COMPACT-C Protocol V1

25th February 2019

A Delphi study to define internationally agreed core clinical outcome measures for Complex Regional Pain Syndrome clinical research studies (COMPACT-C)

Sponsor Name: Royal United Hospitals Bath NHS Foundation Trust

Funder:
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2. Roles and Responsibilities:

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Roles, composition and responsibilities of:

- **Chief Investigator (CI)**
  The CI will oversee the day-to-day running of the project. The CI will lead planning and project management and will organise and lead project management group meetings as required.

- **Study Co-ordinator**
  The Study Co-ordinator will plan and manage the day-to-day running of the project in consultation with the CI. The Study Co-ordinator will be responsible for the data collection, analysis, write up and dissemination of the study. They will also be a member of the project management group. The Study Co-ordinator will be supported by the Study Administrator and members of the study steering group.

- **Study Administrator**
  The Study Administrator will support the CI and Study Co-ordinator with administrative tasks in the day-to-day running of the trial and will be responsible for the screening and input of study data.

- **Study project management group**
  The project management group will consist of all team members (Prof Candy McCabe, Dr Alison Llewellyn, Sharon Grieve, Lisa Buckle, Prof Frank Birklein, Dr Florian Brunner and Dr Andreas Goebel), Professors Norman Harden and Stephen Bruehl from the CRPS International Research Consortium, Robyn Connett, an expert patient representative

from the COMPACT consortium, and Nicole Vaughan-Spickers representing the ALEA team.

All members will be expected to contribute to contribute to the successful delivery of the study and be involved in dissemination of the results.

3. Abbreviations:

CRPS	Complex Regional Pain Syndrome
COMPACT	Core Outcome Measurement set for complex regional PAin syndrome Clinical sTudies
IRC	International Research Consortium
RUH	Royal United Hospitals Bath NHS Foundation Trust
UWE	University of the West of England
IASP	International Association for the Study of Pain
IRC	CRPS International Research Consortium
SIG	Special Interest Group
e-Delphi	Electronic Delphi

Keywords
Complex Regional Pain Syndrome, outcome measures, consensus, Delphi.

4. Rationale & background information:

Complex Regional Pain Syndrome (CRPS) is a chronic pain condition usually affecting a single limb, which manifests in a wide range of sensory, motor, trophic and autonomic abnormalities. In recent years, revised diagnostic and research criteria have been published resulting in improved standardisation across study participants[1]. However, the multidimensional nature of the condition means CRPS clinical trials currently use a diverse range of questionnaire outcome measures[2]. Furthermore, CRPS is categorised as an 'orphan disease' due to the small percentage of the population affected by it (incidence rates range from 5.46 to 26.2 per 100,000 person years[3,4]). This highlights the importance of conducting multi-centre collaborative projects to help achieve sufficient sample sizes for meaningful clinical studies.

Synthesis of clinical trial evidence from a number of different centres has been limited due to the lack of an internationally agreed core set of outcome measurement tools. Historically this has been a significant limiting factor in the advance of our understanding of the mechanisms and management of CRPS. The development of a core measurement set will facilitate the comparison and pooling of data to answer specific research questions agreed

as internationally important and relevant for the advance of the treatment of CRPS. Advocating the use of the core measurement set within all clinical studies would enable these identified research questions to be answered in a timely manner.

A core outcome measurement set can be defined as an agreed, standardised set of outcomes, which should be measured and reported in all clinical studies in a particular condition[5]. In recent years core measurement sets have been increasingly developed in many health conditions in response to the inconsistency of outcome measures used in clinical trials investigating the same disease or condition[6,7]. Previous initiatives have advocated the use of core outcome measurement sets in pain and rheumatology clinical trials; Initiative on Methods Measurement and Pain Assessment in Clinical Trials[8] (IMMPACT) and Outcome Measures in Rheumatology (OMERACT)[9]. This work provided a starting point for the COMPACT collaboration due to a degree of overlap between these disorders and CRPS; a chronic pain condition.

