Pain Medicine, 2025, **26**, 180–188
https://doi.org/10.1093/pm/pnae126
Advance access publication 12 December 2024
Original Research Article

OXFORD

NEUROPATHIC PAIN SECTION

The efficacy of an interdisciplinary pain management program for complex regional pain syndrome compared to low back pain and chronic widespread pain: an observational study

Debbie J. Bean, PhD*[,1], Natalie L. Tuck, PhD[2], Nico Magni, PhD[2], Tipu Aamir, MBBS[3], Catherine Pollard, MHlthPrac[3], Gwyn N. Lewis, PhD[2]

[1]The Centre for Person Centred Research, Auckland University of Technology, Auckland 0627, New Zealand
[2]The Health and Rehabilitation Research Institute, Auckland University of Technology, Auckland 0627, New Zealand
[3]The Auckland Regional Pain Service, Te Toka Tumai, Te Whatu Ora 1010, New Zealand

*Corresponding author: The Centre for Person Centred Research, Auckland University of Technology, 90 Akoranga Drive, Northcote, Auckland 0627, New Zealand. Email: Debbie.bean@aut.ac.nz

Abstract

Background: Little research has assessed the efficacy of interdisciplinary pain management programs (IPMPs) for complex regional pain syndrome (CRPS), whereas evidence shows that IPMPs are effective for low back pain (LBP) and chronic widespread pain (CWP). This study aimed to determine whether outcomes following an IPMP differ for people with CRPS compared to LBP and CWP. In addition, we determined whether it is possible to predict IPMP outcomes using baseline characteristics.

Methods: People with CRPS ($N = 66$) who had completed a 3-week IPMP were compared with age- and gender- matched controls with LBP ($N = 66$) and CWP ($N = 66$). Measures of pain intensity, pain interference and psychological factors were extracted for pre- and post-program, and at 1, 6, and 12 months. Latent class analysis identified recovery trajectories for pain intensity and pain interference, and χ^2 analyses assessed differences between diagnostic groups in recovery trajectories. Machine learning models were implemented to predict recovery trajectories from baseline scores.

Results: Two recovery trajectories for each dependent variable (pain interference and for pain intensity) were identified: Good responders and poorer responders. Following IPMPs, 37% of people belonged to a good responder recovery trajectory for pain interference, and 11% belonged to a good responder recovery trajectory for pain intensity. Recovery trajectories were similar across the three diagnostic groups (CRPS, LBP, CWP) for pain interference ($\chi^2 = 1.8$, $P = .4$) and intensity ($\chi = 0.2$, $P = .9$). Modeling to predict outcomes correctly classified 69% of cases for pain interference and 88% of cases for pain intensity recovery trajectories using baseline scores.

Conclusion: People with CRPS, LBP, and CWP experience similar benefits following an IPMP. This supports the use of IPMPs for people with CRPS.

Keywords: complex regional pain syndrome, interdisciplinary pain management program; cognitive behavioral therapy; rehabilitation; low back pain; fibromyalgia; chronic widespread pain.

Introduction

Complex regional pain syndrome (CRPS) is a debilitating condition which can occur in a person's limb following injury or surgery, or spontaneously.[1] It is characterised by significant pain, sensory changes, temperature disturbance, discolouration, swelling, abnormal sweating, and trophic changes to nails, hair and skin.[2] The pathophysiology of CRPS is complex and includes inflammatory mechanisms, autonomic dysregulation and nociplastic changes to the central nervous system. Full recovery from CRPS is relatively rare and it frequently leads to long-term disability.[3] CRPS often causes significant psychological distress, and people with CRPS generally require support to manage pain, functional limitations and the broader effects of the condition.[4]

Because CRPS is relatively uncommon, large clinical trials are challenging to conduct and there is a paucity of research documenting treatment efficacy.[4] Although there have been some randomized controlled trials (RCTs) of medical and physiotherapy interventions for CRPS, these are relatively few and treatment guidelines focus on functional restoration and physical rehabilitation, in addition to education, psychological intervention and pain relief.[4,5]

Interdisciplinary pain management programs (IPMPs) are typically 3–4 week fulltime programs (30–40 hours per week) provided to people with chronic pain. They deliver cognitive and behavioural interventions including pain education, goal setting and activity planning, graded exercise, cognitive restructuring, relaxation training, and medication management, in an environment designed to reinforce "well" behavior (ie, operant therapy). The efficacy of IPMPs is well established for mixed chronic pain samples, low back pain (LBP), neck pain and chronic widespread pain (CWP).[6–8] Treatment guidelines for CRPS include a recommendation for interdisciplinary pain management,[5] and 80% of

Received: 24 September 2024. **Revised:** 14 November 2024. **Accepted:** 26 November 2024

clinicians report using IPMPs for patients with persistent CRPS[9]; however, there are no published RCTs evaluating the efficacy of cognitive behavioural therapies or IPMPs in this population.[4,5] Several observational studies have reported improvements in physical function, disability and emotional distress following an IPMP for a CRPS population, with mixed findings on outcomes for pain intensity.[10–14] However, no studies of IPMP outcomes for CRPS have included a comparison group to test whether people with CRPS have a comparable treatment response as those with more widely studied conditions, where there is evidence for IPMP efficacy (LBP, CWP).

An additional challenge for IPMPs is the variability in outcomes experienced across individuals. Many studies have sought to identify predictors of outcome to improve or target treatment more effectively.[6] However, these studies often report associations between individual variables and outcomes rather than building models to assess their combined ability to predict IPMP success. In the last decade, a growing amount of medical research has applied machine learning approaches to improve prediction accuracy, showing promising results in the field of diagnostics and personalised treatment.[15,16] However, few studies have applied these techniques to predict recovery from persistent pain.

The first aim of the study was to compare recovery trajectories following an IPMP between people with CRPS and people with other persistent pain conditions where there is good evidence for IPMP efficacy (LBP, CWP). Given that IPMPs do not target particular chronic pain conditions or subtypes, and the observational evidence demonstrating improvements for CRPS,[13,14] we hypothesised that people with CRPS were as likely to present with favourable recovery trajectories for pain interference and pain intensity when compared to people with LBP and CWP. A secondary aim of the paper was to determine whether it is possible to predict the recovery trajectory of people with persistent pain based on baseline characteristics.

