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ORIGINAL ARTICLE

Early versus persistent Complex Regional Pain Syndrome: Is there a difference in patient reported outcomes following rehabilitation?

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Abstract

Background: Expert consensus asserts that early treatment of Complex Regional Pain Syndrome (CRPS) leads to better outcomes. Yet no evidence supports this assumption regarding the recognized gold standard of multidisciplinary functional rehabilitation. To address this, we aimed to establish if there is a difference in outcomes between early CRPS (<1 year symptom duration) and persistent CRPS (= >1 year symptom duration) following rehabilitation and whether any gains are maintained at three months.

Method: Secondary analysis was conducted on previously collected clinical Patient Reported Outcome Measures (PROMS) data from 218 patients attending a residential multidisciplinary rehabilitation programme. Datasets were categorized into early CRPS ($n=40$) or persistent CRPS ($n=178$) dependent on symptom duration. Function, pain, self-efficacy, kinesiophobia and psychological health domains were compared using repeated measures analysis of covariance for a two group design for group difference post rehabilitation and at three month follow-up.

Results: Post-rehabilitation, both groups improved in pain, function, kinesiophobia, psychological health and self-efficacy. At three months, the persistent CRPS group maintained improvements in pain and function. This was not achieved in early CRPS.

Conclusion: This exploratory study is the first to empirically test the assumption that those with early CRPS have better outcomes following rehabilitation. Our clinical data challenges this, as both early and persistent CRPS groups improved following rehabilitation. Findings indicate that rehabilitation benefits those with CRPS, regardless of symptom duration. However, unlike early CRPS, those with persistent CRPS sustain gains at follow-up. Further prospective exploration is warranted.

Significance: Expert consensus recommends early treatment for Complex Regional Pain Syndrome, yet there is little empirical evidence to support this. Our findings are the first to challenge this assumption by revealing no difference in outcomes between early and persistent CRPS post-rehabilitation. However, those

with persistent CRPS maintain gains after three months, unlike people with early CRPS (symptoms < one year). These findings are relevant to clinical practice as they challenge established assumptions, suggesting a focus on improving early CRPS follow-up outcomes.

1 | INTRODUCTION

Complex Regional Pain Syndrome (CRPS) in people presenting with more severe symptoms is difficult to treat (Harden et al., 2006). High pain levels, functional impairment and/or psychological distress are clinical indicators of severity (Bean et al., 2015; Turner-Stokes et al., 2011). In these cases, international clinical guidelines recommend multidisciplinary team (MDT) functional rehabilitation as the gold standard treatment (Béra-Louville et al., 2019; Harden et al., 2013; Perez et al., 2010; Turner-Stokes et al., 2011).

The aim of functional rehabilitation is recovery through improving function and quality of life, reducing pain and promoting self-management (Turner-Stokes et al., 2011). Rehabilitation interventions such as sensory and perceptual re-education, postural control and strategies to increase engagement with the affected limb are commonly delivered in a programme by at least two healthcare professionals, so physiotherapy and occupational therapy play an essential role (Turner-Stokes et al., 2011).

Emerging evidence from clinical and Patient-Reported Outcome Measures (PROMs) suggests that functional rehabilitation is beneficial for CRPS (Elomaa et al., 2019; Kotsougiani-Fischer et al., 2020; Lewis et al., 2019; McCormick et al., 2015; Singh et al., 2004). Functional improvements in lower limb mobility and hand function have been shown (Elomaa et al., 2019; Kotsougiani-Fischer et al., 2020; McCormick et al., 2015). However, findings for pain are mixed as three studies show a reduction in pain intensity (Elomaa et al., 2019; Kotsougiani-Fischer et al., 2020; Lewis et al., 2019) whilst others found no change in pain (McCormick et al., 2015; Singh et al., 2004). Anxiety and depression outcomes are inconsistent as most studies show no change (Elomaa et al., 2019; Kotsougiani-Fischer et al., 2020; Singh et al., 2004). However, McCormick et al. (2015) found improvements in depression and pain-related anxiety.

Existing evidence is limited by relatively modest sample sizes of 89 or less (respectively, Elomaa et al., 2019; Kotsougiani-Fischer et al., 2020; Lewis et al., 2019; McCormick et al., 2015; Singh et al., 2004) therefore limiting the generalizability of findings and highlighting the need for larger scale clinical studies. Whilst post-rehabilitation improvements have been shown, there is little data to establish if improvements are maintained in the longer term. Only Kotsougiani-Fischer et al. (2020) reported pain and hand function improvements at seven-month follow-up.

Expert consensus asserts that early treatment leads to better outcomes (Birklein et al., 2015; Bruehl, 2015; Turner-Stokes et al., 2011; Varenna et al., 2021). Yet, regarding functional rehabilitation, no empirical evidence exists to support this common assumption.

