Musculoskeletal Care

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REVIEW ARTICLE OPEN ACCESS

Rehabilitation Interventions for Adults With Complex Regional Pain Syndrome: A Scoping Review Protocol

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Received: 16 September 2024 | **Accepted:** 23 September 2024

Funding: This work was supported by the University of the West of England and Royal United Hospitals NHS Trust, Bath.

Keywords: complex regional pain syndrome | occupational therapy | physical therapy | physiotherapy | reflex sympathetic dystrophy | rehabilitation

ABSTRACT

Objectives: This scoping review will explore the literature related to rehabilitation interventions for the treatment of adults living with complex regional pain syndrome (CRPS), describe the domains and outcome measures used to assess their effectiveness, and examine the neurophysiological bases of these interventions.

Introduction: The unremitting symptoms of CRPS, a chronic pain condition, are associated with long-term disability, poor psychological health, decreased emotional and social well-being, and reduced quality of life. Effective treatment for persistent symptoms is notoriously difficult. Therapeutic approaches such as graded motor imagery or pain exposure therapy are recommended for CRPS but show mixed results, insufficient effectiveness, variability in outcome measures, and unclear neurophysiological bases.

Inclusion Criteria: This review will consider studies that include any form of non-invasive rehabilitation intervention delivered by a healthcare professional in any setting for adults with a CRPS diagnosis. Quantitative, qualitative and observational studies, text and opinion papers will be considered.

Methods: The Joanna Briggs Institute (JBI) methodology will be used to conduct this scoping review. MEDLINE, Embase, Scopus, APA PsycINFO, CINAHL, Cochrane, OpenGrey Google and ProQuest Dissertations and Theses Global (ProQuest) will be searched for studies in English published between 2007 and 2024. Two independent reviewers will screen the titles, abstracts, and full texts of the selected studies. Data collection will be performed using a tool developed by the researchers based on the standardised JBI tool. Data will be presented in a comprehensive narrative summary.

Trail Registration: https://doi.org/10.17605/OSF.IO/P967T

1 | Introduction

Complex regional pain syndrome (CRPS) is a painful condition that often develops following trauma or surgery to a limb, but on a rare occasion can occur spontaneously (Goebel 2011; Shipton 2009). CRPS is diagnosed using the 'Budapest Criteria' and is classified as type I or type II, depending on whether known major nerve damage is absent or present, respectively (N. R. Harden et al. 2010). Signs and symptoms are usually limited to a single limb, which may include oedema, altered hair, and nail growth, and sensory, motor, and/or autonomic disturbances (N. R. Harden et al. 2010).

With an estimated incidence rate ranging from 5.46 to 26.2 per 100,000 person-years and an estimated prevalence of 1.2% among adults with chronic pain conditions, CRPS is a relatively rare condition (De Mos et al. 2007; Murphy et al. 2017; Sandroni et al. 2003). However, up to 30% of patients following a surgical procedure or fracture are diagnosed with CRPS (Goh, Chidambaram, and Ma 2017; Rolls et al. 2020) and transient features of CRPS are relatively common, occurring in up to 70% of minor limb injuries (Hall et al. 2016). Adults diagnosed with CRPS will have a substantial pain symptom reduction in the first year after syndrome onset, yet only 5% are symptom-free 1 year (Bean et al. 2015). Similarly, evidence has shown that up to 30% of people with CRPS suffer from persistent symptoms, including lasting pain and disability that develops into a long-term condition (Bean et al. 2016). Unremitting symptoms of CRPS are associated with long-term disability, poor psychological health, decreased emotional and social well-being and reduced quality of life (Bean et al. 2015, 2016). Additionally, CRPS is associated with high direct health care costs compared to other chronic hand impairments (Duong et al. 2023; Elsamadicy et al. 2018), generates work incapacity, and ultimately creates a substantial economic burden on society (Elsamadicy et al. 2018).