Methods

Participants

For this retrospective study, we identified patients who: (a) had completed an IPMP at The Auckland Regional Pain Service (Interdisciplinary Pain Center in Auckland, New Zealand) between 2014 and 2022, (b) had pre- and post-IPMP data available, and (c) met the diagnosis of CRPS, LBP, or CWP as described below.

In order to be included in the study, patients had to have a diagnosis of CRPS (type I or II using the Budapest clinical criteria[17]), LBP or CWP (or fibromyalgia)[18] made by a pain medicine specialist (or pain fellow under the supervision of a pain medicine specialist) during a comprehensive 60–90-minute assessment. In addition, clinical records describing symptom reports and patient pain drawings were checked by members of the research team to confirm the diagnoses. To be included in the LBP category, the diagnosis needed to indicate LBP and patients' clinical records needed to show a primary complaint of LBP, but patients were still included if pain additionally affected the leg and/or upper back/neck. We first identified all patients with CRPS meeting the inclusion criteria ($N = 66$) and then identified age- and gender-matched patients with LBP ($N = 66$) and CWP ($N = 66$). Thus, the sample size was determined by the number of eligible CRPS patients who had completed the program. To reduce bias, for each CRPS patient, the first matched LBP and CWP patients identified in clinical records were selected (patient with same gender and within 5 years of target age). A flow chart depicting the identification of patient records for inclusion and reasons for exclusion is displayed in Figure 1.

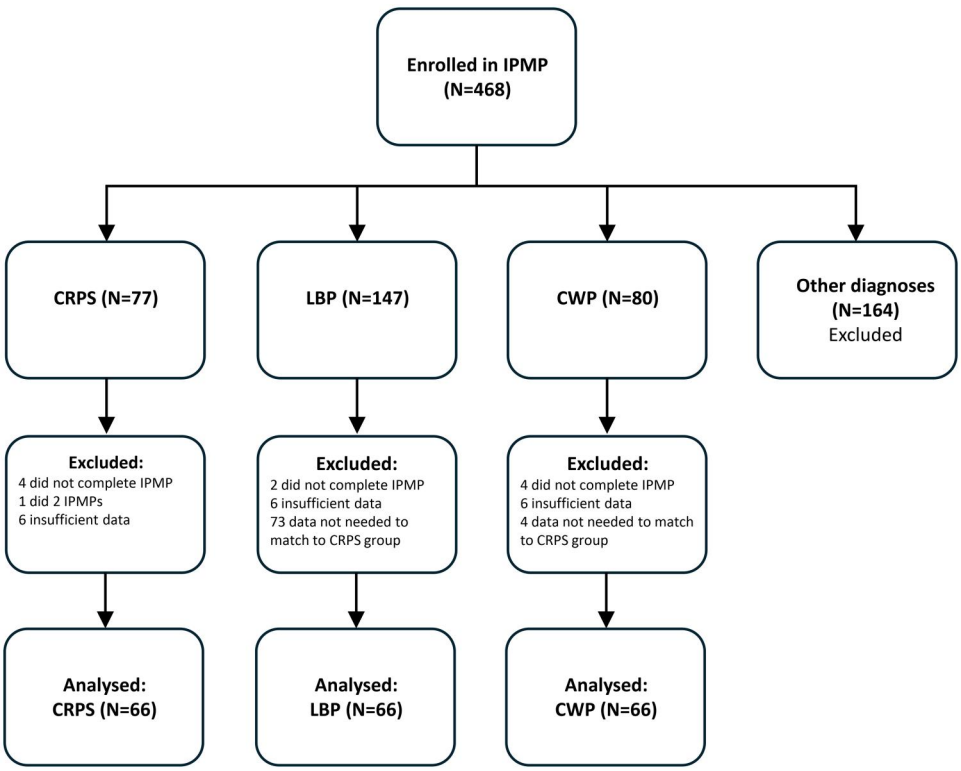

Figure 1. Flow chart of data collection for IPMP for CRPS, LBP, and CWP.

The study was approved by the Auckland University of Technology Ethics Committee and the Auckland District Health Board Research Review Committee prior to commencement. Individual informed consent was not obtained as the study comprised a retrospective chart review. The Strobe Checklist[19] was used to aid quality reporting of this study.

Interdisciplinary pain management program

The treatment comprised a 3-week IPMP (35 hours/week; 105 hours total) and was provided in a group format with up to 10 patients at a time. The program was established in the 1980s and is staffed by physiotherapists, psychologists, pain medicine specialists, an occupational therapist, and a clinical nurse specialist. Therapy includes a graded daily exercise program, individualized exposure to feared activities, goal setting and activity planning, daily relaxation training, pain education, psychological pain management strategies (eg, cognitive therapy, stress management, assertiveness training, sleep management), and medication management (generally individualized pain medication reduction). The pain management program incorporates approximately 2 activity sessions per day. One of these involves an exercise circuit where all participants conduct similar whole body exercises, to improve global movement, fitness and strength. Exercises are modified to suit the individual's abilities, following operant conditioning using a graded activation approach.[20] The second activity session is designed specifically towards the individual's needs, with a strong emphasis on increasing confidence, function and working towards goals. It may include graded exposure therapy, desensitisation training, or neuromodulatory techniques. The team are interdisciplinary and meet regularly to co-ordinate care. The program is provided in an outpatient setting where patients attend daily, and those who do not live locally are provided with motel accommodation offsite. During the COVID-19 pandemic of 2020, the program was switched to an online format with all contact conducted via video conference in participants' own homes. Subsequently, programs have returned to face-to-face format.

Dependent variables

The dependent variables were the 2 subcomponents of the Brief Pain Inventory (BPI),[21] which is routinely administered at the start and end of the program as well as at 1, 6, and 12 month follow-up visits. The BPI Pain Intensity component is assessed using four questions in which respondents rate their worst, least, average and present pain intensity on 11-point Likert scales. The item on present pain intensity was not included in this study as it had not been included in routine clinic questionnaires prior to 2019, so BPI Pain Intensity scores were calculated using the average of the other 3 pain intensity scores. The BPI Pain Interference component is assessed using seven questions regarding the degree to which pain interferes with seven domains of functioning (general activity, mood, walking ability, normal work, relations with other persons, sleep, and enjoyment of life). BPI Pain Interference scores were calculated using an average of these seven questions. The BPI has good psychometric properties.[22] Higher scores indicate higher pain intensity and interference.

