

**COMPLEX REGIONAL PAIN SYNDROME  
(CRPS) PHYSIOTHERAPY MANAGEMENT:  
A COHORT, OBSERVATIONAL,  
PROSPECTIVE, LONGITUDINAL STUDY  
ACROSS THE SOUTH ISLAND  
OF NEW ZEALAND**

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## **Personal Reflection**

Answering questions about physiotherapy practice in any regional domain requires organisational skill and tenacity. Seeking answers to these complex questions has involved a journey across mountain passes, deep ravines and steep cliff ascents that needed diligent scrutiny. A journey was commenced with a goal to form a bridge between relevant clinical practice and academic research. This meant answering questions regarding physiotherapy outcomes and the interventional methods used. It mapped out the journey for physiotherapy management and outcomes over a year for patients presenting to Physiotherapists with Complex Regional Pain Syndrome (CRPS). This covered the South Island of Aotearoa, New Zealand (NZ). A conceptual clinical model of physiotherapy management for CRPS is suggested from this journey.

This journey would not have been possible without the support and guidance of my three supervisors, Ted Shipton, Jonathan Williman and Roger Mulder. I am indebted to their patience, time, constructive advice and help.

I am also grateful for the love, support and care I received from my family who encouraged me to commence this journey and complete it when diligent scrutiny proved arduous or difficult. To them, I owe my thanks, especially for their gracious kindness which accompanied their help and encouragement. I also pledged my late sister, Julie, that I would complete this work. She is not with us to see it, and I have fulfilled my word to her.

## ABSTRACT

Physiotherapy management for CRPS is considered to be essential. However, there is a lack of validated evidence-based treatments. There is controversy between what treatment methods are safe or effective. Physiotherapy outcomes and interventions for patients with CRPS, referred to all outpatient clinics across the South Island of New Zealand, were evaluated. The aim of this project was to determine with an observational, longitudinal study the following: a) to measure patient outcomes and changes over time/natural history for one year after commencing physiotherapy; b) to document and categorise the standard physiotherapy interventional methods received; c) to identify predictors of patient outcomes; d) to investigate the efficacy of the current physiotherapy intervention for CRPS, and (d) to suggest a conceptual clinical model for the physiotherapy management of CRPS. Informed written consent from participants was obtained. Demographic data were collected as follows: the duration of time following injury to CRPS diagnosis and to the commencement of physiotherapy; age; gender; laterality affected; inciting injury; region; work status; ethnicity. Medical and psychological care were also documented. Pre and post outcome measures were measured at 6 weeks, 6 months and 1 year after commencing physiotherapy interventions by an independent telephonic interviewer. The following outcome measures were applied: (a) Pain intensity was measured using the Short form McGill Pain Questionnaire and an 11-point numerical rating scale; (b) functional ability was assessed using the 11-item Quick Disability of the Arm, Shoulder and Hand questionnaire (for those with CRPS of the upper limb), and the 23-item Foot Function Index for those with CRPS of the lower limb; (c) quality of life associated with disability was assessed using the 12-item World Health Organisation Disability Assessment Schedule 2.0 which was chosen as appropriate for both upper and lower extremities; (d) satisfaction of care was measured with the 9-item Deyo and Diehl Satisfaction Questionnaire. Potential predictors were administered once to indicate possible influences on the outcomes. These were the Health Anxiety Index, the Extraversion and Neuroticism scale of the brief-version Eysenck Personality Questionnaire, the Tampa scale for Kinesiophobia, and the 10-item psychological distress Kessler questionnaires. Seventy five participants signed consent to participate between December 2013 and 2018. Nine did not meet inclusion criteria. Fifty-two females and 14 males participated with ages ranging from 11 to 77 years (mean 46 years); New Zealand Europeans predominate as ethnic group; 57 (86%) had a CRPS Type 1 and 9 (14%) had a CRPS Type 2 diagnosis; fractures were the

inciting event for 28 (42%) followed by soft tissue injury 24 (36%) and surgery 14 (21%), respectively. Statistical analysis used standard descriptive statistics: student-t tests to compare pre and post outcome measures; Mann Whitney U tests to determine baseline differences between the categorical or continuous predictor variables, and logistic regression analysis to determine predictive effects of continuous or categorical variables with a power of 0.8 and alpha of 0.05. Effect sizes with logistic regression were strictly determined with confidence intervals not equal to 1. Spearman correlation co-efficients were used with the suggested conceptual model. Results showed all participants had significant improvement; 24 (45%) participants made a complete recovery within one year following commencement of physiotherapy. No specific physiotherapy intervention significantly influenced recovery. Full recovery was correlated with the extraversion personality measure and the concurrent prescription of anticonvulsant analgesia. These findings suggest that the novel factor of personality extraversion warrants further investigation. A proposal was suggested towards a conceptual clinical model for the physiotherapy management of CRPS.

#### Key words

Physiotherapy, Complex Regional Pain Syndrome (CRPS), cohort longitudinal study, outpatient, region, outcomes, intervention methods, intervention categories, telephonic interviewing, independent interviewing, valid and reliable questionnaires, predictors, pain, function, quality of life, satisfaction with care, personality, extraversion, neuroticism, fear avoidance, health anxiety, mental health, kinesiophobia, prevention, inferential statistics, statistical analysis, logistic regression, Spearman correlation, odds ratio, confidence interval, confounding, student-t tests, Mann-Whitney U tests, Kaplan-Meier plot, hypothesis, beliefs, clinical management, clinical practice, conceptual clinical model, psychology, medical family doctor, Specialist Pain Medicine Physician.

## PREFACE

This doctoral thesis has been written to incorporate peer reviewed published journal articles arising from this research project as well as those in submission. All published articles have permission from Journal Editors for inclusion with this thesis. Repetitions may occur between Chapters.

The candidate is the primary author for this thesis of all the publications and presentations, and was responsible for all data collection and analysis. The three supervisors were involved with supervising the direction of the project, providing insight, assistance with statistical analysis, encouragement, critical review and editing the document.

## ACADEMIC PUBLICATIONS AND PRESENTATIONS

The candidate has endeavoured to create a tapestry with coloured threads linking publications to clinical practice along the project's journey. Each individual publication, conference presentation or the provision of continuing education to other Physiotherapists formed a coloured thread woven with the other threads to establish the role of physiotherapy interventions in the management of CRPS in a clinical setting.

The peer reviewed publications which are listed below can also be found in Appendix A.

### Peer reviewed journal publications:

1. Pons, T., Shipton, E.A., Williman, J., and Mulder, R.T., *Potential Risk Factors for the Onset of Complex Regional Pain Syndrome Type 1: A Systematic Literature Review*. *Anesthesiology Research and Practice*, 2015. **2015**(956539): p. 1-15.
2. Pons, T. and Shipton, E.A., *Physiotherapy and the management of complex regional pain syndrome*. *Pain Management*, 2016. **6**(6): p. 515-518.  
<http://www.futuremedicine.com/doi/full/10.2217/pmt-2016-0037>
3. Pons, T., Shipton, E.A., and Mulder, R., *Beliefs and Clinical Practice for Complex Regional Pain Syndrome (CRPS) Managed by Physiotherapists on the South Island of New Zealand*. *International Journal of Clinical Medicine*, 2017. **8**: p. 42-54.
4. Pons, T., Shipton, E.A., Williman, J., and Mulder, R., *Physiotherapy interventions and the outcomes for Complex Regional Pain Syndrome (CRPS) Type 1 on the South*

*Island of New Zealand – a longitudinal, prospective case series.* The Open Pain Journal, 2017. **10**: p. 5-13.

5. Pons T, Shipton EA, Williman J, Mulder RT. *A proposed clinical conceptual model for the physiotherapy management of Complex Regional Pain Syndrome (CRPS).* Musculoskeletal Science and Practice 2018; 38(December):15-22.

**Further publications in review**, also found in Appendix A, are:

6. Pons, T., Shipton, E.A., Williman, J., and Mulder, R., *Standard Physiotherapy for Complex Regional Pain Syndrome (CRPS): ingredients for recovery; a prospective cohort, longitudinal study.*

**Poster presentations** to local and international conferences, also found in Appendix A, were:

1. Poster: Potential Risk Factors for the Onset of Complex Regional Pain Syndrome Type 1: A Systematic Literature Review. *41<sup>st</sup> Annual New Zealand Pain Society Scientific meeting.* April 2016. New Plymouth.
2. Poster: Physiotherapy management for Complex Regional Pain Syndrome (CRPS) on the South Island of New Zealand – a 6 month case series. *37<sup>th</sup> Annual Australian combined Society Scientific meeting.* April 2017. Adelaide.
3. Poster: Recovery for Complex Regional Pain Syndrome (CRPS) with Physiotherapy across the South Island region of New Zealand. *43<sup>rd</sup> Annual New Zealand Pain and Australian combined Society Scientific meeting.* April 2018. Sydney.
4. Poster: How Physiotherapists manage Complex Regional Pain Syndrome (CRPS) across the South Island region of New Zealand. *43<sup>rd</sup> Annual New Zealand Pain and Australian combined Society Scientific meeting.* April 2018. Sydney.

**Oral or plenary speaker presentations** to local and international conferences were:

1. Oral: Physiotherapy management for complex regional pain syndrome. What Physiotherapists believe is important and apply in clinical practice. *39<sup>th</sup> Annual New Zealand Pain Society Scientific meeting.* March 2014, Dunedin.
2. Oral: Physiotherapy management for complex regional pain syndrome. *2014 Annual meeting for New Zealand Orthopaedic Association.* April 2014. Queenstown.

3. Oral: Physiotherapy management for complex regional pain syndrome across the South Island. *Linking the Chain. Biannual Physiotherapy New Zealand Conference.* September 2014. Auckland.
4. Oral: Physiotherapy management for complex regional pain syndrome- a case series for 20 CRPS patients over 1 year. *41<sup>st</sup> Annual New Zealand Society Scientific meeting.* April 2016. New Plymouth.
5. Oral: Physiotherapy management for complex regional pain syndrome on the South Island. *PAIN@Otago Inaugural conference.* November 2016. Dunedin.
6. Plenary speaker invitation; The Assessment of persistent pain. *42<sup>nd</sup> Annual New Zealand Pain Society Scientific meeting.* March 2017. Nelson.
7. Plenary speaker invitation; Physiotherapy for persistent pain. *42<sup>nd</sup> Annual New Zealand Pain Society Scientific meeting.* March 2017. Nelson.
8. Panel discussion speaker invitation. Managing persistent pain in the community. *42<sup>nd</sup> Annual New Zealand Pain Society Scientific meeting.* March 2017. Nelson.
9. Oral: The outcomes of a longitudinal, observational study of Physiotherapy and complex regional pain syndrome on the South Island. *PAIN@Otago conference.* February 2018. Dunedin.

The candidate presented the findings to South Island Physiotherapists:

May 2018, Dunedin, Otago Physiotherapy New Zealand Branch, 2 hours.

May 2018, Dunedin Hospital Physiotherapy Department, 1 hour.

# Table of contents

COMPLEX REGIONAL PAIN SYNDROME (CRPS) PHYSIOTHERAPY MANAGEMENT:.....	i
A COHORT, OBSERVATIONAL, PROSPECTIVE, LONGITUDINAL STUDY.....	i
ACROSS THE SOUTH ISLAND .....	i
OF NEW ZEALAND.....	i
Personal Reflection .....	i
ABSTRACT .....	ii
Key words.....	iii
PREFACE.....	iv
ACADEMIC PUBLICATIONS AND PRESENTATIONS .....	iv
Table of contents.....	vii
List of figures.....	xiv
List of tables .....	xvi
List of abbreviations.....	xix
CHAPTER ONE.....	1
Introduction .....	1
1.1 Context.....	1
1.2 Purpose .....	2
1.3 Aims .....	2
1.4 Ethical and cultural considerations .....	3
1.5 Funding.....	4



CHAPTER TWO .....	5
Literature review .....	5
2.1 The Diagnosis of CRPS .....	5
2.2 The pathophysiology of CRPS.....	7
2.3 The incidence of CRPS .....	8
2.4 The risks for the onset of CRPS.....	8
2.5 The CRPS trajectory.....	10
2.6 Beliefs about the management for CRPS .....	11
2.7 Physiotherapy management for CRPS .....	12
Background.....	12
2.8 Paediatric CRPS physiotherapy .....	20
2.9 Dose of intervention and adherence .....	21
2.10 Medical management of CRPS .....	22
2.11 Alternative therapies and acupuncture for the management of CRPS .....	24
2.12 The multidisciplinary management of CRPS .....	24
2.13 Central sensitisation .....	27
2.14 The therapeutic relationship.....	30
2.15 Mental health and the treating Physiotherapist of a CRPS patient .....	30
2.16 An historical account and evaluation of the models for CRPS management .....	31
2.17 Gaps in the body of knowledge.....	35
CHAPTER THREE.....	37
Initial Survey of South Island Physiotherapists .....	37
3.1. Introduction.....	37
3.2. Purpose .....	37
3.3. Method for Recruitment of Physiotherapists .....	37

3.4. Statistical Analysis .....	38
3.5. Results .....	38
3.5.1. Physiotherapist participation .....	38
3.5.2. The routine physiotherapy interventions used .....	40
3.5.3. Physiotherapists' beliefs.....	44
3.6. Discussion.....	46
CHAPTER FOUR.....	49
Method and Hypothesis Generation.....	49
4.1 Introduction.....	49
4.2 Aims .....	49
4.3 Method.....	49
4.3.1 Recruitment of participants .....	49
4.3.2 Participant inclusion and exclusion criteria.....	52
4.3.3 Demographic and relevant clinical variables.....	52
4.3.4 Medical and Psychological intervention .....	52
4.3.5 Collection of physiotherapy intervention .....	52
4.3.6 Physiotherapy intervention.....	54
4.4 Instruments.....	55
4.4.1 Quantitative instruments .....	56
4.4.2 Quantitative predictors instruments .....	59
4.4.3 Telephone interviewing.....	66
4.5 Hypothesis generation .....	66
4.5.1 Primary hypothesis.....	66
4.6. Secondary objective generation .....	67
4.6.1 Secondary objectives.....	67
4.5.3 Null hypothesis .....	67
4.6 Analytic Approach .....	67

4.7 Statistical power .....	67
4.8 Summary .....	68
CHAPTER FIVE .....	69
Cohort descriptive and baseline statistics .....	69
5.1 Introduction.....	69
5.2 Participation of CRPS patients.....	69
5.3 Demographic characteristics and descriptive statistics .....	71
5.4 Confirmation of CRPS diagnosis according to Budapest criteria.....	74
5.5 Concurrent Medical and Psychological variables .....	75
5.6 Baseline predictor variables .....	76
5.7 Baseline outcome measures .....	77
5.8 Discussion.....	80
CHAPTER SIX.....	82
Description of Physiotherapy, Medical and Psychology interventions applied .....	82
6.1 Introduction.....	82
6.2 Method.....	82
6.2.1 The five aspects of physiotherapy.....	82
6.2.2. Medical and psychology interventions .....	83
6.2.3. Analytic approach .....	83
6.3 Results .....	84
6.3.1 Physiotherapy intensity .....	84
6.3.2 Physiotherapy category of intervention.....	89
6.3.3 The report of physiotherapy homework participation adherence .....	92
6.3.4 Satisfaction with physiotherapy care by participants .....	96
6.3.5 Medical and Psychological support .....	100
6.3.6 The tests for baseline categorical variables .....	104

6.4 Discussion.....	106
CHAPTER SEVEN.....	110
Description of changes over time .....	110
7.1 Introduction.....	110
7.2 Method.....	110
7.3 Results .....	111
7.3.1 The record of autonomic features .....	111
7.3.2 Changes with ability to work.....	111
7.3.3 Changes to outcome measures.....	113
7.3.4 Student t-tests for outcome measure changes.....	117
7.3.5 Changes to outcomes and adherence.....	118
7.4 Hypothesis test 1.1 .....	122
7.5 Discussion.....	123
CHAPTER EIGHT .....	126
Prognostic relationships with complete recovery .....	126
8.1 Introduction.....	126
8.2 Method.....	127
Analytic approach.....	127
8.3 Results .....	127
8.3.1 The tests for baseline continuous variable differences.....	128
8.3.2 The tests for the time to diagnosis and to commence physiotherapy intervention .....	130
8.3.3 Logistic regression analysis continuous variables .....	133
8.3.4 Logistic regression analysis of the timing to diagnosis and to commencement of physiotherapy .....	137
8.4 The hypothesis test 1.2.....	138
8.5 Discussion.....	140

CHAPTER NINE.....	144
The relationships between physiotherapy applied and complete recovery .....	144
9.1 Introduction.....	144
9.2 Method.....	144
9.3 Results .....	144
9.3.1. Physiotherapy intensity relationship with a complete recovery from CRPS .....	144
9.3.2. The effect of individual TIP interventions .....	147
9.3.3. The effects of prescribed homework exercises .....	148
9.4 The objective test 2.1.....	149
9.5. The objective test 2.2.....	150
9.6 Discussion.....	151
CHAPTER TEN.....	154
Development of a conceptual clinical model .....	154
10.1 Introduction.....	154
10.2 Method.....	155
10.3 Results .....	155
10.4 A proposed conceptual clinical model for CRPS management .....	164
10.4.1 The two foundations.....	165
10.4.2 The four pillars .....	165
10.4.3 The four physiotherapy intervention mainstays.....	168
10.5 Discussion.....	172
10.6 Summary.....	173
CHAPTER ELEVEN.....	174
Discussion.....	174
11.1 Synopsis.....	174

11.2 Deliberation.....	177
11.3 Implications for practitioners .....	181
11.4 Strengths .....	183
11.5 Limitations .....	184
11.6 Identifying bias with the Quality in Prognostic study (QUIP) tool .....	186
11.7 Implications for future research .....	187
CHAPTER TWELVE .....	191
Conclusions .....	191
ACKNOWLEDGEMENTS.....	194
REFERENCES .....	195

## List of figures

Figure 2.1. Fear avoidance and central plasticity flow chart. Image by Tracey Pons. ....	15
Figure 2.2. The development of a central sensitisation, flow chart by Tracey Pons. ....	29
Figure 3.1. Flow chart participation with the physiotherapy intervention questionnaire. ....	39
Figure 3.2. Use of graded motor imagery in clinical physiotherapy practice. ....	43
Figure 3.3. The belief about reducing the pain being essential in CRPS to improve the functioning.....	45
Figure 3.4. Improving the function is essential in order to reduce the pain experience. ....	45
Figure 4.1. Flow chart for Physiotherapist referral. ....	53
Figure 5.1. Flow chart of participation. ....	70
Figure 5.2. Age distribution.....	71
Figure 6.1. Kaplan-Meier plot showing numbers of weeks to discharge.....	87
Figure 6.2. Route of discharge from physiotherapy.....	88
Figure 6.3. Discharge from physiotherapy at 12 weeks. ....	88
Figure 6.4. Days of physiotherapy care before discharge. ....	89
Figure 6.5. Weekly averages of each physiotherapy category of intervention.....	91
Figure 6.6. The frequency of homework adhered to in number of days per-week at each interval.....	94
Figure 6.7. The frequency of homework adhered to in number of times per-day at each interval.....	94
Figure 6.8. The rating about homework to relieve pain at each interview.....	96
Figure 6.9. Participant satisfaction with physiotherapy care at 6 weeks with the Deyo and Diehl satisfaction with care. ....	97
Figure 6.10. Participant satisfaction with physiotherapy care at 6months with the Deyo and Diehl satisfaction with care. ....	98
Figure 6.11. Participant satisfaction with physiotherapy care at 1 year with the Deyo and Diehl satisfaction with care. ....	99

Figure 6.11. Participant satisfaction with care being better, the same, worse or do not know when compared with other care. ....	100
Figure 7.1. Work category at baseline and 1 year later. ....	112
Figure 7.2. Raw score, pain, with PRI at each interval. ....	113
Figure 7.3. Raw score, pain, with NRS11 at each interval. ....	114
Figure 7.4. Raw score quality of life and function, WHODAS2 at each interval. ....	115
Figure 7.5. Raw score, FFI, at each interval. ....	116
Figure 7.6. Raw score, upper limb function, QuickDASH, at each interval. ....	117
Figure 8.1. Complete recovery 1 year later for cohort. ....	128
Figure 8.4. WHODAS2 change after 1 year and time in months to diagnosis. ....	131
Figure 8.5. WHODAS2 change after 1 year and time in months to commence physiotherapy. ....	131
Figure 8.6. PRI change after 1 year and time in months to diagnosis. ....	132
Figure 8.7. PRI change after 1 year and time in months to commence physiotherapy. ....	133
Figure 10.1. Spearman Correlation model for relationships between physiotherapy interventions TIP and TIF 6-week, weekly averages and full recovery, $p < 0.05$ . ....	159
Figure 10.2. Model with Spearman correlation factors for complete CRPS recovery, $p < 0.05$ . ....	162
Figure 10.3. A proposed conceptual model of effective physiotherapy for complete recovery from CRPS with four pillars, four revolving physiotherapy mainstays secured on a foundation of prevention and the promotion of good mental health. ....	171



## List of tables

Table 3.1. Physiotherapy interventions for CRPS and frequency of use .....	41
Table 3.2. Significant differences between those Physiotherapists who seldom saw CRPS vs. those who saw CRPS patients often.....	44
Table 3.3. Summary of Physiotherapists' beliefs about what is best for CRPS intervention method.....	46
Table 4.1. Details about questionnaire interview schedule.....	63
Table 4.2. Details of measurement units for Outcome Instrument.....	63
Table 4.3. Details of measurement for potential predictor instrument.....	64
Table 4.4. Details about which questionnaires are used when and approximately how long each one takes to interview.....	64
Table 5.1. Baseline follow up characteristics.....	72
Table 5.2. Baseline descriptive statistics.....	73
Table 5.3. Baseline months to diagnosis, physiotherapy and Pain Medical Specialist.....	74
Table 5.4. Objective baseline autonomic changes recorded at baseline by treating Physiotherapist.....	75
Table 5.5. Baseline Medical and Psychological care.....	76
Table 5.6. Baseline predictor variable descriptive statistics.....	77
Table 5.7. Outcome baseline measures mean, standard deviation median, upper and lower quartiles.....	78
Table 5.8. Student-t tests for differences between baseline categorical and continuous variables of lost to follow up and responders.....	79
Table 6.1. The number of physiotherapy sessions attended in each interval.....	84

Table 6.2. Total cumulative physiotherapy sessions attended by each interval. ....	85
Table 6.3. Mean and. median number of physiotherapy sessions, attended per week, for each interval. ....	86
Table 6.4. Categorised physiotherapy interventions weekly means. ....	90
Table 6.5. Weekly average change of physiotherapy intervention category between 6 weeks and 6 months showing reduction. ....	92
Table 6.6. Physiotherapy homework participation frequency per week and per day. ....	93
Table 6.7. Physiotherapy homework participation frequency per-week and per-day differences between those who self-discharged or were discharged by treating Physiotherapist. ....	95
Table 6.8. Medical and psychological support applied over the year at any time concurrent with physiotherapy. ....	101
Table 6.10. Mann-Whitney U tests for baseline differences with psychological support. ...	102
Table 6.11. Mann-Whitney U tests for differences with medical prescriptions of secondary analgesia tricyclic group. ....	103
Table 6.12. Mann-Whitney U tests for differences with medical prescriptions of secondary analgesia anti-convulsant group. ....	104
Table 6.13. Mann-Whitney U tests for baseline differences between CRPS Type 1 and 2..	105
Table 6.14. Mann-Whitney U tests for baseline differences between inciting injuries. ....	106
Table 7.1. The record of autonomic features of the affected CRPS limb as compared to the unaffected limb at each interval interview. ....	111
Table 7.2. Changes to outcome measures at each interval. ....	118
Table 7.3. Changes to outcome measures and duration of physiotherapy. ....	120

Table 7.4. Unpaired Student t-tests for significance of outcomes measures between duration of physiotherapy for those who were discharged and those who required ongoing care beyond 1 year. ....	121
Table 7.5. Unpaired Student t-tests for significance of outcomes measures between duration of physiotherapy for those who were discharged and those who self-discharged. ....	122
Table 8.1. Continuous predictor variables means and student t-tests for complete recovery. ....	129
Table 8.2. Concurrent psychological support student t-tests for complete recovery. ....	130
Table 8.3. Univariate analysis of continuous independent variables. ....	134
Table 8.4. Univariate analysis of categorical independent variables. ....	135
Table 8.5. Multivariate analysis of continuous independent variables. ....	136
Table 8.6. Multivariate logistic regression for categorical independent variables. ....	137
Table 8.7. Univariate logistic analysis of diagnosis timing and recovery. ....	138
Table 8.8. Univariate logistic analysis of physiotherapy timing and recovery. ....	138
Table 9.1. Physiotherapy category of intervention dose and relationship with complete recovery. ....	145
Table 9.2. Univariate analyses for physiotherapy treatment intervention categories averages on complete recovery. ....	146
Table 9.3. Multivariate analyses for physiotherapy intervention categories averages. ....	147
Table 9.4. Univariate analyses of treatment interventions for pain modulation. ....	148
Table 9.5. Univariate analysis of prescribed homework and its rating on complete recovery. ....	149
Table 10.1. Spearman correlation coefficient matrix: TIF and TIP 6-week, weekly averages and complete recovery. ....	158

## List of abbreviations

CRPS	→	Complex Regional Pain syndrome
NZ	→	New Zealand
RCT	→	Randomised control trial
IASP	→	International Association for the Study of Pain
e.g.	→	For example
viz.	→	Namely
CRPS 1	→	CRPS Type 1
CRPS 2	→	CRPS Type 2
RSD	→	Reflex sympathetic dystrophy
SCS	→	Spinal Cord Stimulation
TENS	→	Transcutaneous Electrical Nerve Stimulation
TSK	→	Tampa Scale for Kinesiophobia
HAI	→	Health Anxiety Index
Kessler10	→	Ten-item psychological distress Kessler scale
GMI	→	Graded motor imagery
RSD	→	Reflex Sympathetic Dystrophy
GEXP	→	Graded exposure
PEXP	→	Pain Exposure
Vs.	→	Versus

PM	→	Pain modulation
DNIC	→	Diffuse noxious inhibitory control
MLD	→	Manual lymphatic drainage
NMDA	→	N-methyl-D-aspartate
AMPA	→	$\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
TIF	→	Treatment interventions for function
TIP	→	Treatment interventions for pain modulation
Educ	→	Education
TII	→	Treatment interventions for immobilisation
Pass	→	Passive treatment interventions
CBT	→	Cognitive behavioural therapy
ACT	→	Acceptance and commitment therapy
SMT	→	Sensory–motor training
DBE	→	Deep breathing exercise
PRI	→	Pain rating index
NRS-11	→	11-point Numerical rating scale
MPQ-SF	→	Short form McGill Pain Questionnaire
WHODAS 2	→	World Health Organisation Disability Assessment Schedule 2.0
QuickDASH	→	Quick Disability of the Arm, Shoulder, Hand questionnaire
FFI	→	Foot Function Index
DDS	→	Deyo and Diehl Satisfaction with care questionnaire

SRI	→	Sensory rating pain index
ARI	→	Affective rating pain index
EVI	→	Evaluative intensity pain
EPQ-BV	→	Eysenck Personality Questionnaire Extraversion and Neuroticism scale, brief version
EPQN	→	Eysenck Personality Questionnaire Neuroticism scale
EPQE	→	Eysenck Personality Questionnaire Extraversion scale
OR	→	Odds Ratio
CI	→	Confidence interval
P	→	Power
Chi <sup>2</sup>	→	Chi squared
POOL	→	Pool based primary exercise
MHP	→	Medical Health Professional

# CHAPTER ONE

## Introduction

### 1.1 Context

What is Complex Regional Pain Syndrome (CRPS)? It is a syndrome which is not yet fully understood. It was previously described as a persistent neuropathic pain condition that followed any trivial injury where the pain experience is severe and disproportionate to the inciting event [1-4]. However, more recently, in 2016, it was suggested that it did not meet the strict criteria for the definition for neuropathic pain, and its formal classification hangs in the balance [5].

Historically, it was first documented in the American Civil War [6, 7] and was broadly named Sudeck's atrophy or algodystrophy [7-9]. Later, during World War I and II it was described as causalgia [10, 11]. In 1953 two types of this syndrome were recognised and were named Reflex Sympathetic Dystrophy (RSD) if the nerve was not damaged, as it was thought to be a problem primarily associated with the sympathetic nervous system, and Causalgia if the nerve had been physically and permanently damaged [12, 13]. It was subsequently identified in 1970s that the problem involved the peripheral as well as central nervous system, but the mechanisms of the physiology involved remained inconclusive [12].

These broad diagnoses raised controversies for both researchers and clinicians [14]. In 1994 the committee for taxonomy of the International Association for the Study of Pain (IASP) met together with clinicians and academics in the area to identify specific diagnostic criteria for this syndrome. The controversy had been that this condition was not exclusively a problem of the autonomic nervous system, so the terms RSD and Causalgia needed to be changed. This syndrome had conclusively been shown not to be a problem primarily related to the sympathetic nervous system [15]. This IASP committee changed the name to Complex Regional Pain Syndrome (CRPS) either Type I or Type 2 to replace the previous names of RSD and Causalgia, respectively [16].

However, CRPS and the IASP nomenclature continued to pose a difficult problem. It was found that the diagnostic criteria decided upon by the IASP were not specific enough and were not used uniformly in clinical or academic published research [13, 17, 18]. It was likely that CRPS was over diagnosed, since other criteria like the Veldman criteria [19] were also used to define it [20, 21]. In 2007, in order to obtain consensus, criteria were debated by the

IASP and the specialist Budapest committee [13, 22]. These Budapest criteria are now considered to be reasonably accurate in making a clinical diagnosis and for research involving CRPS [16, 17, 20, 22-27].

Although CRPS diagnostic criteria were more robustly defined by these criteria, the aetiology and development of the CRPS is not yet fully understood [26]. Effective treatment strategies in both the research and clinical fields are not yet fully developed [28-30]. The need for physiotherapy management for CRPS continues to be widely accepted, despite a lack of understanding about efficacy [31-33]. This project sought to explore and evaluate the current physiotherapy management of CRPS across the out-patient physiotherapy departments and private clinics of the South Island of NZ from July 2013 to March 2017.

## **1.2 Purpose**

The purpose of this project was to answer questions regarding outcomes or predictors associated with the physiotherapy interventional methods used for CRPS patients in a clinical setting across a region, so that a suggested conceptual model could be proposed. Regional, standard physiotherapy practice had not been evaluated before and there is no current valid clinical management model. A systematic review of the evidence for all management of CRPS noted that there is some evidence for physiotherapy intervention being beneficial for both pain reduction and functional improvement, and for the ability of the patient to cope with the condition [31]. However, the actual physiotherapy interventions used were poorly described, and no proposed model for management was provided.

A subsequent systematic review of CRPS intervention methods describes each intervention and provides a critical evaluation about the strength for the evidence [34]. The evidence for physiotherapy interventions used for CRPS in clinical practice is shown to be poor.

## **1.3 Aims**

The primary aims of this project were as follows: To document standard, regional physiotherapy clinical practice; measure patient outcomes and changes over time/natural history for one year after commencing physiotherapy; to document and categorise the physiotherapy interventional methods received; to identify predictors of patient outcomes; to



investigate the associations of the current physiotherapy intervention for CRPS with patient outcomes; and to suggest a conceptual model for physiotherapy CRPS management.

Secondary aims were: To document and categorise the physiotherapy beliefs and usual practice in the treatment of CRPS; to describe the characteristics of CRPS patients living in the South Island of New Zealand (population ~ 1 million, area 150 437 km<sup>2</sup>) [35]; and to determine the risks for the onset of CRPS.

The priority was to achieve these aims with robust evidence that was applicable to everyday physiotherapy clinical practice. A suggestion has been made, in the psychological literature, to address a potential separation between academics with their research findings and everyday clinical practice [36]. It was reported that there was a pressing need for practicing clinicians to have guidelines or suggestions for their effective clinical practice that were available from relevant research, hence the priority of this project's aim.

An additional secondary aim for this project was to document the outcomes in the Māori population affected with CRPS. There is no evidence available about how physiotherapy interventions for CRPS affect ethnic groups. In New Zealand this is particularly important to our Māori community. The Treaty of Waitangi, a unique and valuable treaty, lays a foundation for mutual co-operation and understanding between the Pakeha and Māori ethnic groups in New Zealand [37]. As such, this project aimed to further explore the Māori narrative of their experience with CRPS during outpatient physiotherapy.

Structure of this thesis:

This thesis involved two studies. The first; assessment of what Physiotherapists on the South Island usually applied in everyday clinical practice for their management of CRPS and what they believed to be important. The second and larger study evaluated the outcomes for patients with CRPS who attended Physiotherapy and the associations of their outcomes with the intervention categories applied.

#### **1.4 Ethical and cultural considerations**

It is important for any research to have the scrutiny of independent ethical review. Since the project was an observational analysis of de-identified individuals, the New Zealand National Health Disability and Ethics committee confirmed that this project did not require its review. Ethical approval for this study was provided by the University of Otago Ethics committee (Reference number H13/103). Further ethical approval was granted from each of the four

South Island District Health Boards. The project collected data from December 2013 to December 2017 with formal ethical approval being extended to December 2019.

It is crucial for research in New Zealand to be accountable to and observe the Treaty of Waitangi [37, 38]. New Zealand is unique with its respect for indigenous founders, the Māori. Thus biculturalism is fundamental to the nation's philosophy. For this project, Māori consultation involved engaging with the University Māori research advisor, the Rapaki Māori Women's Welfare League and the Māori iwi advisors associated with each District Health Board in the South Island.

These formal notifications of Ethical approvals and Māori consultations can be found in Appendix B.

Participants and Physiotherapists were not paid for their participation. A full written and verbal explanation about the project was given to each Physiotherapist and participant. All participants were asked to sign informed, written consent in order to participate. This consent was for: a) access to their clinical physiotherapy notes and, b) telephone calls for outcome measures by the researcher or independent interviewer.

All participants were given the option to withdraw from the project at any stage without giving an explanation. The candidate had no commercial association or other relationship with outpatient physiotherapy departments or clinics in New Zealand that might have resulted in a conflict of interest. This project was not anticipated to result in intellectual property, other than academic publication(s).

All participants' information was entered de-identified into the database as a numerical code. It would not be possible to identify any individual from any publication of the data. All data, clinical notes and outcomes measure records were stored in locked cabinets or electronically behind password-protected servers so that anonymity and data security was ensured.

## **1.5 Funding**

The New Zealand Pain Society (NZPS) contributed towards the costs of an independent interviewer and the costs of presentation at the Australian Pain Society conferences in 2017 and 2018.

# CHAPTER TWO

## Literature review

Aspects of this literature review have been published as [39], [40], [41] and [42] and are available in Appendix A.

### 2.1 The Diagnosis of CRPS

The problem is that a myriad of causes for pain are often included in the title of CRPS [43, 44]. The diagnostic controversies resulted in the adoption of the Budapest criteria [45, 46] for the diagnosis of CRPS.

Since there are no gold standards for the diagnosis of CRPS, the diagnosis needs to rely on subjective signs and symptoms [45]. The interaction between neurological dysfunction and neurological plasticity is not yet fully understood in the development of neuropathic pain [47]. Furthermore, it has been suggested the CRPS signs and symptoms do not meet all the criteria needed to be defined as neuropathic pain [5]. Criteria used in the literature to identify a CRPS diagnosis were the Veldman criteria [19] or the International Association for the Study of Pain (IASP) criteria, occasionally also referenced in the literature as Bruehl's criteria [13]. The Budapest consensus meeting confirmed that the Budapest criteria were shown to be reliable and valid and also have better sensitivity and reliability than the other diagnostic criteria for CRPS [22].