An international consortium was established in 2013, under the auspices of the International Association for the Study of Pain (IASP) CRPS Special Interest Group (SIG) to agree a minimum core set of outcome measures advocated for use in all future CRPS clinical studies. The Core Outcome Measures for complex regional PAin syndrome Clinical Trials consortium (referred to hereafter as the COMPACT consortium) comprises patients, clinicians, researchers and representatives from industry from fifteen countries: Switzerland, Germany, Netherlands, Canada, United States, Denmark, Norway, Israel, Australia, New Zealand, South Africa, Japan, Argentina, Brazil and United Kingdom. Members were recruited from the global CRPS community via email and included those with clinical or research expertise in CRPS from within an academic or clinical setting and/ or an interest in treatment outcome measures. Patient representatives were recruited via support groups and were representative of the UK, Netherlands and Switzerland.

The COMPACT consortium agreed that the unique complexity and multifactorial nature of CRPS necessitates the development of a core measurement set specific to this condition. It must reflect the bio-psychosocial presentation and impact of CRPS and therefore must comprise both patient reported outcome data and clinician observed/collected data.

A series of four workshops were convened over a 21 month period at which consortium members agreed an overarching research question ('What is the clinical presentation and course of CRPS, and what factors influence it?'), and a standardised set of patient reported outcome measures to answer this. In addition, one clinician reported measure captured the degree of severity of CRPS.[10,11] This work, published in 2017[12] was endorsed by the IASP SIG for CRPS and they recommended that the resulting questionnaire set (COMPACT-Q) should be used in all future CRPS clinical studies.

The COMPACT consortium recognised at the outset of their work that a later project would be required to define the clinician observed/collected clinical core data set. For example, objective measures of limb temperature, oedema, immunology screen etc. Throughout 2017 preparatory discussions have been conducted to draw together a draft set of clinical outcomes that can be rationalised via consensus methodologies into a clinical core set. These discussions included a one-day workshop, hosted by Prof Frank Birklein in Mainz, Germany. The Mainz meeting particularly benefited from the input of invited clinical academics whose areas of expertise are not directly focused on CRPS, but are closely aligned to it. These experts (Prof. Hans-Georg Schaible, University of Jena, Germany; Prof. Chris Eccleston, University of Bath, UK; Prof. Rolf-Detlef Treede, University of Mannheim, Germany) provided an external perspective on the work of COMPACT and the future research strategy for the International Research Consortium for CRPS (IRC).

Working in collaboration with the Clinical Informatics Research Unit (CIRU) at the University of Southampton, UK we have identified an appropriate COMPACT electronic data capture system and database called ALEA (provided by FormsVision BV). ALEA is widely used in clinical trials internationally and will facilitate the development of a bespoke COMPACT database for our current patient reported outcome measures and future clinical core set. ALEA is designed to allow clinicians/academics to store and view their own data whilst also contributing to an international dataset. The design and testing of this COMPACT data capture tool and database is currently being conducted as part of a 2 year COMPACT-Q feasibility study, which tests the acceptability and feasibility of collecting and storing COMPACT patient reported outcome data across 8 countries.

5. Study hypothesis and research questions

Overarching hypothesis:

A minimum core set of clinical outcomes (COMPACT-C) can be defined that will complement the current COMPACT-Q core outcome measurement set, and together answer the research question: What is the clinical presentation and course of CRPS, and what factors influence it?

Study research questions to be answered:

1. What are the potentially relevant clinical outcomes for use in CRPS?
2. What is the minimum number of CRPS clinical outcomes that together best address the COMPACT consortium's agreed overarching research question?
3. What additional data fields and instructions need adding to the existing COMPACT-Q electronic data management system (ALEA) to collect and manage

the COMPACT-C clinical data efficiently and effectively across an international population?