Predictor variables

The predictor variables also consisted of questionnaires that are routinely administered prior to and following the program. The Depression Anxiety Stress Scale (DASS-21)[23] comprises 3 subscales, one each to measure symptoms of depression, anxiety, and stress. Respondents indicate the degree to which statements such as "I felt that I had nothing to look forward to" and "I found it hard to wind-down" apply to them (0 = "did not apply to me at all," 3 = "applied to me very much of the time"). The maximum score for each negative emotional state is 21, with higher scores indicating greater disturbance. The scale shows excellent reliability though studies suggest that the scale may be interpreted as a general measure of distress using total scores[24] in addition to the 3 subscales originally presented.[25]

The Pain Catastrophizing Scale (PCS)[26] is a 13-item measure of the degree to which a person thinks about pain in a manner characterized by rumination, magnification, and helplessness. The sum of the 13 items is calculated giving a total score out of 52, with higher scores indicating higher pain catastrophizing. The PCS has excellent psychometric properties.[27]

The Pain Self-Efficacy Questionnaire (PSEQ) is a 10-item scale measuring the degree to which an individual perceives themselves as being able to engage in daily activities despite the presence of pain. The maximum score is 60, with higher scores indexing greater confidence. The PSEQ has shown excellent reliability and validity.[28]

In addition to the above questionnaires, demographic and clinical information including age, gender (as identified in hospital records as woman/man/nonbinary), ethnicity (coded using the Stats NZ guidelines), and pain duration (years) were also extracted from clinical records.

Data analysis

Data analyses were performed in R 4.22 (Rstudio v 2023.06.02) and Python 3.9 (Spyder v 5.4.3). Due to limitations of using minimal clinical difference scores to determine those with and without meaningful outcomes from treatment,[29] latent class analysis (LCA) was used to separate participants into 2 groups based on their outcome measure scores over time.[29] To identify recovery trajectories across time points (baseline, end of program, 1 month, 6 months, 12 months), the data were fitted with a LCA linear mixed model (also known as growth mixture model).[30] A model with random slopes forcing 2 classes was applied to both the BPI pain interference and intensity outcome measures, without the inclusion of baseline predictors. The output of the model consisted of two datasets (one for BPI Pain Interference and one for Pain Intensity) with the assigned recovery trajectory for each participant. The two recovery trajectories were named "good responders" and "poorer responders." Data points for which the LCA was unable to indicate a trajectory due to missing data were removed from the datasets. To determine if people with CRPS had a similar response to the program, a χ^2 test was performed to determine whether a difference existed in the proportion of participants belonging to the good and poorer responder trajectories based on diagnostic class (CRPS, LBP, CWP). Although there were missing data, this analysis allowed all individuals to be included in the analyses.

For the secondary aim of the study, several steps were taken to predict the recovery trajectory of participants from baseline characteristics. Data were cleaned, and the following variables were retained within each dataset: Diagnosis, age, gender, ethnicity, duration of pain in years, BPI pain interference, BPI pain intensity, DASS depression, DASS anxiety, DASS stress, PSEQ, and PCS total score. These variables

Table 1. Demographic characteristics and baseline clinical scores of the entire sample. All the numbers are percentages or means and standard deviation.

Variable	Entire sample ($N = 198$)	CRPS ($N = 66$)	LBP ($N = 66$)	CWP ($N = 66$)
Age	47.2 (12.2)	47.6 (12.0)	47.1 (11.7)	46.9 (13.2)
Gender:				
% Woman	141 (71.2%)	47 (71.2%)	47 (71.2%)	47 (71.2%)
% Man	57 (28.8%)	19 (28.8%)	19 (28.8%)	19 (28.8%)
% Nonbinary	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ethnicity:				
European	170 (85.9%)	58 (87.9%)	57 (86.4%)	55 (83.3%)
Māori	15 (7.6%)	7 (10.6%)	5 (7.6%)	3 (4.5%)
Pacific Islander	5 (2.5%)	1 (1.5%)	1 (1.5%)	3 (4.5%)
Asian	5 (2.5%)	0 (0%)	1 (1.5%)	4 (6.1%)
Other	3 (1.5%)	0 (0%)	2 (3.0%)	1 (1.5%)
Pain duration (yrs)	9.3 (13.3)	4.4 (4.2)	4.6 (7.5)	13.4 (12.7)[a]
BPI Pain Intensity	5.9 (1.5)	6.4 (1.6)[b]	5.7 (1.3)	5.8 (1.5)
BPI Pain Interference	6.4 (1.7)	6.5 (1.6)	6.2 (1.8)	6.4 (1.5)
DASS Depression	8.2 (5.3)	8.5 (5.6)	7.3 (5.6)	8.8 (4.5)
DASS Anxiety	7 (5.3)	7.4 (4.6)	5.5 (4.8)	8.2 (6.1)[c]
DASS Stress	10.8 (5.1)	11.7 (4.6)	8.7 (5.3)[a]	11.7 (4.9)
PSEQ Self-Efficacy	25.5 (10.8)	24.3 (11.6)	25.3 (11.4)	26.7 (9.4)
PCS Catastrophizing	21.9 (11.8)	21.1 (11.9)	19.3 (11.4)	25.4 (11.4)

Abbreviations: CRPS, complex regional pain syndrome; LBP, low back pain; CWP, chronic widespread pain; BPI, Brief Pain Inventory; DASS, Depression, Anxiety, and Stress Scale; PSEQ, Pain Self Efficacy Questionnaire; PCS, Pain Catastrophising Scale.
[a] significantly different to both other groups ($P < .05$).
[b] CRPS group significantly different to LBP group.
[c] CWP group significantly different to LBP group.

were selected based on previous studies showing the usefulness of these predictors.[31–34] Missing data were imputed through the k-Nearest Neighbours approach utilising the NKKimputer package from the scikit-learn library. Following this, to provide a more balanced dataset size for each recovery trajectory, the Synthetic Minority Over-sampling Technique (SMOTE) was used.[35] To select the most important variables to use in the multivariable models, a signal to noise ratio (SNR) approach was taken. The top 10 variables out of 12 were retained. The SNR was calculated for each variable across all the diagnostic labels (SNR_{var} = abs (mean var of one good recovery trajectory—mean var of the lower recovery trajectory)/(SD of var of one good recovery trajectory + SD of var of lower recovery trajectory)). Following this process, all the predictors were scaled by subtracting individual values from the mean and dividing this value by the standard deviation.