The recent IASP CRPS SIG consensus defined the clinical course of CRPS into *early* CRPS and *persistent* CRPS (Goebel et al., 2021). Although no precise symptom duration is provided for either term by the Valencia consensus group, *persistent* (previously termed chronic) has been described as CRPS of a year and beyond in duration (Bruehl, 2015; Goebel et al., 2021). Therefore, by definition, *early* CRPS (previously termed acute) is up to 12 months.

Our study addresses the question; *do those with early CRPS have better reported outcomes compared to those with persistent CRPS following MDT rehabilitation?*

We hypothesize that:

1. early CRPS has better PROM outcomes compared to persistent CRPS.
2. early and persistent CRPS rehabilitation outcomes are maintained at follow-up.

2 | METHODS

This retrospective clinical study conducts secondary analysis on previously collected Patient Reported Outcome Measures (PROMS). PROMS were routinely gathered between May 2014 and November 2017 from patients attending a residential rehabilitation programme during the clinical course of the national specialist Complex Regional Pain Syndrome (CRPS) service in Bath, UK. At the point of primary data collection, data were anonymized and a unique identifier was allocated to each case. PROMS measures were collected over three time points, T1; prior to the residential rehabilitation programme, T2; immediately following the programme and T3; three months follow-up post programme.

2.1 | Multidisciplinary functional rehabilitation programme

A two-week CRPS-specific residential programme is delivered at the Royal United Hospital, Bath, UK (Royal National Hospital for Rheumatic Diseases, 2016). Patients who are eligible for the programme have;

1. met the Budapest clinical diagnostic criteria for CRPS (Harden et al., 2010), as confirmed by a physical examination from the team's pain specialist Physician.
2. failed local unidisciplinary treatment and hence require MDT rehabilitation in accordance with the UK CRPS treatment guidelines (Turner-Stokes et al., 2011).
3. a clinical need for rehabilitation as identified by the clinicians.

Delivered by Occupational Therapy, Physiotherapy and Psychology professionals with input from Nursing and Pain Medicine, rehabilitation is guided by the functional goals that the patient identifies as important to them. Treatment approaches are selected by the treating team based on the individual's clinical needs. The treating team meet daily to discuss and review patient progress. Patients participate in up to five hours of daily treatment over ten weekdays delivered via a combination of individual and group sessions (Royal National Hospital for Rheumatic Diseases, 2016). As the treatment focus is rehabilitation, pain medication is reviewed prior to admission and the programme does not include interventional pain procedures.

2.1.1 | Outcome measures

PROMS covered different domains comprising function, pain, self-efficacy, Kinesiophobia and psychological health. Specific measures for each domain are as follows:

2.1.1.1 | *Function*

The EuroQol 5D-5L (EQ-5D-5L) (The EuroQol Group, 1990) requires patients to rate five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) between 1: 'no problems' and 5: 'unable to/extreme problems'. Ratings are converted to a utility index based on the EQ-5D-5L value set for England. Higher scores indicate better function.

Lower limb: Walking Ability Questionnaire (WAQ) measures lower limb function (Roorda et al., 2005). It contains 35 statements related to speed and confidence of mobility and the use of a walking aid using 'yes/no' responses with a maximum score of 35. The scale has good intra-test reliability with an intra-test reliability coefficient $p = 0.95$ and good validity (Roorda et al., 2005). Higher scores indicate greater lower limb function.

Upper limb: Quick Disability of Arm, Shoulder and Hand (Quick-DASH) (Beaton et al., 2005) measures upper limb disability. Patients rate their upper limb symptom severity and ability to perform a range of functional activities in the past week. The measure demonstrates excellent internal consistency (Cronbach's $\alpha = 0.92$) and good construct validity (Beaton et al., 2005). Higher scores indicate greater upper limb disability.

2.1.1.2 | *Pain*

The Short-Form McGill Pain Questionnaire-2 (SF-MPQ-2) consists of 22 statements evaluating neuropathic and non-neuropathic pain in the previous week (Dworkin et al., 2009). Excellent reliability and validity have been shown in chronic pain syndromes (Dworkin et al., 2009), with emerging evidence in CRPS (Packham et al., 2019). A higher score denotes more severe pain.

