic foot. *Diabetes Metab Res Rev* 2004;20 Suppl 1:S68–S77.

133 Grayson ML, Gibbons GW, Balogh K, Levin E, Karchmer AW. Probing to bone in infected pedal ulcers. A clinical sign of underlying osteomyelitis in diabetic patients. *JAMA* 1995;273(9):721–3.

134 Craig JG, Amin MB, Wu K *et al.* Osteomyelitis of the diabetic foot: MR imaging-pathologic correlation. *Radiology* 1997;203(3):849–55.

135 Sorensen LT, Karlsmark T, Gottrup F. Abstinence from smoking reduces incisional wound infection: a randomized controlled trial. *Ann Surg* 2003;238(1):1–5.

136 Hess CT, Kirsner RS. Orchestrating wound healing: assessing and preparing the wound bed. *Adv Skin Wound Care* 2003;16(5):246–57.

137 Guttmann O, Wykes V. Images in clinical medicine. Complex regional pain syndrome type 1. *N Engl J Med* 2008;359(5):508.

138 Pellizzer G, Strazzabosco M, Presi S *et al.* Deep tissue biopsy vs. superficial swab culture monitoring in the microbiological assessment of limb-threatening diabetic foot infection. *Diabet Med* 2001;18(10):822–7.

139 Armstrong DG, Nguyen HC. Improvement in healing with aggressive edema reduction after debridement of foot infection in persons with diabetes. *Arch Surg* 2000;135(12):1405–9.

140 Kremer M, Zuckerman R, Avraham Z, Raz R. Long-term antimicrobial therapy in the prevention of recurrent soft-tissue infections. *J Infect* 1991;22(1):37–40.

141 Williams DT, Harding KG. New treatments for diabetic neuropathic foot ulceration: views from a wound healing unit. *Curr Diab Rep* 2003;3(6):468–74.

142 Kirsner RS, Warriner R, Michela M, Stasik L, Freeman K. Advanced biological therapies for diabetic foot ulcers. *Arch Dermatol* 2010;146(8):857–62.

143 Kjeken I, Darre S, Smedslund G, Hagen KB, Nossum R. Effect of assistive technology in hand osteoarthritis: a randomised controlled trial. *Ann Rheum Dis* 2011;70(8):1447–52.

144 Department of Health. *The National Service Framework for long-term conditions*. London: DH, 2005.

145 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 Med* 2011;12(3):459–65.

146 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. *Clin J Pain* 2011;27(3):203–6.

147 Gustin SM, Schwarz A, Birbaumer N *et al.* NMDA-receptor antagonist and morphine decrease CRPS-pain and cerebral pain representation. *Pain* 2010;151(1):69–76.

148 Picarelli H, Teixeira MJ, de Andrade DC *et al.* Repetitive transcranial magnetic stimulation is efficacious as an add-on to pharmacological therapy in complex regional pain syndrome (CRPS) type I. *J Pain* 2010;11(11):1203–10.

Further reading

Azari P, Lindsay DR, Briones D *et al.* Efficacy and safety of ketamine in patients with complex regional pain syndrome. *CNS Drugs* 2012;26:215–28.

Balsham H, Helfand M, Schünemann HJ *et al*. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epi* 2011;64:401–6.

Birklein F, Schlereth T. Complex regional pain syndrome – significant progress in understanding. *Pain* 156 Suppl 1, 2015;S94–S103.

Bolignano D, Pisano A. Good quality research in rare diseases: trials and tribulations. *Paediatric Nephrology* 2016;Jan 27.

Bruehl S, Harden RN, Galer BS *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.

Brunner F, Schmid A, Kissling R *et al*. Biphosphonates for the therapy of complex regional pain syndrome I – systematic review. *Eur J Pain* 2009;13:17–21.

Cepeda MS, Carr DB, Lau J. Local anaesthetic sympathetic blockade for complex regional pain syndrome. *Cochrane Database Syst Rev* 2005;Oct 19;(4).

Connolly SB, Prager JP, Harden RN. A systematic review of ketamine for complex regional pain syndrome. *Pain Med* 2015,16;943–69.