A leave one out strategy (for the original data only) was then used to separate the test subject prior to training the multivariable model. A personalised approach to training the model was taken by selecting a training subset ($n = 50$) from the whole training dataset. In particular, the personalised approach selects the cluster of training data with predictor values closest to the test subject via assessment of Euclidean distances in the multivariable space.[36] Once the cluster of training data was identified, a support vector machine (SVM) multivariable model was trained and tested on the data point that was initially removed. The overall accuracy of the models was calculated by counting the number of test data that were correctly classified after training the model.

Results

A total of 198 participants with persistent pain were included in the present study. Follow-up data were available for the following proportions of the sample: End of program: 100%, 1 month: 84%, 6 months: 65%, 12 months: 47%, but all individuals were included in the analyses. The demographic characteristics of participants are reported in Table 1. There were several differences in baseline characteristics between the three diagnostic groups. Those with CWP had a longer pain duration ($F(2, 168) = 16.3$, $P < .001$) than both other groups and higher mean anxiety scores ($F(2, 171) = 4.3$, $P = .016$) than those with LBP. Those with CRPS had a higher mean BPI Pain Intensity than those with LBP ($F(2, 171) = 4.1$, $P = .018$). Those with LBP had a lower mean DASS stress scores than both other groups ($F(2, 162)=6.4$, $P = .002$).

Recovery trajectories

For pain interference, class 1 (poorer responder) presented with 114 (63%) participants who had a slight initial reduction in interference followed by a return to baseline scores. Class 2 (good responder) was made up of 66 (37%) participants and showed a sustained decline in interference from baseline scores to the last timepoint (see Figure 2). Pain intensity scores were consistent across all time points for class 1 (poorer responder; $n = 161$, 89%), while class 2 presented a decline in pain over time (good responder; $n = 19$, 11%) (see Figure 3). More detailed mean scores for each group at each time point are also provided in Table S1.

Recovery trajectories across diagnostic class

The number of participants in each recovery trajectory based on diagnostic class is reported in Table 2. There were no differences between the three diagnostic groups in terms of recovery trajectories for BPI Pain Interference ($\chi 2 = 1.8$, $P = .4$) or BPI Pain Intensity ($\chi 2 = 0.2$, $P = .9$).

Prediction modeling for recovery

The baseline predictors for both pain interference and intensity trajectories were identified through SNR values and are

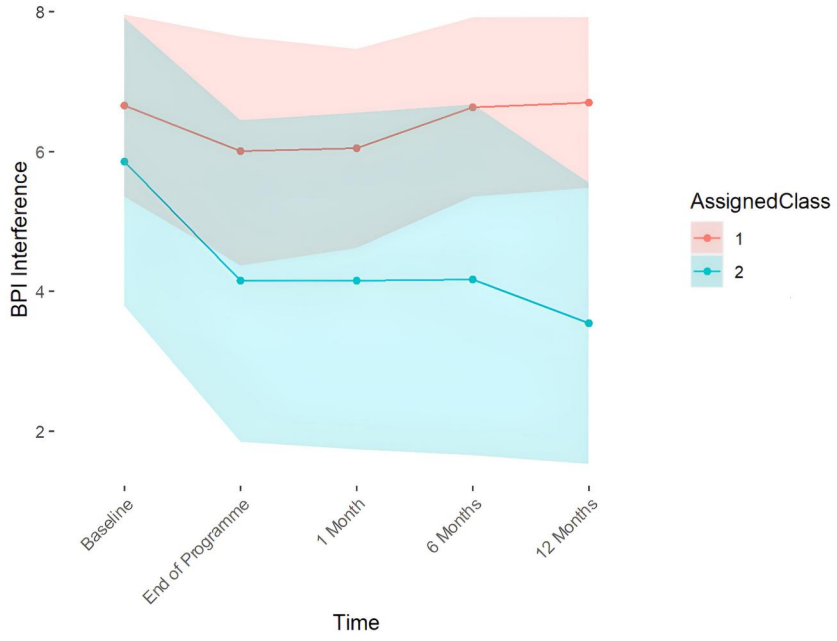

Figure 2. Latent class analysis for the BPI Pain Interference outcome. Shaded areas are 95% confidence intervals.

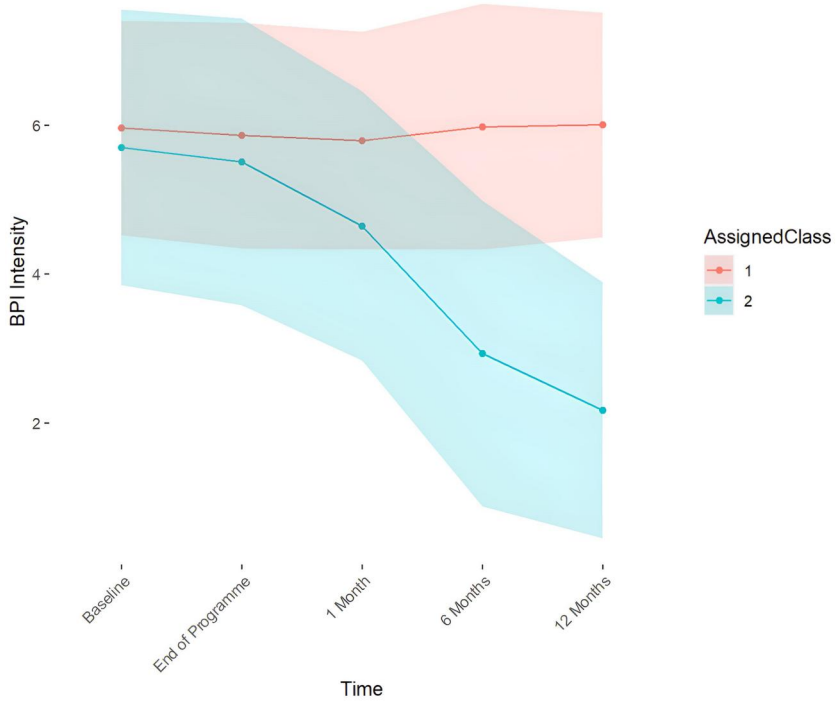

Figure 3. Latent class analysis for the BPI Pain Intensity outcome.

reported in Figure 4. Two separate support vector machine models provided an overall correct classification in 69% of the cases for pain interference and 88% of the cases for pain intensity recovery trajectories. Further details about the classification accuracy of the models are reported in Table 3. For BPI Pain Interference, the baseline predictor variables for a good outcome, and with a signal to noise (SNR) ratio greater than 0.15 were: Lower DASS stress, DASS anxiety, BPI Pain Interference, DASS depression, BPI Pain Intensity, and PCS catastrophizing. For BPI Pain Intensity, the baseline predictors of a good outcome and with a signal to noise (SNR) ratio greater than 0.15 were: Lower BPI pain intensity, gender (women were more likely to have positive trajectory), longer pain duration, higher PCS pain catastrophizing, lower DASS anxiety, and older age.