The Budapest criteria are as follows [22]:

*CRPS describes an array of painful conditions that are characterised by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional (is not a specific nerve territory or dermatome), and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor and/or trophic findings. The syndrome shows variable progression over time.*

*To make the CLINICAL diagnosis, the following criteria must be met:*

1. *Continuing pain which is disproportionate to any inciting event*
2. *Must report at least one symptom in three or four following categories:*
  - **Sensory:** *Reports of hyperaesthesia or allodynia*
  - **Vasomotor:** *Reports of temperature asymmetry or skin colour changes or skin colour asymmetry*

- **Sudomotor/Oedema:** Reports of oedema or sweating changes or sweating asymmetry
  - **Motor/Trophic:** Reports of decreased range of movement and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
3. Must display at least one sign at time of evaluation in two or more of following categories:
- **Sensory:** Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch) and/or temperature sensation and/or deep somatic pressure and/or joint movement
  - **Vasomotor:** Evidence of temperature asymmetry  $>1^{\circ}\text{C}$  and/or skin colour changes or skin colour asymmetry
  - **Sudomotor/Oedema:** Evidence of oedema or sweating changes or sweating asymmetry
  - **Motor/Trophic:** Evidence of decreased range of movement and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
4. There is no other diagnosis that better explains the signs and symptoms

*For RESEARCH PURPOSES; diagnostic decision rule should be at least one symptom **in all four categories** and at least one sign observed at evaluation in two or more sign categories.*

The difficulty around accurate diagnosis is that changes resembling CRPS can be observed following surgery with the usual immobilisation for fractures, especially around the time of cast removal. In most cases, these changes resolve spontaneously [48, 49]. However, a small proportion continue to develop CRPS [50, 51]. A problem is that fifteen per cent of all adult fractures involve the distal radius, and this fracture is the most common seen in Accident and Emergency Departments [52]. Any immobilisation has been shown to be a risk factor for the onset of CRPS [49] and in the development of neuropathic pain [53]. Healthy volunteers are also shown to develop CRPS like symptoms following immobilisation [53, 54]. These studies imply that making a CRPS diagnosis is difficult and the trajectory following a fracture is not predictable.

Importantly, the diagnosis of CRPS does not only follow a fracture, but also follows any trauma surgery or injury. A web base survey of 875 CRPS patients all reported trauma or some injury as the precipitating event: surgery 30.9%; fractures 17%; sprain 11.8%; crush

injury 11.4%; contusions 3.4%; and dislocations 1.4% [55]. Furthermore, CRPS can follow total knee replacement [50].

Diagnosis is difficult since accurate diagnostic tools are not available and clinical evaluation is necessary and shown to be unreliable. It has been found in the Dutch population that CRPS is most likely to be first diagnosed by the General Practitioner, with subsequent medications prescribed and referrals for interventions usually made by the Specialist Pain Medicine Physician [52]. A German study of 158 patients with distal radius fractures showed that for the diagnosis of CRPS, a clinical evaluation had a higher specificity (94%) and sensitivity (78%) than thermography (specificity 66%, sensitivity 58%) or radiography (specificity 91%, sensitivity 33 %) [56]. Diagnostic precision is difficult, for example, a prospective study following fractures showed that for the small proportion of patients who develop CRPS, the time taken to make a diagnosis is sixty three (fourty-six to seventy-two) days following an injury [57]. Investigation by laser Doppler flow was found to be 89.8% accurate in making a diagnosis of sympathetically maintained pain in CRPS [58]. Bone scintigraphy has not been shown to be a useful diagnostic tool in CRPS [59].

## **2.2 The pathophysiology of CRPS**

Historically, CRPS was thought to be Reflex Sympathetic Dystrophy if the nerve was not damaged, as it was understood to be a problem primarily associated with the sympathetic nervous system. CRPS was thought to be Causalgia if the nerve had been physically and permanently damaged [12, 13]. It was identified in the 1970s that the problem involved the peripheral and central nervous system, but the mechanisms for the physiology involved remained inconclusive [12]. Earlier studies had shown mixed results regarding sympathetic involvement and subsequently CRPS has been conclusively shown not to be a problem primarily related to the sympathetic nervous system [15, 60].

CRPS has been suggested to be a multi-factorial disease [61]. Hence the ‘complex’ in CRPS. The following have been suggested as contributing pathophysiological mechanisms: ischaemia then reperfusion; small fibre neuropathy; neurogenic inflammation; sympathetic denervation (as CRPS can be associated with an increased heart rate and reduced heart rate variability, a consequence of the aberrant autonomic nervous system) [62]; aberrant endogenous modulating pain mechanisms [63, 64] or alteration of muscle nociception circuitries [65], especially for those CRPS patients who develop dystonia. Genetic mechanisms, such as the alteration of the Nrf2 single nucleotide polymorphism in sub groups

of patients [66] and the rs1048101 single nucleotide polymorphism in the alpha1a-adrenoreceptor have been found to be significant risk factors in patients who developed CRPS [67].

Other more speculative factors include ischaemia to the lateral medulla due to whiplash injury, or a hereditary predisposition to reduced blood flow through the vertebral artery supply to the anterior cervical spine (case studies in two patients) [68].

### **2.3 The incidence of CRPS**

Information about the incidence for CRPS is sparse. There are only two epidemiological studies available in the literature; both reporting its prevalence to be low, ranging from 5.46 (Olmstead, USA) per 100 000 to 26.2 (The Netherlands) per 100 000 [69, 70]. CRPS Type 1 is more often diagnosed than Type 2 which further dilutes accuracy for Type 2 [71]; this low prevalence has led to difficulty in research, as robust statistical analysis necessitates a larger sample size [72].

#### Summary:

- The diagnostic process for CRPS is not straightforward.
- The most robust diagnostic tool to use is the application of the Budapest criteria.
- Changes resembling CRPS may follow trauma, fractures or immobilisation. Most cases resolve with few progressing to meet the Budapest criteria.
- Clinical evaluation has better sensitivity and specificity for an accurate diagnosis than thermography or radiography.
- A complete understanding about CRPS pathophysiology is lacking.
- CRPS prevalence is low.

### **2.4 The risks for the onset of CRPS**

It has been recommended that early warning signs for the potential for CRPS to develop are heeded [61, 73]. However, CRPS is unlikely to be an exaggerated inflammatory response following trauma or surgery, but seems to form a separate clinical entity [74]. Even with an increased regional inflammatory score and a distal radius fracture, it has been shown that at 6 to 9 weeks post fracture, there is a low risk of developing CRPS as the transitory dysfunction resolves over time [75]. But diligent early detection and a systematic management plan was reported to markedly reduce the onset of CRPS following fracture of the distal radius with an eight-step process used to achieve this [76].

In contrast, the bizarre physical and autonomic features sometimes observed in CRPS had led earlier practitioners to believe that this was possibly an element of somatoform malingering or an hysterical personality associated with being female [77]. This has subsequently been shown to be untrue [78-80]. The reasons for the potential risks associated with gender are however, not yet known since CRPS consistently affects females more frequently than males [55, 69, 70].

Reviews suggest there is no strong evidence for psychological or personality factors that predict the likelihood of CRPS occurring following an injury [79, 80]. Studies show that CRPS-like symptoms following total knee arthroplasty were unable to be predicted by pre-operative psychological distress or pain levels [50]. However, it is recognised in other conditions that psychological, behavioural and perceptions of stress can also exacerbate the pain experience [81, 82]. Catastrophising is shown to be a risk factor for poor outcomes with persistent low back pain [83, 84] or spinal fusion [85]. However, this has not been consistently shown with CRPS [86].

At the start of this project in 2013 there were no systematic reviews about risks for the onset of CRPS Type 1. The candidate undertook a systematic review of these risks. The work was published in *Anesthesiology Research and Practice* [39]. The following is a synopsis of the findings.

Current literature about the risk factors for the onset of Complex Regional Pain Syndrome Type 1 (CRPS 1) remain sparse. Eligible articles were analysed dated January 1996 to April 2014 and potential risk factors for the onset of CRPS 1 were identified from 10 prospective and six retrospective studies. This systematic review showed that accurate potential risk factors for the onset of CRPS 1 remain elusive. Studies remain heterogeneous and are of mixed quality and relevance, and with varied weighting against the risks of bias. The low prevalence of CRPS 1, accompanied by no gold standard for diagnosis, contributed to the difficulty of being able to determine potential risk factors for the onset of CRPS 1.

Potential risk factors identified with strong weighting against bias, good quality and relevance are summarised as follows: being female (particularly post-menopausal); sustaining a fracture of the distal radius; suffering an ankle dislocation or intra-articular fracture; and reporting higher than usual levels of pain in the early phases after trauma. Potential risk factors with weaker weighting against bias and poorer quality and relevance include immobilisation, psychosocial barriers, and a positive diagnostic bone scan. Definite

conclusions cannot be drawn as evidence remains inconsistent across multiple trials, and that homogenous studies are lacking.

Summary:

- This systematic review showed the strongest weighting for strength, lack of bias, quality and relevance for the risks of CRPS onset to be: being female (particularly a post-menopausal female); fracture of the distal radius; an ankle dislocation or intra-articular fracture; and reporting higher than usual levels of pain in the early phases of trauma.

## 2.5 The CRPS trajectory

The outcomes for CRPS show high heterogeneity where early review showed that half the patients diagnosed with CRPS recovered with conservative management [87]. However, follow-up after a year showed that some patients developed deterioration of pain (56%) and function (78%). Furthermore, more than half (67%) were either jobless or had changed jobs because of the pain. A more recent Dutch study assessed 102 CRPS patients over a range of 2-11 years following diagnosis. The study found that 16% (CI 9-22) reported a gradual deterioration of their symptoms, and 31% (CI 19-43) were no longer able to participate in productive work [88]. A 2016 New Zealand study showed that 26.8% of a cohort of 56 CRPS patients still met the Budapest criteria for a CRPS diagnosis one year later [89]. It was also suggested that the trajectory can be unpredictable [90].

On the positive side, a 2003 epidemiological study in the USA reported that 74% exhibited full resolution and that resolution had occurred spontaneously for some, but the proportion of this group was not reported [69]. In 2017 a Spanish study showed that 88.9% of 108 CRPS patients showed a favourable outcome with treatment [91]. In contrast, it has been reported that there is a sub group for whom CRPS becomes recalcitrant [88]. Unfortunately, it may even cost the affected person their life via suicide [44, 69].

There are two systematic reviews evaluating prognostic factors and both report that prognostic factors for CRPS outcomes are difficult to determine [92, 93]. Greater sensory disturbances may be associated with poorer outcomes [93]. The specific factors that predict a poor outcome for the recalcitrant sub-group lack clarity [92]. The early detection and diagnosis of CRPS is suggested to have a positive effect on improving outcomes. This was reported in: a study of 108 patients [91]; for children [94]; following surgery [95]; and for



those receiving physiotherapy for CRPS [96]. However, none provide evidence for effect sizes or confidence intervals (CI).

Higher levels of allodynia to light brushing was predictive of a poorer outcome when Spinal Cord Stimulation (SCS) was used to manage persistent CRPS (sensitivity 75%, specificity 81%) [97]. The presence of allodynia also predicted a poorer outcome in a prospective study for sympathetic blockade [98, 99], but effect sizes were not reported.

However, a cross sectional study suggests that fear avoidance can become problematic for some CRPS patients [100]. The pictorial fear of activity scale was found to be a more significant predictor of functional limitation than pain severity or the Tampa Scale for Kinesiophobia (TSK) ( $\beta = 0.27$ ,  $p < 0.05$ ). It was suggested that fear avoidance may not be predictive with any strong effect on outcomes, but is a factor to be considered with poor recovery [101].

#### Summary:

- Outcomes show high heterogeneity.
- Definitive prognostic factors are not yet known.
- A high level of allodynia is suggested as a predictor of a poor outcome with SCS.

## **2.6 Beliefs about the management for CRPS**

The literature about the beliefs that Medical Practitioners or Allied Health Professionals hold on the management of CRPS is sparse. One study showed that members of a hand team were found to perceive the risk of developing CRPS very differently from each other in their interpretation of clinical signs [102]. In other domains, beliefs held by Medical Practitioners or Allied Health Professionals were shown to affect clinical practice. For example, the report about pain from the elderly to a clinician is not always taken seriously, when compared to a similar report from a younger patient [103].

Physiotherapists have been shown to continue to treat low back pain without evidence of improvement [104], believing that their management was not only about physical treatment, but also about providing emotional support. It was reported that they felt awkward about discharging their patient into a void of no care. Financial gain from such a service was not believed to be the primary motivation.

Beliefs about opioid medications are known to affect prescription practice [105, 106], with prescribers showing a range of beliefs about it being essential, versus those who feel the opposite. Beliefs ranged from feeling helpless versus feeling confident in providing anything else to console a patient's distress.

What Physiotherapists believe to be important for their management of CRPS is not reported in the literature. The current project explored what South Island Physiotherapists believed to be important in their clinical management of CRPS patients. The results were published in 2017 in *International Journal of Clinical Medicine* [40] and Chapter 3 of this thesis outlines the findings about these beliefs.

## **2.7 Physiotherapy management for CRPS**

### **Background**

There are two recent systematic reviews about the physiotherapy management of CRPS. The first found that a specific contribution of physiotherapy for CRPS is difficult to determine as robust trials include other allied or medical management and potentially confound the findings [107]. This review showed level two evidence for Graded Motor Imagery (GMI) for adult management of CRPS Type 1. However, the second review [108] rated all current evidence for physiotherapy management of CRPS as poor, although GMI or mirror therapy were helpful for the reduction of pain and improvement of function. Both these authors called for larger trials and more research to identify the evidence for the physiotherapy management of CRPS.

Physiotherapy management for CRPS is considered to be essential as part of the management for CRPS, despite the paucity of controlled studies [3, 4, 31-33, 107, 109]. It is amusing to read the 1995 4<sup>th</sup> Edition of *Rehabilitation of the Hand: Surgery and Therapy*, where it is recommended that the Physiotherapist should not be aggressive with pain provocation [110]. An early textbook recommends a team approach in the management of CRPS [110]. Physiotherapy management for CRPS continues to be widely accepted as a matter of course [3, 4, 31-33, 100, 111]. However, the specific treatment methods or intensity of physiotherapy in research trials are often not stated [31, 112] which makes it difficult to isolate the ingredient that physiotherapy contributes.

The first model which describes the physiotherapy management of CRPS was proposed in 1998 [23]. Aggressive pain inducing exercise or activity was to be avoided, and exercise was

central to the goal of functional restoration provided through physiotherapy. A fixed protocol of 'standard' physiotherapy was suggested with the first randomised control trial (RCT) in 1999 of physiotherapy vs. occupational therapy for the restoration of active range of movement and the reduction of pain in CRPS [113]. Physiotherapy was shown to be superior to occupational therapy, however no effect size was given. The protocol for physiotherapy was reported as graded exercises for strength, mobility and function twice a week for a minimum of 30 min. No further detail was provided, except that any increase in pain was monitored and graded in the exercise, so that any pain induced resolved within 24 hours. If secondary analgesic medication did not improve pain within 3 weeks, transcutaneous electrical nerve stimulation (TENS) was applied for at least 2 weeks but no details were stated about frequency or the hours of daily use. Occupational therapy was described as to reduce inflammation, protect or support the hand with the most functional or comfortable position, to normalise sensation ability, to improve functional ability of the hand and improve independence with everyday activity.

In 2009, a web survey (N=875) showed that 88.3% patients with CRPS reported to have received physiotherapy with a moderate benefit. No details about the physiotherapy intervention methods they received, the duration of their diagnosis, or the timing of the diagnosis were given. At the time of the survey 8.6% were in physiotherapy care [55].

The literature shows that there are two opposing approaches regarding the physiotherapy management of CRPS: either pain modulation (PM); or pain exposure (PEXP). PEXP is about restoring or improving function, as well as tolerance of pain despite any exacerbation of the pain experience with the intervention method [114, 115]. This method allows as much pain provocation with exercise as the patient tolerates with progressive exercise loading without analgesia towards specific functional goals. It is proposed that avoiding using the limb is detrimental, despite the high experience of pain in using the limb. PEXP has been deemed as safe in reducing pain and improving function with a case series of 106 patients and another small study of 20 patients where it was reported be beneficial [116, 117].

Furthermore, in the two RCTs which have compared PEXP with standard physiotherapy neither showed differences in outcomes, but both suggested that PEXP is less costly than usual physiotherapy management [114, 115]. Standard physiotherapy is reported as 'with pain, no gain' and involved rest of the affected tissue, soft tissue massage, transcutaneous electrical nerve stimulation, exercise aimed at pain reduction, improving skills with compensatory strategies and posture.

There is not enough evidence to show the comparative efficacy of pain exposure or graded exposure [117, 118]. A PEXP approach has been questioned as a possible contributor in worsening the pain experience in CRPS [119]. There is not enough evidence to fully support PEXP [107].

In contrast, PM has a primary focus to reduce the experience of pain, so that functional rehabilitation towards restoration is tolerated. PM applies interventions that do not exacerbate the pain experience. The experience of pain is not ignored, but rather exercise rehabilitation is allowed in a gently graded manner. This occurs from sub-threshold to intolerable pain by constructing an exercise sequence into smaller tolerable actions. As tolerance for exercise is gradually improved, the intensity is progressed. PM interventions are supported by the moderate evidence obtained for graded motor imagery (GMI) [107, 120], mirror exercise [108], sensory-motor training (SMT) [121], graded exposure (GEXP) [100], relaxation [122], psychological techniques [23], and TENS [123].

Pain modulation is similar to graded exposure therapy (GEXP) which has been shown to be helpful for CRPS patients [100] (N=10). The sub-group of patients with CRPS with fear avoidance (which is a potential risk factor for chronic disability with CRPS) when treated with GEXP *in vivo*, report that it was successful at reducing both pain intensity, pain-related fear as well as disability and other physiological signs and symptoms. Graded exposure is thought to activate higher cortical centres which reconcile the motor output and sensory feedback [100, 114, 124] associated with fear avoidance. A summary of the pain related fear and the possible processes contributing to it are displayed in Figure 2.1.

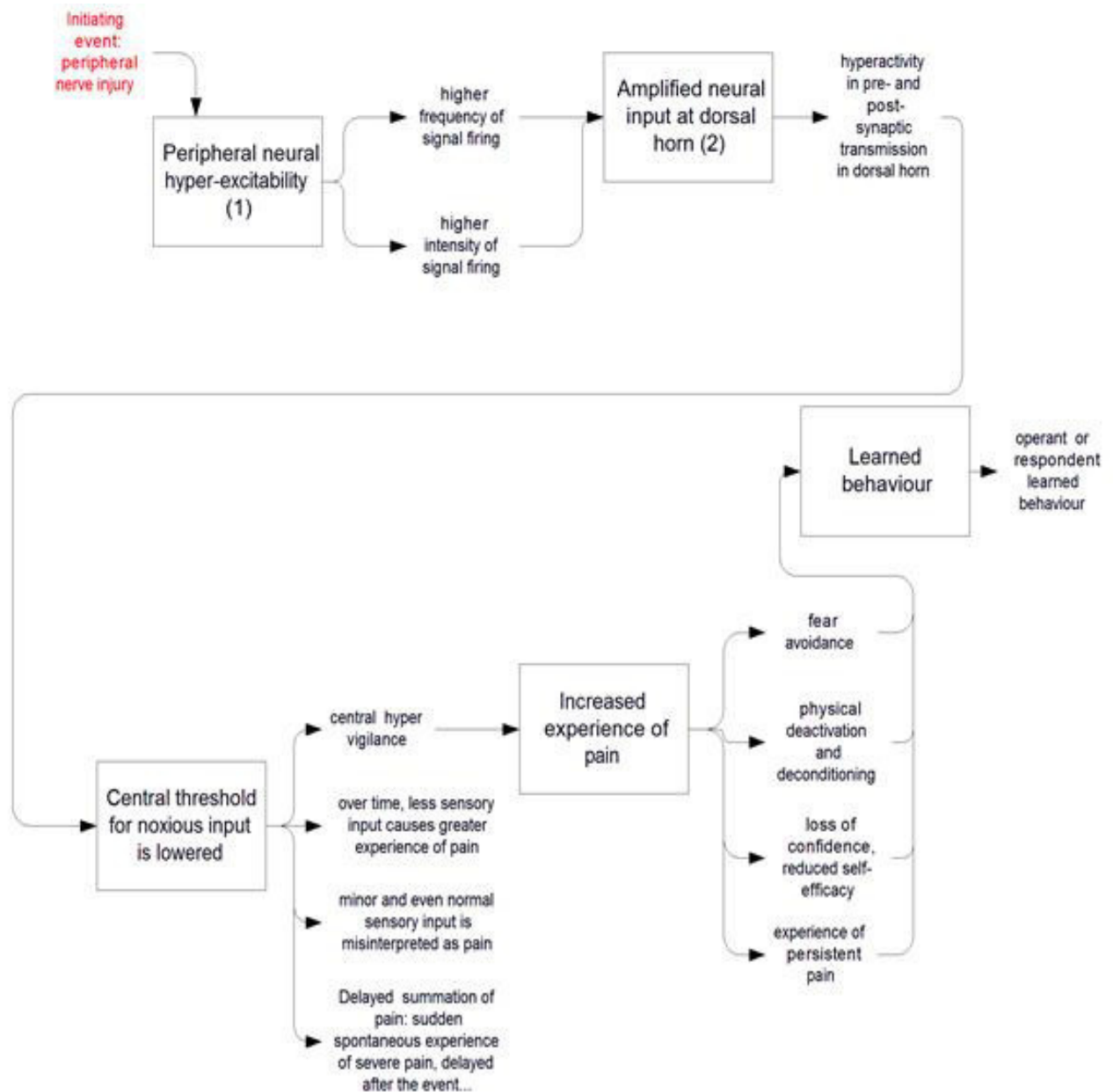


Figure 2.1. Fear avoidance and central plasticity flow chart. Image by Tracey Pons.

It has been proposed that fear avoidance may affect some of those who present with CRPS or develop over time, since the activity that elicits pain is avoided and so behaviour changes occur to accommodate this fear [125]. The activity is avoided in anticipation of pain. Over time physical deactivation, lack of tolerance and lack of confidence with activity occurs, and operant as well as respondent learning become entrenched [126, 127]. The fear of movement and feelings of fear with the anticipation of activity are shown to affect the experience of pain, functioning levels, outcomes, and quality of life [85, 128-130]. It is thought that

cognitive and emotional centres may become hyper-vigilant in observing what is perceived as a potential threat of pain [125]. This is possibly a similar mechanism to the physiological central sensitisation associated with the transmission of nociception [131]. In a small group of 20 CRPS patients, a deliberate progressive loading and managing the pain related fear avoidance of the exercise using specific analgesic medication was reported to be effective and safe [118].

A detailed critical review of interventions applied in physiotherapy follows.

### *2.7.1 Graded Motor Imagery*

Graded motor imagery is reported to involve 6 weeks of intensive therapy with the first 2 weeks using laterality therapy (recognition of left from right); this was followed by 2 weeks of imagined movements and then by 2 weeks of mirror exercise. (The patient views the unaffected limb in the mirror. Since the mirror reflects the image, the image looks like the affected limb performing the action). Exercises are practiced every hour of their waking day. This is shown in several single-centre research studies by Moseley as being positive for pain reduction and tactile discrimination, and for reduced swelling [120, 132-134].

Literature reviews of different treatment methods suggest that GMI has the most support in the research literature for the effective management of CRPS [34, 107, 120, 121, 135-139]. Following the specific sequence described above, GMI has been shown to be more effective than an ad hoc use of the sequencing [132]. It was reported with a RCT (N = 51) of GMI for patients with phantom limb pain (N = 9), brachial plexus avulsion injury (N = 5) or CRPS (N = 37) that pain was reduced by 23.4mm (16.2 -30.4mm) on the visual analogue 100mm scale, ( $\beta = -1.3$ ,  $p < 0.002$ ), when compared with the control group of usual physiotherapy and medical care [140]. Usual physiotherapy was reported as not to include graded motor imagery or mirror exercise. Functional ability improved by 2.2 (1.3 -3.0), using an 11 point functional numerical rating scale ( $\beta = 1.5$ ,  $p < 0.001$ ). The number needed to treat for both reduced pain and improved function of 50% and 4 points of improvement was 3 (2-4), 6 months after the programme [140]. However, no other strong evidence for effect with confidence intervals were provided. Neither did this analysis isolate the effect specifically for the small CRPS group.

It is speculated that GMI corrects the aberrant cortical reorganisation that is shown to occur with CRPS [121, 137]. Central changes associated with CRPS are reported to be reversed through GMI intervention, and maintained a year later with a research trial using functional

magnetic resonance imaging (fMRI), wherein central neuroplastic changes of the somato-sensory cortex functioning of the affected CRPS limb was distorted [137-139] for a small group of CRPS patients and that the reasons for this are yet known. What was interesting to observe was that where pain and functioning had not improved, despite the GMI intervention, the somato-sensory cortex functioning had not changed. It was suggested that the entire problem of CRPS was sustained in the somato-sensory cortex.

Subsequently, in a prospective audit of GMI of two centres in the United Kingdom, the GMI research protocol was recently shown to be ineffective. CRPS patients' pain did not decrease: Centre 1 (N=20), and Centre 2 (N = 12) pre-post pain difference on the 11 point Numerical Rating Scale was 0.6 (95% CI, -0.3 – 1.5) and 0.2 (95% CI, - 0.9 – 1.2), respectively [141]. The authors suggested that perhaps this was because the intense approach applied in the research setting was difficult to replicate in the clinical setting, and in a community based patient's everyday life. In another study of long-standing CRPS patients, no positive differences in outcomes measures of function or of pain were shown with GMI when compared with best practice physiotherapy in an outpatient hospital clinical setting [141]. It is noted that in some studies which refer to GMI being used, prescription details are not shown. It is difficult to determine whether or not the ingredients of this intervention contribute to any effect [142]. The answer to the question about how best to integrate GMI with the previously standard guidelines for clinical physiotherapy practice to date is also unknown [143].

### *2.7.2 Mirror therapy*

Mirror therapy alone has been shown to significantly reduce pain and improve function for CRPS Type 1 [144]. However, effect sizes are not shown or are not strong. fMRI imaging studies show activation of higher order cortical centres with mirrored hand movements [145]. In mirror therapy, alone or in conjunction with GMI, it is suggested that since it is too painful to be active, the affected limb is initially inactive with the exercise, while the unaffected limb performs the exercise required [146, 147]. As the pain experience is reduced over a period of time, through the viewing of the mirrored exercise, the affected limb may also be included in the exercising [148].

Prism glasses have also been investigated on the basis of mirror therapy. These small research trials showed some benefit [149, 150]. However, it is not possible to acquire these prism glasses for use in the clinical field, as the health and safety authorities for medical

equipment have deemed them not safe for public use. This is due to the distortion of the visual field and the potential risk for disorientation and falls.

### *2.7.3 Transcutaneous Electrical Nerve Stimulation (TENS)*

TENS has been investigated for many years. It was shown to be positive in early research in the 1960s for all chronic pain conditions [151]. There is more recent but weak evidence to support it [152-154]. It continues to be used in usual physiotherapy management for CRPS [114]. There is also weak evidence for a sustained placebo effect [155, 156]. Evidence for the use of TENS in CRPS Type 2 in rats is promising; daily placement of the electrodes for an hour on the contralateral limb was shown to be beneficial, and a combination of high and low frequency was used for allodynia [157]. A small study reported that TENS used with progressive weight bearing, tactile discrimination and contrast baths for children and adolescents appeared to be effective [158].

### *2.7.4 Education*

An important role for all physiotherapy is that of educator in a patient centred approach [159]. This involves explaining the diagnosis, the typical trajectory, potential problems and the options used in managing them. However, the literature remains sparse about physiotherapy and CRPS education. It has been reported that most CRPS patients do not meet a minimum standard of basic knowledge about CRPS [160]. Education with graded exposure to activity combined with light touch desensitisation was used to overcome possible fear avoidance. This was shown to be helpful in one study for recalcitrant CRPS where education was specifically focussed on reducing fear avoidance by challenging beliefs about protection behaviour [100].

Information and education are suggested to be fundamental in the CRPS rehabilitation process [161]. Education about other problems such as diabetes has been shown to be helpful, especially where the focus has been on education towards behavioural change rather than simply education to improve knowledge [162]. Education is shown to be particularly important where the PEXP method is applied [115]. The specific effect of education with physiotherapy intervention in CRPS is not yet known.

### *2.7.5 Tactile acuity training*

Research trials show that tactile discrimination, as measured with two point discrimination threshold, was a problem in CRPS [137, 163]. It has also been shown that the mirrored



reflection for tactile training enhanced tactile discrimination [163]. The larger body of trials for tactile acuity problems with CRPS are found in the research setting, rather than in the clinical setting. Specific sensory discrimination training has been found to be effective in resolving the tactile discrimination problem, as well as in reducing the experience of pain and improving function [121, 134]. Tactile discrimination problems and training are shown in other persistent pain conditions. It is an emerging area of research with no strong evidence for it as yet [164, 165].

#### *2.7.6 Cortical plasticity and body perception disturbance training*

Historically, in 1965, the gate control theory of pain laid the theoretical framework for the conceptual model of the sensory, motivational and central control determinants of the pain experience [166]. It is thought that the neuroplasticity of the central nervous system is a complex interaction of upward as well as downward regulation of protein complexes [167]. It appears that interventions aimed at activating cortical centres have been helpful in the research setting to resolve the body perception disturbance [121, 168].

It is theorised that sensory information going into the brain is amplified by the patient's central nervous system, and given priority over other input or not ignored as part of the normal background 'noise'. Phantom pain is an example of centrally generated pain experience [169, 170]. Animal research suggests that persistent nociceptive input can cause central changes of altered perceptual processing that can lead to the persistence of pain [171].

Virtual reality was tested in the research setting for 5 CRPS patients and shown to be helpful [172]. The use of MRI had previously shown that a reduction of the pain can be produced from virtual reality, through the modulating effect it has on the sensory and emotional central centres of the pain experience [173].

Cortical plasticity can be altered from changes in the brain itself. Descending systems can selectively modulate pain [174-176]. Brain stem modulatory systems can exert a bidirectional control, so that peripheral receptors are kept in their switched on state and not switched off [177]. This means more receptors at a given time are responding to sensory input, so the volume of input is larger than normal.

Body perception disturbances e.g. sensations that the limb is not a part of the body or is larger than it is, can be associated with CRPS [178-182]. These are thought to be where the cortical processing mismatches sensory information input [90, 183]. Brain imaging studies of those

with CRPS confirm this, and show that in the painful areas, the central representation of the limb and body parts, sometimes referred to as ‘the map’, become distorted [121, 132, 137, 184]. However, a systematic review of fMRI studies shows a high level of bias, and the evidence to support the theorised neuroplastic changes is lacking [185]. This suggests that these theories need further investigation and development and perhaps also a reconceptualisation.

### *2.7.7 Manual lymphatic drainage*

There is not enough evidence, and a paucity of large trial data to support manual lymphatic drainage [108]. Manual lymphatic drainage (MLD) with physiotherapy vs. physiotherapy (described as physical therapy and exercise programme for 3 weeks) alone showed that MLD was significantly superior at follow up but no statistical analysis is given of its effect [186]. A small controlled trial, involving the placement of topical transdermal isosorbide dinitrate to the affected hand four times daily for 10 weeks with physiotherapy exercises, did not improve regional blood flow in the affected hands [187].

## **2.8 Paediatric CRPS physiotherapy**

Paediatric CRPS is a clinical reality. Early diagnosis and the appropriate medical interventions with intensive physiotherapy for children are suggested to be more favourable for improved function and reduced pain for children with CRPS [94, 188-190].

A prospective longitudinal study for 20 children with CRPS followed up during a 4-year period showed that diagnosis was frequently delayed [191]. A programme of intensive physiotherapy was prescribed: graded exercise aimed at increasing muscle strength; weight bearing and joint active range of motion; hydrotherapy; proprioceptive training; massage; and tactile desensitising techniques. The combination psychological input was reported to help with a high percentage of children who had complete resolution of symptoms. However, 40% required treatment as a hospital inpatient and 20% had a relapse episode over the 4-year period [191]. A recent French study (N = 29) showed that physiotherapy was used for the children with an inpatient, multidisciplinary programme with good outcomes (no co-efficients or odds ratios given), significant reduction of pain 90%, (90% CI, 0.73- 0.98), and ability to walk again 92% (CI 0.73 – 0.99) [192].

Longstanding RSD in children was treated successfully with a combination of physiotherapy, psychology, and an infusion of a prostacycline analogue. Physiotherapy input was not

described other than exercise as an in-patient [193]. A case report in Turkey of an adolescent girl showed that the unnecessary investigations which delayed diagnosis and treatment of CRPS were detrimental to her psychological health [194]. A retrospective study of an intensive hospital programme for children with recalcitrant CRPS described the benefit of 95% regaining full function. However, no statistical analysis was given other than a description of the changes [195]. This physiotherapy programme consisted of timed high intensity aerobic activity, limb and core strengthening, stretching, balance and co-ordination activities. Motivation for the children to move forward to the next level of graded activity was if they were able to beat their time of the activity on the previous day by one second. Occupational therapy (involved with the desensitising programme), art, and recreational therapy with child life specialists were also included but involved less time each day than physiotherapy [195].

## **2.9 Dose of intervention and adherence**

The first documented, standard physiotherapy dose (referred to in 1999) for CRPS was reported to be twice a week for a minimum of 30 min [113]. This has not yet been tested in larger clinical trials. No doses of interventions were calculated in any of the following different interventions: early onset CRPS patients referred to a hand clinic who benefitted from modified GMI to reduce pain where there was no significant change to functional ability [196]; children and adolescents who showed benefits with TENS, progressive weight bearing, and tactile discrimination [158]. Pain exposure physical therapy was reported to be effective and safe for patients unresponsive to accepted standard therapies and described as: traction or translation of affected CRPS joints with passive or active range of movement exercise; stretches and intense manual friction of tender muscle points [117]; physiotherapy in combination with GMI which showed no positive difference in outcomes measure of function or pain in long-standing CRPS [141]; and graded active exercising combined with mirror box therapy [144].

A dose response benefit is shown where mirror exercises performed three times a day for 5 min in combination with cognitive behavioural therapy (CBT) [146]. Whether the unaffected limb participated, or when, was not documented.

Physiotherapy alone was shown to be inferior to a multidisciplinary approach for longer term CRPS [197]. This included physiotherapy of 12 water exercise sessions (not described) and 20 sessions of undefined physiotherapy, and where pain was minimised through medical

intervention of anaesthetic blocks or analgesic medication. In one of the RCTs for PEXP vs. physiotherapy treatment as usual, 17 hours of total duration of intervention time for each participant was given to each of PEXP or physiotherapy as usual [114]. No reasons were given for this treatment dose of intervention other than citing where the treatments took place. The second RCT does not provide details of treatment dose or duration for either treatment method other than that the duration of the study was over 9 months [115].

Furthermore, adherence to any physiotherapy prescription of homework (unsupervised exercise or therapy) was found to be difficult to measure [198]. The effect of an intervention is potentially influenced negatively by poor adherence to the prescribed education/homework exercise/advice [199]. The effect of adherence to either physiotherapy attendance or the prescription of homework exercise is not known in the CRPS literature.

#### Summary:

- Physiotherapy management for CRPS continues to be widely accepted as a matter of course.
- There is no consensus statement about effective physiotherapy CRPS management.
- Evidence for physiotherapy intervention methods are moderate at best.
- Specific standard physiotherapy treatment methods in research trials are often not stated.
- Pain exposure and pain modulation are contrasting intervention methods.
- There is no consensus on doses of intervention and a minimum standard of adherence for a good CRPS outcome.

### **2.10 Medical management of CRPS**

In 1998, Stanton-Hicks described a protocol [23] of topical dimethyl sulfoxide, analgesia, transcutaneous stimulation and sympathetic blockade for CRPS medical management [99]. Subsequent, non-invasive medical management with medication prescription is reported in systematic and other reviews to have poor or moderate evidence in helping adults or children with CRPS [31, 34, 200-203].

Medical non-invasive interventions includes the prescription of opioids, transdermal lignocaine and low doses of oral naltrexone, despite the fact that there is no evidence to support their benefit for CRPS medical management [204]. Robust evidence for

pharmacology prescription is lacking [205] and opioid prescription is no longer recommended [29, 71].

