



BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Quality of life, functioning and participation of adult patients with an amputation following Complex Regional Pain Syndrome I or Brachial Plexus Injury; A scoping review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-079393
Article Type:	Protocol
Date Submitted by the Author:	30-Aug-2023
Complete List of Authors:	Domerchie, Patrick; University Medical Centre Groningen, Rehabilitation van Kammen, Klaske; UMCG, Rehabilitation van Wijk, Iris; Revalidation Centre De Hoogstraat, Rehabilitation Lange, Maaïke; Revalidation Centre De Hoogstraat, Rehabilitation Van der Sluis, Corry; University of Groningen, University Medical Center Groningen, Rehabilitation Medicine
Keywords:	Chronic Pain, NEUROSURGERY, Elbow & shoulder < ORTHOPAEDIC & TRAUMA SURGERY, Quality of Life, REHABILITATION MEDICINE

SCHOLARONE™
Manuscripts

Quality of life, functioning and participation of adult patients with an amputation following Complex Regional Pain Syndrome I or Brachial Plexus Injury; A scoping review

Authors

Patrick N Domerchie¹, Klaske v Kammen¹, Iris v Wijk^{2,3}, Maaïke Lange², Corry K vd Sluis¹

- 1. University of Groningen, University Medical Center Groningen, Department of Rehabilitation Medicine, Groningen, The Netherlands.
- 2. De Hoogstraat Rehabilitation, Utrecht, The Netherlands
- 3. Center of Excellence for Rehabilitation Medicine, UMC Utrecht Brain Center, University Medical Center Utrecht, and De Hoogstraat Rehabilitation, Utrecht, the Netherlands

Correspondence address: Patrick N. Domerchie, MD, Department of Rehabilitation Medicine, University of Groningen, University Medical Center Groningen, Internal postal code CB40, PO box 30.001, 9700 RB Groningen, the Netherlands. Tel: +31 50 36 18506; e-mail: p.n.domerchie@umcg.nl

Abstract

(Maximum - 250 words for Protocols/500 words for Scoping Reviews)

Objective: The objective of this scoping review is to provide insight in what is currently known in literature regarding (perceived) quality of life (QoL), functioning and participation of patients that underwent amputation of their upper limb because of therapy-resistant debilitating complex regional pain syndrome type I (CRPS-I) or brachial plexus injury (BPI).

Introduction: When looking at treatment options for both CRPS-I and BPI, amputation of an upper limb is a last resort. Not much is known about the QoL and functioning after amputation in this patient group. Is it important to gain insight in these outcomes so we can properly inform patients who are eligible for amputation and are considering this treatment option.

Inclusion criteria: All studies regarding patients with either a BPI or CRPS-I who underwent amputation of an upper limb, who are at least 18 years old and without a history of mental illness. Studies should include either one or all of the following topics: QoL, functioning and/or participation.

Methods: Searches will be conducted in the Cochrane database, PubMed, in EMBASE, and in Google Scholar. Search strings will be provided by a licenced librarian. Studies should be written in English or Dutch. Studies will be selected first by title, then abstract and finally full article by two reviewers who will discuss after every selection round. Data will be presented as brief summaries in text, and in tables for clear presentation.

Strengths and limitations

- This scoping review will attempt to provide a full overview of all literature regarding quality of life and functioning after amputation because of brachial plexus injury or CRPS-I
- Strength: All relevant data will be included, regardless of study type, so a full overview can be given
- Weakness: This scoping review is not a systematic review and as such studies will not receive a grade. We will however provide information about the strong and weak points of each study

Introduction

Complex regional pain syndrome type I (CRPS-I) is a pain syndrome in an extremity with debilitating pain and loss of function, for which a number of treatment options exist.(1–4) Therapy-resistant cases exist, for whom amputation is the only option left.(5–7) Similarly, some patients with a complete brachial plexus injury (BPI) can experience severe pain due to for instance traction on the glenohumeral joint apart from having an afunctional ('flail') arm. Amputation can be considered a last resort treatment in these patients as well.(8,9)

Since amputation is an irreversible and last resort treatment, it is important to select these patients that will benefit from this treatment, and to properly inform them about the implications of amputation. Can patients expect a higher quality of life (QoL), will their functionality and participation improve? Literature answers some of these questions, but a clear overview of current literature is, to our knowledge, absent.(10–14) To properly inform these patients who are considering amputation, an overview of current literature is therefore needed.

A preliminary search in the Cochrane database, in PubMed, in EMBASE and by using Google Scholar showed no current or planned reviews (either systematic or scoping) regarding this topic. There is one systematic review by Ayyaswamy et al discussing QoL after amputation in patients with advanced CRPS-I from 2019.(12) A combined scoping review of amputation in either CRPS-I or BPI has not yet been conducted as far as we can tell. Furthermore, Ayyaswamy's review only includes studies up until 2017, and patients with

CRPS-I who have strictly followed the standard diagnostic criteria of CRPS-I. Only QoL outcomes that were reported using descriptive analysis and/or standard tools were included. Our intended scoping review will complement what can be learned from the review of Ayyaswamy et al, as we will look at both quantitative and qualitative reports of QoL, we will look at all studies that have been published at the time of our search, we will also look at functionality and participation, we will also look at BPI and amputation and we will also look at synonyms for CRPS-I (such as Südecks dystrophy). Finally our goal is not to provide the reader with a summarised set of overarching statistics, but rather an overview of what is currently written about QoL, functioning and participation following amputation due to CRPS-I or BPI.