Discussion

This is the first study comparing the recovery trajectories of people with CRPS to other persistent pain conditions following completion of an IPMP. The results showed that, in keeping with the initial hypothesis, people with CRPS were

Table 2. The number of participants in each BPI Pain Intensity and Interference trajectory for each diagnostic class.

	CRPS	LBP	CWP	χ^2, *P*-value
Pain interference				
Poorer responder	42 (70%)	36 (59%)	36 (61%)	1.8, .4
Good responder	18 (30%)	25 (41%)	23 (39%)	
Pain intensity				
Poorer responder	54 (90%)	55 (90%)	52 (88%)	0.2, .9
Good responder	6 (10%)	6 (10%)	7 (12%)	

Abbreviations: CRPS, complex regional pain syndrome; LBP, low back pain; CWP, chronic widespread pain χ^2, chi-square.

equally likely to improve in pain intensity and interference when compared to people with persistent LBP pain or CWP. In addition, a machine learning model was developed to predict recovery trajectories in people with persistent pain attending an IPMP, which showed reasonable prediction accuracy, particularly for pain intensity.

These findings support the use of IPMPs for people with CRPS. It is widely acknowledged that conducting RCTs with the CRPS population is challenging because it is a rare disease.[37] However, because RCTs have demonstrated the efficacy of IPMPs for LBP and CWP,[7,8] the finding that outcomes are similar for CRPS supports the evidence base for interdisciplinary management of CRPS. This is important, because it provides support for clinical guidelines[4,5] and healthcare providers[9] who already recommend or provide IPMPs for CRPS. According to the ICD-11, CRPS is now considered a primary pain condition, like CWP and nonspecific LBP, so it is not surprising that similar management approaches produce equivalent effects for these conditions. However, it is noteworthy that despite limited evidence, there is still a strong emphasis in the literature on providing medical interventions for CRPS,[38–40] and greater evidence for interdisciplinary pain management may support a more nuanced approach to supporting people with CRPS. The finding that IPMPs are equally beneficial for people with CRPS as they for other pain conditions should increase the likelihood of clinicians referring patients to these services. This has the potential of improving patients' quality of life.

It is important to note that the treatment benefits for all three patient groups in the study were modest, with only 37% of people having a positive recovery trajectory for pain interference over the 12-month follow-up period. However, this is consistent with previous research which shows around one third of patients experience a clinically significant improvement following multidisciplinary pain management.[41] Furthermore, the effect sizes from the present study for changes over time were consistent with those of previous studies reporting on inpatient IPMPs.[6] The present data show that a sustained reduction in pain intensity was even less common than reduction in pain interference following interdisciplinary pain management. This suggests that IPMPs are unlikely to result in pain reduction, so should not be recommended to patients on this basis. This reflects the difficulty of treating those with longstanding chronic pain, and particularly of achieving long-term benefits. Whilst specific studies may demonstrate better outcomes than others, it is possible this is due to the specifics of the population, program, measures used and length of follow-up. The present study utilised data from a tertiary referral service where patients are typically only referred after poor outcomes in primary or secondary care, so treatment outcomes can be expected to be somewhat limited.

This limited efficacy of IPMPs for chronic pain suggests that further developments in treatment methods should be prioritised. One approach to optimisation is to identify modifiable predictors of treatment response, and enhance interventions targeting such factors, thereby strengthening the chance of treatment success. Several important modifiable predictors of recovery trajectory were identified in the present study, including stress, anxiety, depression, pain interference and pain catastrophizing. This is consistent with previous literature showing that higher levels of baseline distress are associated with poorer outcomes for cognitive behavioural interventions for chronic pain,[42] for outcomes of multidisciplinary treatment for chronic widespread pain,[31] and for disability outcomes from conservative treatment for low back pain.[43] It was notable that fewer psychological variables were associated with pain intensity trajectory, suggesting that different variables, or perhaps different combinations of variables, are important for different clinical outcomes. Notably the direction of effect for pain catastrophising differed between the two dependent variables, as lower catastrophizing was associated with better outcomes for pain interference, but higher catastrophizing was associated with better outcomes for pain intensity. This may reflect the machine learning approach used, which clusters individuals based on a range of predictor variables rather than considering each predictor separately. Thus, it is the combination of predictors that is important to consider, and the apparently contradictory effect is likely due to how catastrophizing interacts with the other predictor variables. The machine learning analysis also suggested better pain intensity outcomes may be associated with older age, and may occur for women compared to men. The machine learning models used here are exploratory rather than conclusive but the positive effect of older age has also been demonstrated via meta-analysis,[6] though there is mixed evidence on the impact of sex on IPMP outcomes.[44,45] Because machine learning models are able to examine combinations of predictors, expanding the use of machine learning approaches may increase our ability to develop clinical forecasting tools that can better identify personalized care needs taking into account multiple individual factors.