A pharmacology model suggested that prescription needs to be individually tailored [206]. Trials show that vitamin C helped reduce the experience of pain as well the risk of subsequently developing CRPS following a wrist fracture [207, 208]. A RCT (N = 58, with differences outlined in Mann-Whitney U scores and no effect size is given) showed that gabapentin potentially had a small benefit when compared to placebo [209]. A controlled clinical trial showed that gabapentin in combination with a specific graded exercise programme supervised by a Physiotherapist decreased pain significantly in early CRPS, but did not improve function [210]. Both amitriptyline and gabapentin were helpful for sleep and for reducing pain in paediatric CRPS; N = 34, and t-tests showing significant improvement to pain, but no co-efficient, odds ratio or confidence intervals were given to reflect the effect size [211].

Invasive management can involve anaesthetic neural blockade [212]. The administration of intravenous bisphosphonates also showed promise [213, 214], as did intravenous lignocaine, immunoglobulin and ketamine [215]. However, the mechanism by which the intravenous bisphosphonate was effective for some and was ineffective for others remains unknown. It is theorised that the reduced bone turnover and acidosis induced by the bisphosphonate reduces peripheral nerve sensitisation, and thus reduced pain [216].

Spinal cord stimulation (SCS) was used for recalcitrant CRPS, and reported to be helpful for improving quality of life and pain reduction [217]. However, SCS has not been shown to have consistent or excellent results for the restoration of function [217, 218].

The medical prescriptions and the invasive management procedures for CRPS still lack strong supporting evidence for efficacy [219, 220]. Furthermore, longer duration CRPS is speculated to develop a complex hierarchical interaction of peripheral and central factors which remain difficult to manage with medical interventions [221].

#### Summary:

- There is no strong evidence for the use of prescription medications or invasive medical interventions towards the recovery for CRPS.
- Spinal cord stimulation shows limited evidence of being helpful in recalcitrant cases.

## 2.11 Alternative therapies and acupuncture for the management of CRPS

In a well-designed RCT, Qigong exercise was shown to be beneficial for recalcitrant late stage CRPS. Six sessions with two master qigong trainers of 40-min twice weekly for 3 weeks followed with 7 weeks of home practice of the qigong training were reported to be more beneficial than sham training [222].

The quality of research regarding the use of acupuncture is poor [108]. Recent case studies show promising results with acupuncture in paediatric CRPS [223]. Systematic reviews report low grade evidence for acupuncture to relieve pain for CRPS [34, 108]. Small studies show that it was helpful: for 2 patients with previous failed medical and allied health intervention [224]; a single case of recently diagnosed CRPS for a 34-year-old female [225]; and to reduce pain for 3 children [223]. A RCT of physiotherapy vs. electro-acupuncture and massage for shoulder-hand syndrome following stroke, which also included a debatable small sub group of CRPS patients, reported a superior reduction of pain 12 weeks later with electro-acupuncture and massage [226]. The effect size for the improved pain 12 weeks later was reported as 21% (CI 16-26%).

Novel approaches include the use of cutaneous pushpins and a laser for self-maintenance [225], and needle-free electro-acupuncture combined with Chinese herbs [227] Even in poorly controlled studies, acupuncture has been shown to have limited effect [30]. Intensive hydrotherapy, physiotherapy and complementary medicine improved the pain (11 point NRS, reduced from 8 to 2 after 8 weeks) and the description of skin changes is described as ‘significantly improved’ (no statistical analysis is shown) for the case study of a 33-year-old female patient with recalcitrant CRPS [228].

### Summary:

- There is a paucity of evidence for alternative therapies for CRPS recovery.

## 2.12 The multidisciplinary management of CRPS

Persistent pain (including CRPS) has become a growing and significant cost to health care resources [229]. Pain management for persistent pain conditions was developed with the concept of using a biopsychosocial approach [230]. This arose because it had been shown that no single intervention or model was effective for most persistent pain conditions [231].

This approach was proposed as it was recognised that the issues around the experience of most persistent pain conditions are complex, and involve the biological sensory processing and the emotional or cognitive experiences [166].

The complexities of these problems led to the development of a model, validated in a research and clinical setting, that recognised a biopsychosocial rehabilitative approach using multidisciplinary input for persistent pain conditions [232]. This model acknowledged that persistent pain has many different facets which required teamwork of medical and allied health professionals [233]. The model has been extended to children [189], chronic low back pain [234], and persistent pain following whiplash injury [235]. Despite the multidisciplinary management being recommended for CRPS there is no strong evidence, neither is there any RCT that has tested this model [201].

The biopsychosocial practitioner recognises the advances that have been made in the evaluation and management of persistent pain which go beyond the early models of pain [232, 236]. These earlier models ascribed pain as a simply biomechanical, physical experience [237]. The biopsychosocial model integrates the experience of persistent pain in the full biological, psychological and social context of the patient [238]. This means that evaluation, interventions and management should involve all or any of medical, exercise, functional, sleep, family, work, emotional, thoughts, attention, and spiritual needs.

It was also suggested by the early advocates for the biopsychosocial model that an important goal for a successful outcome to any pain management programme was the self-management of the problems by the patient, with a gradual development of confidence and independence from ongoing treatments and formal interventions [239]. This has been applied to the management of low back pain [126, 127]. This is in contrast to the biomedical model for acute pain management where treatment is provided in the hope of a cure or of full resolution of signs and symptoms of the pain problems.

The management of recalcitrant CRPS with a multidisciplinary team in a biopsychosocial model may be a plausible solution for this sub-group who potentially required further support and expert help [71, 240]. However, the CRPS acronym has been also referred to as ‘chronic’ regional pain syndrome [201], which is unfortunate. This phrasing is inappropriate, although for a sub-group CRPS becomes persistent problem, this is certainly not the case for all. Furthermore, the candidate suggests that the proposal for CRPS to be managed by a multidisciplinary team may incorrectly imply that it is an inherently persistent condition,

since the biopsychosocial approach was proposed as a solution for persistent pain, not acute pain conditions.

#### *The role of the Physiotherapist in the multidisciplinary team*

The role of the Physiotherapist was recognised as key in the biopsychosocial rehabilitative model with: effective pain management with thorough and knowledgeable assessments; provision of the tailor-made care; and provision of education about pain mechanisms [241]. The Physiotherapist ensures correct identification of the primary issues and has the necessary skills to apply the appropriate interventions to individual patients [242]. This requires knowledge about persistent pain conditions and the evidence based interventions used in both a research and clinical setting [243].

The primary focus for the Physiotherapists' programme was suggested to build the patient's confidence with self-management and independence through: assisting the a reduction of the pain experience with acceptance; adjustment and the improvement of functional ability with improved self-efficacy [244, 245].

This was since the literature showed that pain related fear may have a relationship with disability across several persistent pain conditions [246]. Specifically, for upper limb out-patient surgery clinics it has been found that pain catastrophising and cognitive fusion were intertwined with higher levels of reported pain as well as with functional disability [124]. It is thought in the context of the biopsychosocial model of pain that pain catastrophising is the source of the pain related fear [246, 247]. Hence a patient will become too afraid to use the affected limb, and a cycle of disuse entrenches the fear of activity, and therefore promotes catastrophic thoughts.

#### *The role of the psychologist in the multidisciplinary team*

The role of psychology is hinged on the gate control theory of pain. This theory proposed that the higher cognitive centres of emotion, affect, meaning, purpose, behaviour and learning were factors to moderate or mediate pain [248]. The Psychologist was instrumental in unravelling the factors that contributed to the negative impact of pain related disability [249, 250]. The Psychologist developed resilience and fostered psychological flexibility [251, 252], and systematically improved cognition, affect, and behavioural responses to pain related disability and coping [253, 254]. A subgroup of CRPS patients require psychological support,



but determining what characterises those who will benefit from this support is not yet determined [255, 256].

Summary:

- The psychologist's role is to assist the self-management of problems rather than trying to cure them.
- There is no strong evidence to support the multidisciplinary management for CRPS in enabling a full recovery.

### **2.13 Central sensitisation**

The concept of central sensitisation is suggested to be an adjustment of the central nervous system to be more sensitive to the experience of pain [237, 257-264]. Acute pain associated with short term central sensitisation is a vital ingredient of life. The primary role of acute pain is protection. However, persistent pain with evidence of central sensitisation poses a challenge to the practitioner [265]. The challenge is to find a cause and make a specific diagnosis when routine laboratory investigations and tests show little or no abnormalities [266]. Central sensitisation could be due to sensitisation of afferent input, activity in the dorsal horn of the spinal column, or due to modulation by the descending central pathways [266].

The theoretical model for central sensitisation was introduced in 1983 [267], and verified in laboratory findings [268]. A state was created which was described as 'wind up' of afferent input in the spinal cord [171, 269-271]. This meant that sensory input otherwise deemed as normal is experienced as pain, with increased activity of both pre-synaptic neurotransmitter release as well as post-synaptic neuronal hyper-excitability [272, 273].

Furthermore, another contributor to the sensitising process is proposed to be small fibre neuropathy and was also suggested as a possible cause of CRPS [21]. This explanation was particularly plausible as the signs and symptoms that are typically present with CRPS are similar to an asymmetrical (i.e. affecting one limb) small fibre neuropathy with central sensitisation. The explanation showed that there can be neural injury without obvious damage to a large fibre neurone. As small fibres degenerated, these became particularly sensitive to injury [21]. In contrast, other studies have shown that the small fibre neuropathy problem to be less likely, and that central sensitisation process are more likely to be involved with regional or central changes in pain processing [274, 275].

Some of the pain and skin changes observed with CRPS, such as spontaneous swelling or colour changes, have been ascribed to an exaggerated response of inflammatory mediators [276, 277], to increased plasma amino acids [278], and following a fracture [69, 70]. The neurogenic response to the inflammation causes sensitisation of the peripheral nerves and receptors [279], resulting in glutamate release which activates the  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors giving rise to calcium release [280]. Consequently, the usually silent N-methyl-D-aspartate (NMDA) receptors are activated, and become the key to unlocking the events that contribute to the persistence of the experience of pain in peripheral and central sensitisation [281, 282]. This caused hyper-excitability of neural activity with reciprocal disinhibition and contributed to a decreased stimulation threshold, an enlarged receptive field, and an increase in the number of responses evoked by natural stimuli.

Another biochemical and histological study reported that following a nerve injury, the central terminals of the C-fibres in the dorsal horn atrophied, thereby creating vacant synaptic sites [283]. A theory was proposed that this atrophy allowed  $\alpha$  (A) fibres to sprout and form novel synapses in lamina II which created inappropriate connections leading to persistent hypersensitivity. This theory offered an explanation to why the experience of the pain can be so intense with only a minor stimulus.

Central sensitisation is reported to also occur in the descending central systems that can selectively modulate pain [174-176]. A comprehensive review of the neurophysiology around descending modulation reported a highly complex system of interaction between central, spinal cord and higher centres of cognitive–affective processing [284]. Brainstem modulatory systems could exert a bidirectional control so that peripheral receptors were kept in their switched on state and were not switched off.

Furthermore, the downward cortical inhibition was described as a failure of the diffuse noxious inhibitory control system (DNIC) [285-287]. Temporal summation, an exponential heightening of the pain experience with repeated motor or sensory input, is an example of DNIC and has been shown to occur in CRPS with tactile sensory input where allodynia is present [288]. The suggestion was that these problems may be associated with central sensitisation and that patients could present with allodynia, hyperalgesia, widespread pain, and spontaneous unpredictable pain. These problems may also be accompanied by out of the ordinary sensations or autonomic responses associated with pain [270].

The central sensitisation inventory (CSI) is a recent, reliable and valid instrument to detect the presence of central sensitisation as a feature affecting all body systems in any patient with persistent widespread pain [289]. However, not all CRPS patients will have evidence for a positive score on the CSI, and the relationship between CRPS and central sensitisation is not yet fully explained [266]. The possible factors developing central sensitisation are summarised by the candidate in the flow chart Figure 2.2.

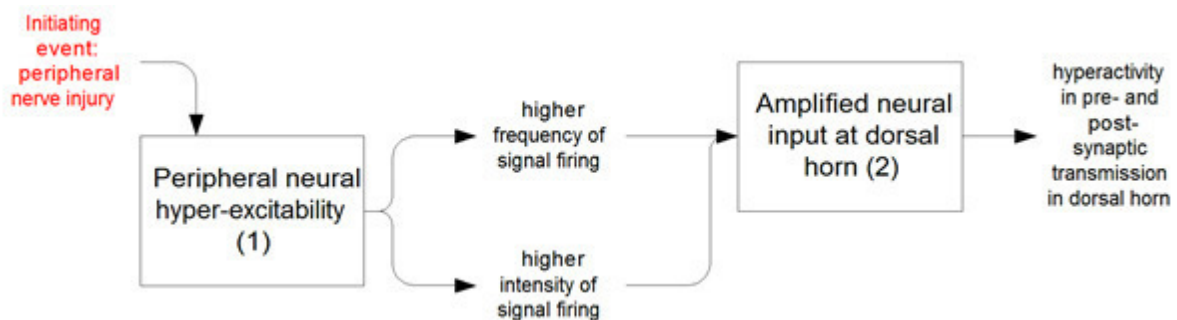


Figure 2.2. The development of a central sensitisation, flow chart by Tracey Pons.

Hence, persistent pain not associated with a precise medical diagnosis can be associated with a known neurophysiological mechanism [290]. The CRPS pain experience, as disproportionate to the inciting injury, was not a reason for a psychiatric or psychological diagnosis [291, 292]. Patients who showed evidence of central sensitisation may not present with the psychosocial yellow flags in the way that patients with other chronic pain conditions did [78, 133]. Sudeck (one of the earlier medical professionals to identify CRPS) is quoted in 1942 as saying: ‘One should be careful not to simply assume psychological reasons for pain disorders one does not sufficiently understand’ [9]. However, at the same time, it is also important to integrate the cognitive-affective factors that can contribute to the neurophysiological processing of central sensitisation and the pain experience [284].

Summary:

- Pain with sensitisation is a neurophysiological phenomenon that is normal for the recovery process in the event of acute injury.
- However, it may persist beyond normal times of tissue recovery and contribute to the CRPS features.
- It is difficult to quantify accurately sensitisation in a clinical setting.
- How central sensitisation process interacts with CRPS is not yet fully understood.

## **2.14 The therapeutic relationship**

Psychotherapy has referred to the therapeutic relationship as a ‘therapeutic alliance’ as it involves the collegial and mutual engagement of both health provider and patient [293-295]. This relationship was shown to have a moderate effect ( $r = 0.22$ ) on influencing outcomes regardless of the instrument or outcome measure used [293]. In mental health research it was reported that it was not simply the conversation or communication about information that was important for an effective therapeutic relationship [296]. There were many other ingredients which involved shared decision making (such as accommodating values, motivation, culture and preferences) that were also important.

The therapeutic relationship in physiotherapy was reported to be an essential component for trust to develop [243] and was suggested to facilitate education about overcoming barriers with participation in exercise [297]. The therapeutic relationship in physiotherapy was shown to be affected by adherence [298]. However, that systematic review showed that the evaluation about adherence was exclusively from the patients’ perspective. There is no literature about what is important for an effective therapeutic relationship for a CRPS trajectory to facilitate good outcomes [298].

### Summary:

- An effective therapeutic relationship is suggested to have a positive effect on outcomes as well as on the process of recovery.
- The ingredients that constitute an effective therapeutic relationship with CRPS patient and Physiotherapist are not yet determined.

## **2.15 Mental health and the treating Physiotherapist of a CRPS patient**

In a recent change to the Declaration of Geneva in October of 2017, it was unanimously accepted that Medical Health Professionals (MHPs) attend to their own health in the same way they attend to the health of their patients [299]. This was in response to the burgeoning exhaustion and weariness affecting MHPs in the modern world, affecting many clinicians [300], and that the associated time off work was costly [301]. The issue of burnout and mental health stresses for the health providers is well known and has been extensively researched [300-302].

However, it is interesting to note that this concept is reflected nowhere in any CRPS literature reviews, models of management, nor in any standard care protocol. This is despite systematic reviews identifying the negative impact of mental health stress affecting the Health Provider sector [303-306]. The interaction of mental health issues with a Physiotherapist who manages CRPS is unknown.

## **2.16 An historical account and evaluation of the models for CRPS management**

It has been recently proposed that a clinical model for CRPS management should also involve the experience of the patients with the diagnosis of CRPS [307]. The literature shows that clinical models for CRPS management are sparse. None to date have been validated.

A history about the models of CRPS management shows that an acronym of CRPS was first proposed in 1998 and was accompanied by a management pathway [23]. This stated that early diagnosis and physiotherapy management were essential. The Physiotherapist was considered to have the central role with a focus on restoring the patient's function. This pathway involved a sequence of steps whereby each step was thought to take 2-3 weeks. If progress was not made in the 2-3 weeks assigned to each step, more aggressive intervention for potential nociceptor drivers and psychotherapy was recommended. Alternatively, if patients were able to progress quicker than 2-3 weeks, they were allowed to progress through the steps, as long as their symptoms allowed for the accelerated progression. The steps of the model given were:

1. Establish the therapeutic relationship.
2. Motivation, mobilisation and desensitisation through both medical (pharmacological and physical interventions) and allied health intervention. It was stated that 'it was essential that movement phobia be overcome, and that the patient begin to actually move and allow the limbs to be touched'.
  - a. Stimulated muscle activity was encouraged.
  - b. Isometric exercise or electrical stimulation was applied as tolerated.
  - c. The treatment of secondary myofascial pain was recommended.
3. Isometric strengthening and stress loading was applied with exercise.
  - a. Aggressive or passive pain provoking exercise or stretches were discouraged.
  - b. The focus was postural normalisation with stabilisation and symmetrical use of both limbs.
4. Complete function recovery.

- a. Normalisation of all functions of the affected limb.
- b. Vocational rehabilitation.
- c. Self-management was promoted as the priority. Dependence on invasive intervention was discouraged.

Around this same time, as mentioned earlier, a RCT showed that physiotherapy was superior to occupational therapy for the management of CRPS [113]. The primary treatment objective given for physiotherapy was ‘to increase control of pain, optimise coping, extinguish the source of ongoing pain, and improve skills’ (p78). The authors emphasised that no pain exposure was applied. All treatment interventions applied used a protocol of ‘with pain, no gain’ (p82). They emphasised that any pain provocation should reduce within 2-3 hours following participation with the activity or exercise. The actual methods or categories of intervention applied were not given. Neither was it clear to what improved skills were. Was this the skill to confidently take cognitive control over the pain experience, or the ability to improve physical dexterity, or was it something else?

Although a pathway was suggested with this early literature, it was not supported with strong evidence. Steps towards functional restoration were proposed in 2001 [308] and a subsequent clinical pathway was proposed in 2002. It was essentially unchanged with physiotherapy intervention as the fundamental component [33]. However, this pathway did recognise that relapse may occur. In the same year, another review showed that the evidence for the treatment of CRPS remained limited for all treatment interventions [30].

In 2006, the Dutch Order of Medical Specialists with the Netherlands Association of Reflex Sympathetic Dystrophy patients proposed their evidence based guidelines for the management of CRPS [309]. These guidelines were about diagnosis risk factors, treatment, and management. Referral for physiotherapy was reported to be indicated when a CRPS patient presented with severe pain, restricted ability to exercise, limited function, sensory disturbances, or was not able to cope. No model was included with these guidelines. Physiotherapy was supposed to be according to the protocol, but no protocol was given in this document, other than listing the strength of evidence for each intervention method that had previously been investigated.

Also in 2006, the literature showed that diagnostic criteria for CRPS were variable. There were many different criteria by which a diagnosis was confirmed. A year later in 2007, the subsequent Budapest criteria helped clarify the diagnostic criteria [22]. The previous lack of

diagnostic clarity had contributed further to the difficulty about determining what effective intervention, especially physiotherapy, should be.

The attempt to identify effective physiotherapy was followed in 2009 with a systematic review about physiotherapy interventions for CRPS. This review showed moderate evidence for efficacy of graded motor imagery. The authors also suggested that a model be developed following the findings of their review, as the evidence in this review was in sharp contrast to previous pathways [107] and they emphasised the urgency of this need.

This call was not heeded. No model was proposed with the evidence based guidelines published in 2010 with a systematic review [31]. This review concluded: CRPS could be prevented with Vitamin C prescription following a wrist fracture; strong opioids were not recommended; the World Health Organisation (WHO) analgesic ladder for pain control should be followed; 'standardised' physiotherapy and occupational therapy was advised (p10); and further research was needed across all aspects of CRPS towards its understanding or management. No description was given of what consisted of 'standardised' physiotherapy.

Neither was this call heeded in 2011 when a comprehensive guideline for the medical diagnostic and interventional management for CRPS was presented [3]. This publication excluded any information about allied health or pharmacology management, and focused on the recalcitrant CRPS pathway. Active physiotherapy rehabilitation was suggested to commence as early as possible as an essential component of the management plan. However, no detail was given about what constituted this physiotherapy rehabilitation or of what it aimed to achieve.

It was a disappointment to find that the 4th publication of Practical Diagnostic and Treatment Guidelines (2013) [310] suggested a physiotherapy pathway unchanged since the 2002 publication. This comprehensive document presented a procedure for each discipline potentially involved in the management of CRPS. However, the new emerging evidence for physiotherapy was omitted, nor was the call for an updated physiotherapy management model acknowledged.

In the same year, the first Cochrane systematic review of CRPS management was published. It showed poor evidence for all aspects of CRPS management [34]. Subsequently, in 2014, two thorough comprehensive reviews were published [71, 311]. However, neither offered any further evidence and both raised questions. One was whether or not CRPS existed as a

separate clinical entity [71]. The other was that since it was shrouded in mystery, how could it be understood?

In 2016, a review reported evidence and potential answers to these questions about CRPS pathophysiology and known progressions [201]. Standard, emerging and uncommon interventions were all evaluated. No strong evidence for effective management was presented and again no model was proposed. A masterclass suggested a functional restoration algorithm based on the model proposed in 2001, where goals of physiotherapy were proposed to normalise abnormal movement patterns, provide understanding about the condition and address pain related fear [161].

This historical account of the literature showed the principles by which the suggested pathways were constituted for CRPS management, and also showed that evidence was poor. A validated and reliable model is not available and the previous guidelines that are suggested are out of date. Neither do any models in the literature include the prevention of CRPS, nor the well-being of either the medical, allied health professional or the CRPS patient. Mental health or well-being is not an integral ingredient to the structure of management as a whole other than being addressed through the proposal of psychological support as necessary for those patients who do not progress through the usual pathway.

The literature only provides speculative stepwise algorithms. These have a physiotherapeutic emphasis, and consistently suggest that more intensive or comprehensive therapy involving multi-disciplinary services is introduced when the initial steps fail to achieve recovery. There is no evidence to support them. The premise of these algorithms is that deterioration reversion to previous steps. Another criticism is that the algorithms fail to recognise that the CRPS trajectory is unpredictable and highly variable.

It would be plausible to consider that an ideal conceptual clinical model would offer concurrent interventions with the recommended pathway, and the elements of this pathway which was flexible according to presentation or trajectory fluctuations. Realistically, relapse or flare ups of symptoms are a feature of the CRPS trajectory and are not accommodated with the stepwise algorithm.

Hence, the call made in 2009 for a new model become a key objective. It was considered important when determining a conceptual model that it would be proposed from the available evidence in both the literature and that gained from this project.



As such, the gaps in the broader knowledge of CRPS management outlined in this Chapter created the stepping stones for the aims developed for this project.

### **2.17 Gaps in the body of knowledge**

There is research activity across all domains affecting CRPS, but with no strong clinical or research evidence for many issues about CRPS in the literature. There is no accurate gold standard for diagnosis. There is controversy whether or not CRPS fits the criteria to be classified as neuropathic pain. Furthermore, although the Budapest criteria show better sensitivity and specificity than previous criteria, they are neither definitive nor conclusive.

The research about the relationships or predictors of the prognosis is limited due to the heterogeneous nature of the CRPS presentation and the variable trajectory of recovery. It is not yet known why a sub-group, sometimes despite the best treatment available, still continue to suffer recalcitrant CRPS. And yet, the literature shows that spontaneous recovery does occur, and surprisingly frequently.

There is a need for the potential risks for the onset of CRPS to be identified, and be a recognised feature in every orthopaedic or physiotherapy practice. Other than a few exceptions, this is not the case and a limitation is that the literature shows no meta-analyses to confirm risk factors. Since the prevalence of CRPS is low and the literature about the prevention of CRPS is sparse, it appears that the focus of most research has been about trying to identify what CRPS is and how to treat it, rather than what is effective to prevent it from occurring in the first instance.

The research about effective intervention methods for either medical or allied health interventions is inconclusive. There is no strong evidence to support any method or protocol. There is no evidence with multiple RCTs across different settings.

Factors associated with adherence and the therapeutic relationship are also not known in CRPS management. This potentially involves factors associated with both the CRPS patient and with the Physiotherapist. The factors showing what constitutes an effective therapeutic relationship, so that adherence is facilitated a good outcome, has not yet been explored.

The literature is sparse about findings that identified what clinicians or patients believed to be important about CRPS prevention or management. It may well be that there are interactive effects as belief systems are potentially multifaceted. There is no literature about this.

Since CRPS is identified as a ‘complex’ syndrome, this implies that it is not a straightforward condition. It stands to reason that treating a CRPS patient may be a difficult process for any clinician, and that the syndrome may be a stressful condition for the patient to live with. Neither is there any research about what is effective to protect mental health or develop resilience for the treating clinician or a CRPS patient in the recovery process.

Hence, this project sought to bridge the gaps for physiotherapy research about:

- Everyday physiotherapy practice intervention methods.
- Regional physiotherapy practice.
- Physiotherapy beliefs about CRPS.
- Relationships between physiotherapy intervention methods and CRPS outcomes.
- Predictors of outcomes for CRPS patients in physiotherapy care.
- Development of a conceptual model that integrates:
  - The current evidence for the management of CRPS.
  - The prevention of CRPS.
  - The well-being or mental health of the Physiotherapist and that of the CRPS patient.

## **CHAPTER THREE**

### **Initial Survey of South Island Physiotherapists**

#### **3.1. Introduction**

Prior to commencing this project, it was important to identify the usual methods of intervention applied in physiotherapy clinical practice across the region of the South Island, New Zealand. Furthermore, it was also necessary to determine what these Physiotherapists believed to be important in their clinical practice in the management of their CRPS patients. This investigation, together with discovering gaps in knowledge in the literature search, provided the platform to generate the aims for this project.

This chapter describes the process and the findings about what the Physiotherapists who accepted CRPS patients reported to use in their clinical practice and what they believed to be important for CRPS management. Aspects of this survey have been published by the candidate [40] and are available in Appendix A.

#### **3.2. Purpose**

The purpose for this initial survey was: a) Determine which Physiotherapists accepted CRPS patients in order to be invited to participate; b) provide Physiotherapists an opportunity to collaborate in the project; c) find out what intervention methods Physiotherapists usually applied; d) determine the project structure that examined and categorised the intervention methods used with their new CRPS patients; e) determine what Physiotherapists believed to be important with their management of CRPS.

The purpose of the results from these findings was to determine the project aims and propose appropriate hypotheses.

#### **3.3. Method for Recruitment of Physiotherapists**

Each individual practice or clinic of the 150 private practices or hospital outpatient departments listed across the South Island of New Zealand by the New Zealand Physiotherapy Society (Physiotherapy New Zealand or PNZ) was contacted to find out whether or not they accepted CRPS patients. Physiotherapy staffing in these practices or clinics vary from solo practitioners to those with high staffing numbers.

Those accepting CRPS patients were asked to fill in a paper-based questionnaire about their usual physiotherapy management of CRPS, and what they believed to be important in the management of pain and for the function in these patients. The questionnaire given to the Physiotherapist contained four sections. The first section asked how frequently CRPS patients were treated by them. A scale containing the following information was used: never; seldom (2-5 times per year); occasionally (5-10 times a year); regularly (2-3 times per month), or often (more than 5 times per month). The second section asked about the precise interventions carried out and their frequency of use. A scale containing the following information was used: Never use this; occasionally use this; often use this, most often use this. The third section enquired about what unlisted interventions the Physiotherapist used and their frequency of use. The fourth section looked at the beliefs the Physiotherapist held about the management of CRPS. The belief choice was as follows: Reducing the pain is essential to improve the function; improving the function is essential to reduce the pain; exercising and increasing pain is contra-indicated; and exercising and increasing pain is indicated.

### **3.4. Statistical Analysis**

Standard descriptive statistics were collated (Statistica 7 ®, Microsoft Excel for windows PC). Data analysis used ANOVA to detect for significance with a  $p < 0.05$ .

### **3.5. Results**

#### **3.5.1. Physiotherapist participation**

Of the 150 physiotherapy practices or outpatient clinics contacted across the South Island of New Zealand, 64 clinics accepted CRPS patients. Questionnaires were posted in self-addressed and pre-stamped envelopes or personally delivered to each of the 141 Physiotherapists employed at these 64 clinics. Eighty-one Physiotherapists answered the questionnaire, and returned it either personally ( $n = 5$ ) or by mail ( $n = 76$ ). This provided a response rate of 57%. Seven (8%) of the 86 clinics contacted did accept patients with CRPS, but declined to answer the questionnaire. Reasons given were as follows: No reason given ( $n = 1$ ); about to retire ( $n = 1$ ); staff shortages ( $n = 1$ ); unwilling to have practice scrutinised ( $n = 2$ ); too busy ( $n = 1$ ), or an assessment only service ( $n = 1$ ). Participation rate in the physiotherapy intervention questionnaire is shown in Figure 3.1.

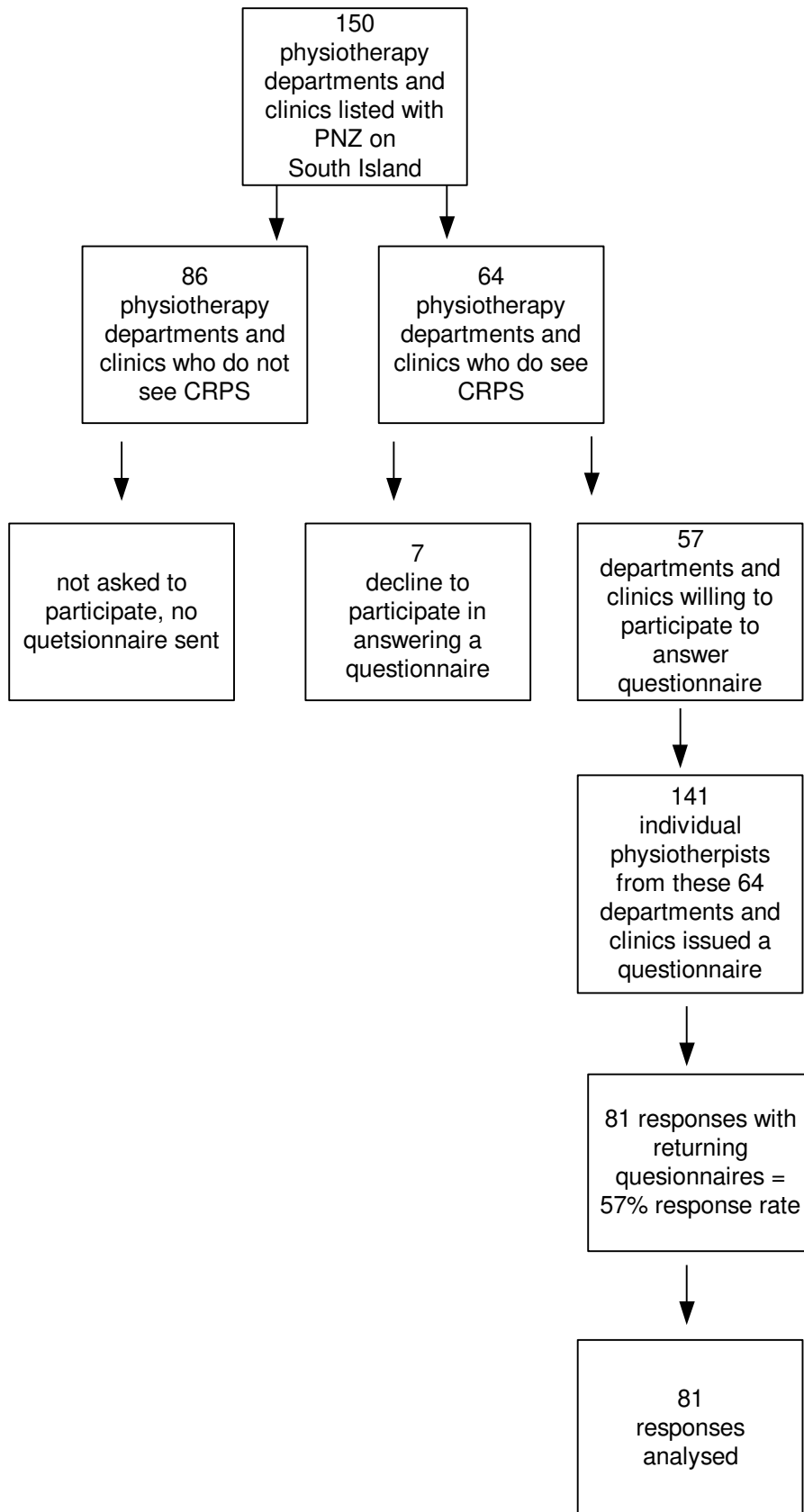


Figure 3.1. Flow chart participation with the physiotherapy intervention questionnaire.

Sixty-three per cent of Physiotherapists in the South Island who accepted patients with CRPS treated them infrequently (2-5 times annually). Twenty per cent treated 5-10 CRPS patients annually. Only 1% of Physiotherapists treated more than 5 CRPS patients in a month; 9% of Physiotherapists treated 2-3 CRPS patients each month. These data were simplified into two categories. Ninety per cent of Physiotherapists were categorised as seldom treating CRPS patients (less than 2 CRPS patients per month). Ten per cent of Physiotherapists were categorised as more frequently treating CRPS patients (more than 2 CRPS patients per month).

### **3.5.2. The routine physiotherapy interventions used**

The routine physiotherapy interventions examined (listed in Table 3.1) were as follows: Active exercises within pain limits; active exercises despite pain; resisted exercises despite pain; eccentric exercises; pain exposure exercises; graded exposure exercises; education; passive exercises within pain limits; passive exercises despite pain; pool exercises; neural stretches; tendon glides; balance exercises; proprioceptive exercises; lymphoedema massage; oedema massage; prescribed homework; scheduled as time contingent or pain contingent; sensory mapping training; discrimination training; desensitising training; GMI in classic order; GMI in ad hoc order; mirror exercises; prism exercises; relaxation exercises; breathing control; cognitive techniques for pain control; problem solving techniques for pain control; cognitive behavioural therapy (CBT); acceptance and commitment therapy (ACT); iontophoresis; soft tissue mobilisation; trigger point release; and other interventions (not listed). Fifteen Physiotherapists used acupuncture.

The frequency of use of all interventions used is listed in Table 3.1. Education was the modality most commonly used as an intervention for CRPS, and is highlighted (by 83% of Physiotherapists). Proprioceptive training and desensitising were often used (by 58% of the Physiotherapists). Forty nine percent of Physiotherapists applied active exercise despite pain occasionally; active and resisted exercises within pain limits were used by 41% and 42% of the Physiotherapists, respectively. The types of interventions listed as occasionally used by the largest groups were trigger points release (53%), active exercise despite pain (49%), pool exercise (44%), and soft tissue mobilisation (41%).