The Brief Pain Inventory-Short Form (BPI) (Cleeland & Ryan, 1991) measures pain severity and pain interference via two subscales. Pain intensity is rated on an 11-point scale for at least and at worst over the past 24 h, along with average and current pain. For the pain interference subscale, patients rate between 0 = 'does not interfere' and 10 = 'completely interferes' the extent to which their pain has interfered with each of seven daily activity items (general activity, mood, walking ability, normal work, relationships, sleep and enjoyment of life) during the past 24 h. A higher score indicates increased severity and/or interference. Psychometric properties have been widely reported in a range of clinical populations, and the scale has good test-retest reliability (Cronbach's $\alpha = > 0.7$) and validity (Cleeland & Ryan, 1991).

2.1.1.3 | *Self-efficacy*

The Pain Self-Efficacy Questionnaire (PSEQ) (Nicholas, 2007) comprises 10 items measuring pain self-efficacy. Patients rate how confident they are in performing 10 different activities despite experiencing pain. Items are rated on a scale of 0 = 'not at all confident' to 6 = 'completely confident'. The scale has high internal consistency (Cronbach's $\alpha = 0.92$), test–retest reliability and validity (Nicholas, 2007). An overall higher score indicates greater pain self-efficacy.

2.1.1.4 | *Kinesiophobia*

The Tampa Scale for Kinesiophobia (TSK-11) measures fear of movement (Woby et al., 2005). Eleven items about fear of movement and re-injury are rated on a 4-point scale, ranging from 1 = 'Strongly disagree' to 4 = 'Strongly agree'. The TSK-11 demonstrates good internal consistency

(Cronbach's $\alpha = 0.79$), test-retest reliability and concurrent and predictive validity (Woby et al., 2005). Higher scores indicate increased kinesiophobia.

2.1.1.5 | *Psychological health*

Depression: The Patient Health Questionnaire (PHQ-9) measures depression via nine items (Kroenke et al., 2001). Each item is rated over the previous 2 weeks on a 4-point scale ranging from 0 = 'not at all' to 3 = 'nearly every day. The PHQ-9 has high internal consistency (Cronbach's $\alpha = 0.86$) and has excellent test–retest reliability and high construct validity (Kroenke et al., 2001). Higher scores indicate increased depression.

Anxiety: The Generalized Anxiety Disorder-7 (GAD-7) (Spitzer et al., 2006) measures generalized anxiety. The measure comprises seven items that reflect the DSM-IV criteria for GAD. Patients rate whether they have been bothered by any of the seven items, such as feeling nervous, anxious or on edge, over the previous two weeks. The GAD has excellent internal consistency (Cronbach's $\alpha = 0.92$) and good test–retest reliability and construct validity (Spitzer et al., 2006). Higher scores denote greater anxiety.

2.2 | Ethics

At the time of primary data collection, all patients had given written consent for their anonymized data to be included on the ethically approved PROMS database (Bath Research Ethics Committee reference number 05/Q2001/320). For the purposes of this secondary data analysis study, additional ethical approval was granted by University of the West of England (UWE), Bristol (reference number HAS.21.01.078).

2.2.1 | Statistical analyses

Datasets were divided into two groups;

(i) Early CRPS comprised datasets with a recorded symptom duration of under one year at T1.
(ii) Persistent CRPS those datasets with symptom duration recorded as one year or more at T1.

It is important to note that within the original PROMS questionnaire format only three tick box options (less than 1 year; 1–2 years; more than 2 years) were provided for patients to report symptom duration, therefore no data were available to calculate symptom duration means and standard deviations for each group.

In order to effectively manage missing data, we applied endpoint analysis if less than 10% of the dataset values were missing (Dong & Peng, 2013).

Descriptive statistics were used to calculate demographic characteristics for the two groups. Mean values and standard deviations (*SD*) were calculated to describe the age and pain intensity of the groups. Gender, reported inciting incident and affected body part were summed per group and are presented as percentages.

2.2.2 | Within group comparisons

Within each group means and *SD*s were calculated for each measure at three timepoints; T1 (prior to the residential rehabilitation programme), T2 (immediately following the programme) and T3 (three months follow-up post programme). Group pre-post programme mean change scores were calculated by subtracting T2 from T1 means. Change at follow-up was calculated by subtracting T3 from T1 means for each group. Paired sample *t*-tests were used to determine statistical significance in pre-post programme changes (T1–T2) and pre to follow-up changes (T1–T3) for each group. Effect sizes were calculated using Cohen's *d* (Cohen, 1988). Effect sizes are represented, respectively, as small ($d = 0.2$), medium ($d = 0.5$) and large ($d = 0.8$).