For those with persistent CRPS (i.e., lasting longer than 12–18 months from onset; Goebel et al. 2021; Lewis et al. 2024) effective treatment is notoriously difficult (R. N. Harden et al. 2006). International clinical guidelines for CRPS recommend multidisciplinary rehabilitation for CRPS as a gold standard treatment, which includes education, pain relief, physical rehabilitation and psychological intervention (Goebel & Turner-Stokes 2018; R. N. Harden et al. 2022; Perez et al. 2010). The goals of multidisciplinary rehabilitation are to restore function to the affected limb, decrease pain and disability, and improve quality of life while minimising medication side effects and toxicities (R. N. Harden et al. 2022). However, these guidelines present some variation in content, are not fully evidence-based, and are not able to provide a definitive clinical pathway (Miller et al. 2019). Furthermore, the gold standard treatment of multidisciplinary rehabilitation is costly, its effectiveness is not clear, and there is no consensus on the optimal rehabilitation input (Ferraro et al. 2023; Goebel and Turner-Stokes 2018; R. N. Harden et al. 2022; Perez et al. 2010).

Rehabilitation interventions are often recommended for CRPS treatment (Goebel and Turner-Stokes 2018; R. N. Harden et al. 2022; Perez et al. 2010). These interventions, generally delivered by physiotherapists and occupational therapists, aim to improve function and quality of life, reduce pain, and promote self-management (Turner-Stokes and Goebel 2011). Although the aims of CRPS rehabilitation interventions among healthcare professionals are consistent with the CRPS clinical guidelines (Grieve et al. 2019), clinicians involved in the rehabilitation of individuals with CRPS use a broad range of modalities commonly delivered in a multimodal format (Ferraro et al. 2023; Miller et al. 2019). These modalities include educational interventions (e.g., facilitation of self-management or pain neuroscience education), physical exercise interventions (e.g., range of movement or strength exercises), passive therapies (e.g., massage or splinting), psychological/brain interventions (e.g., mirror therapy or cognitive behavioural therapy), and exposure-based therapies (e.g., tactile desensitisation or stress loading) (Miller et al. 2019). Yet, recent systematic reviews (Ferraro et al. 2023; Smart et al. 2022) report only very low-quality evidence or no evidence at all on the effects of individual treatment modalities on pain and disability in CRPS because of small sample sizes and high risk of bias. Thus, published national clinical guidelines for CRPS treatment from the United Kingdom, the Netherlands and the United States of America (USA) (Goebel and Turner-Stokes 2018; R. N. Harden et al. 2022; Perez et al. 2010) include data from various sources of evidence, including case series and even in some instances case reports/empirical information (R. N. Harden et al. 2022). Importantly, published evidence regarding the effectiveness of these interventions often focuses solely on pain and disability, neglecting other important CRPS features such as body perception disturbances or kinesiophobia (i.e., fear of movement) (R. N. Harden et al. 2022) and the neurophysiological bases of these widely used CRPS rehabilitation interventions are still under examination and yet not fully understood (Moseley and Flor 2012).

A search of PROSPERO, PubMed, Cochrane Database of Systematic Reviews, the Jonna Briggs Institute (JBI) Systematic Review Register and JBI Evidence Synthesis was conducted in July 2023. We identified four studies in PROSPERO that relate to rehabilitation interventions for adults living with CRPS (Ferraro et al. 2023; O'Connell et al. 2013; Smart et al. 2022; Smart, Wand, and O'Connell 2016). O'Connell et al. (2013) and Ferraro et al. (2023) summarised systematic reviews of evidence exploring the effectiveness of any non-invasive interventions (including rehabilitation interventions) to reduce pain or disability or both in adults living with CRPS. Smart, Wand, and O'Connell (2016), Smart et al. (2022) explored the effectiveness of physiotherapy interventions to treat pain or disability or both including only randomised control trials.

This scoping review differs from previous work as it will first describe any current rehabilitation intervention used to treat adult CRPS, broadening the literature search in our review by including studies of various study designs in order to capture any non-invasive rehabilitation intervention described in literature. Secondly, this review will describe the domains and outcomes that different rehabilitation interventions intend to target and that are used to measure their effectiveness and lastly, this review will characterise the working mechanisms of these interventions when reported.

2 | Review Question

What rehabilitation interventions delivered by healthcare professionals are used to treat adults living with CRPS?

3 | Objectives

The review objectives are:

1. To describe the rehabilitation interventions used to treat adults with CRPS.

2. To explore the domains and outcome measures used to assess the effectiveness of rehabilitation interventions to treat adults with CRPS.
3. To describe the neurophysiological bases that support the use of rehabilitation interventions to treat adults living with CRPS.