Table 3.1. Physiotherapy interventions for CRPS and frequency of use

INTERVENTION METHOD	ANSWER N (%)	FREQUENCY OF USE BY PHYSIOTHERAPISTS WITH PERCENTAGE (%) VALID ANSWERS			
		Never	Occasionally	Often	Mostly
Active exercise within pain limit	77 (95%)	0%	14%	41%	41%
Active exercise despite pain	76 (94%)	20%	49%	20%	5%
Resisted exercise within pain limit	74 (91%)	2%	33%	42%	14%
Resisted exercise despite pain	73 (89%)	38%	40%	11%	0%
Eccentric exercise	72 (89%)	38%	40%	11%	0%
Pain exposure exercise	65 (80%)	30%	32%	11%	7%
Graded exposure exercise	69 (85%)	11%	20%	33%	21%
<b>Education</b>	<b>79 (98%)</b>	<b>0%</b>	<b>1%</b>	<b>14%</b>	<b>83%</b>
Passive exercise within pain limits	71 (88%)	9%	32%	30%	17%
Passive exercise despite pain	71 (88%)	36%	37%	11%	2%
Pool exercise	76 (94%)	22%	44%	20%	7%
Neural stretches	72 (91%)	11%	43%	33%	4%
Tendon glides	72 (91%)	19%	36%	32%	2%
Balance exercise	73 (89%)	9%	22%	51%	9%
Proprioceptive Exc	86 (94%)	2%	20%	58%	14%
Lymphoedema massage	73 (90%)	48%	36%	5%	1%
Oedema massage	86 (95%)	25%	42%	205	9%

<b>Prescribed homework: Scheduled as time contingent</b>	85 (93%)	6%	22%	48%	16%
<b>Prescribed homework: Scheduled as pain contingent</b>	85 (93%)	25%	36%	19%	14%
<b>Sensory mapping training</b>	70 (86%)	42%	32%	12%	1%
<b>Discrimination training</b>	74 (91%)	40%	28%	19%	5%
<b>Desensitising training</b>	76 (94%)	2%	20%	58%	14%
<b>Graded Motor Imagery (GMI) in classic order</b>	71 (90%)	43%	20%	15%	10%
<b>GMI in your own order or ad hoc</b>	73 (90%)	44%	27%	16%	2%
<b>Mirror exercise</b>	78 (96%)	21%	31%	35%	10%
<b>Prism exercise</b>	69 (85%)	78%	7%	0%	0%
<b>Relaxation exercises</b>	73 (90%)	11%	33%	33%	12%
<b>Breathing control</b>	75 (93%)	12%	33%	33%	14%
<b>Cognitive techniques for pain control</b>	73 (90%)	22%	33%	26%	9%
<b>Problem solving techniques for pain control</b>	74 (91%)	20%	31%	25%	16%
<b>Cognitive Behavioural Therapy (CBT)</b>	72 (89%)	48%	15%	22%	4%
<b>Acceptance and Commitment Therapy (ACT)</b>	68 (84%)	705	9%	4%	1%
<b>Transcutaneous Electrical Nerve Stimulation (TENS)</b>	73 (90%)	21%	44%	23%	1%
<b>Iontophoresis</b>	71 (90%)	86%	0%	1%	0%



<b>Soft tissue mobilisation</b>	74 (91%)	9%	41%	37%	5%
<b>Trigger point release</b>	73 (90%)	11%	53%	26%	0%
<b>Acupuncture</b>	81 (100%)	81%	9%	11%	0%

GMI was mostly used in the classic order by 10% versus 2% who used it in an ad hoc sequence. However, 43% never used a GMI classic sequence. Twenty per cent occasionally used the GMI classic sequence. Fifteen percent of the GMI users often applied the classic sequence. Ten percent of Physiotherapists used the classic sequence of GMI as the most common intervention. Those who used the ad hoc sequence showed similar numbers. This is shown in Figure 3.2.

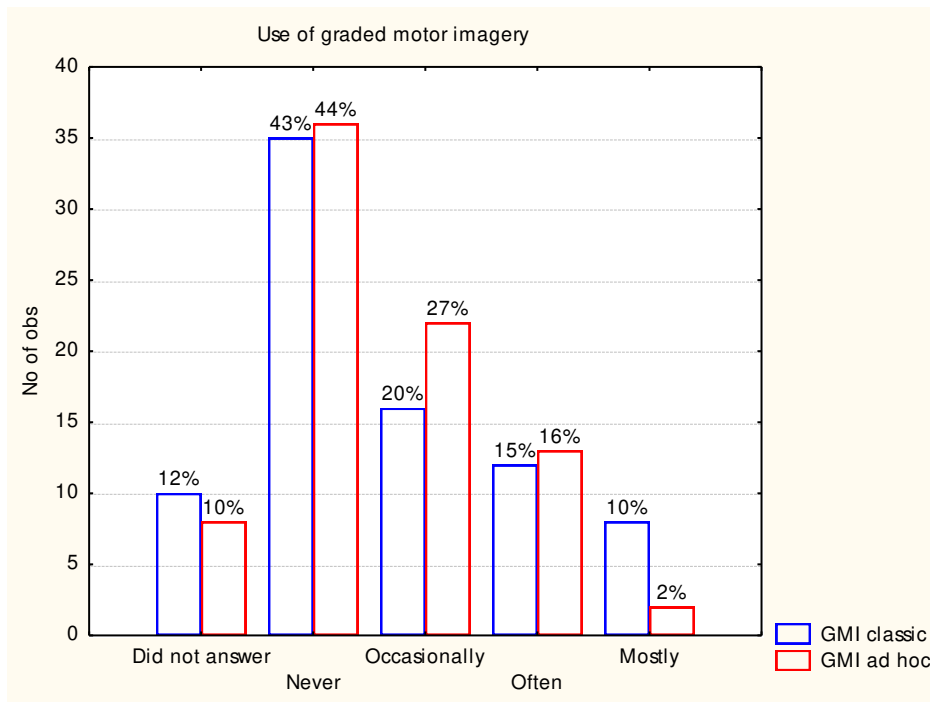


Figure 3.2. Use of graded motor imagery in clinical physiotherapy practice.

These data were further analysed using ANOVA tests for significance to determine if the frequency of seeing CRPS patients was associated with the type of intervention used. The more frequently a Physiotherapist evaluated CRPS patients, the following occurred, namely:

i) they used GMI more often rather than occasionally in the classic order of the 3 phases ( $p = 0.017$ ); ii) they used relaxation techniques often rather than occasionally ( $p = 0.021$ ); iii) the more likely they were to use sensory mapping or discrimination occasionally, rather than never ( $p = 0.00785$ ); and iv) the more often they used oedema massage rather than seldom ( $p = 0.029$ ). Table 3.2 outlines the significant differences between those Physiotherapists who evaluated CRPS patients frequently compared to those who seldom saw CRPS patients. The other variables in Table 3.1 were not significant.

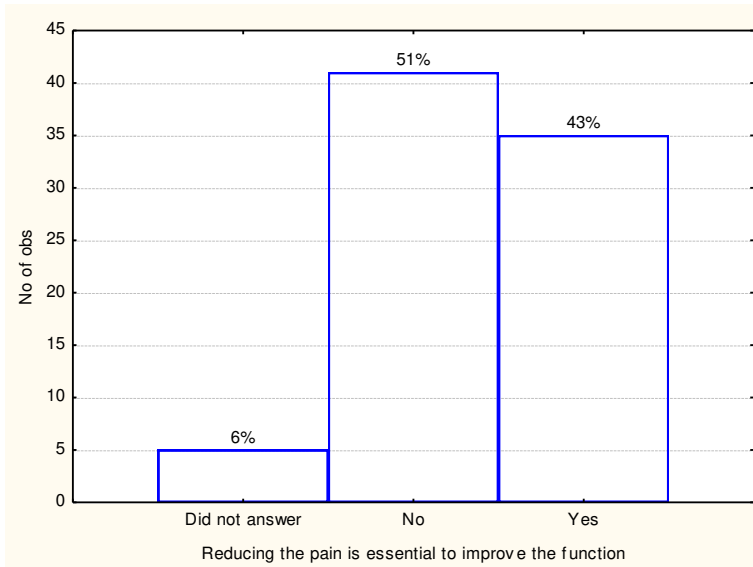
*Table 3.2. Significant differences between those Physiotherapists who seldom saw CRPS vs. those who saw CRPS patients often.*

<b>Physiotherapy intervention method more likely to be used by the physio who sees CRPS patients more often</b>	<b>Frequency of use more likely</b>	<b>P value</b>
<b>Graded Motor Imagery (GMI)</b>	From occasional to often	0.017*
<b>Relaxation techniques</b>	From occasional to often	0.021*
<b>Sensory mapping</b>	From never to occasional	0.007*
<b>Discrimination</b>	From never to occasional	0.007*
<b>Desensitising</b>	From occasional to often	0.007*
<b>Oedema massage</b>	From seldom to often	0.029*

\*= significance with  $p < 0.05$

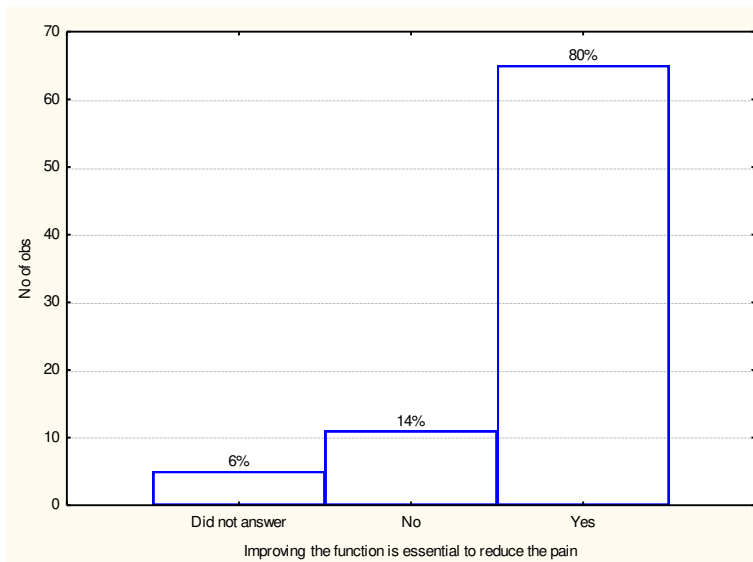
### **3.5.3. Physiotherapists' beliefs**

Physiotherapists' beliefs about what was considered most important for the management of CRPS patients proved highly variable. Physiotherapists were almost equally divided about whether or not reducing the pain experience was essential to improve the functioning (51% and 43%, respectively). This is shown in Figure 3.3.



*Figure 3.3. The belief about reducing the pain being essential in CRPS to improve the functioning.*

Eighty per cent believed that improving the function was essential to reducing the pain; 14% believed that it was not essential. This is shown in Figure 3.4.



*Figure 3.4. Improving the function is essential in order to reduce the pain experience.*

The beliefs for CRPS about whether exercise and increasing pain were indicated or not, showed 72% answered ‘no’ to contra-indicated and 75% answered ‘yes’ to indicated. The beliefs are represented in Table 3.3.

*Table 3.3. Summary of Physiotherapists’ beliefs about what is best for CRPS intervention method.*

<b>Physiotherapists’ beliefs about what is best for CRPS intervention method</b>			
	Did not answer	YES	NO
	N (%)	N (%)	N (%)
Reducing the pain is essential to improve the function	5 (6%)	35 (43%)	41 (52%)
Improving the function is essential to reduce the pain	5 (6%)	65 (80%)	11 (14%)
Exercising and increasing the pain is contra-indicated	6 (7%)	17 (21%)	58 (72%)
Exercising and increasing the pain is indicated	6 (7%)	14 (17%)	61 (75%)

### **3.6. Discussion**

The report about what is usually used for physiotherapy intervention methods had not been evaluated before. It was necessary to document what Physiotherapists reported to apply in everyday usual clinical practice across the South Island, so that the structure of this project could be determined. The interventions applied gave the information required in order to categorise different methods as well as to plan the hypotheses. The information acquired was also useful as it provided a novel contribution to the literature about everyday clinical management, as well as what Physiotherapists believed to be important about usual management of their CRPS patients. There is no literature about physiotherapy beliefs for CRPS management.

These results showed that half of all New Zealand’s South Island physiotherapy practices do not treat CRPS patients. Only a small fraction of the Physiotherapists would treat more than two CRPS patients per month. This confirmed the low prevalence of CRPS reported in the literature [69, 70]. It raised the question about whether or not some CRPS patients never sought physiotherapy help for their CRPS management since it has been shown that CRPS can resolve spontaneously without any intervention [69], or perhaps that some CRPS patients are not referred to physiotherapy.

Education was the modality most often used as an intervention for CRPS, as recorded by 83%. Physiotherapists potentially play an important role in educating patients about the diagnosis, management and prognosis of CRPS. This is because most CRPS patients were shown to possess a minimum standard of basic knowledge regarding the syndrome [160]. Similar to diseases like diabetes, education has been shown to be valuable in enabling behavioural change as well [162]. The provision of information also forms an integral ingredient in an effective therapeutic relationship [295] and registration competency standards [312]. It has been suggested that physiotherapy management for CRPS needs to be specifically tailored for the individual patient's needs [313]. However, it remains difficult with the current body of literature to know what intervention to apply when presentation, progression and outcome of CRPS patients are variable [39].

One third of the Physiotherapists often used cognitive techniques and breathing control with relaxation techniques; another third used them only occasionally. Those treating more CRPS patients were more likely to use these interventions. Less than 15% were most likely to use these techniques. Eighty per cent were familiar with these interventions, but did not apply them regularly. This highly variable presentation of CRPS and the different intervention methods suggested in the literature led the candidate to explore further about what South Island Physiotherapists believed to be important about their CRPS management.

The data showed that the more frequently Physiotherapists evaluate CRPS patients, the more likely they were to use interventions such as GMI and SMT and that these interventions were not used by the other Physiotherapists who see CRPS patients less frequently. It was not possible to determine the reason for these differences.

These data illuminated the inconsistency with which physiotherapy interventions (other than education that is mostly used) are practised in managing CRPS. This finding was conjectured to reflect the differences in Physiotherapists' beliefs about what is important for their management of CRPS patients. This possibly reflected the juxtaposition in research evidence of the pain modulation and pain exposure approaches. The pain modulation approach was supported with the evidence for mirror exercises, relaxation, psychological techniques, SMT, GEXP, GMI, and TENS for reducing the pain experience in order to facilitate function. In contrast, pain exposure is supported by the evidence for progressive exercise loading without analgesia that aims towards restoration of function.

These data showed that Physiotherapists differed in their belief about whether or not reducing the pain experience was essential to improve CRPS function; they were also divided about whether or not pain is indicated with prescribed exercise in CRPS management.

Physiotherapists were divided about believing whether or not pain experience was indicated. Also, Physiotherapists were divided about whether or not the extent to which prescribed exercise provokes pain, is an essential ingredient for potential functional gain. Since there are no studies to show what other clinicians believe to be important for the management of CRPS, other than that members of a hand team were reported to perceive the risk of developing CRPS quite differently from each other in their interpretation of clinical signs [102], it was important to determine what Physiotherapists believed to be important. Hence, these data reflect that it was potentially challenging to determine a management plan with the appropriate exercise, as pain is the hallmark of CRPS [314], even though there are patients with severe pain that present with reasonable function [55]. The reasons for these differences in beliefs about CRPS would benefit from further scrutiny for both practitioners and patients alike.

This survey provided the important information to be able to categorise interventions for the potential longitudinal observational cohort study. Furthermore, it established the relationships and communication channels to enable the research project to go ahead since it was also important to explain the objectives around this potential study. Reassurance was given to physiotherapists that the subsequent project would not be an appraisal of their practice; nor of individual practitioners; nor of their respective clinics. Furthermore, the record of their clinical notes would be anonymous. Any potential influence that the candidate could have on their clinical practice would be minimised. The use of an independent interviewer would help this as well.

## **CHAPTER FOUR**

### **Method and Hypothesis Generation**

#### **4.1 Introduction**

This project sought to bridge the gaps of knowledge in physiotherapy research applied to a clinical setting. The literature search outlined these gaps. These gaps shaped the aims, method and hypothesis generation. This chapter describes the methodology applied to this project.

#### **4.2 Aims**

The aims were: a) to describe the characteristics of CRPS patients living in the South Island; b) to measure patient outcomes and changes over time/natural history for one year after commencing physiotherapy; c) to document and categorise the standard physiotherapy interventional methods received; d) to identify predictors of patient outcomes associated with either baseline or intervention factors; e) to investigate the associations of the current physiotherapy intervention for CRPS; and f) to develop a conceptual model for physiotherapy CRPS management.

#### **4.3 Method**

These aims were pursued as an observational, prospective, longitudinal study across a region, meeting the requirements to be defined as a cohort study [315].

##### **4.3.1 Recruitment of participants**

Physiotherapists accepting CRPS patients across the South Island were invited to participate and informed about the project in person. Patients with a new diagnosis of CRPS, according to the Budapest criteria, who presented to physiotherapy were informed about the project and asked to consent to participate by their treating Physiotherapist. Participation was voluntary. No financial or other gain was given for participation to either the Physiotherapist or the participant. It was explained to Physiotherapists that this project was not an audit of their practice, nor were individuals or groups of Physiotherapists to be compared. The project was to determine the outcomes for all CRPS patients presenting to Physiotherapists across the South Island, to categorise the intervention methods applied, and determine which intervention methods were more effective.

The Physiotherapist involved with the new CRPS patient was asked to: explain the research objectives; obtain signed consent; return the signed consent to the researcher with the participant's details for telephone contact; document the autonomic changes observed; and report back on a provided table. This table listed the possible signs and symptoms associated with Budapest criteria, including changes in colour, temperature, vasomotor, sudomotor, motor, proprioception; and perception of disturbance. The treating Physiotherapist was asked to mark all boxes in the table relevant to the patient's objective examination. This objective record of the signs and symptoms provided the clinical evidence to support the diagnosis of CRPS according to the Budapest criteria. It was a priority to ensure that each participant met the Budapest criteria for the diagnosis of CRPS.

The candidate provided training about the Budapest criteria for the diagnosis of CRPS to the following physiotherapy groups:

October 2013, Christchurch, Redwood Physiotherapy, 1 hour.

October 2013, Christchurch, Merivale Hand Clinic, 1 hour.

October 2013, Christchurch, PhysioSouth private practice, 1 hour.

February 2014, Dunedin Hospital, Hand therapy Department, 1 hour.

February 2014, Invercargill, Windsor Physiotherapy, 1.5 hours.

February 2014, Westport, Buller Health, Physiotherapy Department, 1 hour.

June 2014, Ashburton Hospital, Physiotherapy Department and private practitioners, 2 hours.

August 2014, Nelson Hospital, Physiotherapy Department, 1 hour.

August 2014, Nelson Physiotherapy New Zealand Branch, 2.5 hours.

August 2014, Blenheim Hospital, Physiotherapy Department, 1 hour.

August 2014, Mental Health Special interest group, 1 hour

April 2015, Dunedin, Otago Physiotherapy New Zealand Branch, 2 hours

April 2015, Invercargill, Kew Hospital, Physiotherapy Department, 1 hour.

April 2015, Invercargill, Southland Physiotherapy New Zealand Branch, 2 hours.

April 2015, Timaru, Private and hospital Physiotherapists, 1 hour.



May 2015, Christchurch, Sportsmed private practice Physiotherapists, 3 hours.

August 2015, Rangiora, Central Physiotherapy, Physiotherapists, 1 hour.

September 2015, Christchurch, Private practice, Hand Therapy group, 1 hour.

October 2015, Nelson hospital Physiotherapy Department, 1 hour.

February 2016, Blenheim, Wairau hospital Physiotherapy Department, 1 hour.

February 2016, Timaru, Private and hospital Practitioners, 2 hours.

March 2016, Westport, Buller Health Physiotherapy Department, 1 hour.

May 2017, Christchurch, Waltham Physiotherapy private practice, 2 hours.

Each Physiotherapist was asked if they felt that this subsequent longitudinal study of the clinical outcomes and relationships with physiotherapy intervention would be helpful or not, and also if they would agree to refer patients for inclusion in the cohort study. Interestingly, there were no Physiotherapists who answered negatively. However, when invited later to participate and obtain patients' consent to be interviewed, the unfriendly and unreceptive responses from two managers of a District Health Board's outpatient clinics was a set-back for the candidate. The reason given was that their staff were not paid for spending time on research. This was despite having full locality authorisation from this District Health Board and that the consent process would not require more than 5 or 10 minutes. The folder with all the information about the project was returned. Fortunately, this was not the case for the rest of the South Island.

#### **4.3.2 Participant inclusion and exclusion criteria**

Participants were included if they were confirmed to have a diagnosis of CRPS Type 1 or 2, according to the Budapest criteria [22], by either a General Practitioner, a Medical Specialist or a Physiotherapist within one year of presenting to the treating Physiotherapist. This was recorded by the treating Physiotherapist for this project. Potential participants were excluded: if their CRPS diagnosis had been longer than 1 year; if they had a terminal co-morbid condition; if they were blind (sight was necessary for graded motor imagery); if they were unable to communicate in English or Māori (including deafness and cognitive impairment); or if they chose to decline to participate.

#### **4.3.3 Demographic and relevant clinical variables**

Demographic and relevant clinical data were collected. This included: the diagnosis of either CRPS Type 1 or Type 2; the duration of time with CRPS diagnosis; the length of time from inciting injury to diagnosis; the length of time to see a Specialist Pain Medicine Physician; age; gender; marital status; geographical region; years of education; work status; laterality; adherence to intervention programme homework; and ethnicity as defined by Statistics New Zealand [316].

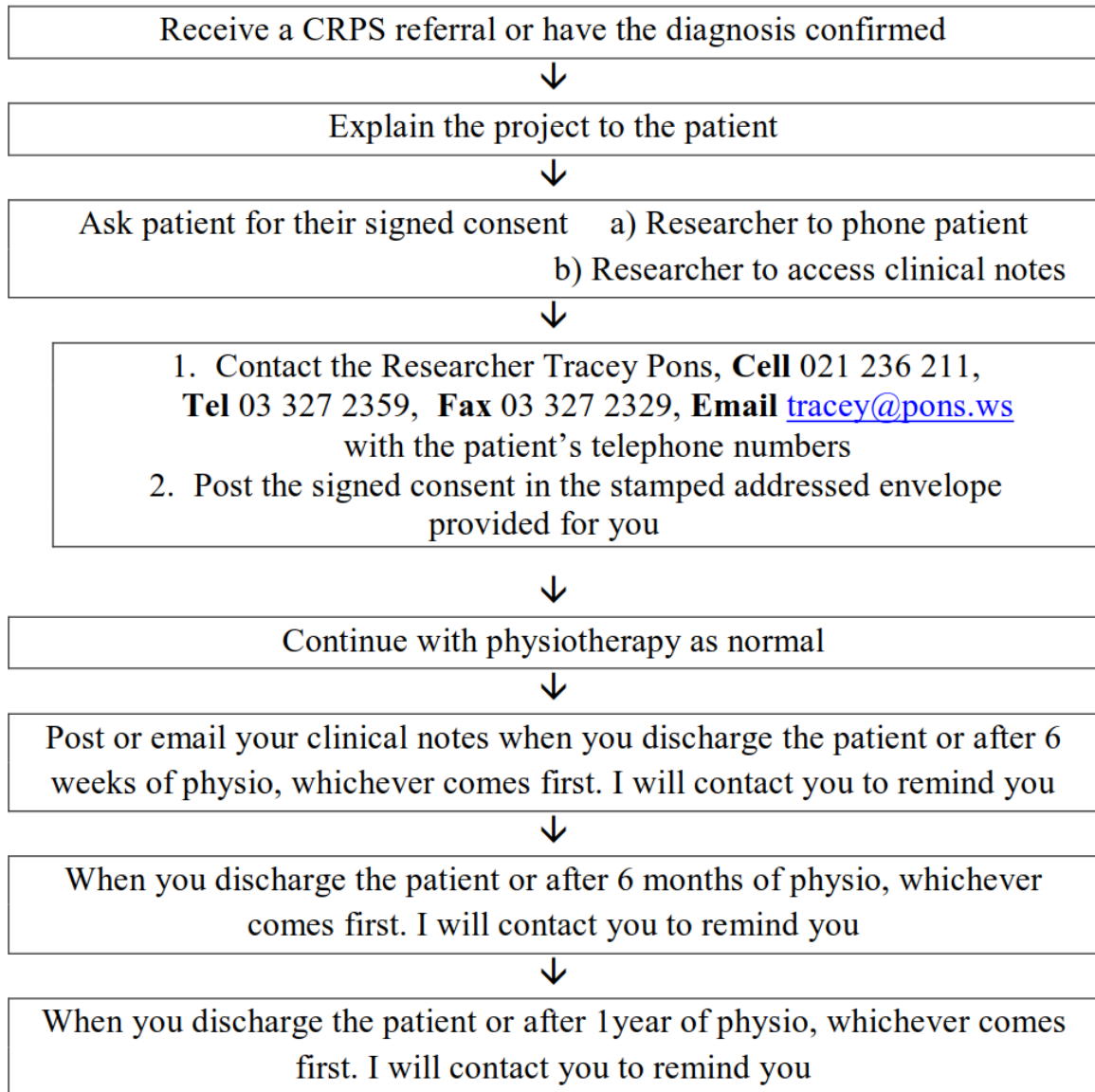
#### **4.3.4 Medical and Psychological intervention**

Medical interventions and psychological input concurrent with physiotherapy were asked about at each interval interview. These were confirmed by the physiotherapy clinical notes if recorded. It is not standard practice for Physiotherapists to record medications prescribed or adherence to psychology if these referrals were concurrent. Hence, it was necessary to obtain this information from participants at each interview. The report of the participant was also taken as compliance with their participation in psychology or with their prescribed medication or procedures. Adherence was not possible to determine in this project and it was not possible to determine those who may have been offered medication, procedures or psychology, but declined to receive them.

#### **4.3.5 Collection of physiotherapy intervention**

A copy of all clinical treatment notes was accessed by the candidate following discharge of each participant from their respective Physiotherapist(s), or 1 year after starting their physiotherapy interventions. The flow chart for Physiotherapist referral and collection of intervention is outlined in Figure 4.1.

### **Flow chart for Physiotherapists**



*As the data collects and I am able to provide some analyses I will be informing you of my findings.*

*I will also inform you when I no longer need participants as I have collected the 75 data points I need.*

***A very big thank you for participating with this research project***

Figure 4.1. Flow chart for Physiotherapist referral.

#### 4.3.6 Physiotherapy intervention

Following the last interview or following the patient's discharge, the treating Physiotherapists were contacted and clinical notes were accessed by the researcher. This was to determine the type, frequency, and duration of interventions administered as well as non-attendance.

Physiotherapy treatment interventions were classified into one of five categories by the researcher (also an experienced Physiotherapist) and by the primary supervisor for this project, a Specialist Pain Medicine Physician. These categories were defined based on the findings from the survey of usual physiotherapy practice intervention methods and what was considered the relevant goal of the intervention.

These assigned categories of physiotherapy intervention were necessary for categorical analysis of intervention methods. Individual intervention methods serve towards different purposes as a group of interventions. Hence, it was considered appropriate that the category of functional restorative interventions target active joint range of motion, muscle strength, soft tissue flexibility, balance and proprioception; that pain modulation interventions targeted central processing; that immobilisation interventions target the restriction or inhibition of active activity; and that passive interventions require no active engagement of the participant with the intervention.

The assigned categories of physiotherapy intervention for this project:

- Treatment Interventions for function (TIF). These were functional restorative exercises: active; passive; resisted; balance; proprioceptive; land/gym based; lymphoedema management exercise; or time contingent homework prescribed.
- Treatment Interventions for pain modulation (TIP). These were exercises for pain modulation: graded motor imagery (GMI); mirror exercise; pool exercise; transcutaneous electrical nerve stimulation (TENS); cognitive behavioural therapy (CBT); acceptance and commitment therapy (ACT); problem solving; relaxation and breathing; sensory–motor training (SMT) including sensory mapping, discrimination and desensitising; positioning for lymphoedema; or pain contingent homework prescribed.
- Education intervention (Educ): This was a written record of education in the clinical notes
- Immobilising interventions (TII): These were bracing, splinting or taping immobilising or restriction of active joint range of motion.

- Passive interventions (Pass): These required no active participation of the patient: massage (scar tissue; lymphoedema or oedema); acupuncture; ultrasound, and application of heat or wax bath

Other interventions, such as medical prescriptions or procedures and other allied or alternative health interventions were recorded from the participant's interview and verified by clinical physiotherapy recorded notes.

#### **4.4 Instruments**

All instruments, other than the record of autonomic changes listed under clinical observations by the treating Physiotherapist were questionnaires for quantitative analysis. The details of each questionnaire instrument can be found in Appendix D.

The instruments chosen have been shown in the literature to be reliable and valid. Short forms were used when known to be reliable with robust inter-item correlation consistency. This was to reduce the potential interference of the time taken to interview participants. It was considered a priority by the candidate to minimise any impact of potential stress or irritation in participants through unnecessarily time-consuming questionnaires.

The instruments chosen evaluated comparable and novel measures in CRPS research. The comparable measures were those chosen for the measure of the pain experience and functional ability of the upper limb. The novel measures evaluated health anxiety, personality, the World Health Organisation quality of life and ability, the functional ability of the lower limb and the satisfaction of care from the treating Physiotherapist.

Since CRPS can affect either the upper or lower limb, a disability measure to assess both limbs and body function was necessary, hence the choice of the World Health Organisation Disability Assessment Schedule [317].

The quantitative tests chosen to be relevant and appropriate for testing the hypotheses and used in other CRPS research for comparison were as follows: the scores of pain rating index (PRI) from Short form McGill Pain Questionnaire (MPQ-SF) [318]; quality of life and functional ability with World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2) [319-321]; the functional ability of upper limb CRPS with the Quick Disability of the Arm, Shoulder, Hand questionnaire (QuickDASH) [322-324]; the functional ability of the lower limb CRPS using the Foot Function Index (FFI) [325, 326]; and the satisfaction of care with the Deyo and Diehl Satisfaction (DDS) Questionnaire [327].

Quantitative outcome measures were undertaken by telephone interview. Baseline measures were performed as physiotherapy intervention commenced. Follow up interviews were performed by an independent interviewer at the interval of 6 weeks, 6 months and 1 year after commencing physiotherapy.

These intervals of 6 weeks, 6 months and 1 year after commencing physiotherapy quantitative outcome measures were chosen as: a) a duration of the benefit or detriment of any intervention is not reliable if only measured in the short term; b) these intervals match other research [92]; c) comparison for changes of associations was made possible with repeated measures.

Contact details were obtained in order to complete the post intervention outcome measurement. The participants were contacted by telephone by the independent interviewer, an appointment time was arranged, or the questionnaires answered at the time of the telephone call.

#### **4.4.1 Quantitative instruments**

##### *Evaluating disability with quality of life*

The assessment of functional ability and quality of life across all cultures was developed with the World Health Organisation (WHO) Disability Assessment Schedule 2.0 (WHODAS 2) in order to define and apply an accurate tool towards an effective and international classification for functioning, disability and health [319, 328, 329]. The scale was developed to cover six constructs of functioning, namely: cognition; self-care; getting along; participation; mobility; and life activities. It was shortened from the previous 36 item questionnaire to a shorter, easier to complete 12 item version [320]. This questionnaire also collected data around work status.

The 12-item version was used in this project as it is time efficient, applicable in a telephone interview, and is a valid and reliable instrument to measure function that reflects the quality of life associated with the multidimensional aspects of disability [317, 321, 330, 331]. It is also an effective instrument that can be applied to population with a disability such as CRPS [328]. However, there is not yet a verified minimal, clinical difference of change to show that a significant difference of improvement has been obtained [331].

The WHODAS 2 uses a Likert scale asking a description of the experience of difficulty over the previous 30 days, ranging from 'none', 'mild', 'moderate', 'severe' or 'extreme' with 2

questions for each of the 6 constructs. It also provided a measure of how many days this difficulty was present in the last 30 days. The Likert scale can be scored by two methods [319]. A simple sum of the response scores where a higher score means a greater the experience of difficulty. The simple sum was used for this project. The second method is described as the weighted method where the scores are converted onto a scale of 1-100. Then the sum of the scores is divided by 48 and converted to a percentage. The WHODAS website provides an SPSS calculator to apply this [320]. This method has been questioned as it may not be valid to accurately measure across multiple constructs [328].

#### *Evaluating functional ability of the upper limb with the Quick Disability of the arm, shoulder and hand questionnaire (DASH)*

The Quick Disability of the arm, shoulder and hand (QuickDASH) is a well-known and long-standing instrument that was developed to assess the functional ability of the upper extremity, including CRPS [322, 332-334]. This study used the short form as it has been shown to be valid and reliable [322, 335, 336], and has been widely used in all forms of interviewing [337]. It has shown better responsiveness to actual clinical changes than Medical Outcomes short form (SF-36) for upper limb functional ability [338].

The Quick DASH questions ability on a 5-point Likert scale ranging from 'no', 'mild', 'moderate', 'severe difficulty' or 'unable'. The constructs evaluate function, social role, work participation, pain experience and sleep with 11 questions. It also has optional further questions about work, musical instrument playing, and sport. The optional questions were not evaluated with this study. The individual response scores are summed and converted to percentage by  $(\text{total sum}/11-1) \times 25$ . This gives a score out of 100, where the higher the score the greater the disability.

#### *Evaluating functional ability of the lower limb with the foot function index*

The Foot Function Index (FFI) is an instrument developed to assess the functional ability of the lower limb. It is a valid and reliable instrument [325, 326] and a suitable instrument for CRPS foot function assessment. The foot function index is scored with a 10 point Likert scale using verbal anchors, and assessing the 3 constructs over the past week. The construct of pain has 5 questions, disability has 9 questions and activity limitations has 3 questions. For the pain construct, the scale uses 'worst pain imaginable' for 10, to 'no pain' as zero. For

disability, 'so difficult, unable to do' 10, to 'no difficulty' scored at zero. For activity limitation disability, it is scaled from 'none of the time' to 'all of the time'.

*Evaluating the pain experience for CRPS using the Numerical Rating Scale-11 and Short form McGill Pain questionnaire*

Pain intensity was measured using the pain rating index from the SF-MPQ Questionnaire, an easy to administer scale [339, 340] and used in CRPS research [341]. This measure consists of 17 items about multiple constructs in three sections. The first section consists of 15 questions that assess the construct of the sensory experience with 11 questions, and the affective experience with 2 questions. The sensory rating index (SRI) questions are on a Likert scale of 'none', 'mild', 'moderate' or 'severe,' with the sensations of 'throbbing, stabbing, shooting, sharp, cramping, gnawing, burning, aching, heavy, tender, or splitting'. The 4 questions which ask about the affective rating index (ARI) included 'tiring-exhausting', 'sickening', 'fearful' and 'punishing-cruel'. The scores for the SRI and ARI are summed to give a total Pain Rating Index (PRI). The higher the PRI score, the greater the sensory and affective experience of pain. The second section evaluates the intensity of the pain experience with the options on a 5-point Likert scale of: 'no pain'; 'mild'; 'discomforting'; 'distressing'; 'horrible', or 'excruciating'. It is termed the evaluative intensity (EVI).

The third section is the Numerical Rating Scale-11 (NRS-11) and is considered sensitive and specific to evaluate the experience of pain; hence it is robust for statistical analysis [342]. For this study, three separate NRS-11 measures were applied, the lowest, the highest scores for the pain experience over the previous week, as well as the current score for the pain at the time of the interview. The use of a single measurement scale has been shown to be as effective as multiple measures, and reliable to repeated measures over time, for the assessment of the pain experience of CRPS Type 1 patients [341].

The recently developed CRPS severity score [343] was not used for this study for several reasons: at the time of preparation for this study in 2010, the severity score had not yet been validated; it was also not possible for the independent interviewer to provide an objective assessment for a valid score at each interview interval; and a treating Physiotherapist would not be available if a participant had been discharged prior to an interview.



### *Evaluating participant satisfaction of their physiotherapy care*

The satisfaction of participant's care by their respective treating Physiotherapist was measured using the Deyo and Diehl Satisfaction (DDS) Questionnaire. It is valid, reliable, short and easy to administer [327]. Satisfaction with physiotherapy care is important to determine as an ingredient in the therapeutic relationship. Meta-analysis shows that the therapeutic relationship has a moderate effect ( $p < 0.05$ ,  $r = 0.22$ ) to potentially affect the outcome for many health problems [293]. Satisfaction with care is shown to be high with those who show improved CRPS recovery [96]. It was measured with the choice of 3 options; 'dissatisfied/no'; 'satisfied/yes'; 'don't know' to each of 9 questions about satisfaction with care: These are: 'Were you satisfied with your contact with your Physiotherapist?'; 'Did you have an adequate explanation of your CRPS?'; 'Do you feel the Physiotherapist was concerned about you?'; 'Do you feel the Physiotherapist understood what was bothering you?'; 'Do you feel you understand what was wrong?'; 'Did your Physiotherapist spend enough time with you?'; 'Would you like to see the same Physiotherapist if you were to go back to that clinic/department?'; 'Was your care with your Physiotherapist for your CRPS better, worse or the same as your visits to your specialist or doctor?'; 'Did you seek help from a Doctor or allied health professional or hospital after your last visit with your Physiotherapist? If yes, whom?'