2.2.3 | Between group comparisons

To test our hypotheses that (1) early CRPS has better PROM outcomes compared to persistent CRPS, and (2) early and persistent CRPS rehabilitation outcomes are maintained at three-month follow-up, repeated measures analysis of co-variance (ANCOVA) was applied for each hypothesis. The advantage of using this test is that it can control for differences at baseline and is valid with unequal sample sizes which makes it highly suitable for this previously collected clinical dataset (Koepsell et al., 1991; Krueger & Tian, 2004). For hypothesis (1) ANCOVA compares the two groups at T2 controlling for T1; for hypothesis (2) ANCOVA compares groups at T3 controlling for T1, that is whether the two groups differ at T2 or T3 after controlling for baseline. Results found to be significant are presented graphically.

Tests of normality of the distribution and homogeneity of variance between groups were applied.

Statistical significance levels were set at $p = 0.05$. Confidence intervals were calculated at 95%. All analyses were undertaken using IBM SPSS Statistics v.28 (IBM corp.).

3 | RESULTS

Datasets from 218 patients who attended the Bath CRPS rehabilitation programme were categorized into early CRPS ($n=40$) or persistent CRPS ($n=178$) dependent on symptom duration. Table 1 presents patient characteristics for each group.

Early CRPS PROMs outcomes for pre-post rehabilitation (T1–T2) and pre-follow-up (T1–T3) are presented in Table 2a,b, respectively.

Results at post programme for the early CRPS group show a significant improvement in function and anxiety with small effect sizes and pain, kinesiophobia, depression and self-efficacy with medium effect sizes.

Follow-up results demonstrate improvements are sustained in kinesiophobia and self-efficacy with medium effect sizes. No evidence of differences at baseline other than self-efficacy ($p=0.04$) were found between those early CRPS patients that completed measures at T3 and those that did not (see Table S1).

Persistent CRPS PROMs outcomes for pre-post rehabilitation (T1–T2) and pre-follow-up (T1–T3) are presented in Table 3a,b, respectively.

Post programme results for the persistent CRPS group show a significant improvement in function with small effect sizes and pain, kinesiophobia, anxiety, depression and self-efficacy with medium effect sizes.

Follow-up results reveal that improvements in pain, upper limb function, self-efficacy, kinesiophobia, depression and anxiety are maintained with small effect sizes.

A comparison between the early and persistent CRPS groups at pre and post programme (T1, T2) is presented in Table 4.

Assumptions of normality and homogeneity were met. Results show no significant differences pre-post programme between the early and persistent CRPS groups.

A comparison between the early and persistent CRPS groups at pre-programme to follow-up (T1, T3) is presented in Table 5.

Assumptions of normality and homogeneity were met. Results show a significant difference between the early and persistent CRPS groups at follow-up for pain ($p=0.006$) (see Figure 1a), lower limb function (WAQ) ($p=0.026$), (see Figure 1b) and upper limb function (QDash) ($p=0.007$) (see Figure 1c). ANCOVA results indicate a significant effect on anxiety ($p=0.036$), but it should be noted that the two groups were different at baseline; therefore, less reliance can be placed on this result.

Figure 1a illustrates that for pain, significance is in the opposite direction indicating that whilst the persistent group have improved at three months, pain has worsened in the early CRPS group.

Figure 1b illustrates that for lower limb mobility the persistent group maintain baseline function whilst the early group deteriorate at follow-up.

Figure 1c shows that improvements- in upper limb function are maintained for the persistent group and worsen for the early group at follow-up.

There is no significant difference at baseline ($p=0.24$) between the early and persistent groups that completed T3 providing evidence that they are from the same population (see Table S2).

In summary, these results reveal that at three-month follow-up, the persistent CRPS group show significant improvements in pain and upper limb function that are sustained when compared to the early CRPS group.

4 | DISCUSSION AND CONCLUSION

This is the first study to empirically test the assumption that those with early CRPS have better rehabilitation outcomes compared to persistent CRPS. Our findings provide valuable results that are contrary to what would be expected with regard to this important clinical question.

We aimed to establish whether there is a difference in outcomes between early CRPS and persistent

TABLE 1 Comparison of patient characteristics by group.

	Early CRPS $n=40$	Persistent CRPS $n=183$	Test of significance (independent samples *t*-test)
Age	45.9 (*SD* 13.66)	46.17 (*SD* 12.60)	0.884
Gender (Male/Female)	35 (87.5%)	123 (67.2%)	0.011*
Body part affected	13 Lower limb 17 Upper limb Both 10	49 Lower limb 95 Upper limb Both 39	0.333
Pain intensity baseline (SFMPQ-2)	5.70 (*SD* 2.12)	6.24 (*SD* 2.03)	0.138

Note: Age and pain intensity analysed using independent samples *t*-test; Body Part and Gender analysed using chi-square test of association.

*$p<0.05$.

TABLE 2 Early CRPS PROMS outcomes pre, post programme and follow-up.