The data also revealed several baseline differences between the 3 diagnostic groups. Those with LBP had lower stress levels than both other groups, and lower anxiety than those with CWP, consistent with prior literature.[46,47] It might be that psychological factors such as anxiety play less of a role in the development of LBP,[47] or it may be that LBP causes less distress than CWP, which is associated with high levels of uncertainty[48] and social stigma.[49]

Strengths and limitations

This study presents with several strengths. First, because CRPS is a relatively rare condition, it is challenging to recruit adequate sample sizes for clinical trials. Using data collected over a 10-year period, this study accrued data from 66 CRPS patients, which is a reasonable size for research in this condition. Second, the real-world clinical data from a tertiary service that tends to see the most complex patients makes the results applicable to such settings. Third, the machine learning approach employed is novel and innovative, and provides a template for further analyses predicting treatment outcome in this population. In terms of limitations, this was a

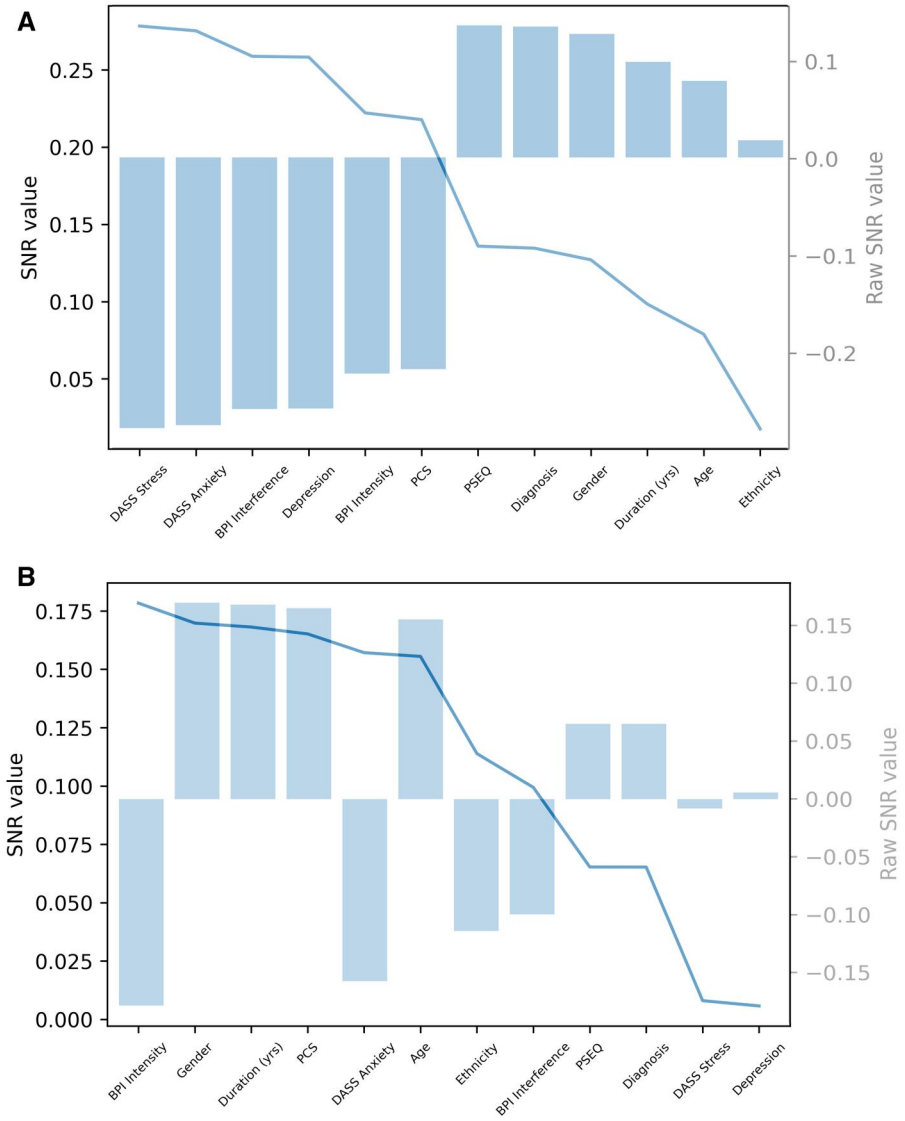

Figure 4. Signal to noise ratio (SNR) for the (**A**) BPI Pain Interference (**B**) and BPI Pain Intensity outcomes.

Table 3. Sensitivity, specificity, and likelihood ratios for pain interference and intensity predictions obtained through the support vector machine model.

Outcome	Sensitivity (ratio)	Specificity (ratio)	LR+	LR−
BPI Pain Interference	58% (38/66)	76% (87/114)	2.4	0.55
BPI Pain Intensity	95% (18/19)	90% (145/161)	9.5	0.056

Abbreviations: LR+, Positive likelihood ratio; LR−, Negative likelihood ratio; BPI, Brief Pain Inventory.

secondary analysis of an existing dataset, hence, no a-priori power calculations were completed to determine the sample size required to test the hypotheses. However, based on the (small) between group effect sizes, it is unlikely that a greater sample size would demonstrate significant differences in outcomes between those with CRPS, CWP, and LBP. In terms of generalizability, although the findings are likely relevant to tertiary pain service populations, they may not be generalizable to less complex clinical populations. The sample were predominantly European, and future work is needed to assess the generalizability to minority groups. Further, the study was observational in nature with no placebo control group, and the clinical dataset had considerable loss to follow-up. Medication data were not systematically collected so could not be included as a variable in the analyses. Additionally, the machine learning approach utilized, and the combination of predictors included has not been tested on an external dataset. It is therefore likely that the accuracy obtained when testing the model was an overestimation of its actual capability. In the future, similar machine learning approaches will be applied to a much larger dataset, which will allow a more precise model induction and validation on a separate sample subset. Machine learn models must be validated on an external dataset before being applied so no recommendations for changing clinical care based on predictive factors should be made at this time.

Conclusion

People with CRPS show equivalent benefits from IPMP to those with other primary pain conditions (LBP and CWP).

These results support the use of interdisciplinary pain management for CRPS. The combination of baseline pain, psychological factors and demographics may prove useful in predicting IPMP outcomes in people with persistent pain. If the accuracy of these models was validated in a different group of participants, it may be possible to identify additional strategies to improve outcomes of people who are currently less likely to benefit from IPMPs.

Author contributions

D.B.: Concept and design, acquisition of data, analysis and interpretation of data, drafting manuscript, approval of final version.
N.T.: Concept and design, acquisition of data, analysis and interpretation of data, revising manuscript, approval of final version.
N.M.: Study concept and design, analysis & interpretation of data, revising manuscript, approval of final version.
C.P.: Acquisition of data, revising the manuscript, approval of final version.
T.A.: Acquisition of data, revising the manuscript, approval of final version.
G.L.: Study concept and design, analysis & interpretation of data, revising manuscript, approval of final version.