6. Study aims & objectives

Aims:

1. To define a core set of clinical outcomes that complement the current COMPACT-Q core set to answer the research question that has been agreed as internationally important and relevant to advance the treatment of Complex Regional Pain Syndrome.
2. To modify the current electronic data management system (ALEA) to ensure clinical data are accurately and safely collected and stored.
3. To encourage the use of this core set of outcomes within all clinical studies so the identified research question is answered in a timely manner.

Objectives:

1. Via a face-to-face workshop and online survey with experts in the field, agree a list of validated clinical outcomes, which could address the COMPACT consortium research question.
2. Using an electronic-Delphi survey[13,14] with members of the IRC and IASP SIG for CRPS define a draft clinical outcome measurement set to address the agreed research question.
3. Via a second face-to-face workshop with members of COMPACT, agree the final core set and consider if any of those outcomes not included in the core set should be included within ALEA as 'optional' for specific research groups/sub-questions.
4. Consider cultural or language barriers to the use of these outcomes and conduct the work required to address these.
5. Develop inclusive and robust communication systems and data collection techniques within ALEA.

7. Methodology

Study design:

An electronic-Delphi study, supported by face-to-face workshops.

Study population:

We recognise the importance of getting a multi-disciplinary perspective on this work. The COMPACT consortium, IRC and the IASP CRPS SIG, all have a multi-disciplinary membership.

Patient and industry representatives are also key members of COMPACT. The population for each stage of the study will be as follows:

- Project Preparation Workshop 1: Clinicians, academics and Industry representatives who are members of the COMPACT consortium.
- Workshop 2: The COMPACT consortium including patient representatives.
- E-Delphi survey: Clinicians and academics who are able to communicate in written English and are members of the IASP SIG for CRPS and/or members of the IRC for CRPS at the time that the invitation to participate in this study is circulated to both organisations.

Sample size:
Delphi surveys can range from quite small sample sizes (n=15-50) up to much larger samples (n>300)[15]. It is common to have some attrition at each stage so that the final number of participants completing all stages of the process is considerably smaller than the total potential sample at the outset. The study team have experience of successfully conducting a Delphi survey in a large study population (n=> 300)[16]. We are aware that within our 'expert' groups of the IASP CRPS SIG (current membership n=270) and IRC (currently n=70) there is some overlap in membership so we anticipate the total potential sample will be < 300 but above the desirable minimum of 50.

Recruitment and consent:
Email notification of the COMPACT-C workshops will be circulated to clinicians and academics within the COMPACT consortium. Prior to recruitment into this study, all participants will have the nature and scope of the study explained to them via the email invitation and/or at the start of each workshop. Consent to participate in the study will be assumed by attendance at the workshops

Potential e-Delphi survey participants will be contacted via a personal email invitation sent by the IASP SIG for CRPS, and the IRC administrator, Debra Nelson-Hogan, to the members of their respective organisations. Permissions have already been agreed by the Chair of the IASP SIG for CRPS (Dr Goebel) and Amy Kirsling (previous administrator) IRC, to use this recruitment approach. We will also approach the chair of the IASP Neuropathic SIG (NeuPSIG) to request that its members are also invited. This method of recruitment has been successfully used in the past by members of the study team. The email invitation will include an overview of the study and a link to access further information and the first round of the e-Delphi survey. This invitation will be circulated again two weeks after the first email in an attempt to optimise recruitment.

The two rounds of the e-Delphi study will be presented to participants as "Survey 1" and "Survey 2" for ease of understanding.

On accessing the Round 1 survey, potential participants will be reminded of the study aims and why they have been invited to take part on the first screen. A link to a private You-Tube video-scribe will be given. The video-scribe will include an explanation of the sequential process of the study and the aims of each round of questionnaires. A full participant information sheet will also be provided via a link on the first page of the electronic survey, and before the respondent decides whether to participate. Providing this type of information to potential participants has been shown to increase commitment to the study and improve response rates in subsequent rounds[17,18]. Consent to participate in the study will be received by the respondent clicking the appropriate option to access the Round 1 survey questions. Respondents who choose not to participate will be asked to explain why and no further data will be captured.