Since our main goal is to provide insight into what is currently known in literature, we felt that a scoping review was most appropriate, as it describes and gives an overview of all articles, without quantifying the quality of the included articles. For instance, a case series describing the experiences of patients following an amputation can be as valuable as a large study with questionnaires regarding QoL when the goal is to provide insight into a patient's perceived QoL, functioning and participation.

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Supérieur (ABES).

Review question

What is currently known in literature regarding (perceived) QoL, functioning and participation of patients that underwent amputation of their upper limb because of therapy-resistant debilitating CRPS-I or BPI?

Keywords

QoL, functioning, CRPS-I, BPI, amputation, upper limb

Eligibility criteria

Participants

Studies that have included adults with either a BPI (including obstetric BPI) or therapy-resistant CRPS-I who underwent amputation. Patients should be 18 years or older. For CRPS-I specifically, we will also include studies that use (older) synonyms for CRPS-I, such as posttraumatic dystrophy and Südecks dystrophy.

Concept

All studies that have included the above mentioned patients and that describe either QoL, functioning and/or participation will be considered for inclusion. The World Health Organization defines QoL as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns".⁽¹⁵⁾ Indicators that qualify QoL are employment status, mental and emotional health, physical health, education, freedom, recreation and leisure, and the ability to perform activities of daily living (ADL).

The international classification of functioning (ICF) defines functioning as: "an umbrella term for body function, body structures, activities and participation. It denotes the positive or neutral aspects of the interaction between a person's health condition(s) and that individual's contextual factors (environmental and personal factors)." ⁽¹⁶⁾

The ICF defines participation as involvement in a life situation.⁽¹⁶⁾

We will include all studies that discuss/measure (aspects of) the above definitions. This includes, but is not limited to, questionnaires, qualitative studies, experts opinions and case reports.

Context

All studies will be included if they are written in either English or Dutch. While we are aware that culture and perhaps even geographic location may play a role in perceived QoL and possibilities of participating in society, we will also include articles that are not from 'western countries' as they provide valuable insight as to what encompasses perceived QoL in these cultures and/or countries.

Types of Sources

This scoping review will consider both experimental and quasi-experimental study designs including randomized controlled trials, non-randomized controlled trials, before and after studies and interrupted time-series studies. In addition, analytical observational studies including prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies will be considered for inclusion. This review will also consider descriptive observational study designs including case series, individual case reports and descriptive cross-sectional studies for inclusion.

Qualitative studies will also be considered that focus on qualitative data including, but not limited to, designs such as phenomenology, grounded theory, ethnography, qualitative description, action research and feminist research.

In addition, systematic reviews that meet the inclusion criteria will also be considered, depending on the research question; we will use the relevant original articles from these reviews.

Text and opinion papers will also be considered for inclusion in this scoping review.

Methods

The proposed scoping review will be conducted in accordance with the JBI methodology for scoping reviews and reported as per PRISMA-SCR guidelines.(17,18)

Search strategy

An initial limited search of the Cochrane database, in PubMed, in EMBASE and Google Scholar was undertaken to identify articles on the topic. The text words contained in the titles and abstracts of relevant articles, and the index terms used to describe the articles were used to develop a full search strategy for Cochrane database, in PubMed, in EMBASE and by using Google Scholar (see Appendix 1). The search strategy, including all identified keywords and index terms, will be adapted for each included database and/or information source. The reference list of all included sources of evidence will be screened for additional studies.

Studies published in either English or Dutch will be included. All published articles that are available at the time of conducting our search will be considered. Since the goal of this scoping review is to provide the reader with a summary of all available studies regarding this topic, we felt no earlier date limit should be set.

The databases to be searched include Cochrane database, in PubMed, in EMBASE and Google Scholar. Furthermore, a search on PROSPERO was carried out and confirmed no similar or identical reviews are currently being conducted.

Study/Source of Evidence selection

Following the search, all identified citations will be collected and uploaded into Mendeley. Data will then be transferred to Rayyan for removal of duplicates and to make notes of included articles. Titles and abstracts will then be screened by two independent reviewers for

assessment against the inclusion criteria for the review. An initial selection round will be made on title alone, then another selection round after thoroughly reading the abstract and finally a selection round after reading the entire article. After every selection round, the two reviewers will discuss any differences in included articles. The full text of selected citations will be assessed in detail against the inclusion criteria by the same independent reviewers. Reasons for exclusion of sources of evidence at full text that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion, or with (an) additional reviewer(s). The results of the search 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.(18)

Data Extraction

Relevant data from the selected papers will be extracted using a data extraction form we have developed specifically for this scoping review. Relevant data will include details regarding type of study, year in which the study has been conducted, country in which the study has been conducted, number of patients included, relevant in- and exclusion criteria, primary and secondary outcome(s), and strong and weak (deemed as such by the reviewers) points of each study. This data will be presented both in a table, and as part of a summary of the article in plain text.