Supplementary material

Supplementary material is available at *Pain Medicine* online.

Funding

This study did not receive any funding.

Conflicts of Interest: All authors declare that they have no conflicts of interest.

References

1. Taylor SS, Noor N, Urits I, et al. Complex Regional Pain Syndrome: a comprehensive review. *Pain Ther*. 2021;10(2):875-892.
2. Goebel A, Birklein F, Brunner F, et al. The Valencia consensus-based adaptation of the IASP complex regional pain syndrome diagnostic criteria. *Pain*. 2021;162(9):2346-2348. https://doi.org/10.1097/j.pain.0000000000002245
3. Bean DJ, Johnson MH, Heiss-Dunlop W, Kydd RR. Extent of recovery in the first 12 months of complex regional pain syndrome type-1: a prospective study. *Eur J Pain*. 2016;20(6):884-894. https://doi.org/10.1002/ejp.813
4. Harden RN, McCabe CS, Goebel A, et al. Complex Regional Pain Syndrome: practical diagnostic and treatment guidelines, 5th edition. *Pain Med*. 2022;23(suppl 1):S1-S53. https://doi.org/10.1093/pm/pnac046
5. Goebel A, Barker C, Turner-Stokes L. Complex Regional Pain Syndrome in Adults: UK guidelines for diagnosis, referral and management in primary and secondary care. *RCP*. 2018.
6. Lewis GN, Bean DJ. What influences outcomes from inpatient multidisciplinary pain management programs? A systematic review and meta-analysis. *Clin J Pain*. 2021;37(7):504-523. https://doi.org/10.1097/AJP.0000000000000941
7. Waterschoot FPC, Dijkstra PU, Hollak N, de Vries HJ, Geertzen JHB, Reneman MF. Dose or content? Effectiveness of pain rehabilitation programs for patients with chronic low back pain: a systematic review. *PAIN®*. 2014;155(1):179-189. https://doi.org/10.1016/j.pain.2013.10.006
8. Geraghty AWA, Maund E, Newell D, et al. Self-management for chronic widespread pain including fibromyalgia: a systematic review and meta-analysis. *PLoS One*. 2021;16(7):e0254642.
9. Miller C, Williams M, Heine P, Williamson E, O'Connell N. Current practice in the rehabilitation of complex regional pain syndrome: a survey of practitioners. *Disabil Rehabil*. 2019;41(7):847-853.
10. Singh G, Willen SN, Boswell MV, Janata JW, Chelimsky TC. The value of interdisciplinary pain management in Complex Regional Pain Syndrome Type I: a prospective outcome study. *Pain Physician*. 2004;7(2):203-209.
11. McCormick ZL, Gagnon CM, Caldwell M, et al. Short-term functional, emotional, and pain outcomes of patients with Complex Regional Pain Syndrome treated in a comprehensive interdisciplinary pain management program. *Pain Med*. 2015;16(12):2357-2367. https://doi.org/10.1111/pme.12817
12. Lewis JS, Kellett S, McCullough R, et al. Body perception disturbance and pain reduction in longstanding Complex Regional Pain Syndrome following a multidisciplinary rehabilitation program. *Pain Med*. 2019;20(11):2213-2219. https://doi.org/10.1093/pm/pnz176
13. Schneider S, Wertli MM, Henzi A, Hebeisen M, Brunner F. Effect of an interdisciplinary inpatient program for patients with Complex Regional Pain Syndrome in reducing disease activity—a single-center prospective cohort study. *Pain Med*. 2024;25(7):459-467. https://doi.org/10.1093/pm/pnae021
14. Lewis JS, Wallace CS, White P, et al. Early versus persistent Complex Regional Pain Syndrome: is there a difference in patient reported outcomes following rehabilitation? *Eur J Pain*. 2024;28(3):464-475. https://doi.org/10.1002/ejp.2196
15. Elfanagely O, Toyoda Y, Othman S, et al. Machine learning and surgical outcomes prediction: A systematic review. *J Surg Res*. 2021;264:346-361. https://doi.org/10.1016/j.jss.2021.02.045
16. Krittanawong C, Virk HUH, Bangalore S, et al. Machine learning prediction in cardiovascular diseases: A meta-analysis. *Sci Rep*. 2020;10(1):16057. https://doi.org/10.1038/s41598-020-72685-1
17. Harden NR, Bruehl S, Perez RSGM, et al. Validation of proposed diagnostic criteria (the "Budapest Criteria") for Complex Regional Pain Syndrome. *Pain*. 2010;150(2):268-274. https://doi.org/10.1016/j.pain.2010.04.030
18. Wolfe F, Clauw DJ, Fitzcharles M, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res (Hoboken)*. 2010;62(5):600-610.
19. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Ann Intern Med*. 2007;147(8):573-577. https://doi.org/10.7326/0003-4819-147-8-200710160-00010
20. Magalhaes MO, França FJR, Burke TN, et al. Efficacy of graded activity versus supervised exercises in patients with chronic non-specific low back pain: Protocol of a randomised controlled trial. *BMC Musculoskelet Disord*. 2013;14:36. https://doi.org/10.1186/1471-2474-14-36
21. Cleeland CS, Ryan KM. Pain assessment: global use of the brief pain inventory. *Ann Acad Med Singap*. 1994;23(2):129-138.
22. Tan G, Jensen MP, Thornby JI, Shanti BF. Validation of the brief pain inventory for chronic nonmalignant pain. *J Pain*. 2004;5(2):133-137.
23. Lovibond SH, Lovibond PF. *Manual for the Depression Anxiety Stress Scale*. 2nd ed. Psychology Foundation; 1995.
24. Zanon C, Brenner RE, Baptista MN, et al. Examining the dimensionality, reliability, and invariance of the Depression, Anxiety, and Stress Scale–21 (DASS-21) across eight countries. *Assessment*. 2021;28(6):1531-1544.