Participants who continue to the Round 1 survey will be asked to proved their email address so they can be contacted directly, without the need to go back through the IASP SIG, IRC or NeuPSIG for the conduct of the subsequent round. Participant email addresses will only be seen by the research team. All data presented within the second round of the e-Delphi survey, and in future publications will be presented in an anonymised manner. The survey rounds will be hosted on the Qualtrics Insight Platform as provided and licensed via the University of the West of England, UK.

A study specific email address will be made available for participants, to address any questions relating to the study.

Method:

Project Preparation Workshop 1

A single workshop will be convened which ideally will run alongside an international meeting (e.g. IASP World Congress 2018, Boston). Email notification of this workshop will be circulated to clinicians and academics within the COMPACT consortium. A representative from ALEA will also be in attendance. This COMPACT-C workshop will review the data arising from the Mainz 2017 meeting and from a literature search, in order to compile a list of validated clinical outcomes that have relevance to the COMPACT research question. The resulting list will comprise the first round of the Delphi survey, that study participants will be invited to consider.

The e-Delphi Survey

The Delphi technique comprises a series of sequential questionnaires (usually 2-3), which are interspersed by controlled feedback that seeks to combine opinion into a group

consensus[15]. Consensus methods are useful for situations where there is incomplete knowledge or a requirement to set an agreed set of priorities.[15,19] A particular strength of a consensus approach is that each participant has an equal say so that no one voice is dominant[15]. As there is no published data on the minimum core set of clinical outcomes for CRPS then this is an appropriate technique to use to explore this topic and to set a priority list. The Delphi Technique has been used successfully before by members of the research team to answer other questions in relation to the care and treatment of those with CRPS.[16, 20]

- e-Delphi Round 1

Participants will be reminded of the overarching COMPACT research question: What is the clinical presentation and course of CRPS, and what factors influence it? They will be asked to review the list of clinical outcomes arising from Workshop 1 and to rate the relevance of each outcome to the research question on a 9-point Likert scale where 1=not relevant and 9 =highly relevant. There will be space beneath each response for free text to be added so participants can justify their selected response or add a comment if they choose.

The responses to this questionnaire will be collated so as to create Round 2.

- e-Delphi Round 2

Those respondents who completed Round 1 will be presented with an individualised questionnaire. This will comprise the full list of outcomes from Round 1; their individual score of relevance for each outcome; and the group median score for each outcome. Any comments added in Round 1 will also be displayed in an anonymised manner. After considering the group median and free-text comments, study participants will be invited to re-rate each outcome.

Those outcomes that have a final group median score of ≥ 7 as agreed by 75% of the study group[15] will be considered the draft 'core clinical outcome measurement set'.

Workshop 2

It is anticipated the second COMPACT-C workshop will coincide with the IASP CRPS SIG meeting scheduled for September 2019 in Valencia, Spain prior to the 2019 EFIC meeting. A representative from the ALEA team will also be invited to ensure the final core clinical set can be appropriately presented and supported on the data management system. The draft core clinical measurement set will be presented to, and discussed by members of the COMPACT consortium to determine the final core set. The rationale for this stage is to consider any practical limitations to the final selected outcomes (financial or time restrictions), and consider which measures should be included in the core set, and which measures should be included within the ALEA data set as 'optional for research purposes'. Where/if problems arise in achieving group consensus within this workshop then Nominal Group techniques,[15,21] such as ranking and voting will be used to achieve the goals of the

workshop. These discussions will be audio recorded to allow post-event validation of confirmation of the core clinical outcomes and optional research outcomes. The final agreed 'core' and 'research optional' outcomes will inform the design and content of the ALEA data collection forms and database.

8. Data Analysis:

All data will be exported from the e-Delphi survey tool (Qualtrics) and entered on to an Excel spreadsheet.