### *Evaluating adherence*

Adherence to prescribed homework by the Physiotherapist was considered important to evaluate as a factor that potentially affects outcomes or the therapeutic relationship [298]. A 7-point Likert scale about adhering to prescribed homework was used. This ranged over the week from: 'never'; 'once'; 'twice', etc. to 'every day' of the week, as well as over the period of a day from: 'never'; 'once a day'; 'twice a day'; 'three times a day'; 'four times a day'; 'five times a day', to 'more than every hour'. It also had the option of 'other' to define a point of difference. Participants were also asked 'how would you rate how much your prescribed homework exercise helped to make your pain feel less' on a Likert scale with the options: 'always'; 'almost always'; 'sometimes'; 'rarely', or 'never'.

#### **4.4.2 Quantitative predictors instruments**

It is possible in any quantitative research that the effect of predictors on outcome measures can be determined with robust statistical methods. The literature reviews outlined in Chapter

2 showed that potentially anxiety, mental health, psychological distress, catastrophising and fear of movement all affect CRPS outcomes, but with no strong statistical evidence of a relationship.

Since psychosocial measures like catastrophising, anxiety or depression had not been shown to be strongly associated with poor CRPS outcomes [39, 255], health anxiety, a specific facet of anxiety associated with body sensations and physical health, was chosen as a novel measure to contribute to the understanding about CRPS. This was measured using the Health Anxiety Index (HAI) [344]. In addition, the 10-item psychological distress Kessler (Kessler10) measure was chosen as it is comprehensive to evaluate mental health [345, 346]. The Kessler10 provided another novel contribution as it had not been applied in CRPS research before.

Personality and CRPS was also explored. Hence the inclusion of the Eysenck Personality Questionnaire Extraversion and Neuroticism scale, brief version (EPQ-BV) [347] which is a novel application. The Tampa scale for Kinesiophobia (TSK) [125] had been used in CRPS research before to evaluate the fear of movement or kinesiophobia [101]. It was felt important to include this measure to compare with other research findings.

In summary, the potential predictors for possible influences on the outcomes chosen for this project were the following: health anxiety with the HAI; Personality Extraversion and Neuroticism with the EPQ-BV; fear of movement with the TSK, and mental health with the Kessler10 questionnaires. These predictors were only administered once with the pre-intervention measures. Further details about each measure follow. The exploratory nature of this study was to determine potential associations.

### *Evaluating health anxiety*

Anxiety about general health has been shown to be associated with some persistent pain [348-350]. Hence the development of an instrument, the HAI, to exclusively measure the construct of anxiety about physical health [344]. The short form of this instrument was used as it determines the extent of the pre-occupation with bodily symptoms, and anxiety related to the experience of symptoms. This factor has not been explored before with those who have a diagnosis of CRPS and is a novel application. It is a valid and reliable instrument to measure the construct health related anxiety [351, 352]. The short form has four statements about potential health anxiety with each of the 18 questions. These are scored from zero to three

over each of the four statements for each of the 18 questions. The total score is the sum of responses to all questions. The higher the score the higher the anxiety about health.

The Hospital Anxiety and Depression scale (HAD) was not used for this project. It was developed as a questionnaire to determine the extent of general anxiety related to possible depressive symptoms during illness or trauma [353-355]. This questionnaire was not used as depression was already being assessed with the Kessler10 questionnaire and it assesses anxiety as a whole construct, not the specific construct of health-related anxiety which determines the pre-occupation with bodily symptoms. The specific construct of health-related anxiety was considered to be better addressed with the HAI.

#### *Evaluating neuroticism or extraversion in personality*

The bizarre physical and autonomic features sometimes observed in CRPS led earlier practitioners to believe that there was possibly an element of somatoform malingering [77], but this has since been shown to be untrue [78-80]. However, it is recognised in all persistent pain conditions that psychological, behavioural and perceptions of stress can contribute to exacerbating the pain experience [81]. A higher level of neuroticism in personality has been shown to be associated with some persistent pain conditions [356-358].

Extraversion has been shown to be associated with greater ability to tolerate distress [359] and teenage extraversion is shown to be a protective factor for mental health at age 30 [360]; hence this study used the EPQ-BV to evaluate the influence of personality traits extraversion or neuroticism [361, 362]. The brief version is a quick, reliable, valid and easy to apply tool which assesses both these constructs [363]. Personality extraversion and neuroticism had not been evaluated in CRPS research before. The EPQ-BV uses a Likert scale of 1-4 from 'not at all', to 'slightly', 'moderately', 'very much', 'extremely' to each question with two reversed questions. The higher the score the greater the extent of the neuroticism or extraversion.

#### *Evaluating the fear of movement*

The TSK determines the extent the pain experience represented a belief that pain was equivocal to tissue damage or harm. It also reflects the extent of the belief that avoiding activity was helpful to reduce pain [128, 130]. When it was originally developed, it was not published and instead it was used with permission by further developers of the fear avoidance model [364, 365]. The TSK has been shown to have good reliability and internal consistency [366], and was used in this project to measure the extent a CRPS participant

feared movement. The TSK has 17 questions with a Likert scale of 1 to 4 ascribed to strongly disagree, disagree, agree, and strongly agree to each statement with four reversed questions.

### *Evaluating Mental Health*

Mental health was considered to be important to evaluate, since the construct of depression has been shown in numerous studies to be a factor associated with persistent pain [345, 367, 368], fibromyalgia [369], and the neglect-like symptoms that can present with CRPS [370]. The Kessler10 was developed as a brief, easy to apply, time-efficient and accurate screening tool for telephonic or personal interviewing to determine mental health or psychological distress, where it has been shown to be accurate, valid and reliable [346]. The Kessler10 was shown as more reliable than the General Health Questionnaire 12 which was also used to determine psychological distress [346].

It has been used extensively in health research for a broad variety of applications including for those who attempt to quit smoking [371], and is able to determine the presence of potential mental health issues and can discriminate between those who have mental health issues and those who do not [346, 372], and across all population groups [372]. It uses a Likert scale of 1-5 anchored at 'none of the time' to 'a little', 'some of', 'most of', 'all of the time', for 10 questions. The higher the score the greater the depression.

### *Longitudinal instrument application*

Table 4.1 summarises which questionnaires were used and at what interval. Table 4.2 shows details about each instrument's unit measurement scale. Table 4.3 shows the details about measurement units with the predictor instruments.

#### **KEY to Abbreviations for Tables 4.1-4:**

MPQ-SF - Short form McGill Pain Questionnaire

WHODAS2 - World Health Organisation (WHO) Disability Assessment Schedule 2.0

QuickDASH - The Quick Disability of the arm, shoulder and hand

FFI – Foot Function Index

TSK – Tampa Scale for Kinesiophobia

HAI – Health Anxiety Index

Kessler10 – Ten item psychological distress Kessler

EPQ-BV - Eysenck Personality Questionnaire Brief Version

DDS - Deyo and Diehl Satisfaction

Table 4.1. Details about questionnaire interview schedule.

<b>INTERVIEW SCHEDULE</b>	<b>MPQ-SF</b>	<b>WHODAS2</b>	<b>Quick DASH or FFI</b>	<b>TSK</b>	<b>HAI</b>	<b>Kessler10</b>	<b>EPQ-BV</b>	<b>DDS</b>	<b>Homework Adherence</b>
<b>Baseline</b>	√	√	√	√	√				
<b>6 weeks</b>	√	√	√			√		√	√
<b>6 months</b>	√	√	√				√	√	√
<b>1 year</b>	√	√	√					√	√

Table 4.2. Details of measurement units for Outcome Instrument.

<b>Name</b>	<b>Outcome Measures</b>	<b>Unit of measurement</b>
MPQ-SF	a. Descriptive words for pain (PRI) b. Numerical rating scale-11 (NRS11) c. Intensity of pain (EVI)	a. Likert Scale (0-4) + (n) words b. Likert Scale (0-10) b. Likert Scale (0-5)
WHODAS2	a. Functional ability b. Disability experience	a. Likert scale (1-4) b. Numbers of days
DASH	Upper limb functional ability	Likert scale (1-4)
FFI	Lower limb functional ability	Likert scale (0-10)
DDS	Satisfaction with physiotherapy	Dissatisfied/no Satisfied/yes Don't know
Homework participation	a. Days per week b. Number of times per day c. Rating about helpfulness to reduce pain	a. Likert Scale (0-7) b. Likert Scale (0-8) b. Likert Scale (0-4)

Table 4.3. Details of measurement for potential predictor instrument.

Possible Predictor Measures	Unit of measurement
TSK	Likert scale (1-4)
HAI	Likert scale (1-72)
Kessler10	Likert scale (0-50)
EPQ-BV EPQN EPQE	Likert scale (1-60) Likert scale (1-60)

Table 4.4. Details about which questionnaires are used when and approximately how long each one takes to interview

Interview schedule	Instrument	Approximate length of time to take
As physiotherapy intervention commences	<p><u>Introduction</u></p> <p><u>Baseline measures</u></p> <p>MPQ-SF</p> <p>WHODAS 2</p> <p>DASH or FFI (limb dependent)</p> <p><u>First predictor</u></p> <p>TSK, HAI</p>	<p>1 min</p> <p>2 min</p> <p>4 min</p> <p>1 min</p> <p>2 min, 3min</p>
6 weeks following commencing physiotherapy	<p><u>Introduction</u></p> <p><u>Baseline measures</u></p> <p>MPQ-SF</p> <p>WHODAS 2, section 4 only</p> <p>DASH or FFI (limb dependent)</p> <p><u>Satisfaction</u></p> <p>DDS</p>	<p>1 min</p> <p>2 min</p> <p>3 min</p> <p>1 min</p> <p>1 min</p>

	<u>Adherence</u> Homework questions 2 min  <u>Second predictor</u> Kessler 10 2 min	
6 months following commencing physiotherapy	<u>Introduction</u> 1 min  <u>Baseline measures</u> MPQ-SF 2 min WHODAS 2, section 4 only 3 min 1 min DASH or FFI (limb dependent)  <u>Satisfaction</u> DDS 1 min  <u>Adherence</u> Homework questions 2 min  <u>Third predictor</u> EPQ 2 min	
1 year following commencing physiotherapy	<u>Introduction</u> 1 min  <u>Baseline measures</u> MPQ-SF 2 min WHODAS 2, section 4 only 3 min 1 min DASH or FFI (limb dependent)  <u>Satisfaction</u> DDS 1 min  <u>Adherence</u> Homework questions 1 min  <u>Conclusion and thanks</u> 1 min	

#### **4.4.3 Telephone interviewing**

This project involved an independent interviewer to reduce potential bias, and improve the validity of the data collected. The independent interviewer also contributed to minimising the potential interference of the researcher with the treating Physiotherapist through conversations with their respective patient, as well as reducing the concern that some Physiotherapists raised about feeling vulnerable.

Telephone interviewing has been shown to be valid and reliable to determine disability or psychological health [337]. It was reported to have excellent reliability when compared with personal interviewing in a recent publication about upper limb disability and function [337]. Telephone interviewing has been shown to be valid with the Kessler10 [346].

The advantage of the telephonic interview is the time efficiency and reduced transport costs for the face-to-face interviews for both parties involved. This is especially since the region of South Island of New Zealand covers a large area. The disadvantage is that telephonic interviews have been shown to reveal greater dissatisfaction with treatment than those who mail back their questionnaires [373, 374].

#### **4.5 Hypothesis generation**

The survey findings of the usual physiotherapy clinical practice, and the gaps found in the literature, provided the necessary information to determine the structure of this project. Two primary and two secondary hypotheses were explored. The regional physiotherapy intervention methods, and the respective CRPS patient outcomes, were evaluated. This evaluation was by prospective observation and independent interviewing. This permitted the objective measurement of individual physiotherapy interaction with different intervention methods, in a clinical environment, on subsequent outcomes.

##### **4.5.1 Primary hypothesis**

The primary hypothesis was to determine if a positive outcome for CRPS is associated with: 1) Adherence with Physiotherapy intervention, and 2) early diagnosis defined as within 4 months of injury event.

Tests for Hypothesis 1.1 are presented in Chapter 7 and for Hypothesis 1.2 in Chapter 8.



## **4.6. Secondary objective generation**

### **4.6.1 Secondary objectives**

The secondary objective explored was to determine if 1) that physiotherapy intervention specifically aimed at central processes (described as treatment interventions for pain) has a positive association on CRPS outcomes, and 2) that different physiotherapy treatment modalities have dissimilar associations for the outcomes for CRPS.

Tests for objectives 2.1 and 2.2 are presented in Chapter 9.

### **4.5.3 Null hypothesis**

The null hypothesis was that any observed changes to outcomes of CRPS are due to chance.

## **4.6 Analytic Approach**

Quantitative statistical methods were used. Data from the physiotherapy clinical record data were collated using Microsoft Excel®. Standard descriptive statistics were used to compare categorical variables. Analysis used statistical software Statistica 7.1®. The primary analysis was for significance between pre and post outcome measures, and used student t-tests for significance. Secondary analyses compared variables and demographic data, and tested for significance differences with Mann-Whitney U tests. Possible predictors and relationships between different categories or intensity of physiotherapy intervention associated with outcome measures were analysed using logistic regression models. A Spearman correlation matrix determined relationships, and a conceptual clinical model was proposed.

## **4.7 Statistical power**

To detect for significance a power  $1 - \beta$  (1-beta) of 0.8, and  $\alpha$  (alpha) of 0.05 was used. Significance was further refined so that despite a p-value of significance as  $p < 0.05$  with logistic regression, any potential predictive effect was excluded if the upper or lower quartiles of the confidence intervals showed a ratio of 1:1 around the odds ratio.

The nature of this project was as a Hypothesis generating study and not as a clinical trial. Hence, there was no randomisation nor control group was applied. To determine meaningful information it was required that an appropriate sample size was necessary to meet this significance. To meet this significance, assuming a small association for physiotherapy

intervention of  $r = 0.2$ , a sample size of 153 participants [375] was required. However, in order to accommodate the low prevalence of CRPS [69], as well as manage a potential dropout rate, a sample of 75 was sought as this sample size is relevant to other CRPS studies, N = 59 [89], N = 39 [25], N = 26 [120], N = 46 [114] and N = 49 [98].

#### **4.8 Summary**

The candidate sought six broad aims for the longitudinal study, in the context of the literature review and the prior survey information obtained from South Island Physiotherapists for CRPS management. Ethical approval was obtained and appropriate Māori consultation accomplished. Hypotheses and objectives were proposed and in order to evaluate them, reliable and valid quantitative instruments were used to measure variables at baseline, 6 weeks, 6 months and 1 year following commencing with physiotherapy. Participants were invited to be interviewed by an independent interviewer with signed, informed consent if they met the inclusion criteria.

## CHAPTER FIVE

### Cohort descriptive and baseline statistics

#### 5.1 Introduction

This Chapter provides the information about the cohort's characteristics and baseline statistics. Aspects of this data were published as a case series for the first 20 participants in *The Open Pain Journal* [42], see Appendix A.

The aim of this Chapter is to describe the full sample demographic characteristics; clinical features; Budapest criteria; concurrent medical or psychological intervention; baseline measures; and predictor variable measures.

#### 5.2 Participation of CRPS patients

The full cohort consisted of 75 participants who signed consent to participate between January 2014 and December 2017. Nine participants were excluded for the following reasons: 1 due to their duration of CRPS being greater than a year; 2 due to diagnoses not being CRPS; 1 due to the language barrier with interviewing; 2 were not able to be contacted for baseline interview; 1 withdrew with no reason given; and 2 withdrew for personal reasons. Thirteen were lost to follow up for the final interview for outcome measures one year later. However, their physiotherapy intervention data were available. A total of 66 participants were included in the analyses for categories of physiotherapy applied and 53 for outcome measures. Figure 5.1 shows the participation process.

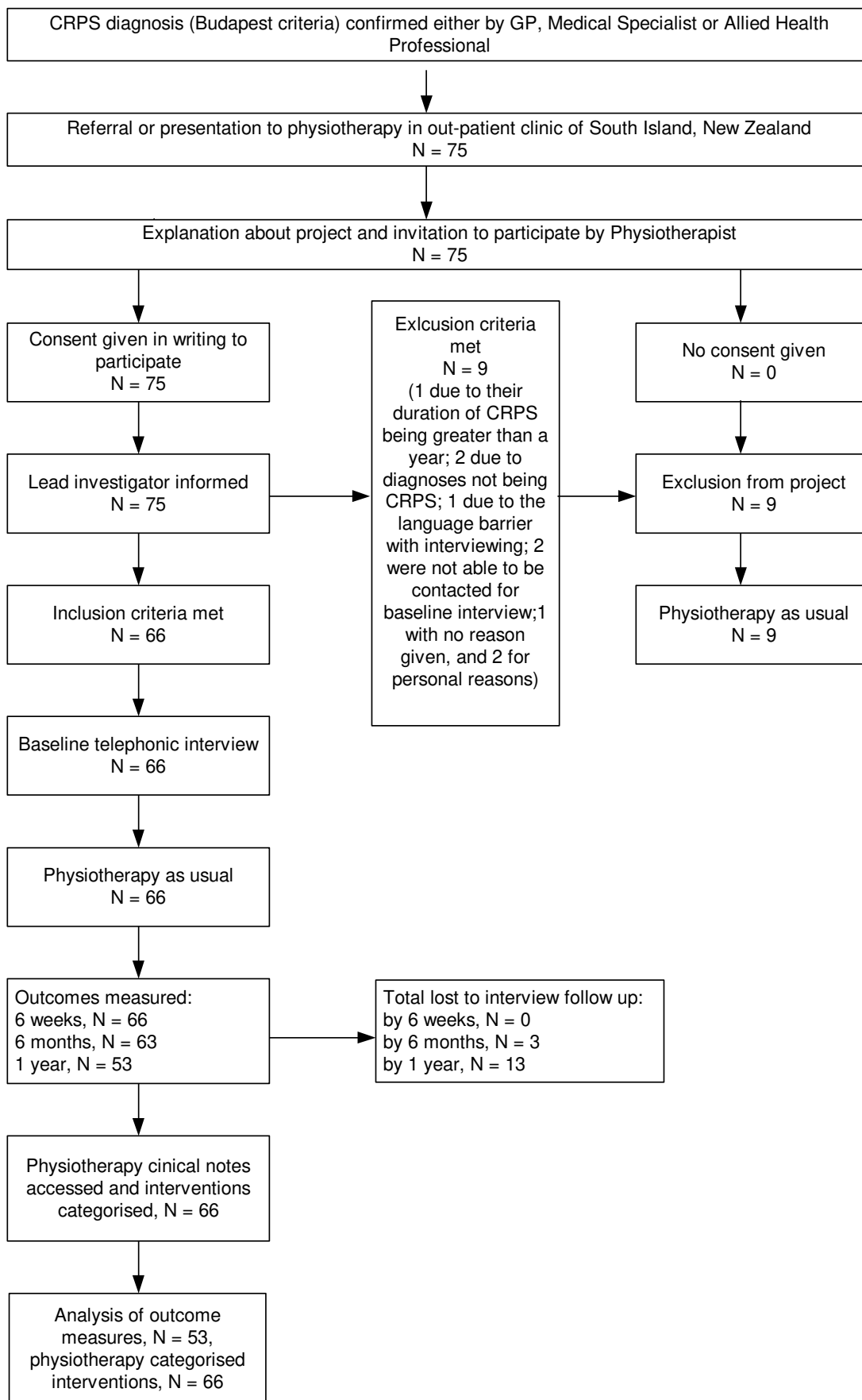


Figure 5.1. Flow chart of participation.

### 5.3 Demographic characteristics and descriptive statistics

Fifty-two females and 14 males participated with ages ranging from 11 to 77 years (mean 46 years). The age distribution is presented in Figure 5.2.

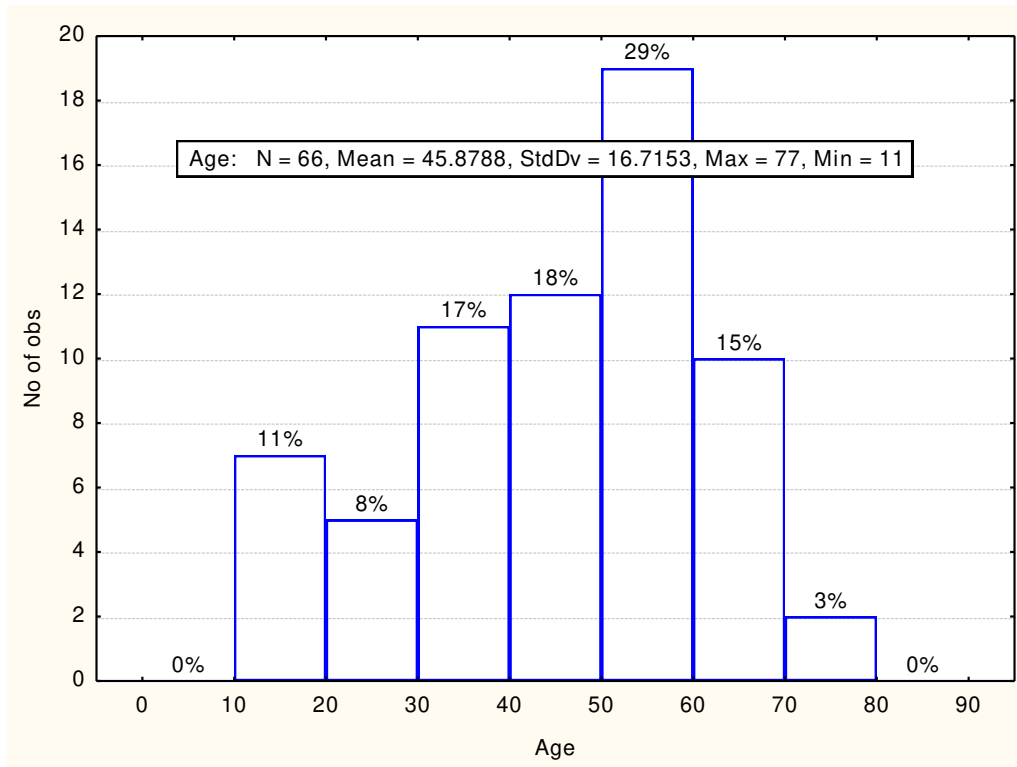


Figure 5.2. Age distribution.

New Zealand Europeans were the predominant ethnic group: fifty seven (86%) had a CRPS Type 1 and 9 (14%) had a CRPS Type 2 diagnosis; fractures were the inciting event for 28 (42%); followed by soft tissue injury for 24 (36%); and surgery for 14 (21%) participants. The upper limb was more frequently affected than the lower limb with 49 (74%), and 17 (26%) participants, respectively.

The Nelson/Marlborough and West Coast regions were represented in this sample with one participant each, and the other South Island regions were represented in proportion to their population densities with the largest sample from Mid and North Canterbury, 37 (56%) which represents the area supporting the largest South Island city, South Canterbury, 14 (21%), Southland, 9 (14%) and Otago, 4 (6%) participants.

The largest group of 26 (40%) were employed with 20 (30%) participants not employed due to their CRPS; 7 (11%) scholars or tertiary students; 6 (9%) retired; 4 (6%) home maker; 2 (3%) not working for other reasons; and 1 (2%) was a non-paid volunteer. These data are shown in Table 5.1.

*Table 5.1. Baseline follow up characteristics.*

<b>CHARACTERISTICS</b>	<b>Baseline N (%)</b>
<b><i>Gender</i></b> Female Male	53 (79) 14 (21)
<b><i>Ethnicity</i></b> New Zealand European Māori Tongan Other European	57 (86) 6 (9) 1 (1) 2 (3)
<b><i>Diagnosis CRPS Type</i></b> CRPS 1 CRPS 2	57 (86) 9 (14)
<b><i>CRPS precipitating event</i></b> Fractures Soft tissue injury Surgery	28 (42) 24 (36) 14 (21)
<b><i>Affected limb</i></b> Upper limb Lower limb	49 (73) 17 (27)
<b><i>Marital status</i></b> Currently married Never married Cohabiting Divorced/separated Widowed	29 (42) 16 (24) 10 (15) 9 (14) 2 (3)
<b><i>Region</i></b> Nelson/Marlborough West Coast Mid/North Canterbury South Canterbury Otago Southland	1 (2) 1 (2) 37 (56) 14 (21) 4 (6) 9 (14)
<b><i>Employment</i></b> Paid employment Not working due to CRPS Student or scholar Retired Home maker Not working for other reasons Non-paid volunteer	26 (40) 20 (30) 7 (11) 6 (9) 4 (6) 2 (3) 1 (2)

The time taken to diagnosis, from the inciting injury, was the same percentage of 28 (42%) participants for 1 month and 2–4 months. For 10 (15%) diagnosis took longer than 4 months. The mean time to diagnosis found with this cohort was 2.4 months (with a SD of 1.87). Greater than half, 45 (68%) of this cohort were evaluated by a Specialist Pain Medicine Physician; 17 (26%) were seen from 1-3 months from their inciting injury, and 11 (17%) were seen in 3-6 months; and 18 (27%) waited for longer than 6 months to be seen. These data are shown in Table 5.2.

*Table 5.2. Baseline descriptive statistics.*

<b>DESCRIPTION</b>	<b>N (%)</b>
<i>Time to diagnosis from injury</i>	
1 month	28 (42)
2-4 months	28 (42)
≥ 4 months	10 (15)
<i>Time taken to physiotherapy from injury</i>	
Less than 1 month	20 (30)
1-2 months	21 (31)
2 and < 3 months	9 (13)
3 and <6 months	10 (14)
≥ 6 months	7 (10)
<i>Referred to a Medical Pain Specialist (MPS)</i>	
Yes	45 (68)
No	21 (32)
<i>Time taken to see the MPS from injury</i>	
1 month up to 3 months	17 (26)
3 months up to 6 months	11 (17)
≥ 6 months (SD)	18 (27)

The time taken to commence with physiotherapy shows similarity as within 1 month for 20 (30%), and within 2 months for 21 (31%). Nine commenced physiotherapy (13%) within 3 months. Ten (14%) took 4 to 6 months to commence; seven (10%) waited for more than 6

months before they commenced physiotherapy. The mean time to the commencement of physiotherapy was 2.8 months (with a SD of 1.87). These data are shown in Table 5.3.

*Table 5.3. Baseline months to diagnosis, physiotherapy and Pain Medical Specialist.*

<b>MONTHS</b>	<b>N</b>	<b>Mean</b>	<b>SD</b>	<b>Median</b>	<b>Lower Quartile</b>	<b>Upper Quartile</b>
<b>Time to diagnosis</b>	66	2.4	1.9	2.0	1.0	3.0
<b>Time to commence physiotherapy</b>	66	1.9	0.9	2.0	1.0	3.0
<b>Time to see Pain Medical Specialist</b>	53	4.4	4.4	3.0	1.0	6.0

SD – Standard Deviation

#### **5.4 Confirmation of CRPS diagnosis according to Budapest criteria**

The diagnosis was confirmed at baseline by the use of the objective record of all autonomic or other signs according to the Budapest criteria provided by the treating Physiotherapist. This record was completed on the provided tables at the time of the CRPS diagnosis, or at the time of commencement of physiotherapy. These tables used by the treating Physiotherapist can be viewed in Appendix C.

The baseline findings demonstrated that most of this cohort showed the following: vasomotor signs with changes of skin temperature (91%) and colour (91%); sudomotor changes of oedema (83%); sweating (89%); hyperalgesia (70%); and allodynia (48%). It is possible that participants might have presented with both allodynia in one area and hyperalgesia in another area in the region affected by their CRPS. These data are presented in Table 5.4.



*Table 5.4. Objective baseline autonomic changes recorded at baseline by treating Physiotherapist.*

<b>AUTONOMIC CHANGE PRESENT</b>	<b>N (%)</b>
<b>Skin temperature to physical touch change of affected area in comparison to unaffected other limb</b>	60 (91)
<b>Skin colour</b>	60 (91)
<b>Skin texture</b>	43 (65)
<b>Oedema</b>	55 (83)
<b>Skin sweating</b>	59 (89)
<b>Hair growth</b>	32 (48)
<b>Nail changes</b>	28 (42)
<b>Skin sensation: Hyperalgesia</b>	46 (70)
<b>Skin sensation: Allodynia</b>	32 (48)
<b>Skin sensation: Hypoaesthesia</b>	25 (38)

### **5.5 Concurrent Medical and Psychological variables**

The concurrent medical or psychological support data were documented at each interview interval. Psychological support was already in place for one participant at baseline.

Prescription (or over the counter) oral medication adherence was as follows: Paracetamol, the largest group, (over the counter or prescribed) with 27 (41%) participants; followed by gabapentin with 15 (23%); over the counter or prescribed non-steroidal, anti-inflammatories by 14 (21%); amitriptyline by 13 (20%); nortriptyline by 9 (14%) and tramadol by 6 (9%).

Use of other opioids such as codeine was low with 1 (2%) participant. Oral cortisone, dothiepin and pregabalin were not prescribed at the time of baseline measure. These data are represented in Table 5.5.

Table 5.5. Baseline Medical and Psychological care.

Management	Description	Baseline, N (%)
<b>Medical</b>	Pamidronate infusion	1 (2)
	Prescription of codeine	1 (2)
	Prescription of tramadol	6 (9)
	Prescription of panadeine	1 (2)
	Prescription of amitriptyline	13 (20)
	Prescription of nortriptyline	9 (14)
	Prescription of dothiepin	0 (0)
	Prescription of gabapentin	15 (23)
	Prescription of pregabalin	0 (0)
<b>Over the counter or prescribed</b>	Over the counter or prescribed paracetamol	27 (41)
<b>Over the counter or prescribed</b>	Over the counter or prescribed non-steroidal, anti-inflammatory	14 (21)
<b>Psychological support</b>	Individual psychological sessions	1 (2)

## 5.6 Baseline predictor variables

The higher the score for the TSK, Kessler10, HAI and EPQ reflect a greater extent of the construct being measured viz.; TSK, higher fear avoidance; Kessler10, poorer mental health; HAI, poorer health anxiety; EPQE, greater personality extraversion trait; and EPQN, greater personality neuroticism trait. The standard deviation (SD) and inter-quartile range (IQR) with these data showed a mean TSK of 37, (SD 10.7 IQR 29-45); Kessler10, mean 10.5, (SD 8.9, IQR 3-17); HAI mean 30.5, (SD 10.4, IQR 21-40); EPQE mean 39.6, (SD 9.0, IQR 33-47); EPQN mean 38.3, (SD 10.4, IQR 31-46). These data are shown in Table 5.6.

Table 5.6. Baseline predictor variable descriptive statistics.

Predictor/Confounder measure	N	Mean	SD	Median	Lower quartile	Upper quartile
<b>TSK</b>	66	37.0	10.7	38.0	29.0	45.0
<b>Kessler10</b>	65	10.5	8.9	9.0	3.0	17.0
<b>HAI</b>	66	30.5	10.4	28.0	21.0	40.0
<b>EPQE</b>	64	39.6	9.0	41.0	33.0	47.0
<b>EPQN</b>	64	38.3	10.4	39.5	31.0	46.0

TSK – Tampa Scale for Kinesiophobia

HAI – Health Anxiety Index

Kessler10 – Ten item psychological distress Kessler

EPQE - Eysenck Personality Questionnaire Extraversion

EPQN - Eysenck Personality Questionnaire Neuroticism

## 5.7 Baseline outcome measures

Each outcome measure score for pain, PRI and NRS11 produced a higher score to represent higher/worse pain experience. Each functional measure, the WHODAS2, DASH and FFI scored greater disability with a higher score. The PRI mean was 26.1, (SD 8.4, IQR 20-33); NRS11 mean 6.2, (SD 1.7, IQR 5-7); WHODAS2 mean 31.3, (SD 9.6, IQR 23-40); FFI mean 45.9, (SD 14.9, IQR 31.2-55.9); DASH mean 69.2, (SD 14.9, IQR 59.1-79.5). These data are shown in Table 5.7.

*Table 5.7. Outcome baseline measures mean, standard deviation median, upper and lower quartiles.*

<b>Outcome measure</b>	<b>N</b>	<b>Mean</b>	<b>Std Dev</b>	<b>Median</b>	<b>Lower quartile</b>	<b>Upper quartile</b>
<b>PRI</b>	66	26.1	8.4	26.0	20.0	33.0
<b>NRS11</b>	66	6.2	1.7	6.0	5.0	7.0
<b>WHODAS2</b>	66	31.3	9.6	9.0	23.0	40.0
<b>FFI</b>	17	45.9	16.5	45.3	31.2	55.9
<b>QuickDASH</b>	49	69.2	14.9	72.7	59.1	79.5

PRI - Short form McGill Pain Questionnaire pain rating index

NRS11 – 11-point Numerical pain rating scale

WHODAS2 - World Health Organisation (WHO) Disability Assessment Schedule 2.0

QuickDASH - The Quick Disability of the arm, shoulder and hand

Those lost to follow up showed no differences from the responders with baseline categorical or continuous variables with Student-t tests. These data are shown in Table 5.8.

Table 5.8. Student-t tests for differences between baseline categorical and continuous variables of lost to follow up and responders.

	<b>N Baseline</b>	<b>Mean</b>	<b>SD</b>	<b>N Lost to follow up</b>	<b>Mean</b>	<b>SD</b>	<b>t-value</b>	<b>p</b>
<b>TSK</b>	54	36.1	11.2	12	40.8	7.3	-1.4	0.13
<b>HAI</b>	54	30.4	10.1	12	31.1	12.2	-0.2	0.35
<b>EPQE</b>	54	38.6	9.9	10	36.3	12.8	0.7	0.25
<b>EPQN</b>	54	23.5	8.7	10	25.2	10.7	-0.5	0.34
<b>PRI</b>	54	25.5	8.9	12	28.5	5.2	-1.1	0.06
<b>NRS11</b>	54	6.2	1.7	12	6.0	1.9	0.4	0.65
<b>FFI</b>	16	45.4	16.9	1	54.1	0.0	-0.5	1.00
<b>QuickDASH</b>	38	68.2	15.5	11	72.7	12.5	-0.9	0.48
<b>Kessler10</b>	54	10.2	9.0	11	11.5	9.0	-0.4	1.00

TSK – Tampa Scale for Kinesiophobia

QuickDASH - The Quick Disability of the arm, shoulder and hand

PRI - Short form McGill Pain Questionnaire pain rating index

NRS11 – 11-point Numerical pain rating scale

Kessler10 – Ten item psychological distress Kessler

HAI – Health Anxiety Index

FFI – Foot Function Index

EPQN - Eysenck Personality Questionnaire Neuroticism

EPQE - Eysenck Personality Questionnaire Extraversion

## 5.8 Discussion

The following was described in this cohort of 75 participants, namely: demographic, descriptive characteristics as well as their diagnosis confirmation and timing; the commencing of physiotherapy; the use of concurrent medical or psychological support; and their baseline outcome measures as well as potential predictor variable measures.

These cohort data closely represented other large epidemiological studies [55, 69, 70, 292] and also a single North Island New Zealand study [89]. The data showed predominantly female Europeans, a mean age of 46 years, and a ratio of one male to four females, with 44% a fracture as the precipitating injury. Fracture had been identified as a potential risk for the onset of CRPS [39] as well as being the most common precipitant for the injury that subsequently develops into CRPS [55, 69, 70, 292]. These data also showed that the upper limb was more frequently affected than the lower limb, in keeping with the literature [69, 70, 86]. The reasons for this are not known. Furthermore, CRPS of the lower limb is shown to be frequently excluded in research trials [107]. In contrast, one large web-based study, N = 875, showed a higher incidence affecting the lower limb [55] and the reasons for this discrepancy are not known. The affected laterality showed similar proportions of left or right being affected with these data; this is in keeping with other studies [178, 376].