25. Henry JD, Crawford JR. The short-form version of the Depression Anxiety Stress Scales (DASS-21): Construct validity and normative data in a large non-clinical sample. *Br J Clin Psychol*. 2005;44(Pt 2):227-239.Https://doi.org/10.1348/014466505X29657
26. Sullivan MJL, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. *Psychol Assess*. 1995;7(4):524-532.
27. Osman A, Barrios FX, Gutierrez PM, Kopper BA, Merrifield T, Grittmann L. The pain catastrophizing scale: further psychometric evaluation with adult samples. *J Behav Med*. 2000;23(4):351-365. https://doi.org/10.1023/A:1005548801037
28. Dubé MO, Langevin P, Roy JS. Measurement properties of the pain self-efficacy questionnaire in populations with musculoskeletal disorders: a systematic review. *Pain Rep*. 2021;6(4):e972. https://doi.org/10.1097/PR9.0000000000000972
29. Dumenci L, Perera RA, Keefe FJ, et al. Model-based pain and function outcome trajectory types for patients undergoing knee arthroplasty: a secondary analysis from a randomized clinical trial. *Osteoarthritis Cartilage*. 2019;27(6):878-884. https://doi.org/10.1016/j.joca.2019.01.004
30. Wardenaar KJ. Latent Class Growth Analysis and Growth Mixture Modeling Using R: A Tutorial for Two R-Packages and a Comparison with Mplus. 2022. Accessed April 16, 2024. https://doi.org/10.31234/osf.io/m58wx
31. de Rooij A, Roorda LD, Otten RHJ, van der Leeden M, Dekker J, Steultjens MPM. Predictors of multidisciplinary treatment outcome in fibromyalgia: a systematic review. *Disabil Rehabil*. 2013;35(6):437-449. https://doi.org/10.3109/09638288.2012.699582
32. Hayward R, Stynes S. Self-efficacy as a prognostic factor and treatment moderator in chronic musculoskeletal pain patients attending pain management programmes: a systematic review. *Musculoskelet Care*. 2021;19(3):278-292. https://doi.org/10.1002/msc.1533
33. McCracken LM, Turk DC. Behavioral and cognitive–behavioral treatment for chronic pain: Outcome, predictors of outcome, and treatment process. *Spine (Phila Pa 1976)*. 2002;27(22):2564-2573.
34. Craner JR, Sperry JA, Evans MM. The relationship between pain catastrophizing and outcomes of a 3-week comprehensive pain rehabilitation program. *Pain Med*. 2016;17(11):2026-2035. https://doi.org/10.1093/pm/pnw070
35. Elreedy D, Atiya AF, Kamalov F. A theoretical distribution analysis of synthetic minority oversampling technique (SMOTE) for imbalanced learning. *Mach Learn*. 2024;113(7):4903-4923. https://doi.org/10.1007/s10994-022-06296-4
36. Doborjeh M, Doborjeh Z, Merkin A, et al. Personalised predictive modelling with brain-inspired spiking neural networks of longitudinal MRI neuroimaging data and the case study of dementia. *Neural Netw*. 2021;144:522-539. https://doi.org/10.1016/j.neunet.2021.09.013
37. Shafiee E, MacDermid J, Packham T, Walton D, Grewal R, Farzad M. The effectiveness of rehabilitation interventions on pain and disability for Complex Regional Pain Syndrome: a systematic review and meta-analysis. *Clin J Pain*. 2023;39(2):91-105.
38. Wie C, Gupta R, Maloney J, Pew S, Freeman J, Strand N. Interventional modalities to treat Complex Regional Pain Syndrome. *Curr Pain Headache Rep*. 2021;25(2):10. https://doi.org/10.1007/s11916-020-00904-5
39. Duong S, Bravo D, Todd KJ, Finlayson RJ, Tran DQ. Treatment of Complex Regional Pain Syndrome: An updated systematic review and narrative synthesis. *Can J Anaesth*. 2018;65(6):658-684. https://doi.org/10.1007/s12630-018-1091-5
40. Her YF, Kubrova E, Dombovy-Johnson M, ElSaban M, Mostert K, D'Souza RS. Complex Regional Pain Syndrome: updates and current evidence. *Curr Phys Med Rehabil Rep*. 2024;12(1):50-70. https://doi.org/10.1007/s40141-023-00426-2
41. Wilson IR. Management of chronic pain through pain management programmes. *Br Med Bull*. 2017;124(1):55-64.
42. Forden G, Ronaghan S, Williams P, Fish S, Ford C. Predictors of treatment outcome in cognitive behavioural therapy for chronic pain: a systematic review. *Disabil Rehabil*. 2024;46(21):4877-4888. https://doi.org/10.1080/09638288.2023.2283113
43. Alhowimel AS, Alotaibi MA, Alenazi AM, et al. Psychosocial predictors of pain and disability outcomes in people with chronic low back pain treated conservatively by guideline-based intervention: a systematic review. *J Multidiscip Healthc*. 2021;14(null):3549-3559. https://doi.org/10.2147/JMDH.S343494
44. Racine M, Solé E, Sánchez-Rodríguez E, et al. An evaluation of sex differences in patients with chronic pain undergoing an interdisciplinary pain treatment program. *Pain Pract*. 2020;20(1):62-74. Https://doi.org/10.1111/papr.12827
45. Flegge LG, Lake E, Truesdale C, Craner JR. Sex differences in interdisciplinary pain rehabilitation outcomes: a systematic review. *Scand J Pain*. 2022;22(2):218-231. https://doi.org/10.1515/sjpain-2021-0188
46. Angst F, Benz PT, Lehmann S, Erich P. Measurement of depression and anxiety in chronic low back pain and fibromyalgia: a validity comparison of four patient-reported outcome measures. *J Depress Anxiety Disord*. 2024;6(1):162-172. https://doi.org/10.36959/362/489
47. Couëpel B, Tremblay M, Bernier M, Abboud J, Descarreaux M. What are the functional and clinical characteristics shared by fibromyalgia and low back pain? A scoping review. *BMC Rheumatol*. 2024;8(1):56. https://doi.org/10.1186/s41927-024-00430-6
48. Cedraschi C, Luthy C, Girard E, Piguet V, Desmeules J, Allaz AF. Representations of symptom history in women with fibromyalgia vs chronic low back pain: a qualitative study. *Pain Med*. 2012;13(12):1562-1570. https://doi.org/10.1111/j.1526-4637.2012.01501.x
49. Quintner J. Why are women with fibromyalgia so stigmatized? *Pain Med*. 2020;21(5):882-888.

Pain Medicine, 2025, 26, 180–188
https://doi.org/10.1093/pm/pnae126
Original Research Article