- Round 1: Participants' demographic data will be reported using descriptive statistics.. Free text comments for each item will be collated.
- Round 2: Median scores and level of dispersion (standard deviation and the interquartile range) of each questionnaire item will be calculated[15.] Measures that have a final group median score of ≥ 7 as agreed by 75% of the study group[15] will be identified.

9. Safety considerations

As this is an electronic-Delphi study supported by face-to-face workshops involving Clinicians, academics, industry representatives, and only patients who are members of the COMPACT consortium, the risk to participants is very low.

10. Data collection and management

The Chief Investigator will ensure that the confidentiality of participants taking part in the study (as per General Data Protection Regulation and Data Protection Act 2018). Self-reported questionnaires, non-anonymous data regarding subjects (including identity and contact details) and the study Master File will be physically kept in a digitally locked office on secure premises (at the RUH).

Data generated will be stored on the RUH password protected computer system. The data will be anonymised and managed by the research team. Research data and all appropriate documentation will be stored for a minimum of 5 years after the completion of the study, in accordance with the General Data Protection Regulation and Data Protection Act 2018. Personal identifiable data will be kept for 2 years after the close of the study in order to address any queries that may arise during the dissemination of the work.

11. Project management

Day to day responsibility for the trial will be held by the CI (CM) and the Study Co-ordinator (AL). The overall responsibility for the project will be held by the Chief Investigator (CM). The project management group will convene approximately every 4-6 months via teleconference to review study progress including recruitment, protocol adherence, data quality, milestones, deliverables and budget. These meetings will be chaired by the CI (CM). Monthly research meetings with members of the core research team (the CI, Study Co-ordinator and Study Administrator) will be also be held.

12. Quality assurance

All members of the core research team (the CI, Study Co-ordinator and Study Administrator) will be trained to the appropriate level of Good Clinical Practice (GCP) standards. To ensure the collection of good quality data the following data collection processes will be followed. The collected data will be inputted by the Study Administrator (LB) and double checked by the Study Co-ordinator (AL). A sample of data will be further checked by the CI (CM). The Study Co-ordinator will contact research participants for any missing data. However, to ensure that participants are not overburdened they will be contacted a maximum of three times.

13. Dissemination of results and publication policy

A final report of the study outcomes, in addition to a peer-reviewed publication, will be circulated to members of the IRC and IASP CRPS Special Interest group. Publications arising from this study will have all project management group members as co-authors.
We plan to present at appropriate national and international conferences and will provide links to the findings from our research across the RUH and UWE social media platforms.

14. Duration of the project & time schedule

The project will run for 20 months. We anticipate this will be from the 1st September 2018 until 30th April 2020.
The anticipated time schedule is as follows:

- 1 mth project preparation workshop 1 (Boston, September 2018)
- 2-5 mths Creation of e-Delphi content
- 5-6 mths University ethical approval
- 7-8 mths and recruitment and conduct of Delphi Round 1, analysis of data
- 9-10 mths preparation and conduct of Delphi Round 2
- 11 mths analysis of Round 2 data and preparation of documents for workshop 2
- 12 mths Conduct of workshop 2 (Valencia, September 2019),
- 12-14 mths Preparation of publication and other dissemination activities.

- 15-20 mths Modification of ALEA to accommodate core clinical set and feasibility testing using 'mock data' by applicants. Translation of online/paper data collection tools as required*

* As COMPACT is an international collaborative initiative then data collection and data storage systems need to be accessible to the global community. Where translation is required for use of the clinical core set within ALEA, then this will be undertaken by the research partners within the COMPACT consortium under strict adherence to the 'best practice' translation standards established in a protocol for the CRPS Recovery Study.[16] This uses a forwards and backwards translation approach to ensure the meaning of text is the same across each of the countries. Permissions will be sought for translation as required for any clinical outcome measure included in the core set that may have publication or protocol author restrictions.