The draft extraction form has been made following the template provided by the Joanna Briggs Institute and the article by Pollock et al.(19,20) This form has been discussed with the research group before finalization. During the data extraction process conducted by two independent reviewers, this form will be modified and revised as necessary, and modifications will be mentioned in detail in the scoping review. Should disagreements occur between the reviewers regarding any modifications, a third reviewer will be asked to help resolve this and guide the reviewers to consensus.

If any relevant data is missing from the article, the reviewers will try to acquire this data by contacting the authors of the papers. As this is a scoping review, with the goal to inform what is currently known in literature, no critical appraisal of individual articles shall be conducted. We will check the references of our included articles, to verify whether we have missed relevant literature in our searches.

Data Analysis and Presentation

Data will be presented in tables, as discussed in the above paragraph. Furthermore, a short summary of relevant full articles will be given in text with regard to most important outcomes and study objectives.

Patient and Public Involvement Statement

Neither patients nor the public were involved in the design of this protocol.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Acknowledgements

We would like to thank Karin Sijtsma, medical librarian at the Central Medical Library of the Rijksuniversiteit Groningen and University of Groningen Medical Centre for her contributions to our search strategies.

Funding

For this review no funding or grants were received

Conflicts of interest

The authors declare that there are no conflicts of interest in this project

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Supérieur (ABES).

References

1. Urits I, Shen AH, Jones MR, Viswanath O, Kaye AD. Complex Regional Pain Syndrome, Current Concepts and Treatment Options. *Curr Pain Headache Rep*. 2018;22(2):1–9.
2. NVA/VRA. Richtlijn Complex Regionaal Pijn Syndroom type 1 [Internet]. https://richtlijndatabase.nl/richtlijn/complex_regionaal_pijn_syndroom_type_1/startpagina_-_complex_regionaal_pijsyndroom.html. 2021 [cited 2022 Oct 7]. Available from: https://richtlijndatabase.nl/richtlijn/complex_regionaal_pijn_syndroom_type_1/startpagina_-_complex_regionaal_pijsyndroom.html
3. Royal College of Physicians. Complex regional pain syndrome in adults [Internet]. 2018 [cited 2022 Oct 7]. Available from: <https://www.rcplondon.ac.uk/guidelines-policy/complex-regional-pain-syndrome-adults>
4. Casale R, Atzeni F, Sarzi-Puttini P. The therapeutic approach to complex regional pain syndrome: Light and shade. *Clin Exp Rheumatol*. 2015;33:126–39.
5. Krans-Schreuder HK, Bodde MI, Schrier E, Dijkstra PU, van den Dungen JA, den Dunnen WF, et al. Amputation for long-standing, therapy-resistant type-I complex regional pain syndrome. *J Bone Joint Surg Am*. 2012;94(24):2263–8.
6. Schrier E, Dijkstra PU, Zeebregts CJ, Wolff AP, Geertzen JHB. Decision making process for amputation in case of therapy resistant complex regional pain syndrome type-I in a Dutch specialist centre. *Med Hypotheses*. 2018;121:15–20.
7. Bodde MI, Dijkstra PU, den Dunnen WFA, Geertzen JHB. Therapy-resistant complex regional pain syndrome type I: to amputate or not? *J Bone Joint Surg Am*. 2011;93(19):799–805.
8. Resnik L, Fantini C, Latlief G, Phillips S, Sasson N, Sepulveda E. Use of the DEKA Arm for amputees with brachial plexus injury: A case series. *PLoS One*. 2017 Jun 1;12(6).
9. Wilkinson' MCP, Birch2 R, Bonney3 G. Brachial plexus injury: when to amputate? *Injury*. 1993.
10. Midbari A, Suzan E, Eisenberg E, Adler T, Vulfsons S, Melamed E, et al. Amputation in patients with complex regional pain syndrome: A comparative study between amputees and nonamputees with intractable disease. *Bone Jt J*. 2016;98B(4):548–54.
11. Kang JE, Kim YC, Lee SC, Kim JH. Relationship between complex regional pain syndrome and working life: a Korean study. *J Korean Med Sci*. 2012;27(8):929–33.
12. Ayyaswamy B, Saeed B, Anand A, Chan L, Shetty V. Quality of life after amputation in patients with advanced complex regional pain syndrome: A systematic review. *EFORT Open Rev*. 2019;4(9):533–40.
13. Gray B. Quality of life following traumatic brachial plexus injury: A questionnaire study. *Int J Orthop Trauma Nurs*. 2016 Aug 1;22:29–35.
14. Bodde MI, Schrier E, Krans HK, Geertzen JHB, Dijkstra PU. Resilience in patients with amputation because of Complex Regional Pain Syndrome type I. *Disabil Rehabil*. 2014;36(10):838–43.
15. GROUP TW. The World Health Organization Quality of Life Assessment (WHOQOL): Position Paper From The World Health Organization. *SocSciMed*. 1995;41(10):1403–9.

16. The ICF: An overview.

17. Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil H. JBI Manual for Evidence Synthesis. JBI. 2020.

18. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. Ann Intern Med. 2018;169(7):467–73.

19. Pollock D, Peters MDJ, Khalil H, McInerney P, Alexander L, Tricco AC, et al. Recommendations for the extraction, analysis, and presentation of results in scoping reviews. JBI Evid Synth. 2023;21(3):520–32.

20. N.a. Appendix 11.1 JBI template source of evidence details, characteristics and results extraction instrument. Available from: <https://jbi-global-wiki.refined.site/space/MANUAL/4687579/Appendix+11.1+JBI+template+source+of+evidence+details%2C+characteristics+and+results+extraction+instrument>

Appendices

Appendix I: Search strategy

Cochrane database: ("Brachial Plexus" OR "Plexus brachial" OR "Complex Regional Pain Syndrome" OR "Complex Regional Pain Syndromes" OR "Reflex Sympathetic Dystrophy" OR "Reflex Sympathetic Dystrophies" OR sudeck* OR "Obstetric plexus lesion" OR "Obstetric plexus lesions" OR "Erbs palsy") AND Amput*

Pubmed: ("Brachial Plexus"[Mesh] OR Brachial Plex*[tiab] OR Plexus brachial*[tiab] OR "Complex Regional Pain Syndromes"[Mesh:NoExp] OR "Reflex Sympathetic Dystrophy"[Mesh] OR crps[tiab] OR Complex Regional Pain Syndrome*[tiab] OR Reflex Sympathetic Dystroph*[tiab] OR sudeck*[tiab] OR Obstetric plexus lesion*[tiab] OR Erbs palsy[tiab]) AND ("Amputation, Surgical"[Mesh] OR amput*[tiab])

EMBASE: ('brachial plexus'/exp OR 'complex regional pain syndrome'/de OR 'complex regional pain syndrome type I'/exp OR ('Brachial Plex*' OR 'Plexus brachial*' OR crps OR 'Complex Regional Pain Syndrome*' OR 'Reflex Sympathetic Dystroph*' OR sudeck* OR 'Obstetric plexus lesion*' OR 'Erbs palsy'):ab,ti,kw) AND ('amputation'/exp OR amput*:ab,ti,kw)

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Ensignment Supérieur (ABES).

Appendix II: Data extraction instrument

#Only append the JBI or non-JBI data extraction instrument if the standardized tool has been modified in any way, otherwise simply cite the tool used in the text. Any modifications made to the instrument should also be described in the text.

We have used the example of a data extraction table from Pollock et al (table 1) as a template, and expanded from there.

Author, year	
Country	
Aim	
Study type/source	
Population (age, inclusion criteria)	
Sample size (total <i>n</i> and per group if applicable)	
Country in which the study has been conducted	
Gender	
Other relevant demographics: level of amputation, side of amputation, years post-amputation, prosthesis use, education, work, co-morbidities	
CRPS or BPI (or both)	
Outcome measures (how did the author measure the outcomes; questionnaires etc)	
Results (statistical evidence, p-values, CI's, effect sizes)	
Strong points of this study	
Weak points of this study	

BMJ Open

Quality of life, functioning and participation of adult patients with an amputation following Complex Regional Pain Syndrome I or Brachial Plexus Injury; A scoping review protocol

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-079393.R1
Article Type:	Protocol
Date Submitted by the Author:	06-Dec-2023
Complete List of Authors:	Domerchie, Patrick; University Medical Centre Groningen, Rehabilitation van Kammen, Klaske; UMCG, Rehabilitation van Wijk, Iris; Revalidation Centre De Hoogstraat, Rehabilitation Lange, Maaik; Revalidation Centre De Hoogstraat, Rehabilitation Van der Sluis, Corry; University of Groningen, University Medical Center Groningen, Rehabilitation Medicine
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Surgery
Keywords:	Chronic Pain, NEUROSURGERY, Elbow & shoulder < ORTHOPAEDIC & TRAUMA SURGERY, Quality of Life, REHABILITATION MEDICINE

SCHOLARONE™
Manuscripts

Quality of life, functioning and participation of adult patients with an amputation following Complex Regional Pain Syndrome I or Brachial Plexus Injury; A scoping review protocol

Authors

Patrick N Domerchie¹, Klaske v Kammen¹, Iris v Wijk^{2,3}, Maaïke Lange², Corry K vd Sluis¹

- 1. University of Groningen, University Medical Center Groningen, Department of Rehabilitation Medicine, Groningen, The Netherlands.
- 2. De Hoogstraat Rehabilitation, Utrecht, The Netherlands
- 3. Center of Excellence for Rehabilitation Medicine, UMC Utrecht Brain Center, University Medical Center Utrecht, and De Hoogstraat Rehabilitation, Utrecht, the Netherlands

Corresponding author: P.N.Domerchie, University of Groningen, University Medical Center Groningen, Department of Rehabilitation Medicine, Groningen, The Netherlands.
email-address: p.n.domerchie@umcg.nl

Abstract

(Maximum - 250 words for Protocols/500 words for Scoping Reviews)

Introduction: This planned scoping review aims to provide insight in current literature regarding perceived quality of life (QoL), functioning and participation of patients with upper limb amputations (ULA) because of therapy-resistant debilitating complex regional pain syndrome type I (CRPS-I) or brachial plexus injury (BPI). It is important to gain insight into these outcomes so we can properly inform and select patients eligible for amputation.