Cornu C, Kassai B, Fisch R *et al.* Experimental designs for small randomised clinical trials: an algorithm for choice. *Orphanet J Rare Dis* 2013;Mar 25;8:48.

Daly AE, Bailocerkowski AE. Does evidence support physiotherapy management of adult Complex Regional Pain Syndrome type one? A systematic review. *Eur J Pain* 2009;13,339–53.

Dworkin RH, O'Connor AB, Backonja M *et al.* Pharmacologic management of neuropathic pain: evidence-based recommendations. *Pain* 2007;132(3):237–51.

Dworkin RH, O'Connor AB, Audette J *et al.* Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. *Mayo Clin Proc* 2010; 85(3 Suppl):S3–14.

Farrar JT, Young Jr JP, LaMoreaux L *et al.* Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain* 2001;94:149–58.

Goebel A, Pope C, Poole H *et al.* The nature and impact of complex regional pain syndrome: Patients' views. *Eur J Pain* 13(S1):2009.

Grieve S, Jones L, Walsh N, McCabe C. What outcome measures are commonly used for Complex Regional Pain Syndrome clinical trials? A systematic review of the literature. *Eur J of Pain* 2016;331–40.

Guyatt G, Oxman AD, Akl EA *et al.* GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epi* 2011;64:383–94.

Harden RN. Complex regional pain syndrome. *Br J Anaesth* 2001;87(1):99–106.

Harden RN, Bruehl S, Perez RSGM *et al.* Development of a severity score for CRPS. *Pain* 2010;151(3):870–6.

Higgins JPT, Green S (eds.) *Cochrane Handbook for Systematic Reviews of Interventions, v5.1.0*. The Cochrane Collaboration, 2011 (www.handbook.cochrane.org).

Lundborg G, Rosen B. Hand function after nerve repair. *Acta Physiol* 2007;189:207–17.

O'Connell NE, Wand BM, McAuley J *et al.* Interventions for treating pain and disability in adults with complex regional pain syndrome. *Cochrane Database Syst Rev* 2013;Apr 30;(4).

Rowbotham MC. What is a 'clinically meaningful' reduction in pain? *Pain* 2001;94:131–2.

de Souza NS, Carolina A, Martins G *et al.* Motor imagery and its effect on complex regional pain syndrome: an integrative review. *Neurology International* 2015;7:58–61.

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 Syst Rev* 2016;Issue 2.

Stanton-Hicks MD, Burton AW, Bruehl SP *et al.* An updated interdisciplinary clinical pathway for CRPS: report of an expert panel. *Pain Pract* 2002;2(1):1–16.

Tran DQ, Duong S, Bertini P, Finlayson RJ. Treatment of complex regional pain syndrome: a review of the evidence. *Can J Anaesth* 2010;57,149–66.

van Bussel CM, Stronks DL, Huygen FJ. Dorsal column stimulation versus dorsal root ganglion stimulation for complex regional pain syndrome confined to the knee; patients' preference following the trial period. *Pain Practice* 2017;Mar 23 epub ahead of print.

van Buyten JP, Smet I, Liem L *et al.* Stimulation of dorsal root ganglia for the management of complex regional pain syndrome: a prospective case series. *Pain Practice* 2015;15:208–16.

van der Lee JH, Wesseling J, Tanck MWT, Offringa M. Efficient ways exist to obtain the optimal sample size in clinical trials in rare diseases. *J Clin Epidem* 2008;61,324–30.

Wertli MM, Kessels AG, Perez RS *et al.* Rational pain management in complex regional pain syndrome 1 (CRPS 1) – a network meta-analysis. *Pain Med* 2014;15,1575–89.

Complex regional pain syndrome in adults

These guidelines concern the diagnosis and management of patients with complex regional pain syndrome (CRPS). They provide recommendations for diagnosis, treatment and referral in a variety of clinical settings (primary care, occupational therapy and physiotherapy, surgical practice, rheumatology, neurology and neurosurgery, sport and exercise medicine (SEM), dermatology, pain medicine, rehabilitation medicine, emergency medicine and long-term care). Their purpose is to provide coherent guidance for professionals working in the different health specialties who care for these patients.

11 St Andrews Place
Regent's Park
London NW1 4LE
www.rcplondon.ac.uk

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