15. Ethical and legal considerations

Participation will be voluntary. Consent to participate, and on-going engagement in the study, is via return of completed e-documents at each stage of the Delphi survey and/or attendance at the workshops. It will be made clear in the online study information that research participants may withdraw from the study at any time but data that has already been collected will be included in the study. There will be no requests for any further data when a study participant has asked to withdraw from the study or when no response has been received from the preceding round in the Delphi survey. Where possible, the reason for withdrawal from the study will be elicited and documented.

Prior to commencement of the study, the study protocol and all other relevant documentation will be submitted for approval to the University of the West of England's ethics committee. A record of this approval will be stored within the Master File at the lead site (RUH). The Chief Investigator will be responsible for adhering to research governance and good clinical practice as required locally, including data protection and storage of data.

Permissions for use will be sought as required for any clinical outcome included in the core set that has publication or protocol author restrictions.

The protection of human subjects in research is of great importance. This study will adhere to the principles defined in the declaration of Helsinki 2008.

16. Confidentiality

Personal data collected will be in the form of the names and email addresses of workshop attendees and e-Delphi respondents. A unique study participant identifier will be allocated to participants, linking them to their email address. This information will be stored separately from the study data and will only be accessed by the Bath administrative team for the purposes of conducting the e-Delphi survey. All study data will be stored using the study participants' unique identifier. No participant identifiable data will be shared outside of the Bath administrative team at any time. In Round 2 of the Delphi survey each participant will only see their own Round 1 responses, anonymised free text comments, and the group median score. Direct access to the source data and documents will be permitted for local monitoring, audits, Research Ethics Committees and review.

For the purposes of this study, no patient data will be stored on ALEA. Any work related to ALEA will be in terms of formatting the data collection tools and database design in order to accommodate future data from the core clinical set. Work is being conducted as part of the current COMPACT-Q feasibility study to define and complete the necessary ethical and governance approval processes for the future use of ALEA. It is anticipated that this work will be nearing completion at the same time as the study within this protocol comes to an end. Information gained in this study can then easily be added in to the ALEA ethical and governance approval processes for the whole COMPACT data set (patient reported outcome measurements and clinical data).

After the e-Delphi data set has been closed, the RUH will have access to this and the entire dataset.

17. References

1. Harden RN, Bruehl S, Perez RSGM, Birklein F, Marinus J, Maihofner C, Lubenow T, Buvanendran A, Mackey S, Graciosa J, Mogilevski M, Ramsden C, Chont M and Vatine J-J. Validation of proposed diagnostic criteria (the "Budapest Criteria") for Complex Regional Pain Syndrome. Pain 2010; 150(2): 268-274
2. 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 Pain. 2015; 20(3), 331-340
3. De Mos M, de Brujn AGJ, Huygen FJPM, Dielman JP, Stricker BHC, Sturkenboom MCJM. The incidence of complex regional pain syndrome" a population-based study. Pain 2007; 129(1.2): 12-20.
4. Sandroni P, Benrud-Larson LM, McClelland RL, Low PA, Complex regional pain syndrome type 1: incidence and prevalence in Olmsted county, a population-based study. Pain 2003; 103 (1-2): 199-207