(a) Early CRPS PROMS pre-post programme (T1–T2) comparisons and effect size (Cohen's *d*)				
Domain **/ measure**	**Pre-programme T1 *n* = 40 mean (*SD*)**	**Post-programme T2 *n* = 40 mean (*SD*)**	**Pre-post programme change T2–T1 mean (*SD*)**	**Effect size**
Pain				
BPI	6.56 (2.02)	5.81 (1.92)	−0.75 (1.32)*	0.57
SFMPQ-2	5.59 (2.17)	5.31 (2.25)	−0.28 (1.24)	0.23
Self efficacy				
PSEQ	18.44 (10.35)	25.97 (10.80)	7.53 (10.85)**	−0.69
Function				
EQ-5D-5L	0.22 (0.27)	0.34 (0.28)	0.12 (0.24)*	−0.50
WAQ	22.22 (12.82)	22.2 (12.74)	0.00 (1.61)	0.00
QDASH	65.40 (22.76)	64.92 (18.80)	−0.48 (10.77)	0.05
Kinesiophobia				
TSK	28.44 (6.91)	24.63 (5.85)	−3.81 (3.87)**	0.99
Psychological health				
PHQ-9	14.73 (6.11)	11.49 (6.28)	−3.24 (5.41)**	0.60
GAD-7	11.05 (5.04)	9.30 (5.62)	−1.75 (4.93)*	0.36
(b) Early CRPS PROMS pre-programme to follow-up (T1–T3) comparisons and effect size (Cohen's *d*)				
Domain **measure**	**Pre-programme T1 *n* = 18 mean (*SD*)**	**Follow-up T3 *n* = 18 mean (*SD*)**	**Follow-up change T3–T1 mean (*SD*)**	**Effect size**
Pain				
BPI	6.86 (2.00)	7.33 (1.57)	0.47 (1.37)	−0.34
SFMPQ-2	5.84 (2.05)	6.00 (2.30)	0.16 (1.33)	−0.12
Self efficacy				
PSEQ	14.47 (9.40)	20.37 (12.56)	5.90 (8.05)*	−0.73
Function				
EQ-5D-5L	0.16 (0.26)	0.20 (0.27)	0.04 (0.21)	−0.22
WAQ (*n* = 9)	21.44 (13.75)	19.78 (14.61)	−1.66 (5.27)	0.32
QDASH (*n* = 13)	65.33 (23.22)	69.93 (22.10)	4.6 (17.27)	−0.27
Kinesiophobia				
TSK	28.47 (6.71)	24.60 (6.40)	−3.87 (5.21)*	0.74
Psychological health				
PHQ-9	14.28 (5.94)	13.67 (7.22)	−0.61 (4.00)	0.15
GAD-7	10.11 (5.28)	10.05 (6.45)	−0.06 (3.00)	0.02

Note: Significant difference (paired samples *t*-test).

*$p < 0.05$; **$p < 0.001$.

CRPS following rehabilitation and whether any improvements gained are maintained at three months. Our findings did not support the hypothesis that those with early CRPS have better rehabilitation outcomes compared to persistent CRPS. In fact, results showed that there are improvements for both early and persistent CRPS groups following rehabilitation, suggesting that those with persistent CRPS do equally well. Therefore, rehabilitation benefits those with CRPS regardless of symptom duration. On this basis our findings challenge the long-held assumption that treating CRPS early results in better clinical outcomes.

For both groups following rehabilitation improvements were made in function, pain kinesiophobia, psychological health and self-efficacy.

Notably, at three-month follow-up, the persistent CRPS group maintained improvements in function and pain,

TABLE 3 Persistent CRPS PROMS outcomes pre, post programme and follow-up.