4 | Methods

The proposed review will be conducted in accordance with the JBI methodology for scoping reviews (Peters et al. 2020). The final manuscript will also follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) (Tricco et al. 2018).

4.1 | Inclusion Criteria

The PCC model (Participants, Concept, Context) was used for developing the research question and objective(s), informed the inclusion and exclusion criteria, and consequently the literature search strategy (Peters et al. 2020). A summary of the eligibility criteria can be found in Table 1, and inclusion and exclusion criteria can be found in Table 2.

4.2 | Participants

This review will consider studies that include participants with a clinical diagnosis of CRPS type 1 or 2 (Goebel 2011; Shipton 2009) who are 18 years of age or older. The diagnosis of CRPS is clinical and is commonly based on the new International Association for the Study of Pain (IASP) criteria, also referred to as the Budapest criteria (N. R. Harden et al. 2010). For the purposes of this scoping review, CRPS will be categorised as a physician diagnosis based on current clinical practices, including studies where CRPS diagnosis is not established using the Budapest Criteria (N. R. Harden et al. 2010). This review will also consider articles with participants diagnosed with CRPS that present with co-morbidities (e.g., stroke participants diagnosed with CRPS) and articles with participants diagnosed with CRPS even if the study population is not exclusively CRPS participants (articles will be included if CRPS population ≥ 50% of the total study population).

4.3 | Concept

Rehabilitation interventions for adult CRPS are delivered by a healthcare professional. This review will consider all rehabilitation interventions to treat adult CRPS such as educational interventions, physical exercise interventions, passive therapies,

TABLE 1 | Scoping literature review eligibility criteria.

Participants	• A clinical diagnosis of CRPS type 1 or 2 (Goebel 2011; Shipton 2009). For the purposes of this scoping review, CRPS was categorised as a physician diagnosis based on current clinical practices, including studies where CRPS diagnosis was not established using the Budapest Criteria (R. N. Harden et al. 2007) • 18 years of age or older • CRPS diagnosis with co-morbidities (e.g., stroke participants diagnosed with CRPS) • CRPS diagnosis even if the study population was not exclusively CRPS participants (articles will be included if CRPS population ≥ 50% of the total study population)
Concept	Rehabilitation interventions for adults living with CRPS delivered by a healthcare professional. This includes (Miller et al. 2019): • Educational interventions • Physical exercise interventions • Passive therapies • Psychological/brain intervention • Exposure-based therapies • Interventions in combination with other non-rehabilitative interventions (e.g., ketamine infusions with Cognitive Behavioural Therapy) This review will explore their neurophysiological basis where reported
Context	All studies conducted in any clinical or research setting, from any geographical location or country

TABLE 2 | Overview of inclusion and exclusion criteria for the scoping literature review.

	Inclusion	Exclusion
Types of studies	Treatment clinical guidelines systematic reviews and meta-analyses	
	Observational	
	Experimental	
	Quasi-experimental study design	
	Clinical and case series	
	Grey literature (theses, conference papers, dissertations, research reports, articles that have not been peer-reviewed yet [pre-prints])	
	Opinion papers	
Types of population	Adults living with CRPS	
Types of intervention	Any form of rehabilitation intervention delivered by a healthcare professional	
Setting	Any clinical or research setting	
	Any geographical location or country	
Mode of delivery	Interventions delivered by a healthcare professional	
Language of publications	English	Other languages
Date of publication	From 2007 to date	

psychological/brain interventions, and exposure-based therapies (Miller et al. 2019) delivered by a wide range of healthcare professionals in combination with other non-rehabilitative interventions (e.g., ketamine infusions with Cognitive Behavioural Therapy) or as a standalone intervention. This review will also include articles reviewing rehabilitation interventions for CRPS or exploring their neurophysiological bases.

4.4 | Context

All studies in English conducted in any clinical or research setting, from any geographical location or country will be considered.

4.5 | Types of Sources

All sources including treatment clinical guidelines, systematic reviews and meta-analyses, observational, experimental, and quasi-experimental study designs, clinical and case series, grey literature, and opinion papers between 2007 and 2024 will be examined. This will allow examination of a broad range of up-to-date rehabilitation interventions for adult CRPS in different contexts since the establishment of the Budapest diagnostic criteria (N. R. Harden et al. 2010).