These data also showed their baseline pain to be within the range of other CRPS studies [89, 114, 141, 148]. Fear of movement with the TSK was shown to be greater when compared with a North Island study; N= 59, mean TSK=28,6 [255]; but lower when compared with a sample who had CRPS for more than 2 years, N=8 with a mean score of 54.5 [100]. The QuickDASH score mean is higher than reported in two French studies N=20, as 62.8 [377] and N=8 as 40.8 [196]; also in a Turkish study N=36 as 55.3 [378]. Since there is no literature for WHODAS2 for CRPS populations, these baseline data were compared with a healthy Australian population sample and were shown, as expected, to have a greater disability and poorer quality of life with WHODAS2 [379].

The novel aspects of the Kessler10 explored with this cohort showed a mean score of 10.2 (SD 9.0) which reflects better mental health when compared with mean of 14.5 reported from normative data for the healthy Australian population in 2007 [380], and also reflects that this sample of patients with CRPS are within 92% of the population norm who score between 10 and 29 [381]. These data provide new information to the field.

The following Chapter 6 describes the five aspects to the physiotherapy as well as the medical and psychology interventions as applied by practitioners across the South Island for CRPS intervention.

## **CHAPTER SIX**

### **Description of Physiotherapy, Medical and Psychology interventions applied**

#### **6.1 Introduction**

This Chapter outlines the five aspects to the physiotherapy, medical, and psychology interventions as applied by practitioners across the South Island for CRPS intervention. It was important to evaluate concurrent intervention with physiotherapy and describe an account of what was applied. This was necessary to provide the platform for comparison with other potential future studies and to provide the information necessary to determine specific or interactive effects.

The structure of this Chapter describes the method and follows with the results describing a) the physiotherapy intervention: the number of sessions, discharge route, categories applied, intensity of categories applied; b) the participant's report about: adherence to prescribed homework, satisfaction with physiotherapy care, and c) the baseline differences between those who received psychological support or medical prescriptions.

#### **6.2 Method**

##### **6.2.1 The five aspects of physiotherapy**

Physiotherapy was assessed in five different ways.

First, the intensity of the physiotherapy, that is the number, frequency or duration of sessions that were attended for each interval and the accumulated sum over the year.

Second, the when or how participants were discharged. It would be a plausible assumption that when formal discharge was prescribed by the Physiotherapist that a satisfactory outcome was achieved. There were also those who self-discharged and were no longer willing to adhere to appointments. Then, there were those for whom on-going care continued beyond one year.

Third, physiotherapy interventions (as described in Chapter 4) which were categorised as treatment interventions for: pain (TIP); function (TIF); education (Educ); immobilisation (TII); or were passive (Pass). These were collated from the clinical records and compared.



Fourth, the extent to which there was adherence to the prescribed homework. This was determined through the interview at each interval where participants reported on how often in a day, as well as a week they performed their prescribed homework; and how they rated its helpfulness towards a reduction of their pain experience.

Fifth, the satisfaction with care reported by participants with the Diehl and Deyo questionnaire at each interval.

Physiotherapy clinical data records were accessed and attendance, contact hours and duration of physiotherapy sessions attended were documented. The full data set for all 66 participants was completed for their respective physiotherapy clinical data. All data were collated accordingly between each interview interval, as well as the accumulated sum from baseline (the first measure when physiotherapy commenced) to each interval. This means that the sum from baseline to 6 months or 1 year would include the data from baseline to 6 weeks.

### **6.2.2. Medical and psychology interventions**

Baseline differences for all categorical or continuous variables between those who received psychological support or medical intervention were explored. This was because their contribution to the recovery and potential influence on physiotherapy intervention may have influenced the outcomes.

### **6.2.3. Analytic approach**

These data were entered into the Microsoft Excel® and the Statistic 7® spreadsheet and cleaned when all data entry was completed in November 2017. Standard descriptive statistics were applied and the Kaplan Meier plot used to show survival analysis between the discharge routes. ANOVA and Mann-Whitney U Tests were applied to determine differences between the categorical and continuous variables in baseline differences, psychological support, the medical prescription of the anticonvulsant, and the tricyclic medication groups.

## 6.3 Results

### 6.3.1 Physiotherapy intensity

#### *The number of session attended*

The number of sessions attended per interval showed larger upper interquartile range than lower quartile ranges i.e. was skewed to the upper quartile range. The greatest number of sessions attended occurred in the 18 weeks between the 6-week and 6-month interviews with a mean of 10.4 (SD 8.2) per week. The mean for the first interval of baseline to 6 weeks was less; it showed a mean of 6.9 (SD 3.2) per week. The lowest number of sessions per week was for the third interval from 6 months to 1 year with a mean of 3.6 (SD 6.0). These data are shown in Table 6.1.

*Table 6.1. The number of physiotherapy sessions attended in each interval.*

<b>N=66</b>	<b>Mean</b>	<b>SD</b>	<b>Median</b>	<b>Lower quartile</b>	<b>Upper quartile</b>	<b>Sum</b>
<b>TOTAL N physio sessions from baseline to 6 weeks</b>	6.9	3.2	6.5	5.0	9.0	456.0
<b>TOTAL N physio sessions from 6 weeks to 6 months</b>	10.4	8.2	9.5	3.0	16.0	687.0
<b>TOTAL N physio sessions from 6 months to 1 year</b>	3.6	6.0	0.0	0.0	5.0	240.0

The cumulative sum of sessions for each interval was also documented. This was considered more useful information. It disclosed that the greatest numbers of physiotherapy sessions were applied in the first 6 months, showing a sum of 1,143 at 6 months and only increasing by another 247 sessions for the next 6 months. In contrast, the sum for the first 6 weeks was almost twice that at 456. There are variations around the interquartile ranges from 5-9 for the first 6 weeks, 10-25 for 6 months, and from 10-33 over the year. This showed that most had completed their physiotherapy by 6 months. These data are shown in Table 6.2.

*Table 6.2. Total cumulative physiotherapy sessions attended by each interval.*

<b>N=66</b>	<b>Mean</b>	<b>Std. Dev.</b>	<b>Median</b>	<b>Lower quartile</b>	<b>Upper quartile</b>	<b>Sum</b>
<b>N physio sessions at 6wk</b>	6.9	3.2	6.5	5.0	9.0	456
<b>TOTAL N physio 6 mo</b>	17.3	10.0	16.0	10.0	25.0	1,143
<b>TOTAL N physio 1yr</b>	21.2	14.7	16.0	10.0	33.0	1,396

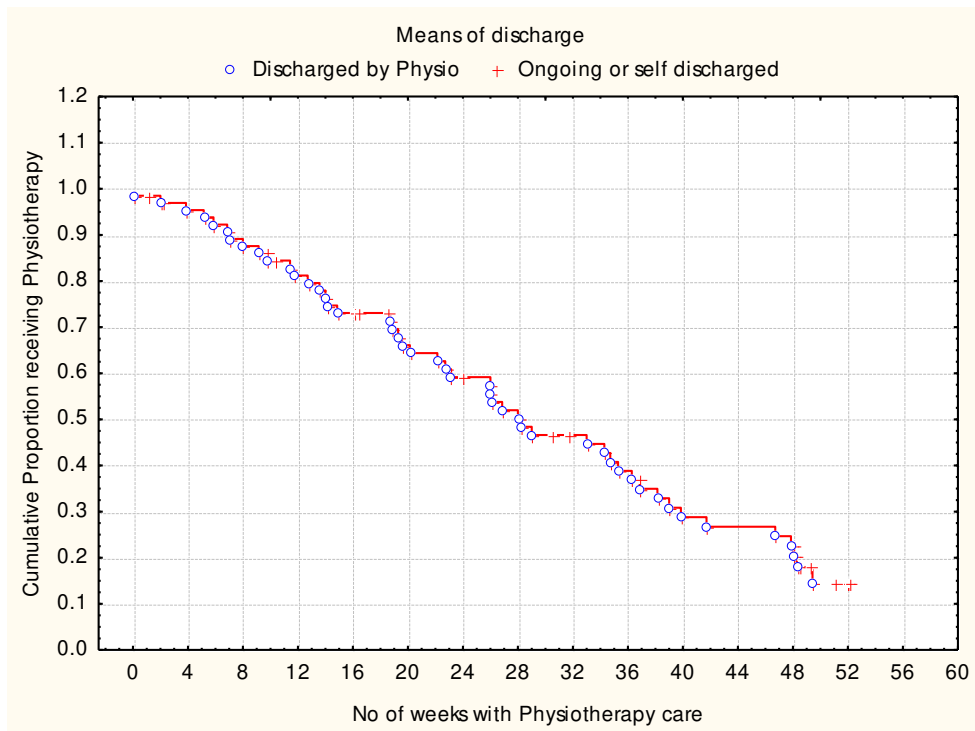
The mean and median number of weekly sessions attended with their treating Physiotherapist was calculated for each outcome measure interval. The intervals are: baseline to 6 weeks; 6 weeks to 6 months; and 6 months to one year. These data showed that for the first six weeks most were seen approximately weekly with 1.1 times per week, (IQR 0.8 - 1.5). This was more frequent than from 6 weeks to 6 months which showed 0.5 times per week, (IQR 0.2 - 0.7). This is similar for the longer interval of 6 months to one year, where the smaller group of 26 participants who were not yet discharged in this interval are seen 0.4 times per week, (IQR 0.2-0.6). These data are shown in Table 6.3.

*Table 6.3. Mean and median number of physiotherapy sessions, attended per week, for each interval.*

No of physiotherapy sessions per week	Attending physiotherapy N	Discharged N	Mean	SD	Median	Min	Max	Lower quartile	Upper quartile
<b>Baseline to 6 weeks</b>	66	0	1.1	0.5	1.1	0.2	3.0	0.8	1.5
<b>6 weeks to 6 months</b>	60	6	0.5	0.3	0.4	0.0	1.3	0.2	0.7
<b>6 months to 1 year</b>	26	40	0.4	0.3	0.3	0.0	1.3	0.2	0.6

### *The discharge route*

The time at which discharge occurred over the year is graphically represented with a Kaplan-Meier plot shown in Figure 6.1. The results showed the trend of an almost linear gradual reduction in in number of weeks attending physiotherapy before discharge. This was for those who self-discharged or were formally discharged by their treating Physiotherapist. There was no apparent difference between these two groups regarding the time at which discharge occurred, with a steady spread over the year.



*Figure 6.1. Kaplan-Meier plot showing numbers of weeks to discharge.*

The route for discharge was documented. Forty-seven (71%) participants were discharged by their Physiotherapist. Small and similar groups, 9 (14%) and 10 (15%) participants respectively, either self-discharged (they chose to discontinue their physiotherapy despite follow up being arranged) or they required ongoing care beyond the year. These data are shown in Figure 6.2.

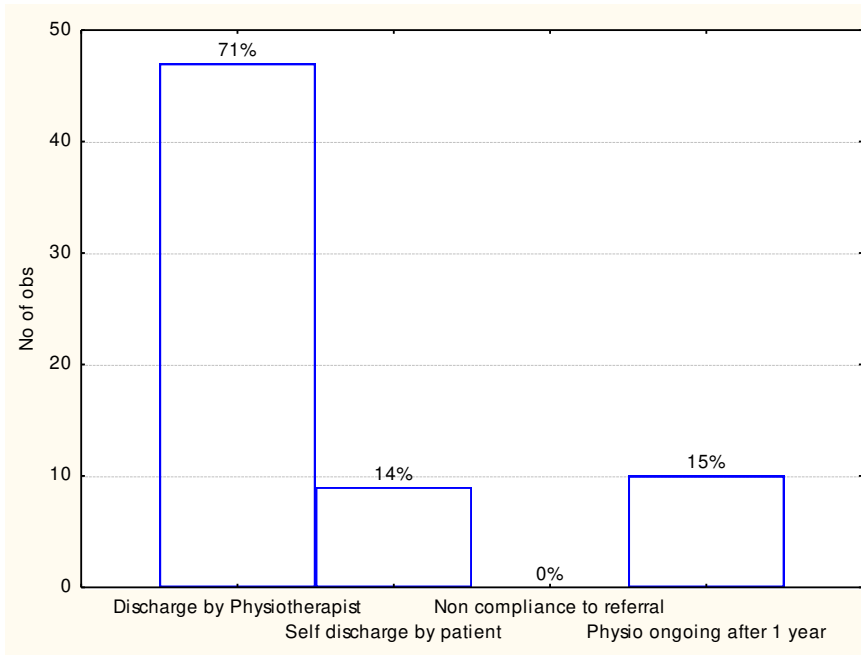


Figure 6.2. Route of discharge from physiotherapy.

The number of days in physiotherapy care was also documented. Most of the cohort were discharged after 12 weeks (3 months) and a small group 16 (24%) were discharged by 12 weeks. These data are shown in Figure 6.3.

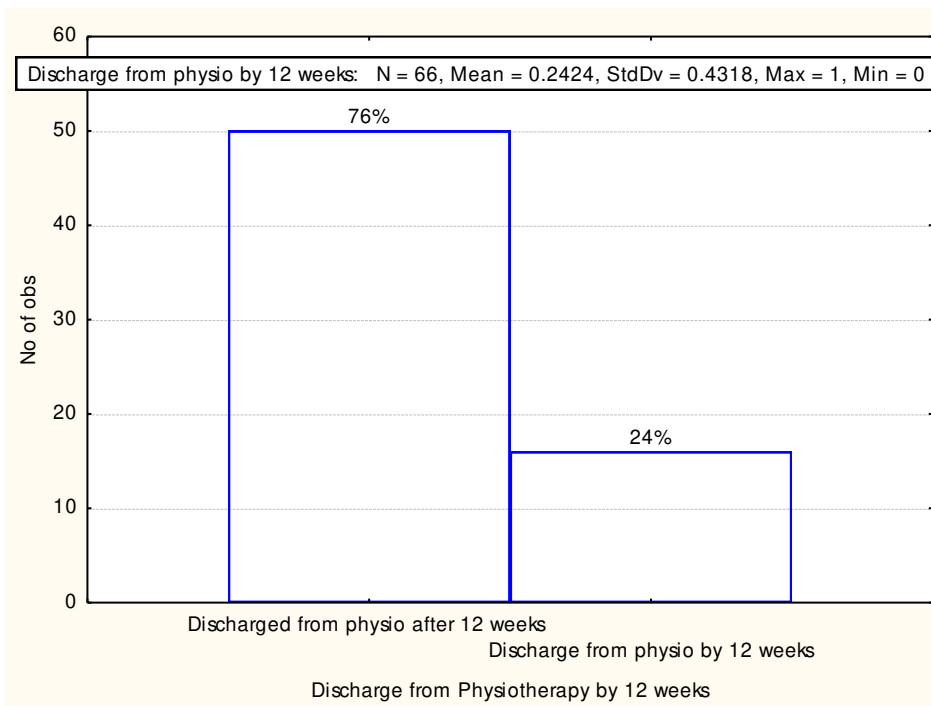


Figure 6.3. Discharge from physiotherapy at 12 weeks.

A total of thirty nine participants (59%) were discharged by 200 days; a further fifteen (22%) were discharged by 300 days (which is just short of 10 months). Thirteen (19%) were seen up to one year. One participant was seen only once and self-discharged following the initial physiotherapy contact. These data are shown in Figure 6.4.

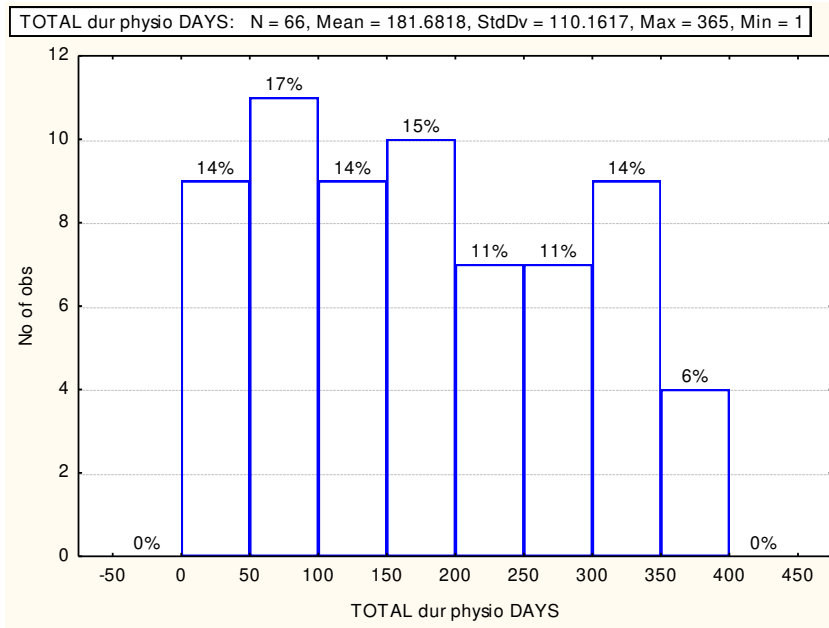


Figure 6.4. Days of physiotherapy care before discharge.

### 6.3.2 Physiotherapy category of intervention

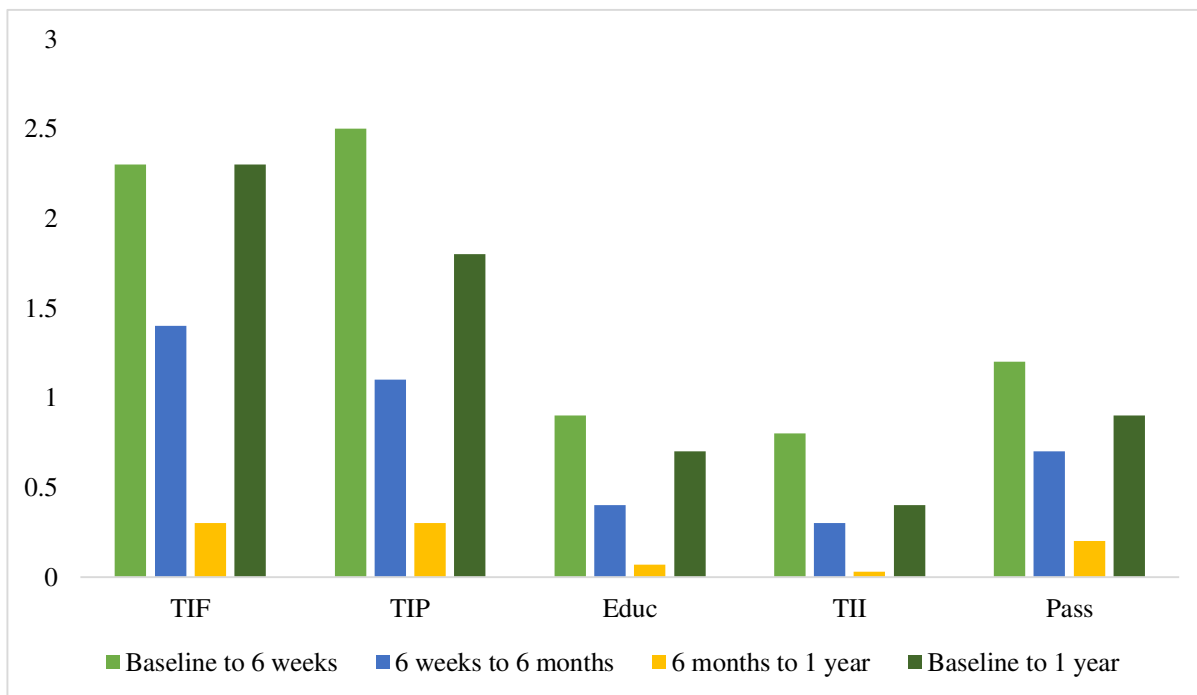
The weekly average for each category of intervention was calculated by each outcome measure interview interval, at 6 weeks, 6 months and 1 year as explained in Chapter 4. Weekly average was considered necessary to provide a suitable measure of intensity for comparison to provide meaningful data. The number of actual sessions may have been influenced by confounding and the weekly average was considered a suitable measure to reduce this possibility. These categories were treatment intervention for pain modulation (TIP), treatment intervention for functional restoration (TIF), treatment intervention for immobilisation (TII), education (Educ), or passive (Pass) intervention (where intervention required no active participation of the patient). The weekly averages showed that TIP interventions were similar and slightly greater than TIF at 6 weeks. TIF had dropped less than TIP by 6 months.

TIF was the highest proportion of intervention applied at 20.4%, followed with TIP at 15.9%. Pass interventions were shown to be slightly higher than education at 8.0% and 6.2%, respectively, while TII was lowest at 3.5%. These data are shown in Table 6.4, and graphically represented in Figure 6.5.

*Table 6.4. Categorical physiotherapy interventions weekly means.*

Category of physiotherapy intervention	Interventions per week, Mean (SD)				Percent proportion of physiotherapy interventions
	Baseline to 6 weeks N=66	6 weeks to 6 months N=66	6 months to 1 year N=63	Baseline to 1 year N=66	
<b>Functional restoration (TIF)</b> N = 66 (100%)	2.3 (1.8)	1.4 (1.6)	0.3 (0.6)	2.3 (2.8)	20.4
<b>Pain Modulation (TIP)</b> N = 64 (96%)	2.5 (3.1)	1.1 (1.5)	0.3 (0.7)	1.8 (1.8)	15.9
<b>Education (Educ)</b> N = 66 (100%)	0.9 (0.6)	0.4 (0.4)	0.07 (0.1)	0.7 (0.9)	6.2
<b>Immobilisation (TII)</b> N = 43 (64%)	0.8 (1.2)	0.3 (0.8)	0.03 (0.1)	0.4 (0.5)	3.5
<b>Passive interventions (Pass)</b> N = 46 (69%)	1.2 (0.9)	0.7 (0.9)	0.2 (0.5)	0.9 (0.8)	8.0





TIP: Physiotherapy treatment interventions for pain modulation;  
TIF: Physiotherapy treatment interventions for functional restoration,  
TII: Physiotherapy treatment interventions for immobilisation,  
EDUC: Physiotherapy treatment interventions for education,  
PASS: Passive Physiotherapy treatment interventions.

*Figure 6.5. Weekly averages of each physiotherapy category of intervention.*

The changes between the weekly averages for each category of intervention at 6 weeks and 6 months were calculated. The weekly average between 6 months and one year was not included as it was considered not statistically sound, due to being skewed with the larger group being discharged by 6 months. The results for these differences showed that all categories of intervention were reduced after 6 weeks. None were increased. The TIF category was reduced by 0.9 and TIP by 1.4 with all other categories being reduced by half. Since it was a reduction of applications, it was represented by a negative number. These data are shown in Table 6.5.

Table 6.5. Weekly average change of physiotherapy intervention category between 6 weeks and 6 months showing reduction.

Category of physiotherapy intervention	Change of weekly average between 6 weeks to 6 months
<b>TIF</b>	- 0.9
<b>TIP</b>	- 1.4
<b>Educ</b>	- 0.5
<b>Pass</b>	- 0.5
<b>TII</b>	- 0.5

TIP: Physiotherapy treatment interventions for pain modulation;  
TIF: Physiotherapy treatment interventions for functional restoration,  
TII: Physiotherapy treatment interventions for immobilisation,  
EDUC: Physiotherapy treatment interventions for education,  
PASS: Passive Physiotherapy treatment interventions.

### 6.3.3 The report of physiotherapy homework participation adherence

The prescribed homework given by the Physiotherapist was determined from three questions using an 8-point Likert scale. There is no literature available about adherence to prescribed physiotherapy homework or home exercises. Neither is their literature about the appropriate nomenclature to be used as the prescription by a Physiotherapist for a CRPS patient may include cognitive techniques, emotional regulation, and application of TENS or visualisation, to name a few examples, which are not technically physical exercises. Hence the term homework was applied and not home exercises.

For question one: ‘How often do you do your physiotherapy homework exercises *in a week*,’ this ranged from ‘never’, ‘once’, ‘twice’, ‘three times’, ‘four times’, ‘five times’, ‘six times’ or ‘every day.’

For question two: ‘How often do you perform your physiotherapy homework exercises *in a day*,’ a 9-point Likert scale was used. It ranged from ‘never’, ‘once’, ‘twice’, ‘three times’, ‘four times’, ‘five times’, ‘every hour’, ‘more than every hour’ or ‘other’.

These data showed the greatest effort reported with homework participation in the first 6 weeks with most applying their homework every day of the week (76%) and half 2-3 times daily (48%), with the other half less often during the day, but two participants consistently never did their prescribed homework. Thirty-nine (59%) participants were discharged by 6

months and only 10 (15%) required ongoing physiotherapy beyond the year. One year later, 53 (84%) participants were discharged but only 13 had stopped participating with their prescribed homework.

At the six-week interview, half the sample, 32 (48%) reported that they did their homework two or three times a day, with 26 (40%) doing it more often, and a smaller group, 5 (8%) doing their homework only once a day. These data are shown in Table 6.6 and the visual representations for the six weeks participation are shown in Figure 6.6-7.

*Table 6.6. Physiotherapy homework participation frequency per week and per day.*

<b>Frequency of homework participation</b>	<b>N responses</b>	<b>Lower quartile</b>	<b>Upper quartile</b>	<b>Mean</b>	<b>SD</b>
<b>Homework weekly frequency 6 weeks</b>	66	6.0	7.0	6.1	1.8
<b>Homework weekly frequency 6 months</b>	64	4.0	7.0	5.2	2.7
<b>Homework weekly frequency 1 year</b>	53	0.0	7.0	3.7	3.3
<b>Homework daily frequency 6 weeks</b>	66	2.0	4.0	3.4	1.9
<b>Homework daily frequency 6 months</b>	62	1.0	5.0	3.0	2.2
<b>Homework daily frequency 1 year</b>	53	0.0	3.0	1.9	2.1

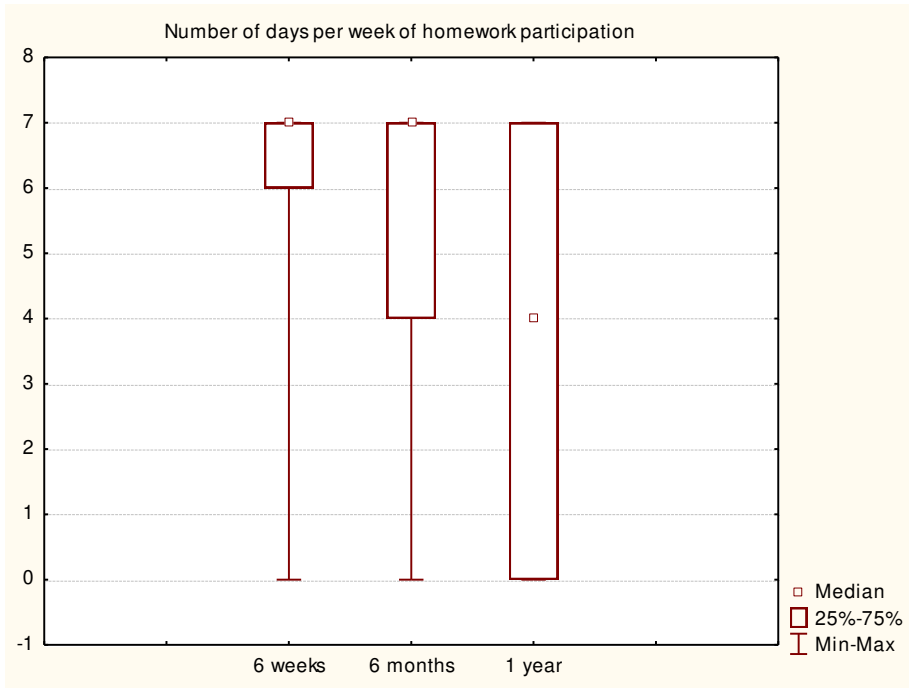


Figure 6.6. The frequency of homework adhered to in number of days per-week at each interval.

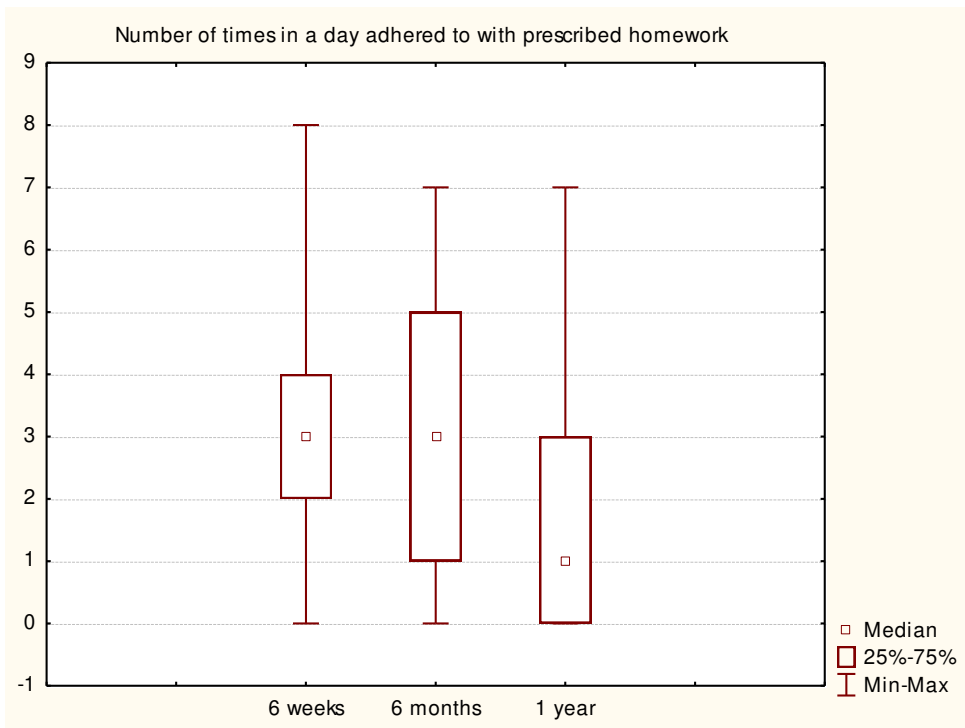


Figure 6.7. The frequency of homework adhered to in number of times per-day at each interval.

The frequency of homework participation between those participants who self-discharged reported a similar weekly frequency mean of homework participation with those who were discharged by their treating Physiotherapist. Their daily frequency showed differences where those who were discharged by their treating Physiotherapist doing their homework more often during the day than those who self-discharged with the IQR's of 3.0-3.5 vs 2.0-2.6 respectively. These data are shown in Table 6.7.

*Table 6.7. Physiotherapy homework participation frequency per-week and per-day differences between those who self-discharged or were discharged by treating Physiotherapist.*

<b>Frequency of homework participation</b>	<b>N responses</b>	<b>25th percentile</b>	<b>75th Percentile</b>	<b>Mean</b>	<b>SD</b>
<b>Homework weekly frequency 6-weeks with self-discharge</b>	9	6.0	7.0	7.0	2.3
<b>Homework weekly frequency 6-weeks with treating Physiotherapist discharge</b>	47	5.9	0	7.0	5.0
<b>Homework daily frequency 6-weeks with self-discharge</b>	9	2.6	2.0	0	5.0
<b>Homework daily frequency 6-weeks with treating Physiotherapist discharge</b>	47	3.5	3.0	0	8.0

Question three inquired about 'How would you rate how much your prescribed homework exercise helped to make your pain feel less'. A 5-point Likert scale was used which ranged from 'never', 'rarely', 'sometimes', 'almost always', or 'always'.

These data showed the rating about how the prescribed homework helped to relieve pain. Seven to 8 (11-15%) participants reported their prescribed homework was 'always' helpful at each interval. Twelve to nineteen (18-31%) participants reported that it was 'sometimes' helpful. On the contrary, 14-22 (27-33%) participants reported it was 'never' helpful, and 5-10 (10-15%) participants reported it was 'rarely' helpful.

A small group (11-15%) consistently showed that their prescribed homework was always helpful for their pain. These data are visually represented in Figures 6.8.

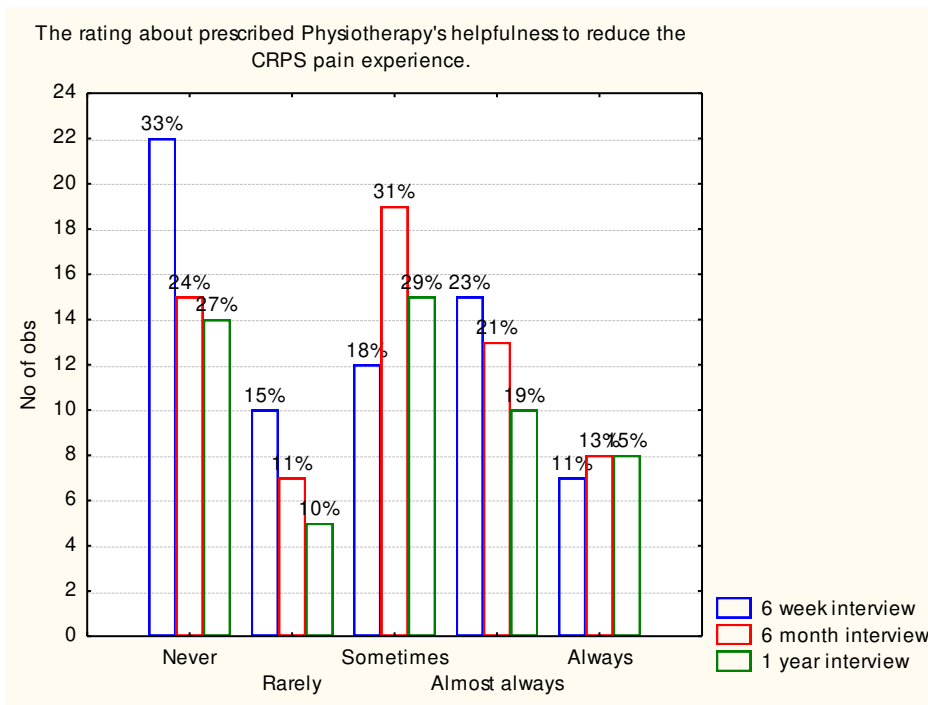
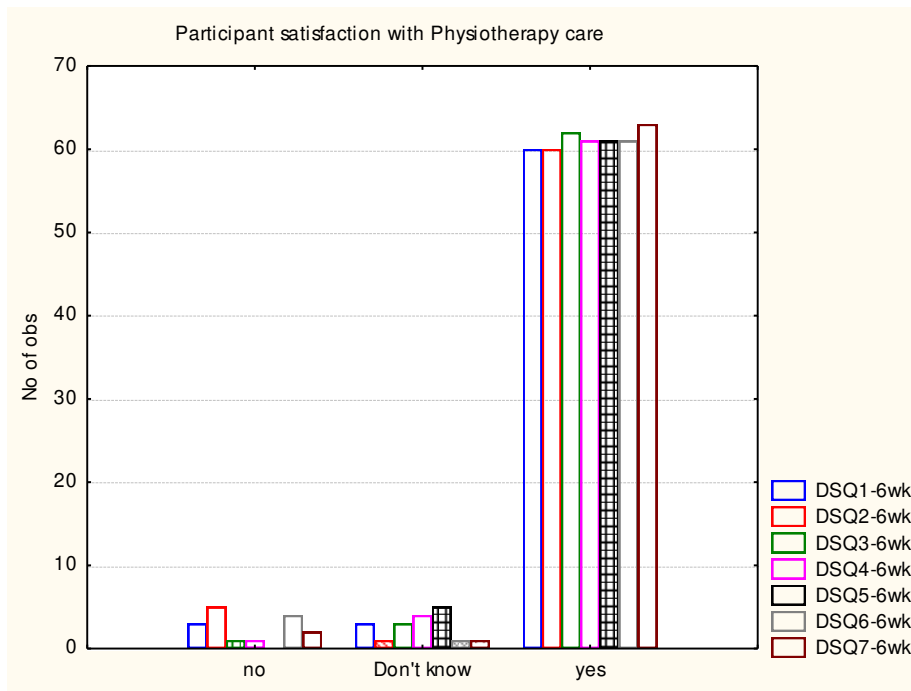


Figure 6.8. The rating about homework to relieve pain at each interview.