5. Williamson PR, Altman DG, Blazeby JM, Clarke M, Devane D, Gargon E, Tugwell P. Developing core outcome sets for clinical trials issues to consider. Trials 2012;13:132
6. Boers M, Kirwan JR, Wells G, Beaton D, Gossec L, d'Agostino MA, Conaghan PG, Bingham III, C., Brooks P, Landewe R, March L, Simon LS, Singh JA, Strand V,Tugwell P. Developing Core Outcome Measurement Sets for Clinical Trials: OMERACT Filter 2.0. Journal of Clinical Epidemiology 2014; 67(7): 745-53
7. Gargon E, Gurung B, Medley N, Altman DG, Blazeby J M, Clarke M, Williamson PR. Choosing important health outcomes for comparative effectiveness research: a systematic review. PloS One 2014; 9(6): e99111.
8. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, Kerns RD, Stucki G, Allen RR, Bellamy N, Carr DB, Chandler J, Cowan P, Dionne R, Galer BS, Hertz S, Jadad AR, Kramer LD, Manning DC, Martin S, McCormick CG, McDermott MP, McGrath P, Quessy S, Rappaport BA, Robbins W, Robinson JP, Rothman M, Royal MA, Simon L, Stauffer JW, Stein W, Tollett J, Wernicke J, Witter J. Immpact. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 2005; 113(1-2): 9-19
9. Fried BJ, Boers M, Baker PR. A method for achieving consensus on rheumatoid arthritis outcome measures: the OMERACT conference process.J Rheumatol. 1993 Mar;20(3):548-51
10. Harden RN, Bruehl S, Perez RSGM, Birklein F, Marinus J, Maihofner C, Lubenow T, Buvanendran A, Mackey S, Graciosa J, Mogilevski M, Ramsden C, Schlereth T, Chont M and Vatine JJ. Development of a severity score for CRPS. Pain 2010; 151(3): 870-876
11. Harden N, Maihofner C, Abousaad E, Vatine J-J, Kirsling A, Perez R.S.G.M, Kuroda M, Brunner F, Stanton-Hicks M, Mackey S, Birklein F, Schlereth T, Mailis-Gagnon A, Graciosa J, Connoly S.B, Dayanim D, Massey M, Frank H, Livshitz A, Bruehl S. A prospective, multisite, international validation of the Complex Regional Pain Syndrome Severity Score. Pain 2017; 158(8):1430–1436
12. Grieve S, Perez RSGM, Birklein F, Brunner F, Bruehl S, Harden RN, Packham T, Gobeil F, Haigh R, Holly J, Terkelsen A, Davies L, Lewis J, Thomassen I, Connett R, Worth T, Vatine J-J, McCabe CS. Recommendations for a first Core Outcome Measurement set for complex regional PAin syndrome Clinical sTudies (COMPACT). Pain 2017; June 158(6): 1083-109
13. Linstone HA, Turoff M. The Delphi survey: method techniques and applications. Reading: Addison-Wesley; 1975.
14. Avery AJ, Savelyich BSP, Sheikh A, Cantrill J, Morris CJ, Fernando B, et al. Identifying and establishing consensus on the most important safety features of GP computer systems: e-Delphi study. Inform Prim Care. 2005;13:3–11.
15. McMillan SS, King M, Tully MP. How to use the Nominal Group and Delphi techniques. Int J Clin Pharm 2016;38:655–662

16. Llewellyn A & McCabe CS. White P, Hibberd Y, Davies L, Marinus J, Perez RSGM, Thomassen I, Brunner F, Sontheim C, Birklein F, Goebel A, Haigh R, Connett R, Maihöfner C, Knudsen L, Harden N, Zyluk A, Shulman D, Small H, Gobeil F, Moskovitz P. Are you better? A multi-centre study exploring the patients' definition of recovery from Complex Regional Pain Syndrome. Eu. J. Pain 2018;22(3):551-564
17. Buck AJ, Gross M, Hakim S, Weinblatt J. Using the Delphi process to analyse social policy implementation; a post hoc case from vocational rehabilitation. Policy Sciences 1993;26:271-288
18. Whitman N. The committee meeting alternative using the Delphi technique. Journal of Nursing Administration 1990; 20(7):30-37
19. Delbecq AL, van de Ven AH, Gustafson DH. Group techniques for program planning, a guide to nominal group and Delphi processes. Glenview, IL: Scott, Foresman and Company; 1975.
20. Brunner F, Lienhardt FB, Kissling RO, Bachmann LM, Weber U. Diagnostic criteria and follow-up parameters in complex regional pain syndrome type 1-a Delphi survey. Eu. J. of Pain 2008; 12:48-52
21. Jones J, Hunter D. Consensus methods for medical and health services research. BMJ. 1995;311:376–80.