4.6 | Search Strategy

The research librarian and the primary author conducted an initial limited search of MEDLINE (PubMed), CINAHL, JBI Evidence Synthesis, Cochrane Database of Systematic Reviews and PROSPERO to identify articles on the topic and to review other search strategies. The research librarian and primary author used key terms contained in the titles and abstracts of relevant articles and the associated index terms to develop a full search strategy for EMBASE (see Table 3). The search strategy, including all identified keywords and index terms, will be adapted for each included database. Additionally, the reference lists of all included studies will be reviewed to identify any additional relevant studies. The initial search will include only studies on CRPS adult populations. A limit on the search strategy will be the English language. Studies published in languages other than English will be excluded due to limited financial resources for translation services. Another limitation is the publication date. To capture the most up-to-date rehabilitation interventions for adult CRPS, we used the establishment of the Budapest Criteria (N. R. Harden et al. 2010) for CRPS diagnosis (2007–2024). The databases to be searched include MEDLINE, Embase, Scopus, APA PsycINFO, CINAHL, Cochrane, OpenGrey Google and ProQuest Dissertations and Theses Global (ProQuest).

4.7 | Study Selection

Following the search, all identified citations will be collated and uploaded into Rayyan (Ouzzani et al. 2016), and duplicates removed. Two independent reviewers (MPB and JL/AVDW/NW) will then screen titles and abstracts for assessment against inclusion criteria for the review. Reasons for exclusion of any studies that do not meet the inclusion criteria will be recorded and reported in the final scoping review. Potentially relevant studies will be retrieved in full, and their citation details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia) (Munn et al. 2018). The full text of potentially relevant studies will be assessed in detail for further review against the inclusion criteria by two independent reviewers (MPB and JL/AVDW/NW). Reasons for exclusion of any full-text studies that do not meet the inclusion criteria will be recorded and reported in the final scoping review. Any disagreements that arise

TABLE 3 | Scoping literature review search conducted in EMBASE.

	Query
#1	(Therapy or Treatment or Training or Retraining or Re-training or Rehabilitation).ti.
#2	(psychology or behaviour therapy).sh. or psycholog*.ti. or behaviour.ti. or behaviour.ti. or cogniti*.ti. or acceptance.ti.
#3	(occupational therapy or occupational therapists).sh. or "OT".ti. or "ergotherap*".ti. or "occupational therap*".ti.
#4	Physical Therapy Specialty.sh. or "physiotherap*".ti. or "Physical Therap*".ti.
#5	#1 OR #2 OR #3 OR #4
#6	"Complex Regional Pain Syndrome*".ti. or Complex Regional Pain Syndromes.sh. or "CRPS".ti.
#7	#5 AND #6