(a) Persistent CRPS PROMS pre-post programme (T1–T2) comparisons and effect size (Cohen's *d*)				
Domain measure	**Pre-programme T1 (*n* = 178) mean (*SD*)**	**Post-programme T2 (*n* = 178) mean (*SD*)**	**Pre-post programme change T2–T1 mean (*SD*)**	**Effect size**
Pain				
BPI	6.80 (1.67)	6.05 (2.00)	−0.75 (1.64)**	0.45
SFMPQ-2	6.23 (2.05)	5.70 (2.19)	−0.53 (1.60)**	0.34
Self-efficacy				
PSEQ	20.19 (12.04)	26.93 (12.63)	6.74 (10.08)**	−0.67
Function				
EQ-5D-5L	0.24 (0.28)	0.32 (0.30)	0.08 (0.27)**	−0.31
WAQ	24.09 (10.53)	23.04 (11.23)	−1.05 (5.14)	0.20
QDASH	70.00 (18.04)	63.21 (17.64)	−6.79 (14.59)**	0.46
Kinesiophobia				
TSK	27.92 (6.29)	24.18 (5.86)	−3.74 (5.83)**	0.64
Psychological health				
PHQ-9	14.81 (7.08)	11.20 (6.06)	−3.61 (5.89)**	0.61
GAD-7	11.46 (6.14)	8.67 (5.48)	−2.79 (5.33)**	0.52
(b) Persistent CRPS PROMS pre-programme to follow-up (T1–T3) comparisons and effect size (Cohen's *d*)				
Domain measure	**Pre-programme T1 (*n* = 75) mean (*SD*)**	**Follow-up T3 (*n* = 75) mean (*SD*)**	**Follow-up change T3–T1 mean (*SD*)**	**Effect size**
Pain				
BPI	6.77 (1.71)	6.14 (2.51)	−0.63 (1.67)*	0.37
SFMPQ-2	6.34 (2.04)	5.76 (2.57)	−0.58 (1.79)*	0.34
Self-efficacy				
PSEQ	22.27 (11.87)	25.79 (15.61)	3.52 (10.05)*	−0.35
Function				
EQ-5D-5L	0.28 (0.28)	0.30 (0.33)	0.02 (0.24)	−0.08
WAQ	25.95 (8.86)	25.92 (8.23)	−0.03 (5.63)	0.01
QDASH	67.55 (19.64)	61.78 (24.52)	−5.77 (12.31)*	0.47
Kinesiophobia				
TSK	29.00 (6.32)	26.51 (7.34)	−2.49 (5.07)**	0.49
Psychological health				
PHQ-9	14.59 (6.85)	13.16 (7.55)	−1.43 (5.16)*	0.28
GAD-7	11.51 (5.91)	9.73 (6.24)	−1.78 (3.60)**	0.50

Note: Significant difference (paired samples *t*-test).

*$p < 0.05$; **$p < 0.001$.

demonstrating that gains were sustained in the medium term. This was not achieved in early CRPS.

In the following discussion, we place these findings within the context of current literature and explore potential reasons why these differences between early and persistent CRPS are observed.

This pragmatic study involves the largest clinical population of people with CRPS of its type to be conducted to date. With a cohort of 218 it is over double the sample size of the previous largest study (Kotsougiani-Fischer et al., 2020.

Post rehabilitation functional improvements across both groups support those previously found by McCormick et al. (2015), Elomaa et al. (2019) and Kotsougiani-Fischer et al. (2020).

Improvements in anxiety and depression following rehabilitation across groups are consistent with McCormick et al. (2015) but have not been found in the

TABLE 4 Early versus persistent CRPS: Group comparison pre and post programme (T1, T2) with *p*-value for between groups ANCOVA contrast.

	Early ($n=40$) mean (*SD*)		Persistent ($n=178$) mean (*SD*)		*p*-Value
Domain	**T1 pre**	**T2 post**	**T1 pre**	**T2 post**	
Pain					
BPI	6.56 (2.02)	5.81 (1.92)	6.79 (1.67)	6.14 (2.51)	0.881
SFMPQ-2	5.59 (2.17)	5.31 (2.25)	6.23 (2.05)	5.70 (2.19)	0.506
Self-efficacy					
PSEQ	18.44 (9.40)	25.97 (10.80)	20.19 (12.04)	26.93 (12.63)	0.259
Function					
EQ-5D-5L	0.22 (0.27)	0.34 (0.28)	0.24 (0.28)	0.32 (0.30)	0.707
WAQ	22.22 (12.82)	22.22 (12.74)	24.09 (10.53)	23.04 (11.23)	0.973
QDASH	65.40 (22.76)	64.92 (18.80)	69.89 (18.04)	63.21 (17.64)	0.963
Kinesiophobia					
TSK	28.44 (6.91)	24.63 (5.85)	27.92 (6.29)	24.18 (5.86)	0.176
Psychological health					
PHQ-9	14.73 (6.11)	11.49 (6.28)	14.81 (7.08)	11.20 (6.06)	0.797
GAD-7	11.05 (5.04)	9.30 (5.61)	11.46 (6.14)	8.67 (5.48)	0.876

Note: Some means differ from Table 2 due to a small difference in the numbers of cases in each analysis.

TABLE 5 Early versus persistent CRPS: Group comparison pre-programme and follow up (T1, T3) with *p*-value for between groups ANCOVA contrast.