Methods and analysis: Joanna Briggs Institute methodology for scoping reviews, PRISMA-ScR guidelines and Arksey and O'Malley's framework will be used. Studies regarding adult patients with either BPI or CRPS-I who underwent ULA, will be considered for inclusion. Studies should include one or more of the following topics: QoL, functioning or participation and should be written in English, German or Dutch. Searches will be conducted in the Cochrane database, PubMed, EMBASE and Google Scholar. Search strings will be provided by a licenced librarian. All relevant literature will be considered for inclusion, regardless of published date, in order to give a full scope of available literature. Studies will be selected first by title, then abstract and finally by full article by two reviewers who will discuss after

every round. A third reviewer will make final decisions to reach consensus if needed. Data will be presented as brief summaries and in tables using a modified data extraction table.

Ethics and dissemination: No ethical approval is required since no original data will be collected. Results will be disseminated through publication in a peer-reviewed journal and presentations at (inter)national conferences.

Keywords

Quality of Life, functioning, Complex Regional Pain Syndrome Type I, Brachial Plexus Injury, amputation, upper limb

Strengths and limitations of this study:

- The quality of our scoping review will be assured by adhering to the guidelines provided by the Joanna Briggs Institute, Preferred Reporting Items for Systematic Reviews and Meta-Analyses Scoping Reviews (PRISMA-ScR) reporting guidelines and using Arksey and O'Malley's framework.
- Using search algorithms provided by a certified medical librarian will contribute to methodological quality.
- The search algorithms cover three major databases as well as Google Scholar.
- Dutch, German and English articles are considered for this review, meaning that there is a possibility of excluding potentially interesting articles written in different languages
- There are limited studies available concerning amputation after CRPS-I or BPI, and the quality of these studies varies widely.

Introduction

Complex regional pain syndrome type I (CRPS-I) is a pain syndrome with debilitating pain and loss of function in a limb, for which a limited number of treatment options exist.(1–4) Not all patients recover from CRPS-I after treatment and for therapy-resistant cases amputation might be the only remaining treatment option.(5–7) Similarly, some patients with a complete brachial plexus injury (BPI) can experience therapy-resistant severe pain due to traction on the glenohumeral joint or on the neck and upper back because of the flail arm's weight. Another important reason is hindrance of their afunctional arm. Amputation can be considered a last resort treatment for these patients as well.(8,9) To our knowledge, no data regarding incidence of amputation in these patient categories are available.

Since amputation is an irreversible and last resort treatment, it is important to select those patients that will benefit from this treatment, and to properly inform them about the implications of amputation. Can patients expect a higher quality of life (QoL), will their functionality and participation improve? Literature answers some of these questions, but a clear overview of current literature is, to our knowledge, absent.(10–14) To properly inform clinicians who treat patients considering amputation, an overview of current literature is needed, so that they can select and inform patients eligible for amputation better.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

A preliminary search in the Cochrane database, PubMed, EMBASE, Open Science Framework (OSF), The International Prospective Register of Systematic Reviews (PROSPERO) and Google Scholar showed no current or planned reviews (either systematic or scoping) regarding this topic. There is one systematic review by Ayyaswamy et al (2019) discussing QoL after amputation in patients with advanced CRPS-I .(12) A combined scoping review of amputation because of either CRPS-I or BPI has, to our knowledge, not been conducted yet. Furthermore, Ayyaswamy’s review only includes studies up until 2017, and patients with CRPS-I who were diagnosed following the standard diagnostic CRPS-I criteria . Only QoL outcomes that were reported using descriptive analyses and/or standard tools were included.

Our intended scoping review will complement what can be learned from the review of Ayyaswamy et al, as we will look at both quantitative and qualitative reports of QoL, functionality and participation for both CRPS-I and BPI. Furthermore, we will also look at synonyms for CRPS-I (such as Südecks dystrophy). We will consider all articles that mention either BPI or CRPS-I and amputation concerning QoL, functioning and/or participation, regardless of publication date. Finally our goal is not to provide the reader with a summarised set of overarching statistics, but rather an overview of what is currently written about QoL, functioning and participation following amputation due to CRPS-I or BPI.

Our rationale for combining BPI and CRPS-I is that despite the differences in cause and (types of) pain, both diseases share that in some therapy-resistant cases, amputation is considered a last resort treatment and is always performed as an elective surgery. Furthermore, both diseases share a peripheral origin, meaning that (not taking comorbidities into account) both patients with BPI and CRPS-I have a clear view of their life before and after their amputation with regard to QoL, functioning and participation. Finally both CRPS-I and BPI have a great impact on the functionality of an upper limb.