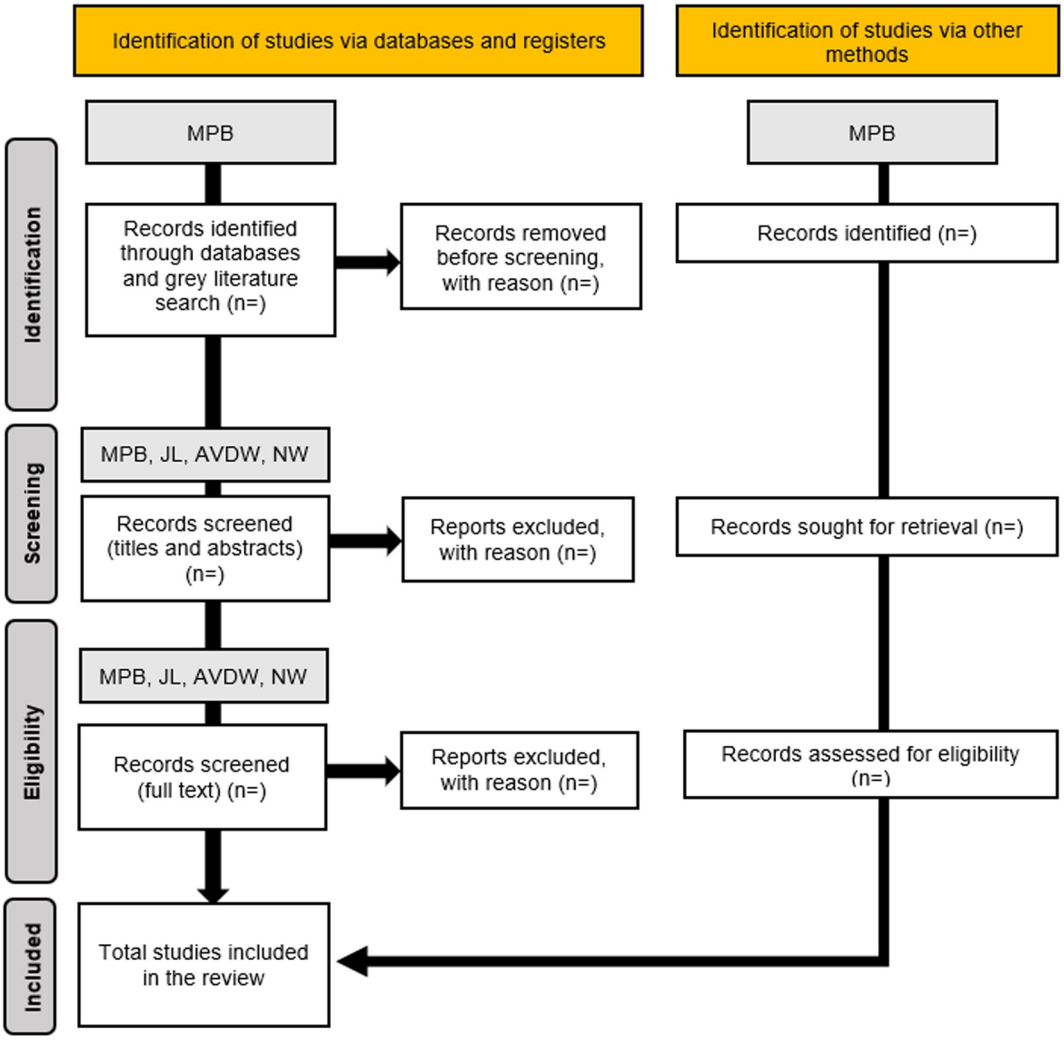

FIGURE 1 | PRISMA flowchart of the scoping literature review.

between the reviewers at any stage of the study selection process will be resolved through discussion or with an additional reviewer/s. The search results and the study inclusion process will be reported in full in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping review (PRISMA-ScR) flow diagram (see Figure 1; Tricco et al. 2018).

4.8 | Data Extraction

Data will be extracted from studies included in the scoping review by the main reviewer (MPB). Using a modified data extraction tool developed by the reviewers based on the standardised tool from JBI SUMARI (Munn et al. 2018). The data extracted will include specific details about the population,

concept, context, study methods, and key findings relevant to the review objective. A draft data extraction form is provided (see Appendix I). Modification of the JBI data extraction tool involved the addition of the following items: study design, rehabilitation interventions, outcome measures, neurophysiological bases of the intervention(s), and main findings. The draft data extraction tool was piloted during the protocol stage and will be refined and revised as necessary during the review stage. Modifications to the data extraction tool will be detailed in the final scoping review. If necessary, authors of the included studies will be contacted to request missing or additional data.

4.9 | Data Analysis and Presentation

The extracted data will be grouped and presented as descriptive summaries in text, diagrammatic and tabular formats that align with the objectives of this scoping review. To answer the research question, a table will be developed to present the types of interventions, their main characteristics, the areas of impairment addressed, and their theoretical frameworks. The search strategy and selection process results will be presented in a PRISMA flow diagram. A narrative summary will accompany the tabulated and/or charted results.

Author Contributions

M.A.P.B., N.E.W., A.V.d.W., and J.S.L.: Developing the concept and strategy, developing the search strategy, conducting the search, and writing and reviewing the manuscript.

Acknowledgements

Lisa Hirst, Librarian, for peer-review and assisting with the search strategy.

Ethics Statement

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

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Appendix I: Draft Data Extraction Instrument

First author, year, country, journal, and DOI & Study details (study design, age, sex, dominance, areas affected, symptom duration, medication, previous/current treatments)
Rehabilitation intervention details and outcome measures
Main findings
Neurophysiological bases for the intervention