	Early ($n=18$) mean (*SD*)		Persistent ($n=75$) mean (*SD*)		
Domain	**T1**	**T3**	**T1**	**T3**	**ANCOVA *p*-value**
Pain					
BPI	6.86 (2.00)	7.33 (1.57)	6.77 (1.72)	6.14 (2.51)	**0.006***
SFMPQ-2	5.84 (2.05)	6.00 (2.30)	6.34 (2.04)	5.76 (2.57)	0.628
Self-efficacy					
PSEQ	14.47 (9.40)	20.37 (12.56)	22.27 (11.87)	25.79 (15.61)	0.624
Function					
EQ-5D-5L	0.16 (0.26)	0.20 (0.27)	0.28 (0.28)	0.30 (0.33)	0.781
WAQ	21.44 (13.75)	19.78 (14.61)	25.95 (8.86)	25.92 (8.23)	**0.026***
QDASH	65.33 (23.22)	69.93 (22.10)	67.55 (19.64)	61.78 (24.51)	**0.007***
Kinesiophobia					
TSK	28.47 (6.71)	24.60 (6.40)	29.00 (6.32)	26.51 (7.34)	0.517
Psychological health					
PHQ-9	14.28 (5.94)	13.67 (7.22)	14.59 (6.85)	13.16 (7.55)	0.538
GAD-7	10.11 (5.28)	10.05 (6.45)	11.51 (5.91)	9.73 (6.24)	**0.036***

Note: Some means differ from Table 2 due to a small difference in the numbers of cases in each analysis.

*Significance $p \leq 0.05$.

majority of studies (Elomaa et al., 2019; Kotsougiani-Fischer et al., 2020; Singh et al., 2004). This could be due to a combination of factors related to the duration, content and format of rehabilitation, as both ours and McCormick et al.'s (2015) rehabilitation programmes involve five disciplines compared to fewer disciplines in the other studies (Elomaa et al., 2019; Kotsougiani-Fischer et al., 2020; Singh et al., 2004).

Pain changes are in line with Lewis et al. (2019), Elomaa et al. (2019) and Kotsougiani-Fischer et al. (2020). These studies were in clinical samples with a broad disease duration ranging from 7 months to 3.4 years. Conversely, our

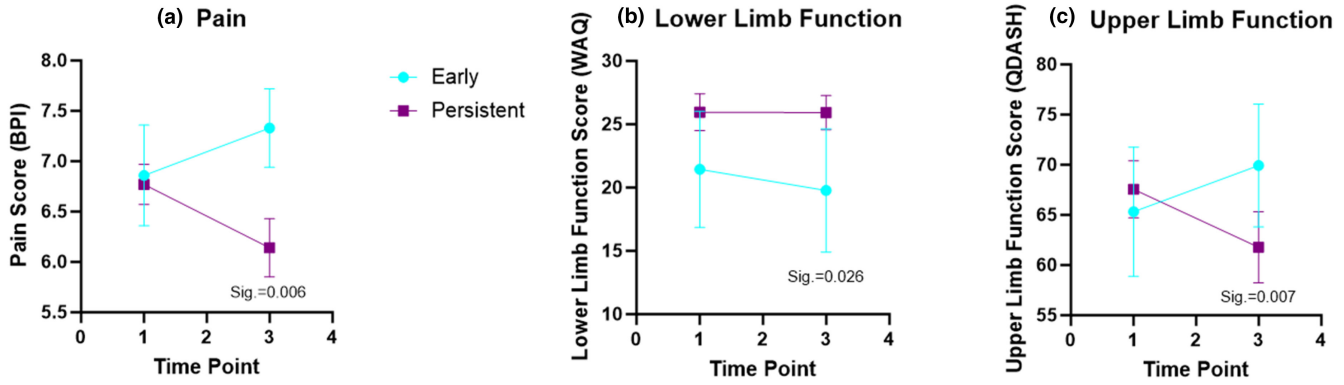

FIGURE 1 (a–c) Significant T1, T3 between group results.

pain findings were not consistent with Singh et al. (2004) and McCormick et al. (2015). Their results were only in persistent CRPS (mean duration range 1.7–3 years). Sample sizes were considerably smaller than ours which may well account for the difference in findings.

Of note is that the early CRPS group showed no pain reduction at follow-up after rehabilitation. One explanation is that those with persistent CRPS are more likely to have developed secondary myofascial pain due to altered use of the affected limb (Bruehl, 2015) and consequent postural maladaptation over time. This presentation is more rapidly responsive to rehabilitation methods such as postural correction and hydrotherapy as delivered by our programme, which typically results in more sustained pain reduction, as observed in our findings.

Interestingly, there was no significant improvement in lower limb function at follow-up for either group, which is contrary to that found in other studies (Elomaa et al., 2019; McCormick et al., 2015).

In terms of PROM outcomes over a year, Bean et al. (2015, 2016) conducted a prospective study reviewing 56 patients 12 months after symptom onset and found improved pain, depression and anxiety compared to baseline. These patients received various treatments, including occupational therapy and physiotherapy (98%), although only a minority (21%) participated in multidisciplinary pain management over the year, and unlike our findings, a comparison between those with more persistent CRPS was not undertaken.