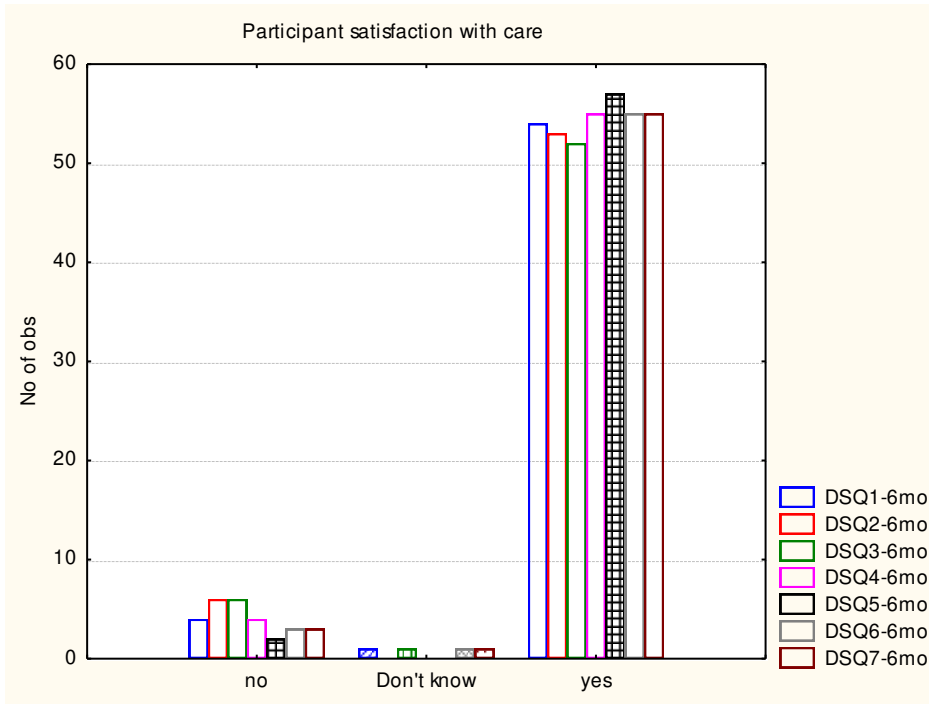
### 6.3.4 Satisfaction with physiotherapy care by participants

Physiotherapy satisfaction with care was shown to be positive with close to 100% satisfaction at each interval. Since satisfaction of care was uniformly positive, statistical analysis of its potential effect was not possible. The similar results about the treating Physiotherapist for each question of the Deyo and Diehl Questionnaire, can be seen with each interview responses that are shown in Figures 6.9-11.



DSQ- Deyo and Diehl Questionnaire

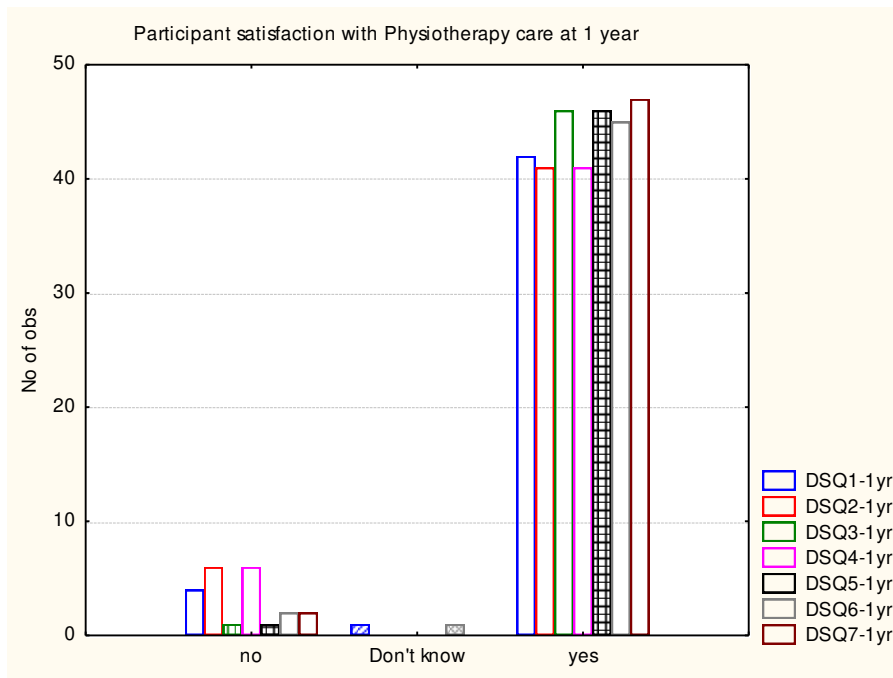
Figure 6.9. Participant satisfaction with physiotherapy care at 6 weeks with the Deyo and Diehl satisfaction with care.



DSQ- Deyo and Diehl Questionnaire

Figure 6.10. Participant satisfaction with physiotherapy care at 6months with the Deyo and Diehl satisfaction with care.

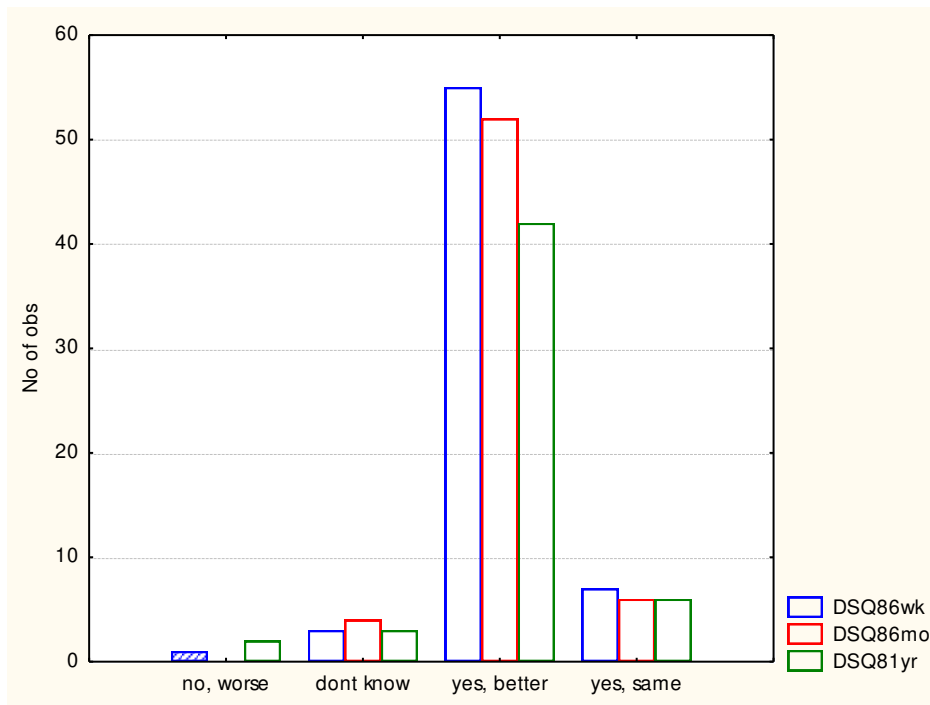




DSQ- Deyo and Diehl Questionnaire

*Figure 6.11. Participant satisfaction with physiotherapy care at 1 year with the Deyo and Diehl satisfaction with care.*

It is important to note that it was not an objective of this project to compare disciplines or individual practitioners. However, it was important to determine how patients felt about their care and whether it was satisfying. Another question from the Deyo and Diehl Questionnaire asked: ‘Was your care with your Physiotherapist for your CRPS better, worse or the same as your visits to your Specialist or Doctor?’ Results again show that physiotherapy care was ‘better’ at 6 weeks as well as at 1 year. These are shown in Figure 6.11.



DSQ- Deyo and Diehl Questionnaire

*Figure 6.11. Participant satisfaction with care being better, the same, worse or do not know when compared with other care.*

### 6.3.5 Medical and Psychological support

The description for medical intervention and psychological support at baseline is described in Chapter 5. Data were collated for medical and psychological support over the year and is shown in Table 6.8.

*Table 6.8. Medical and psychological support applied over the year at any time concurrent with physiotherapy.*

<b>Management</b>	<b>Description</b>	<b>N of full sample (%)</b>
<b>Medical</b>	Pamidronate infusion	5 (7)
	Neural blockade	3 (3)
	Prescription of non-steroidal, anti-inflammatories	12 (21)
	Prescription of oral cortisone	2 (4)
	Prescription of any oral morphine derivatives	12 (21)
	Prescription of tricyclic secondary analgesia	39 (58)
	Prescription of gabapentin or pregablin secondary analgesia	34 (51)
	Over the counter or prescribed paracetamol	27 (41)
<b>Psychology</b>	Individual sessions	19 (28)

Mann-Whitney U Tests were applied to determine differences in baseline characteristics, those who received (or did not) psychological support, the medical prescription of the anticonvulsant or tricyclic medication groups. Those who received psychological support showed higher health anxiety ( $p = 0.01$ ), poorer mental health ( $p = 0.02$ ), as well as poorer baseline quality of life and functional ability ( $p = 0.03$ ). Those who were prescribed tricyclic antidepressants showed higher health anxiety ( $p = 0.02$ ), greater baseline pain experience ( $p = 0.04$ ), as well as poorer mental health ( $p = 0.04$ ). Those who were prescribed anticonvulsants showed higher fear avoidance ( $p = 0.01$ ) and higher personality neuroticism ( $p = 0.04$ ). These data are shown in Tables 6.10-12.

Table 6.10. Mann-Whitney U tests for baseline differences with psychological support.

Mann-Whitney U Test for baseline differences with psychological support, N = 19					
	Rank Sum	Rank Sum	U	Z	p
Age	1557	654	429	-0.2	0.80
Gender	1510	702	382	-1.3	0.19
TSK	1454	757	326	-1.7	0.09
HAI	<b>1391</b>	<b>821</b>	<b>263</b>	<b>-2.6</b>	<b>0.01</b>
EPQE	1508	572	382	0.7	0.50
EPQN	<b>1313</b>	<b>767</b>	<b>278</b>	<b>-2.2</b>	<b>0.03</b>
Kessler10	<b>1390</b>	<b>755</b>	<b>262</b>	<b>-2.4</b>	<b>0.02</b>
PRI Baseline	1569	643	441	-0.1	0.93
WHODAS2 Baseline	<b>1417</b>	<b>794</b>	<b>289</b>	<b>-2.2</b>	<b>0.03</b>

Significance\* p<0.05

TSK – Tampa Scale for Kinesiophobia

PRI - Short form McGill Pain Questionnaire pain rating index

Kessler10 – Ten item psychological distress Kessler

HAI – Health Anxiety Index

EPQN - Eysenck Personality Questionnaire Neuroticism

EPQE - Eysenck Personality Questionnaire Extraversion

WHODAS2 - World Health Organisation Disability Assessment Schedule 2.0

Table 6.11. Mann-Whitney U tests for differences with medical prescriptions of secondary analgesia tricyclic group.

<b>Mann-Whitney U Test for medical prescription of secondary analgesia tricyclic group, N = 39</b>					
	<b>Rank Sum</b>	<b>Rank Sum</b>	<b>U</b>	<b>Z</b>	<b>p</b>
<b>Age</b>	910	1301	521	0.1	0.94
<b>Gender</b>	848	1364	470	-1.0	0.29
<b>TSK</b>	962	1249	469	0.8	0.45
<b>HAI</b>	<b>1079</b>	<b>1132</b>	<b>352</b>	<b>2.3</b>	<b>0.02</b>
<b>EPQE</b>	833	1247	482	-0.2	0.87
<b>EPQN</b>	868	1213	472	0.3	0.76
<b>Kessler10</b>	<b>1065</b>	<b>1147</b>	<b>367</b>	<b>2.1</b>	<b>0.04</b>
<b>PRI Baseline</b>	<b>1059</b>	<b>1152</b>	<b>372</b>	<b>2.0</b>	<b>0.04</b>
<b>WHODAS2 Baseline</b>	850	1295	499	-0.1	0.91

Significance\* p<0.05

TSK – Tampa Scale for Kinesiophobia

PRI - Short form McGill Pain Questionnaire pain rating index

Kessler10 – Ten item psychological distress Kessler

HAI – Health Anxiety Index

EPQN - Eysenck Personality Questionnaire Neuroticism

EPQE - Eysenck Personality Questionnaire Extraversion

WHODAS2 - World Health Organisation Disability Assessment Schedule 2.0

Table 6.12. Mann-Whitney U tests for differences with medical prescriptions of secondary analgesia anti-convulsant group.

Mann-Whitney U tests for differences with medical prescriptions of secondary analgesia of anti-convulsant group, N = 34					
	Rank Sum	Rank Sum	U	Z	p
Age	1185	1027	466	1.0	0.31
Gender	1040	1172	479	-1.2	0.23
TSK	<b>907</b>	<b>1304</b>	<b>346</b>	<b>-2.5</b>	<b>0.01</b>
HAI	992	1220	431	-1.5	0.14
EPQE	1210	870	374	1.8	0.06
EPQN	<b>921</b>	<b>1160</b>	<b>360</b>	<b>-2.0</b>	<b>0.04</b>
Kessler10	981	1230	420	-1.6	0.11
PRI Baseline	956	1256	395	-1.9	0.05
WHODAS2 Baseline	1022	1124	494	-0.5	0.65

Significance\* p<0.05

TSK – Tampa Scale for Kinesiophobia

PRI - Short form McGill Pain Questionnaire pain rating index

Kessler10 – Ten item psychological distress Kessler

HAI – Health Anxiety Index

EPQN - Eysenck Personality Questionnaire Neuroticism

EPQE - Eysenck Personality Questionnaire Extraversion

WHODAS2 - World Health Organisation Disability Assessment Schedule 2.0

### 6.3.6 The tests for baseline categorical variables

Mann-Whitney U Tests were applied to determine baseline differences between the categorical variables of: inciting event as fracture or not; and CRPS Type 1 or 2. No differences were shown between those whose initial event was a fracture or not. Those who had CRPS Type 2 showed greater health anxiety (p = 0.04) than those with CRPS Type 1. These data are shown in Table 6.13-14.

Table 6.13. Mann-Whitney U tests for baseline differences between CRPS Type 1 and 2.

Mann-Whitney U Test for CRPS Type 1 or 2								
CRPS Type 1 N= 57, CRPS Type 2 N= 9								
	Rank Sum	Rank Sum	U	Z	p-level	Z	p-level	2*1sided
Age	1948	263	218	0.7	0.47	0.7	0.47	0.48
Gender	1874	338	221	-0.7	0.50	-0.9	0.34	0.51
TSK	1858	354	205	-1.0	0.33	-1.0	0.33	0.34
HAI	<b>1802</b>	<b>410</b>	<b>149</b>	<b>-2.0</b>	<b>0.04</b>	<b>-2.0</b>	<b>0.04</b>	<b>0.04</b>
EPQE	1799	282	203	-0.4	0.66	-0.4	0.66	0.67
EPQN	1807	274	211	-0.3	0.78	-0.3	0.78	0.79
Kessler10	1819	393	166	-1.7	0.09	-1.7	0.09	0.09
PRI Baseline	1928	284	239	0.3	0.74	0.3	0.74	0.74
WHODAS2 Baseline	1785	360	189	-1.2	0.23	-1.2	0.23	0.24

Significance\* p<0.05

TSK – Tampa Scale for Kinesiophobia

PRI - Short form McGill Pain Questionnaire pain rating index

Kessler10 – Ten item psychological distress Kessler

HAI – Health Anxiety Index

EPQN - Eysenck Personality Questionnaire Neuroticism

EPQE - Eysenck Personality Questionnaire Extraversion

WHODAS2 - World Health Organisation Disability Assessment Schedule 2.0

Table 6.14. Mann-Whitney U tests for baseline differences between inciting injuries.

Mann-Whitney U Test for fracture, Fracture N= 28, No fracture N= 26								
	Rank Sum	Rank Sum	U	Z	p-level	Z	p-level	2*1sided
Age	713	773	362	-0.0	0.97	-0.0	0.97	0.97
Gender	761	724	318	0.8	0.43	1.1	0.25	0.43
TSK	617	868	266	-1.7	0.09	-1.7	0.09	0.09
HAI	711	775	360	-0.1	0.94	-0.1	0.94	0.94
EPQE	708	777	357	-0.1	0.90	-0.1	0.90	0.91
EPQN	820	666	260	1.8	0.07	1.8	0.07	0.07
Kessler10	617	868	266	-1.7	0.09	-1.7	0.09	0.09
PRI Baseline	743	743	337	0.5	0.63	0.5	0.63	0.64
WHODAS2 Baseline	773	713	307	1.0	0.32	1.0	0.32	0.32

Significance\* p<0.05

TSK – Tampa Scale for Kinesiophobia

PRI - Short form McGill Pain Questionnaire pain rating index

Kessler10 – Ten item psychological distress Kessler

HAI – Health Anxiety Index

EPQN - Eysenck Personality Questionnaire Neuroticism

EPQE - Eysenck Personality Questionnaire Extraversion

WHODAS2 - World Health Organisation Disability Assessment Schedule 2.0

## 6.4 Discussion

The literature as outlined in Chapter 2 showed that there was little evidence for CRPS physiotherapy management to indicate what intensity, type, or ingredients for standard physiotherapy were effective. Neither were data available for standard clinical practice across a region.

The median for this sample shows 16 contact sessions with an inter-quartile range (IQR) of 10–33 sessions attended over a period around six months. It is plausible to assume that healthy functional ability and reduced pain had been achieved for the patient, so that further physiotherapy care was not deemed necessary for those discharged. This is despite the fact that all patients may not necessarily have obtained normal or full functional ability, quality of life or complete resolution of pain. Since a smaller proportion continued with their



physiotherapy care for longer than 6 months, a smaller cumulative number of 247 sessions were reflected by 1 year for the remaining 41% participants.

These data showed a similar trend for all routes of discharge over the year with the smaller group who self-discharged (10%) vs. the larger group (71%) who exited physiotherapy care with formal discharge. These data showed that TIF, TIP, TII, Educ, Pass interventions and prescribed homework formed the ingredients of physiotherapy. The greatest intensity of physiotherapy interventions and participation in prescribed homework exercises occurred in the first 6 weeks. The interval between 6 months and 1 year showed that the intensity of physiotherapy as well as participation with homework had reduced for the group (41%) who continued with the physiotherapy care. Those who self-discharged reported a participation with homework exercises at a slightly lower daily frequency than those who were discharged by their treating Physiotherapist, but participated similarly with their weekly frequency. It is plausible to conjecture that benefit was appreciated from prescribed homework for those who self-discharged. However, the possible reasons would need further investigation.

It is interesting to note that prescribed homework was rated by a small group to be helpful to relieve pain (11-15%). This was in contrast to a larger group (27-33%) of participants who reported it as 'never' helpful and 10-15% who reported it as 'rarely' helpful. This was despite the overwhelming positive response to satisfaction with physiotherapy care and that rating was better than other support or intervention. This finding was a positive reflection for physiotherapy care across this large region. However, this particular response about a better rating for care was taken with caution as there was no comparison group who did not receive physiotherapy. When placed in the context of the other questions and that an independent interviewer (and not a Physiotherapist) collected the data; it suggests that the therapeutic relationship associated with physiotherapy care on the South Island was positive. However, prescribed homework that did not help to relieve pain was reported by 37-48% of participants. The reasons or interactive effects for this were beyond the scope of this project but it is suggested that they could be worth exploring.

Medical or psychological support was provided for less than half this cohort with the exception of the prescription of tricyclic analgesia with 39 (58%). It was not possible to determine adherence to prescriptions or appointments; hence there may have been those who were offered medical or psychological help but declined to take it or did not adhere due either to side effects from the medication or that they chose not to attend. Adherence with

prescription medication is reported to be an area needing research and difficult to accurately measure [382].

### *Implications for practitioners*

The literature showed that in a recent RCT comparing standard care with the pain exposure intervention method for CRPS management [114] that standard physiotherapy involved 17 sessions. However, no reasons were given for this number of sessions. The first RCT to compare physiotherapy with occupational therapy did not describe the number of sessions for CRPS physiotherapy intervention [113]. The predominant feature of the literature is that outcomes were presented in all studies but consistently without reporting the number of sessions attended. Hence comparisons were not possible with the present study.

What was reflected in the present data is that the median of 16 was not an accurate reflection of intervention applied, because the interquartile range was large, from 10-33. Hence, it is potentially difficult to manage a CRPS patient if only a specific number of sessions are prescribed by the funding body.

It was beyond the scope of this project to explore how an overwhelming positive rating was given to physiotherapy care across nine questions but prescribed homework exercise was rated as unhelpful to relieve pain. It is speculated that physiotherapy care as a whole was positive and the possible irritation of the unhelpful homework was not a major detracting factor from the patient's perspective. Alternatively, communication by the treating Physiotherapist with the patient about the unhelpful homework was taken seriously and reassurance or appropriate adjustment was provided.

The outcomes still improved significantly over the year despite that homework did not relieve pain for most. It has been suggested that the GMI research protocol of performing homework exercises every hour was not possible to replicate in a clinical setting [141] and reflected the poor outcomes related to the GMI intervention. Despite the dominant clinical paradigm being that prescribed homework is important to the management of CRPS, neither the literature nor the present study support this. If prescribed homework is effective at all, it is not yet known what its components would be.

Nonetheless, homework did not appear to have a negative consequence associated with an outcome and neither did it affect satisfaction with care in this cohort. Hence, it would be prudent to continue with homework prescription until further clarity obtained.

### *Implications for research*

Future research could explore what intensity of physiotherapy provides an optimal outcome. Is it duration over a period of time or is it the number of sessions? Furthermore, it could be useful to determine the potential relationship and interactive effects between these two factors for a positive outcome for CRPS. It may also be helpful to determine the ingredients for effective homework components and strategies in future research. It is reasonable to expect that health care goals for any patient are independence. Possibly prescribed homework would foster independence. The factors around all aspects of prescribed homework for an effective CRPS outcome are not known and are important for future investigation.

In the next Chapter 7, the analyses for the outcome measures changes over the year are reported.

## CHAPTER SEVEN

### Description of changes over time

Aspects of this literature review have been published as [42] and are available in Appendix A.

#### 7.1 Introduction

An aim for this project was to document the CRPS trajectory over the period of one year for patients attending outpatient physiotherapy across a region. This Chapter describes the changes over the year and analyses outcome measures changes for significance.

The structure of this Chapter describes the method, analytic approach with the results over the year of the record of Budapest criteria autonomic changes; changes with the ability to work; changes to outcome measures; and the outcome for Hypothesis test 1.1.

#### 7.2 Method

The objective record of signs and symptoms was provided by the treating Physiotherapist at the time of the CRPS diagnosis that fulfilled the Budapest criteria. The telephone interviews at each interval included the subjective report of the CRPS patient about their signs, symptoms, and autonomic changes as compared to their unaffected limb. Each outcome measure data was obtained via telephone interviews with an independent interviewer 6 weeks, 6 months, and 1 year later.

##### *Analytic approach*

The changes to autonomic features, signs and symptoms according to the Budapest criteria and the ability to work were collated for each interval. Paired Student *t*-tests were applied to the PRI, NRS-11, WHODAS2, FFI and QuickDASH determine for significant change using  $p < 0.05$ . The hypothesis test 1.1 was explored. Adjustment for confounding was not applied to the *t*-tests as the scope of the present study was to determine the natural time course and was also not a clinical trial. The unpaired *t*-tests sample sizes were too small to apply adjustment to.

## 7.3 Results

### 7.3.1 The record of autonomic features

Over the course of one year: hyperalgesia and allodynia were reduced with only 4% reporting this symptom one year later. Skin temperature (cold, warm, hot or very hot), texture (dry, scaly or glossy), and sweating of the affected limb showed a reduction in 40-50% of the cohort. However, the presence of the altered sensations listed for Budapest criteria were still reported in all criteria for some 1 year later. There was no criterion that showed no presence a year later. These data are shown in Table 7.1.

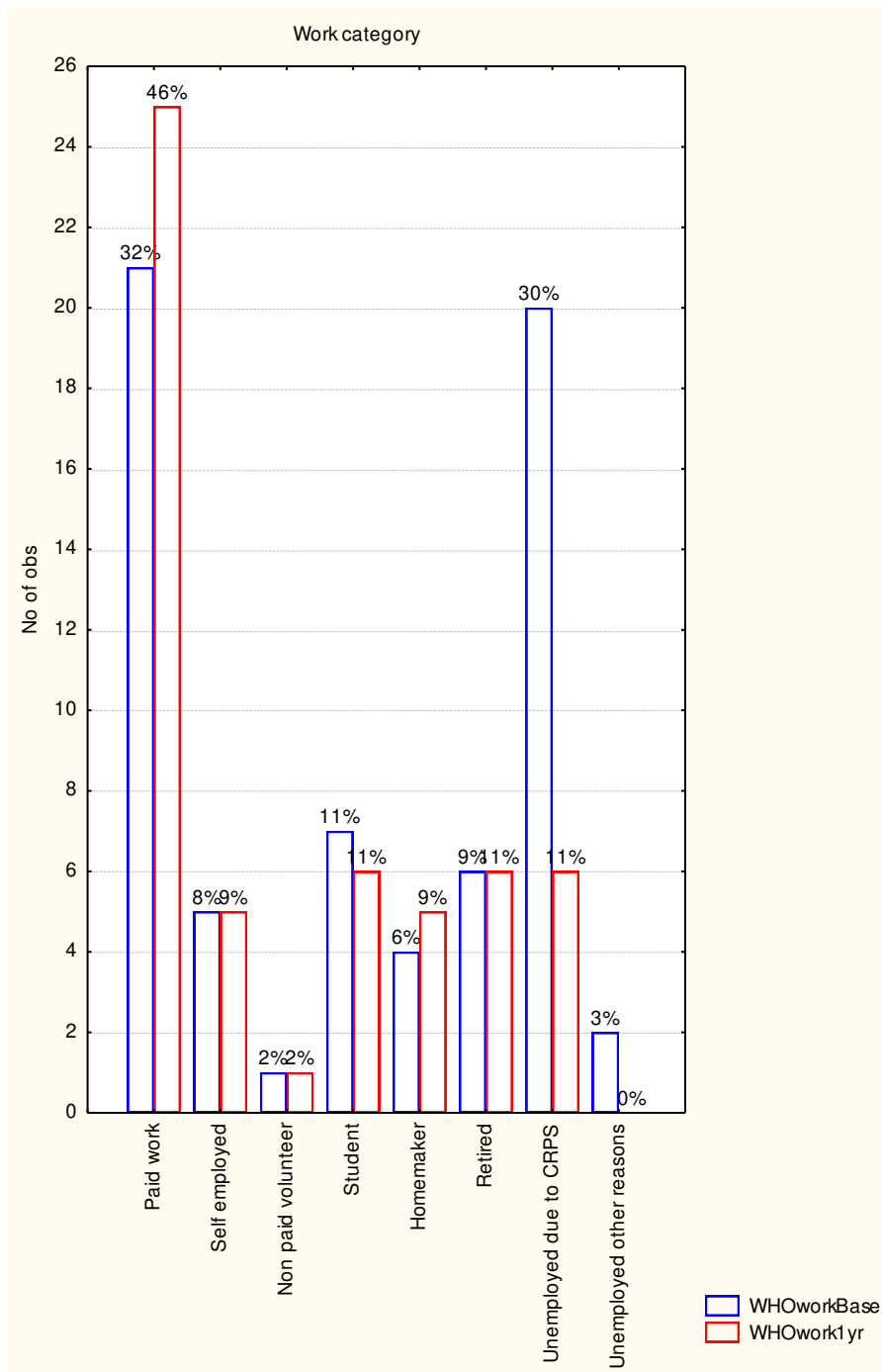
*Table 7.1. The record of autonomic features of the affected CRPS limb as compared to the unaffected limb at each interval interview.*

<b>AUTONOMIC CHANGE PRESENT CHANGE OF AFFECTED CRPS LIMB IN COMPARISON TO UNAFFECTED OTHER LIMB</b>	<b>Baseline N=66 N (%)</b>	<b>6 weeks N=66 N (%)</b>	<b>6 months N=64 N (%)</b>	<b>1 year N=54 N (%)</b>
<b>Skin temperature to physical touch</b>	60 (91)	46 (70)	37 (56)	27 (50)
<b>Skin colour</b>	60 (91)	50 (76)	36 (53)	24 (44)
<b>Skin texture</b>	43 (65)	35 (53)	24 (36)	28 (52)
<b>Oedema</b>	55 (83)	14 (21)	41 (62)	24 (44)
<b>Skin sweating</b>	59 (89)	29 (44)	24 (36)	17 (31)
<b>Hair growth</b>	32 (48)	24 (36)	15 (23)	9 (17)
<b>Nail changes</b>	28 (42)	27 (41)	26 (39)	16 (30)
<b>Skin sensation: Hyperalgesia</b>	46 (70)	46 (70)	16 (24)	2 (4)
<b>Skin sensation: Allodynia</b>	32 (48)	8 (14)	2 (3)	3 (4)
<b>Skin sensation: Hypoaesthesia</b>	25 (38)	16 (24)	15 (25)	6 (13)

### 7.3.2 Changes with ability to work

Work category was collected and categorised according the WHODAS2. These data showed that at baseline, 20 participants (30%) were not able to work due to their CRPS. There was a positive change with a reduction of 14 participants to 6 (11%) who were still not able to work 1 year later due to their CRPS. This change showed a similar proportion at baseline: 21

(32%) working, versus 20 (30%) not working. One year later these percentages were changed to 25 (46%) and 6 (11%), respectively. These data are shown in Figure 7.1.



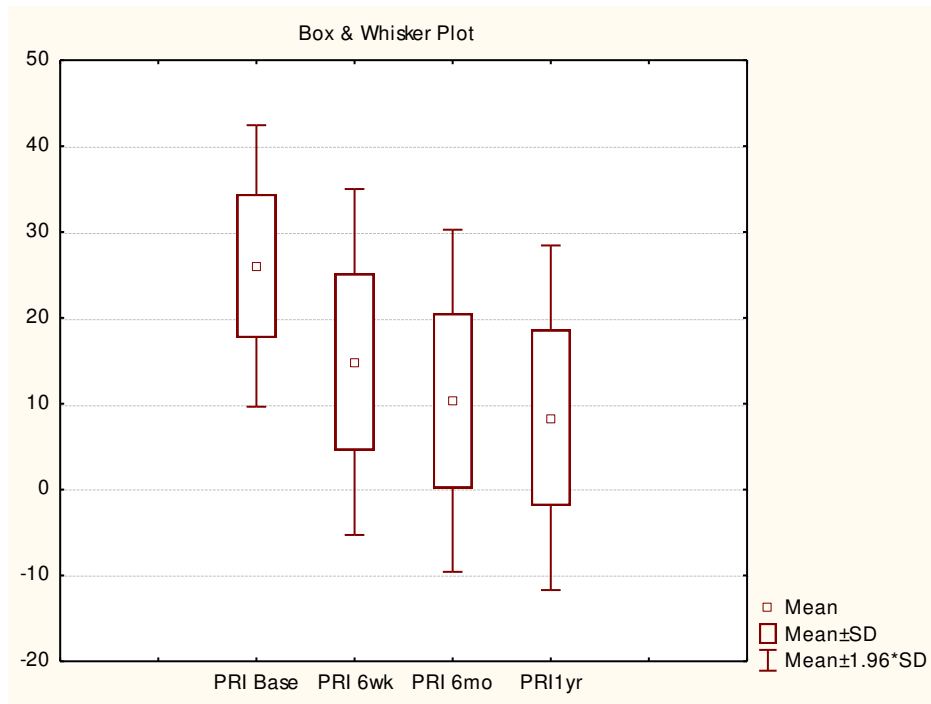
WHOworkBase - World Health Organisation Disability Assessment Schedule 2.0 work category baseline

WHOwork1yr - World Health Organisation Disability Assessment Schedule 2.0 work category after 1 year.

Figure 7.1. Work category at baseline and 1 year later.

### 7.3.3 Changes to outcome measures

Each outcome measure raw score was plotted with box plots for each interview interval. Results showed that that most had recovered by 50% at six weeks; recovery in the interval from 6 weeks to 6 months was similar to that for the interval between 6 months and 1 year. These data are represented in Figures 7.2-6.



PRI - Short form McGill Pain Questionnaire pain rating index

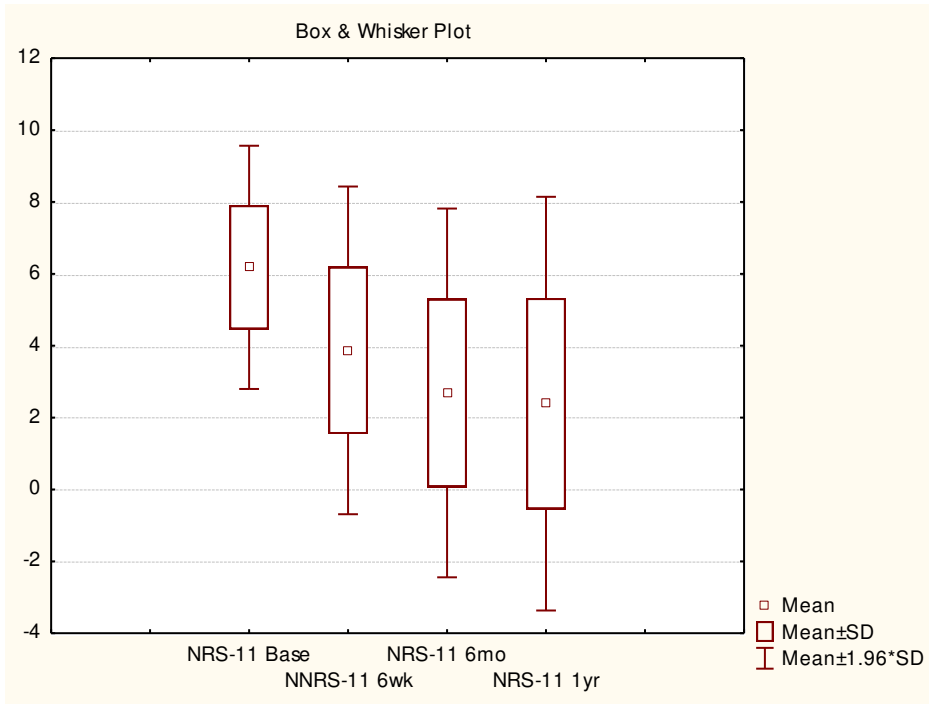
Base-Baseline

6wk-6 week interval

6mo-6 month interval

1 yr-1 year interval

*Figure 7.2. Raw score, pain, with PRI at each interval.*



NRS-11 – 11-point numerical rating scale

Base-Baseline

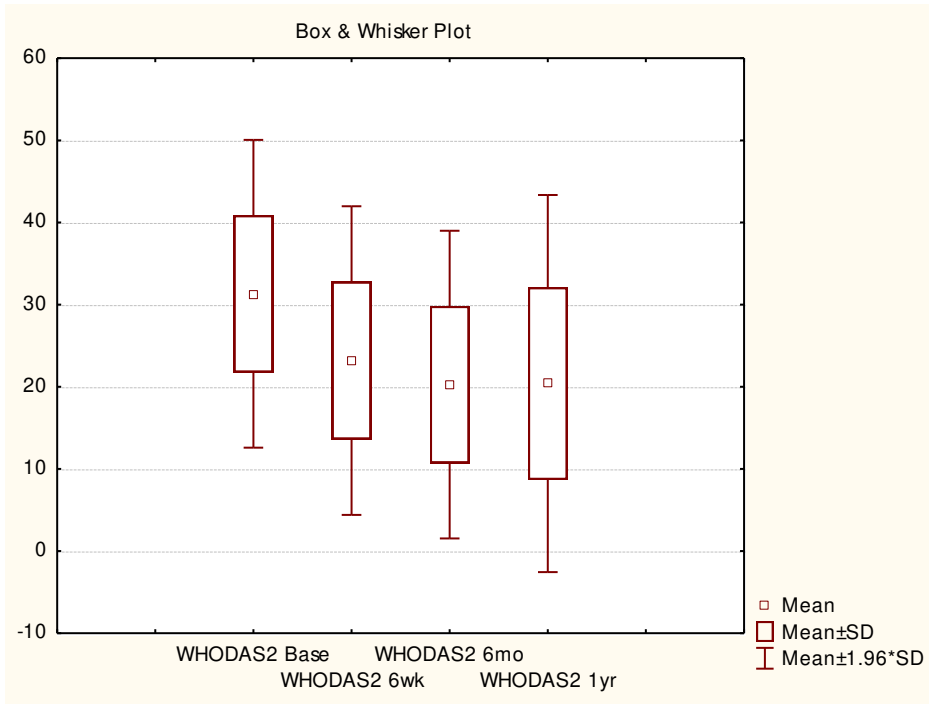
6wk-6 week interval

6mo-6 month interval

1 yr-1 year interval

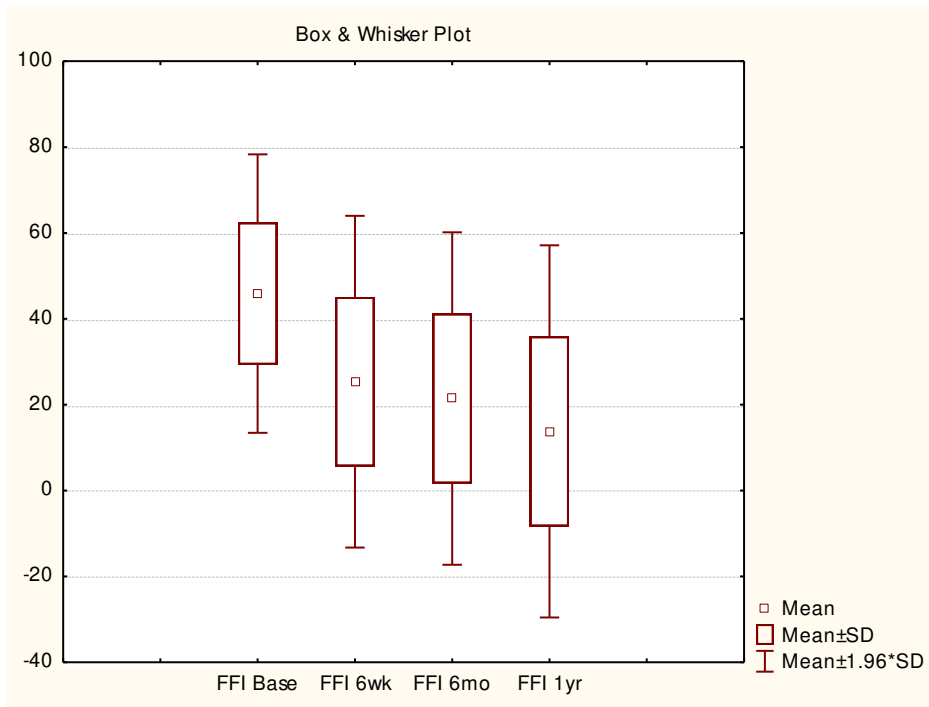
*Figure 7.3. Raw score, pain, with NRS11 at each interval.*





WHODAS2 - World Health Organisation Disability Assessment Schedule 2.0 work  
 Base-Baseline  
 6wk-6 week interval  
 6mo-6 month interval  
 1 yr-1 year interval

Figure 7.4. Raw score quality of life and function, WHODAS2 at each interval.