Methods and analysis

The proposed scoping review will be conducted in accordance with the JBI (Joanna Briggs Institute) methodology for scoping reviews and reported as per PRISMA-ScR.(15,16) Furthermore, we will follow the steps as described in Arksey&O'Malley’s framework.(17) Finally we have registered the scoping review on OSF under “Quality of life, functioning and participation of patients with an amputation following Complex Regional Pain Syndrome I or Brachial Plexus Injury; A scoping review” (registration number: <https://doi.org/10.17605/OSF.IO/JMBGK>)

Inclusion criteria

Studies that have included adults with either a BPI (including obstetric BPI) or therapy-resistant CRPS-I who underwent amputation. Patients should be 18 years or older. For CRPS-I specifically, we will also include studies that use (older) synonyms for CRPS-I, such as posttraumatic dystrophy and Südecks dystrophy. All studies that describe either QoL, functioning and/or participation will be considered for inclusion. Studies published in either English, German or Dutch will be included. All published articles that are available at the time of conducting our search will be considered. Since the goal of this scoping review is to provide the reader with a summary of all available studies regarding this topic, we felt no earlier date limit should be set.

Exclusion criteria

Studies about limb amputation due to other diagnoses than CRPS-I or BPI (acquired or by

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Supérieur (ABES)

birth) and studies that do not mention either quality of life, functioning and/or participation after amputation, studies that have no full text in English, German or Dutch will not be taken into account.

Concept

The World Health Organization defines QoL as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns".(18) Indicators that qualify QoL are employment status, mental and emotional health, physical health, education, freedom, recreation and leisure, and the ability to perform activities of daily living (ADL).

The international classification of functioning, disability and health (ICF) defines functioning as: "an umbrella term for body function, body structures, activities and participation. It denotes the positive or neutral aspects of the interaction between a person's health condition(s) and that individual's contextual factors (environmental and personal factors)." (19)

The ICF defines participation as involvement in a life situation.(19)

We will include all studies that discuss or measure (aspects of) the above definitions. This includes, but is not limited to, questionnaires, qualitative studies, experts opinions and case reports, as per Arksey and O'Malley's framework.(17)

Context

All studies will be included if they are written in either English, German or Dutch. Since we are aware that culture and perhaps even geographic location may play a role in perceived QoL and possibilities of participating in society, we will also include articles that are not from 'western countries' as they will provide valuable insight as to what encompasses perceived QoL in these cultures and/or countries.

Types of Sources

This scoping review will consider both experimental and quasi-experimental study designs including randomized controlled trials, non-randomized controlled trials, before and after studies and interrupted time-series studies. In addition, analytical observational studies including prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies will be considered for inclusion. This review will also consider descriptive observational study designs including case series, individual case reports and descriptive cross-sectional studies for inclusion.

Studies that focus on qualitative data will also be considered including, but not limited to, designs such as phenomenology, grounded theory, ethnography, qualitative description, action research and feminist research.

In addition, systematic reviews that meet the inclusion criteria will also be considered, depending on the research question; we will use the relevant original articles from these reviews.

Text and opinion papers will also be considered for inclusion in this scoping review

Search strategy

First a search on PROSPERO and OSF was carried out, which confirmed that no similar or identical reviews are currently being conducted. Subsequently, an initial limited search of the Cochrane database, PubMed, EMBASE and Google Scholar was undertaken to identify

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

articles on the topic. The text words contained in the titles and abstracts of relevant articles, key words and the index terms used to describe the articles were employed to develop a full search strategy in the aforementioned databases [see Appendix 1]. The search strings, including all identified keywords and index terms, will be adapted for each included database and/or information source. The reference list of all included studies will be screened for additional eligible studies.

To assess whether we would be missing valuable articles, we used the search string provided by our certified librarian in Pubmed both with and without exclusively including articles that were written in English, German or Dutch. Including all languages, a total of 590 articles came up (search conducted on the 16th of November 2023). Excluding English, German and Dutch articles, 54 articles came up, none of which have titles or abstracts that seem relevant to the topic of our review.

Study/Source of Evidence selection

Following the search, all identified citations will be collected and uploaded into Mendeley Reference Manager (Elsevier, Mendeley Desktop version v1.19.8). Data will then be transferred to Rayyan for removal of duplicates and to be able to make notes of included articles.(20) Titles and abstracts will then be screened by two independent reviewers for assessment against the review’s inclusion criteria. An initial selection round will be conducted on title screening, followed by a second selection round after thorough reading of the abstract and finally a third selection round will take place after reading the entire article. After every selection round, the two reviewers will discuss any differences in included articles. Reasons for exclusion of studies after full text reading will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion, or with an additional reviewer to reach consensus. The results of the search and the study inclusion process will be reported in full in the final scoping review and presented in a PRISMA-ScR flow diagram.(15)

Data Extraction, Analysis and Presentation

Relevant data from the selected papers will be extracted using a data extraction form we have developed specifically for this scoping review, following the template provided by the Joanna Briggs Institute and the article by Pollock et al [table 1].(20,21) This form has been discussed within the research group before finalization. During the data extraction process conducted by two independent reviewers, this form will be modified and revised if necessary, and modifications will be mentioned in detail in the scoping review. Should disagreements occur between the reviewers regarding any modifications, a third reviewer will be asked to help resolve this and guide the reviewers to consensus. Relevant data will include details regarding type of study, year in which the study has been conducted, country in which the study has been conducted, number of patients included, relevant in- and exclusion criteria, primary and secondary outcome(s), and strong and weak (deemed as such by the reviewers) points of each study. This data will be presented both in a table, and as part of an overview of the articles in plain text. We will report data from CRPS-I and BPI studies separately in the Tables and in the Results section, so that the readers of our manuscript will be able to judge the outcomes of the limb amputations separately for both disorders.