At three months, findings revealed a clear difference between persistent CRPS where gains in function and pain were maintained compared to early CRPS where this was not achieved. It is vital for clinical practice that reasons for a lack of maintenance in those with early CRPS should be explored.

We speculate that psychological factors play a large part in the differences observed between early and persistent CRPS. Those with early CRPS may not have come to terms with living with the condition. Our clinical experience is that patients early in the disease course often continue to seek a pathophysiological cause for their pain so that it can be 'fixed' with the hope of 'curing' CRPS. This search for a cause is expressed in qualitative interviews by those with persistent CRPS from New Zealand (Antunovich et al., 2021). Rodham et al. (2013) identified this stage as 'ambivalence' given the conflict between acceptance of having CRPS and battling against it. Accepting the condition was considered an important factor by those with persistent CRPS in regaining control over and successfully self-managing the condition although it was acknowledged that this was hard to accomplish (Antunovich et al., 2021; Rodham et al., 2013).

Once home, issues arise with expectations from the family as patients express that they lack understanding about the condition and struggle to provide support. Without this support, the motivation to continue rehabilitation exercises at home is likely to decline, which is a further explanation for why improvements are not maintained in early CRPS (Rodham et al., 2013).

4.1 | Clinical implications

Our findings show that people with persistent CRPS considered to be resistant to traditional pain treatments, benefit from functional rehabilitation as much as those with early CRPS and maintain these gains. Therefore, rehabilitation benefits those with CRPS regardless of symptom duration.

However, there are clinical implications for rehabilitation given that those with early CRPS did not maintain functional improvements at follow-up. Identifying those with early CRPS and tailoring treatment to enhance their knowledge about the pathophysiological processes and impact of CRPS will help in their understanding and make seeking an explanation for their condition more straightforward (Antunovich et al., 2021; Rodham et al., 2013). Further emphasis on setback planning and family education to prepare those with early CRPS to better self-manage at home would be beneficial.

4.2 | Limitations

This is a pragmatic study conducting secondary analysis on primary clinical data previously collected as part of routine clinical practice. It is important to note that this cohort is not representative of the CRPS population as a whole, as only those with more severe CRPS that necessitated multidisciplinary rehabilitation participated in the programme and were therefore part of this dataset.

We recognize that the early CRPS sample at follow-up is small. Early CRPS dataset dropout rates (55%) at three-month follow-up was slightly higher than previous studies of a similar type (46%, Kotsougiani-Fischer et al. (2020). Despite using analyses that account for unequal sample size comparisons, there is still a possible risk of bias. It is acknowledged that absence of evidence is not evidence of absence, particularly when arising from smaller sample sizes. This highlights the need for this exploratory work to be replicated in prospective clinical studies with larger samples of early onset CRPS to establish whether our findings can be substantiated.

A smaller number of early CRPS patients within our dataset is consistent with expectations given the two-year average time frame from symptom onset to receiving specialist CRPS rehabilitation (Shenker et al., 2015).

A further limitation of this clinical dataset was that accurate recording of symptom duration had not been previously collected; therefore, it was not possible to calculate the means and range of symptom duration for each group. The collection of more detailed symptom duration data within future clinical datasets is recommended.

Randomized control trials of MDT rehabilitation in CRPS would be classed as higher quality evidence yet there are ethical considerations with regard to the possible content of the control intervention as this has the potential to deny patients of the gold standard recommended treatment.

4.3 | Future research

Our findings provide sufficient evidence to support further research in a larger early CRPS sample to establish whether rehabilitation outcomes are sustained at follow-up. A multimodal approach of combining objective clinical measures with PROMs would add strength and depth to future studies. Exploration of barriers and facilitators to sustaining improvements made during rehabilitation by those with early onset CRPS and ways to enhance changes in the long term would inform advances in treatment. Results would help to inform future clinical service provision and international clinical guidance recommendations.

5 | CONCLUSION

In summary, our study reports on the largest clinical dataset of its kind and the first to test the assumption that those with early CRPS have better outcomes following rehabilitation. Data from this study suggests that this assumption is wrong as those with persistent CRPS do equally well following rehabilitation and sustain these gains at follow-up unlike those with early CRPS. Given the limitations of this retrospective pragmatic clinical study, this assumption warrants further exploration in future prospective clinical studies. Furthermore, investigating the barriers and facilitators to sustaining rehabilitation improvements in early CRPS are essential for clinical practice so that patient outcomes can be improved.

AUTHOR CONTRIBUTIONS

All authors discussed the results and commented on the manuscript.

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CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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