If any relevant data is missing from the article, the reviewers will try to acquire this data by contacting the authors of the papers. As this is a scoping review, with the goal to inform what is currently known in literature, no critical appraisal of individual articles shall be conducted.

Patient and public involvement

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Ensignement Supérieur (ABES) .

217 No patients were involved in making this study protocol, nor will they be involved in making
218 the actual review.

219 Ethics and dissemination

220
221 No ethics approval is required since no original data will be collected. Results will be
222 disseminated through publication in a peer-reviewed journal and presentations will be given
223 at (inter)national conferences.

224 Acknowledgements

225 We would like to thank Karin Sijtsma, medical librarian at the Central Medical Library of the
226 Rijksuniversiteit Groningen and University of Groningen Medical Center for her contributions
227 to our search strategies. Funding

228 For this review no funding or grants were received

229

230 Contributor statement

231 P.D. wrote the manuscript with help from K.K., I.W., M.L. and C.S.
232 P.D., K.K., I.W., M.L. and C.S. all conceived the idea for this review protocol and fabricated
233 the format for the review protocol. K.K., I.W., M.L. and C.S. all supervised the protocol.
234 All authors (P.D., K.K., I.W., M.L. and C.S.) have met the 4 criteria as described in the
235 ICMJE criteria for authorship; all authors have made substantial contributions to the
236 manuscript, have reviewed the manuscript critically for important intellectual content, have
237 given final approval for the upload of the definitive version and all authors state that they are
238 accountable for all aspects of the manuscript

239

240 Conflicts of interest

241 The authors declare that there are no conflicts of interest in this project

242

243 References

- 244 1. Urits I, Shen AH, Jones MR, Viswanath O, Kaye AD. Complex Regional Pain Syndrome, Current
245 Concepts and Treatment Options. Curr Pain Headache Rep. 2018;22(2):1–9.
- 246 2. NVA/VRA.
247 [https://richtlijnendatabase.nl/richtlijn/complex_regionaal_pijn_syndroom_type_1/startpagina](https://richtlijnendatabase.nl/richtlijn/complex_regionaal_pijn_syndroom_type_1/startpagina_-_complex_regionaal_pijnsyndroom.html)
248 [a_-_complex_regionaal_pijnsyndroom.html](https://richtlijnendatabase.nl/richtlijn/complex_regionaal_pijn_syndroom_type_1/startpagina_-_complex_regionaal_pijnsyndroom.html). 2021 [cited 2022 Oct 7]. Richtlijn Complex
249 Regionaal Pijn Syndroom type 1. Available from:
250 [https://richtlijnendatabase.nl/richtlijn/complex_regionaal_pijn_syndroom_type_1/startpagina](https://richtlijnendatabase.nl/richtlijn/complex_regionaal_pijn_syndroom_type_1/startpagina_-_complex_regionaal_pijnsyndroom.html)
251 [a_-_complex_regionaal_pijnsyndroom.html](https://richtlijnendatabase.nl/richtlijn/complex_regionaal_pijn_syndroom_type_1/startpagina_-_complex_regionaal_pijnsyndroom.html)
- 252 3. Royal College of Physicians. Complex regional pain syndrome in adults [Internet]. 2018 [cited
253 2022 Oct 7]. Available from: [https://www.rcplondon.ac.uk/guidelines-policy/complex-](https://www.rcplondon.ac.uk/guidelines-policy/complex-regional-pain-syndrome-adults)
254 [regional-pain-syndrome-adults](https://www.rcplondon.ac.uk/guidelines-policy/complex-regional-pain-syndrome-adults)

- 255 4. Casale R, Atzeni F, Sarzi-Puttini P. The therapeutic approach to complex regional pain
256 syndrome: Light and shade. *Clin Exp Rheumatol*. 2015;33:126–39.
- 257 5. Krans-Schreuder HK, Bodde MI, Schrier E, Dijkstra PU, van den Dungen JA, den Dunnen WF, et
258 al. Amputation for long-standing, therapy-resistant type-I complex regional pain syndrome. *J*
259 *Bone Joint Surg Am*. 2012;94(24):2263–8.
- 260 6. Schrier E, Dijkstra PU, Zeebregts CJ, Wolff AP, Geertzen JHB. Decision making process for
261 amputation in case of therapy resistant complex regional pain syndrome type-I in a Dutch
262 specialist centre. *Med Hypotheses*. 2018;121:15–20.
- 263 7. Bodde MI, Dijkstra PU, den Dunnen WFA, Geertzen JHB. Therapy-resistant complex regional
264 pain syndrome type I: to amputate or not? *J Bone Joint Surg Am*. 2011;93(19):799–805.
- 265 8. Resnik L, Fantini C, Latlief G, Phillips S, Sasson N, Sepulveda E. Use of the DEKA Arm for
266 amputees with brachial plexus injury: A case series. *PLoS One*. 2017 Jun 1;12(6).
- 267 9. Wilkinson' MCP, Birch2 R, Bonney3 G. Brachial plexus injury: when to amputate? *Injury*. 1993.
- 268 10. Midbari A, Suzan E, Eisenberg E, Adler T, Vulfsons S, Melamed E, et al. Amputation in patients
269 with complex regional pain syndrome: A comparative study between amputees and
270 nonamputees with intractable disease. *Bone and Joint Journal*. 2016;98B(4):548–54.
- 271 11. Kang JE, Kim YC, Lee SC, Kim JH. Relationship between complex regional pain syndrome and
272 working life: a Korean study. *J Korean Med Sci*. 2012;27(8):929–33.
- 273 12. Ayyaswamy B, Saeed B, Anand A, Chan L, Shetty V. Quality of life after amputation in patients
274 with advanced complex regional pain syndrome: A systematic review. *EFORT Open Rev*.
275 2019;4(9):533–40.
- 276 13. Gray B. Quality of life following traumatic brachial plexus injury: A questionnaire study. *Int J*
277 *Orthop Trauma Nurs*. 2016 Aug 1;22:29–35.
- 278 14. Bodde MI, Schrier E, Krans HK, Geertzen JHB, Dijkstra PU. Resilience in patients with
279 amputation because of Complex Regional Pain Syndrome type I. *Disabil Rehabil*.
280 2014;36(10):838–43.
- 281 15. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for
282 scoping reviews (PRISMA-ScR): Checklist and explanation. *Ann Intern Med*. 2018;169(7):467–
283 73.
- 284 16. Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil H. JBI. 2020. JBI Manual for
285 Evidence Synthesis.
- 286 17. Arksey H, O'Malley L. Scoping studies: Towards a methodological framework. *International*
287 *Journal of Social Research Methodology: Theory and Practice*. 2005 Feb;8(1):19–32.
- 288 18. The World Health Organization quality of life assessment (WHOQOL): Position paper from the
289 World Health Organization. *Soc Sci Med*. 1995 Nov 1;41(10):1403–9.
- 290 19. The ICF: An overview. The International Classification of Functioning, Disability, and Health :
291 ICF. (2001). Geneva :World Health Organization [Internet]. Available from:
292 https://www.cdc.gov/nchs/data/icd/icfoverview_finalforwho10sept.pdf

20. Pollock D, Peters MDJ, Khalil H, McInerney P, Alexander L, Tricco AC, et al. Recommendations for the extraction, analysis, and presentation of results in scoping reviews. *JBI Evid Synth.* 2023;21(3):520–32.
21. N.a. Appendix 11.1 JBI template source of evidence details, characteristics and results extraction instrument. Available from: <https://jbi-global-wiki.refined.site/space/MANUAL/4687579/Appendix+11.1+JBI+template+source+of+evidence+details%2C+characteristics+and+results+extraction+instrument>

For peer review only

Table 1: Data extraction instrument

Author, year	
Country	
Aim	
Study type/source	
Population (age, inclusion criteria)	
Sample size (total <i>n</i> and per group if applicable)	
Country in which the study has been conducted	
Gender	
Other relevant demographics: level of amputation, side of amputation, years post-amputation, prosthesis use, education, work, co-morbidities	
CRPS or BPI (or both)	
Outcome measures (how did the author measure the outcomes; questionnaires etc)	
Results (statistical evidence, p-values, CI's, effect sizes)	
Strong points of this study	
Weak points of this study	

Appendix I: Search strategy

Cochrane database: ("Brachial Plexus" OR "Plexus brachial" OR "Complex Regional Pain Syndrome" OR "Complex Regional Pain Syndromes" OR "Reflex Sympathetic Dystrophy" OR "Reflex Sympathetic Dystrophies" OR sudeck* OR "Obstetric plexus lesion" OR "Obstetric plexus lesions" OR "Erbs palsy") AND Amput*

Pubmed: ("Brachial Plexus"[Mesh] OR Brachial Plex*[tiab] OR Plexus brachial*[tiab] OR "Complex Regional Pain Syndromes"[Mesh:NoExp] OR "Reflex Sympathetic Dystrophy"[Mesh] OR crps[tiab] OR Complex Regional Pain Syndrome*[tiab] OR Reflex Sympathetic Dystroph*[tiab] OR sudeck*[tiab] OR Obstetric plexus lesion*[tiab] OR Erbs palsy[tiab]) AND ("Amputation, Surgical"[Mesh] OR amput*[tiab])

EMBASE: ('brachial plexus'/exp OR 'complex regional pain syndrome'/de OR 'complex regional pain syndrome type I'/exp OR ('Brachial Plex*' OR 'Plexus brachial*' OR crps OR 'Complex Regional Pain Syndrome*' OR 'Reflex Sympathetic Dystroph*' OR sudeck* OR 'Obstetric plexus lesion*' OR 'Erbs palsy'):ab,ti,kw) AND ('amputation'/exp OR amput*:ab,ti,kw)