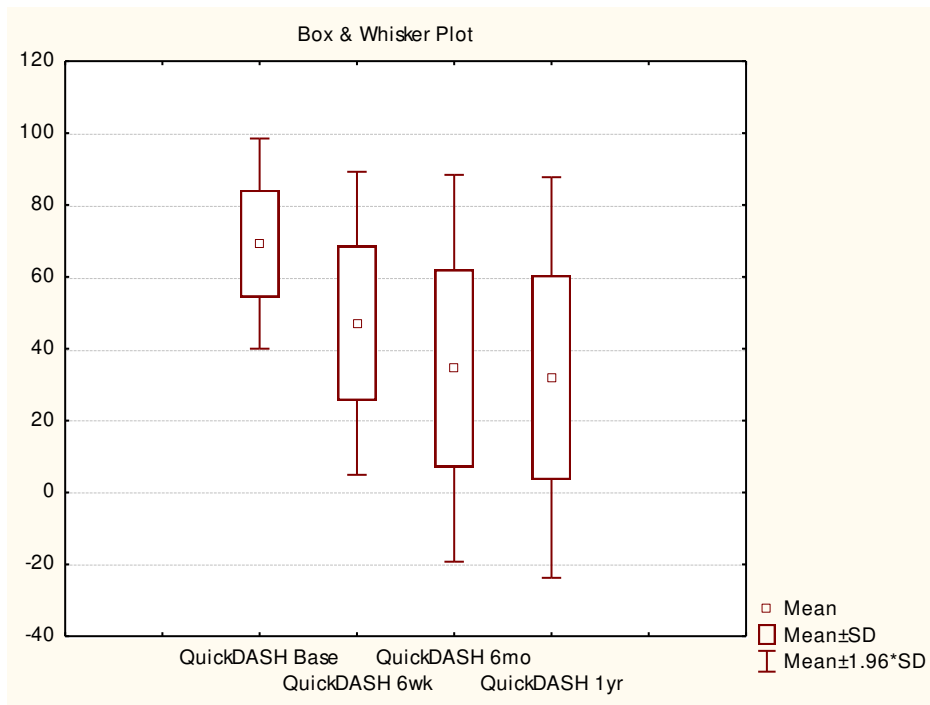
FFI-Foot Function Index

6wk-6 week interval

6mo-6 month interval

1 yr-1 year interval

*Figure 7.5. Raw score, FFI, at each interval.*



QuickDASH - The Quick Disability of the arm, shoulder and hand  
 6wk-6 week interval  
 6mo-6 month interval  
 1 yr-1 year interval

Figure 7.6. Raw score, upper limb function, QuickDASH, at each interval.

### 7.3.4 Student t-tests for outcome measure changes

All outcome measures changes showed a similar trend with most of the positive changes occurring in the first 6 weeks, followed by approximately half as much positive change again occurring by 6 months. The trend for positive change slowed between 6 months and 1 year for pain reduction and remained stagnant for further gains of both functional ability with QuickDASH and quality of life and function with the WHODAS2. However, further functional gain did gradually continue for those with lower limb CRPS as reflected with the further improvement with the FFI score.

Each outcome measure score for pain or for function were represented with a higher score for higher or worse pain experience, or for higher or worse functional disability. Hence, a change towards recovery was attributed as a negative number.

Paired Student t-tests for dependent samples from baseline measure to the same measure after 1 year showed significant improvement ( $p < 0.001$ ). These data are shown in Table 7.2.

Table 7.2. Changes to outcome measures at each interval.

Outcome dependent variable (Score range, clinically important change)	Baseline score, mean (SD) N = 66	Change at 6 weeks, mean (SD) N = 66	Change at 6 months, mean (SD) N = 64	Change at 1 year, mean (SD) N = 54	t-test p: change at 1yr
<b>PRI</b> (0 to 45, >10)	26.0 (8.4)	-11.2 (-10.9)	-15.4 (-11.4)	-17.1 (11.3)	<0.001 *
<b>NRS-11</b> (0 to 10, > 3)	6.2 (1.7)	-2.3 (-2.2)	-3.5 (-2.6)	-3.8 (3.1)	<0.001 *
<b>WHODAS2</b> (1 to 60, > 10)	33.5 (9.5)	-8.1 (-7.9)	-11.0 (-9.1)	-10.7 (11.9)	<0.001 *
	<b>N = 17</b>	<b>N = 17</b>	<b>N = 15</b>	<b>N = 15</b>	
<b>FFI</b> (0 to 100, >10)	45.8 (16.5)	-20.5 (-13.2)	- 23.9 (15.8)	- 31.6 (18.5)	<0.001 *
	<b>N = 49</b>	<b>N = 49</b>	<b>N = 48</b>	<b>N = 38</b>	
<b>QuickDASH</b> (1 to 100, >15)	69.2 (14.9)	-22.2 (19.6)	-34.6 (-23.8)	-36.9 (24.7)	<0.001 *

PRI - Short form McGill Pain Questionnaire pain rating index

NRS-11- 11-point Numerical Rating Scale

WHODAS2 - World Health Organisation (WHO) Disability Assessment Schedule 2.0

QuickDASH - The Quick Disability of the arm, shoulder and hand

FFI – Foot Function Index

Significance\* p<0.05

### 7.3.5 Changes to outcomes and adherence

The effect of adherence to physiotherapy on outcomes was further analysed with paired t-tests for dependent samples from baseline measure to the same measure 1 year later between three groups. These groups were those who self-discharged, those completing a course of physiotherapy with formal discharge from physiotherapy care, and those requiring ongoing physiotherapy beyond 1 year. The discharged group showed significant improvement with their outcome measures 1 year later (p < 0.001). However, 1 year later, one participant with lower limb affected CRPS required ongoing physiotherapy care and two with upper limb

affected CRPS self-discharged. Hence, it was not possible to make statistical analysis for the FFI and QuickDASH for these two outcome measures with respect to these two small groups. Those who required on-going physiotherapy beyond the year showed half the improvement, in comparison with those who completed their course of physiotherapy within the year. These are shown in Table 7.3.

Table 7.3. Changes to outcome measures and duration of physiotherapy.

Outcome dependent variable (Score range, clinically important change)	Self-discharge by participant			Discharge by Physiotherapist			On-going physiotherapy		
	Baseline score, Mean (SD)	Change at 1 year, Mean (SD)	t-test P: change from baseline at 1yr	Baseline score, Mean (SD)	Change at 1 year, Mean (SD),	t-test P: change from baseline at 1yr	Baseline score, Mean (SD)	Change at 1 year, Mean (SD)	t-test P: change from baseline at 1yr
	N = 9	N = 7		N = 47	N = 36		N = 10	N = 10	
<b>PRI</b> (0 to 45, >10)	27.9 (8.1)	-15.6 (12.6)	0.02*	24.1 (8.3)	-19.5 (9.5)	<0.001 *	28.5 (10.5)	-9.6 (14.1)	<0.001 *
<b>NRS-11</b> (0 to 10, > 3)	5.9 (1.9)	-1.8 (3.1)	0.2	6.1 (1.8)	-4.9 (2.5)	<0.001 *	7.1 (1.1)	-1.5 (3.1)	<0.001 *
<b>WHODAS2</b> (1 to 60, > 10)	32.7 (9.5)	-3.9 (14.1)	0.5	29.3 (9.3)	-13.4 (9.4)	<0.001 *	36.6 (11.5)	-5.7 (15.6)	0.8
	N = 6	N = 5		N = 11	N = 10		N = 1	N = 1	
<b>FFI</b> (0 to 100, >10)	48.6 (24.9)	-19.1 (15.9)	0.06	42.7 (13.3)	-40.5 (14.11)	<0.001 *	55.8	-4.7	N/A
	N = 4	N = 2		N = 36	N = 27		N = 9	N = 9	
<b>QuickDASH</b> (1 to 100, >15)	71.0	-5.7 (20.9)	N/A	65.9 (14.6)	-44.1 (22.5)	<0.001 *	75.8 (18.4)	-22.2 (21.4)	<0.001 *

Significance\* p<0.05; N/A = not applicable, sample size too small

PRI - Short form McGill Pain Questionnaire pain rating index

NRS-11- 11-point Numerical Rating Scale

WHODAS2 - World Health Organisation (WHO) Disability Assessment Schedule 2.0

QuickDASH - The Quick Disability of the arm, shoulder and hand

FFI – Foot Function Index

Despite their overall significant improvement, those who required on-going physiotherapy beyond the year showed a significant difference using unpaired t-tests (NRS-11, p <0.001;

PRI,  $p=0.005$ ; WHODAS2,  $p < 0.01$ ; QuickDASH,  $p < 0.002$ ) in outcome measure from those who completed their course of physiotherapy within the year. These are represented in Table 7.4.

*Table 7.4. Unpaired Student t-tests for significance of outcomes measures between duration of physiotherapy for those who were discharged and those who required ongoing care beyond 1 year.*

<b>Outcome dependent variable</b>	<b>Discharge by Physiotherapist Change at 1 year, Mean (SD) N = 47</b>	<b>On-going physiotherapy Change at 1 year, Mean (SD) N = 10</b>	<b>t-value</b>	<b>t-test P: change from baseline at 1yr</b>
<b>PRI</b>	-19.5 (9.5)	-9.6 (14.1)	-2.9	<b>0.005*</b>
<b>NRS11</b>	-4.9 (2.5)	-1.5 (3.1)	-4.1	<b>&lt;0.001 *</b>
<b>WHODAS2</b>	-13.4 (9.4)	-5.7 (15.6)	-2.7	<b>0.01*</b>
<b>QuickDASH</b>	-44.1 (22.5)	-22.2 (21.4)	-2.5	<b>0.002*</b>

PRI - Short form McGill Pain Questionnaire pain rating index

NRS-11- 11-point Numerical Rating Scale

WHODAS2 - World Health Organisation (WHO) Disability Assessment Schedule 2.0

QuickDASH - The Quick Disability of the arm, shoulder and hand

Significance\*  $p < 0.05$

Those who self-discharged also showed significantly less improvement except for their PRI score (NRS-11,  $p = 0.01$ ; PRI,  $p = 0.03$ ; WHODAS2,  $p = 0.03$ ; QuickDASH,  $p = 0.02$ ).

These data are shown in Table 7.5.

Table 7.5. Unpaired Student t-tests for significance of outcomes measures between duration of physiotherapy for those who were discharged and those who self-discharged.

Outcome dependent variable	Discharge by Physiotherapist Change at 1 year, Mean (SD) N = 47	Self-discharge Change at 1 year, Mean (SD) N = 10	t-value	t-test P: change from baseline at 1yr
<b>PRI</b>	-19.5 (9.5)	-16 (12.6)	-0.9	0.35
<b>NRS11</b>	-4.9 (2.5)	-2 (3.1)	-2.8	<b>0.01*</b>
<b>WHODAS2</b>	-13.4 (9.4)	-4 (14.1)	-2.3	<b>0.03*</b>
<b>QuickDASH</b>	44.1 (22.5)	-6 (20.9)	-2.5	<b>0.02*</b>

PRI - Short form McGill Pain Questionnaire pain rating index

NRS-11- 11-point Numerical Rating Scale

WHODAS2 - World Health Organisation (WHO) Disability Assessment Schedule 2.0

QuickDASH - The Quick Disability of the arm, shoulder and hand

Significance\* p<0.05

## 7.4 Hypothesis test 1.1

The primary hypothesis 1.1 was to explore that positive outcomes for CRPS were associated with adherence to physiotherapy intervention. All participants showed significant improvement. However, these results showed that there was a positive association between the completion of physiotherapy intervention and outcomes for CRPS. Those who self-discharged (with less contact time, intervention and adherence) showed significantly poorer outcomes than those who were formally discharged by their treating Physiotherapist. Hence, the null hypothesis was rejected.

It was unethical to withhold treatment. This study was designed to be observational and prospective; care was taken not to interfere with everyday clinical practice. There was no control group or waiting list for comparison. There was no randomisation of participants. It could be argued that there was a possibility of Type 1 error with this analysis and association. This error would be that rejections of the null hypothesis assumed a relationship between physiotherapy intervention positively affecting outcomes, when in fact, there was no



relationship. However, the argument to refute the possibility of Type 1 error is that potential bias was less likely since the collection of these data used an independent interviewer. The interviewer was also not a Physiotherapist but was well qualified with a doctorate; so that potential social desirability or coercion bias was reduced.

No other study has consistently shown what the specific ingredient of physiotherapy contributes to a recovery in CRPS. This does not mean that physiotherapy is unnecessary or ineffective. These data showed improved outcomes with meaningful clinical changes, despite not identifying the specific recovery ingredient with this statistical analysis.

Furthermore, psychotherapy interventions showed that not giving an intervention is potentially detrimental, however, all interventions have a similar positive effect with little difference in outcomes between the different intervention methods [383].

## **7.5 Discussion**

All outcome measures showed clinically relevant score improvements as represented by a change of 15 points with the QuickDASH, [26]; FFI as 10 [21]; the WHODAS2 with 15 [27]; the PRI as 5; and NRS-11 as 3 [28]. All outcome measures were improved in the first 6 weeks, followed by slower improvement over the next 6 months. The improvement over the year was shown to be significant. Those who self-discharged or needed ongoing physiotherapy care also showed this significant improvement by approximately half, in comparison with those who completed their course of physiotherapy within the year.

These results showed that positive change slowed between 6 months and 1 year for pain reduction and remained stagnant for further gains of upper limb functional ability with QuickDASH, and quality of life and function with the WHODAS2. Further functional gain was obtained gradually for those with lower limb CRPS. The reasons for this quicker pace of change in the early phases which either slows or leads to resolution from 6 months to 1 year later is not able to be explained with this study. The trends for the trajectory of CRPS show high variability which are consistent with the literature as outlined in Chapter 2.

Those who participated in work showed an improvement with 25 (46%) not in work at baseline being reduced to 6 (11%) one year later. A North Island study reported 21% who had not returned to work due to their CRPS [89]. The improved ability to return to work shown with these results was a positive reflection for this cohort, but the reasons for it are

beyond the scope of this project. A Korean retrospective study of 63 participants, where the number of males was greater than the number of females (unlike this cohort), reported that CRPS patients who had a white-collar jobs and had been diagnosed within 8 months were more likely to be employed. No information was provided in this paper about the medical or allied health interventions these CRPS patients received [384]. A Turkish study with a male cohort (N=168) showed that 72% had returned to work [385] but no time frame was reported. Autonomic features also showed positive changes with the CRPS patients' reports of a reduction in their symptoms. These signs and symptoms were evaluated according to the Budapest criteria at baseline by the treating physiotherapist, but were not able to be objectively measured at the subsequent intervals due to the geographical distances across the South Island. These symptoms were self-reported to the independent interviewer. The findings could not be analysed for significance due to the potential poor reliability of the findings to confirm the participants' reports with an objective examination of their signs.

#### *Implications for practitioners*

These results and the literature provide weak support that physiotherapy for the management of CRPS is beneficial. A positive therapeutic relationship is thought to contribute to better health outcomes [293]. The ingredients towards attaining an effective therapeutic relationship involves: the application of the best available evidence together with the Physiotherapist's clinical proficiency and collaborative patient involvement in a personalised management plan [298]; patient-centred communication [295]; and being sensitive to the patient's background and situation [243, 294]. The candidate suggests that a management plan could have ongoing reflection and review between both patient and physiotherapist throughout the process.

#### *Implications for research*

The prevalence of CRPS is low and the relationship between specific physiotherapy intervention methods and the respective outcomes for patients is known to be difficult to determine. Possible future research directions could include international collaborations by obtaining greater Physiotherapist participation in referring their CRPS patients for independent interviewing, or by longitudinal studies where follow up is continued over many years (e.g. 10-20 years).

However, it is questionable whether or not a larger sample size over a longer period of time would be able to accurately identify the stand-alone contribution of physiotherapy to CRPS

recovery. This is due to the highly variable presentation of each CRPS patient presenting to any Physiotherapist who accepts CRPS patients, as well as the research method focusing exclusively on intervention methods and outcomes.

There are no studies in the literature which evaluate the physiotherapist's perspective of the interaction with their patient. Rather the focus is on the patient's perspective about their satisfaction with care e.g. DDS and outcomes. The candidate suggests it could also be important to include the potentially bidirectional ingredient of Physiotherapist expertise; beliefs about CRPS management; factors affecting their perspective of the therapeutic relationship about their CRPS patient's culture, preferences and temperament. Harassment by patients may also be an issue to explore since the literature reports that in other domains, poorer outcomes were also associated with poorer mental health [386].

It is suggested that to determine the effect of physiotherapy on CRPS outcomes, the relationship between a Physiotherapist and CRPS patient could perhaps be further clarified through qualitative and quantitative investigation in a mixed research method [387]. However, to implement this method with a prospective study and across a region (as in this project) may be difficult. Furthermore, the scrutiny of individual practitioners may be perceived as intimidating.

### *Limitations*

Limitation is the low sample size which may have contributed to confounding or errors. Since a small group showed little improvement despite all intervention, and the physios do not discharge these patients the associations need to be interpreted with caution.

A further limitation is that an ANOVA analysis may have been applied with adjusted p-values to outcome measure instead of the t-test since multiple scales are presented. Only a single t-test is conducted for each scale (i.e. a test that there was no change from baseline to 1 year).

The following Chapter 8 explores the associations between the outcomes changes with the characteristics of the participants as well as the continuous and categorical variables.

# CHAPTER EIGHT

## Prognostic relationships with complete recovery

### 8.1 Introduction

These cohort sample characteristics were similar to the only two epidemiological studies about CRPS published (as shown in Chapter 5). The literature review outlined in Chapter 2 demonstrated consistent evidence for a diagnosis of CRPS gender female: male ratio of 4:1, and that fewer are diagnosed with CRPS Type 2 than with CRPS Type 1. An early diagnosis and intervention was suggested to improve the outcomes for CRPS. Furthermore, at one centre, it was also shown that the incidence of CRPS was reduced to zero through aggressive management of any early signs of symptoms suggestive of CRPS [76].

However, there is no conclusive evidence regarding either the risks for the onset of CRPS [39] or the definitive prognostic factors determining CRPS outcomes in either gender [92, 93]. It is unethical in clinical practice to deny treatment for any patient presenting with pain, especially if the pain experience is severe (allodynia, hyperalgesia), and associated with the autonomic signs and symptoms (sweating, colour, temperature changes) as found in CRPS.

Other persistent pain conditions show fear avoidance, anxiety and depression to be predictors of outcomes following medical or allied health management. Hence, the Tampa Scale for Kinesiophobia, Health Anxiety Index and Kessler10 measures were applied at baseline to determine their effect on the outcomes following physiotherapy management (as shown in Chapter 4). Furthermore, the novel concept of personality and the possibility of neuroticism or extraversion being a factor affecting outcome was explored.

This Chapter describes and analyses the effect that continuous and categorical factors had on participants' outcome measures with a complete recovery.

The structure of this Chapter describes the method, the tests for baseline continuous variable differences, the tests for the timing to diagnosis and the commencement of physiotherapy with the outcome to Hypothesis test 2.2.

## 8.2 Method

This study was not a clinical trial. It was an observational study, hence, the Patient/Problem/Population Intervention Comparison Outcome (PICO) [388] format was not applied. There was not randomisation or control group as this was not possible to implement, hence, intervention control could not apply. Continuous variable multivariable analyses were applied, however, categorical variable multivariate analyses could not be applied as sample sizes were too small and the potential errors of co-linearity also limited this analysis.

The full resolution from all pain and a full restoration of function are considered the best outcome for any Physiotherapist treating a CRPS patient [389]. In order to determine the effect of predictor variables on full resolution from pain and full restoration of function and quality of life, this cohort's outcome variables were combined into two groups; those who made a *complete recovery*, as determined as a zero PRI pain score from their MPQ-SF and obtained full restoration of their function on the WHODAS score, vs those who did not make this complete recovery. The primary outcome variable is for the whole group and includes both upper and lower limb affected CRPS.

### Analytic approach

The approach taken with these data was to apply logistic regression to test for the effect of continuous or categorical variables on the outcome of a complete recovery with CRPS.

The logistic regression analysis was applied to continuous and categorical variables to determine the odds ratio (OR) with the respective 95<sup>th</sup> percentile confidence intervals for a predictive effect on the outcome of a complete recovery. The OR was considered not relevant for a predictive effect if it showed a ratio of 1:1 within the 95<sup>th</sup> percentile confidence interval range. The relevance was strictly applied, even if there was a  $p < 0.05$  value of significance.

## 8.3 Results

The DASH or FFI outcome scores were not included in this combination, as each sample was too small for robust statistical testing. The DASH score only applies to those with upper limb CRPS. The FFI score only applies to those with lower limb CRPS. The PRI and WHODAS-2 are outcomes measures that were applied to the full cohort, since they do not separate the upper limb from the lower limb with their measures; they were used to determine full

recovery. The data showed that 24 participants (45%) obtained a full recovery of function with zero pain PRI and zero functional disability on the WHODAS-2 scores. These are represented in the histogram in Figure 8.1.

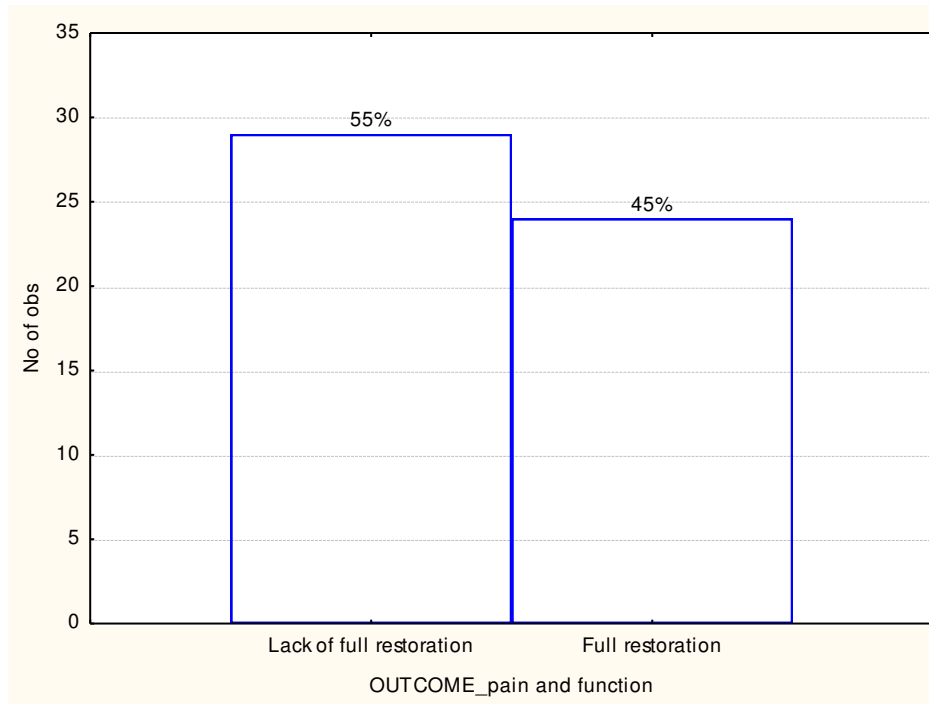


Figure 8.1. Complete recovery 1 year later for cohort.

### 8.3.1 The tests for baseline continuous variable differences

The continuous variables analysed were the following: age; baseline PRI and WHODAS2; health anxiety (HAI); personality extraversion (EPQE) or neuroticism (EPQN); fear of movement (TSK); and mental health (Kessler10). A higher score for the HAI, TSK and Kessler10 indicate higher anxiety, fear avoidance and poorer mental health, respectively. A higher score for the EPQE and EPQN indicate higher levels of extraversion or neuroticism, respectively.

Student-t tests were applied and showed the following similarities with baseline measures between the complete recovery vs. lack of recovery groups: a difference of only three points greater with the baseline PRI; TSK, 35.7 and 36.0; and HAI, 29.7 and 31.1, respectively. The following significant differences ( $p < 0.05$ ) were shown for the complete recovery group: better mental health Kessler10 (6.7 vs. 13.5); a higher EPQE (43.6 vs 34.4); a lower EPQN

(20.0 vs. 26.5). These data are shown in Table 8.1 where significant findings are highlighted in bold.

*Table 8.1. Continuous predictor variables means and student t-tests for complete recovery.*

	<b>Complete recovery, Mean (SD) N=24</b>	<b>Lack complete recovery, Mean (SD) N=29</b>	<b>t- value</b>	<b>P</b>
<b>Age</b>	42.0 (18.8)	46.5 (15.8)	-0.9	0.35
<b>TSK</b>	35.7 (11.2)	36.0 (11.3)	-0.1	0.93
<b>HAI</b>	29.7 (9.4)	31.1 (11.3)	-0.5	0.62
<b>EPQE</b>	<b>43.6 (9.2)</b>	<b>34.4 (10.9)</b>	<b>3.7</b>	<b>&lt;0.001</b>
<b>EPQN</b>	<b>20.0 (6.7)</b>	<b>26.5 (8.8)</b>	<b>-2.9</b>	<b>0.01</b>
<b>Kessler10</b>	<b>6.7 (7.6)</b>	<b>13.5 (0.5)</b>	<b>-2.9</b>	<b>&lt;0.001</b>
<b>Baseline PRI</b>	23.4 (9.0)	26.9 (9.3)	-1.5	0.15
<b>Baseline WHODAS2</b>	<b>28.1 (9.7)</b>	<b>33.6 (8.5)</b>	<b>-2.0</b>	<b>0.05</b>

PRI - Short form McGill Pain Questionnaire Pain Rating Index

WHODAS2 - World Health Organisation (WHO) Disability Assessment Schedule 2.0

TSK – Tampa Scale for Kinesiophobia

HAI – Health Anxiety Index

Kessler10 – Ten item psychological distress Kessler

EPQE - Eysenck Personality Questionnaire Extraversion

EPQN - Eysenck Personality Questionnaire Neuroticism

Significance\* p<0.05

Student t-test showed a significant difference between those who did not receive psychological support to be more likely to have a full recovery than those who did receive this intervention, p=0.02. These data are shown in Table 8.2.

Table 8.2. Concurrent psychological support student t-tests for complete recovery

Psychological support	Complete recovery	Lack complete recovery	t- value	P
Yes, N=19 No, N=47	N=3	N=12	2.4	<b>0.02*</b>

Significance\* p<0.05

### 8.3.2 The tests for the time to diagnosis and to commence physiotherapy intervention

#### *Differences to the WHODAS2 score*

There was a 13-point difference between the WHODAS2 changes with a diagnosis within 1 month vs. 2 months. The diagnosis timing of 3 months or longer showed a difference of 10 points from the diagnosis timing of 2 months. The time to diagnosis of 2 months showed the largest change to the WHODAS2 score. This change represents improvement of functional ability and quality of life as the WHODAS2 score is reduced and represented as a negative number.

The timing to start physiotherapy showed a different trend. The greatest improvements were: 17 points with commencing 1 month following injury; and 16 points with 3 or more months. The least improvement was shown with commencing physiotherapy 2 months following injury represented by an improvement of 5 points. These are graphically shown in Figures 8.4-5 where the bars represent the 95<sup>th</sup> percentile confidence intervals.



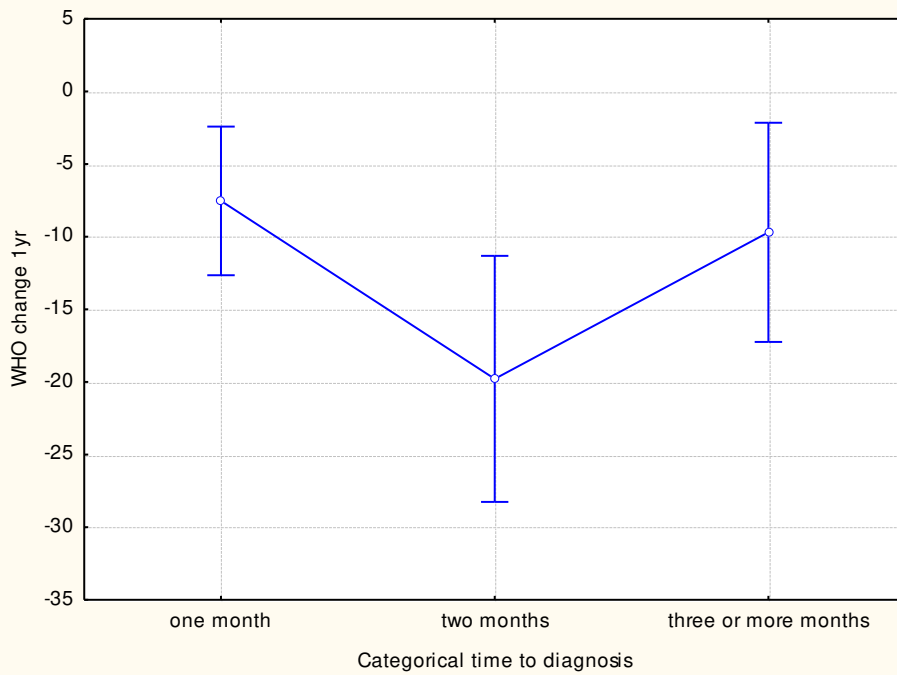


Figure 8.4. WHODAS2 change after 1 year and time in months to diagnosis.

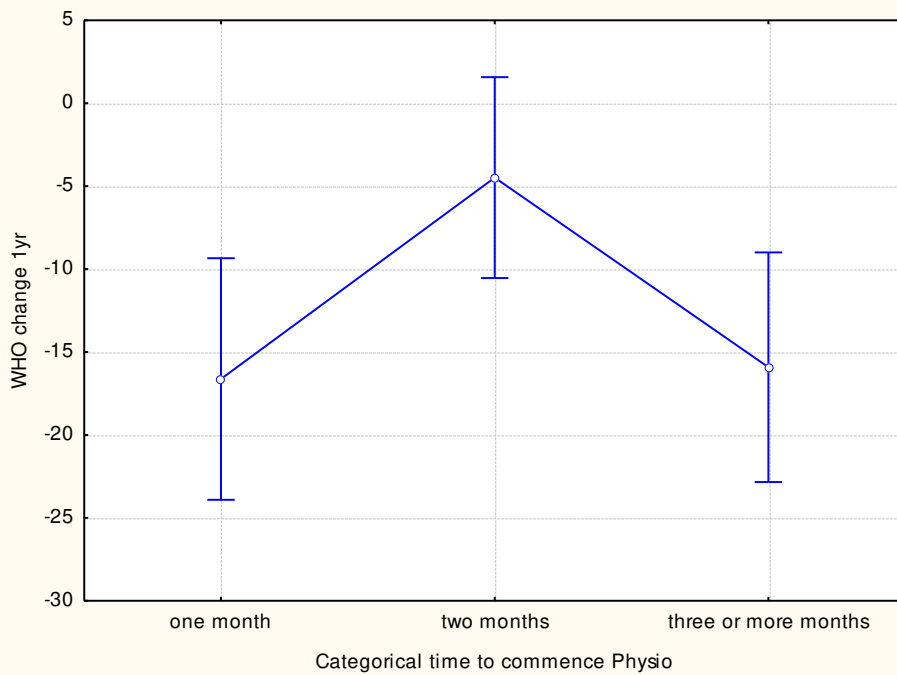


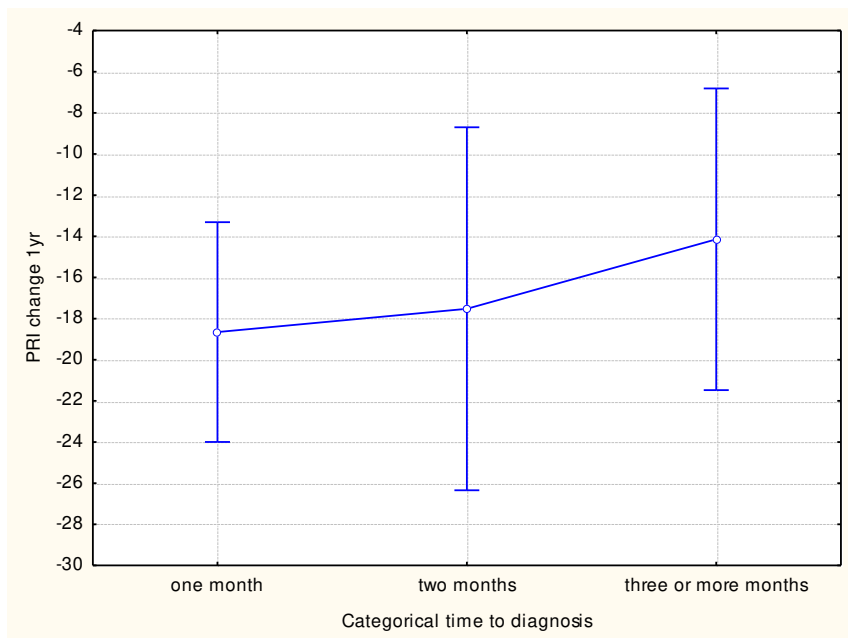
Figure 8.5. WHODAS2 change after 1 year and time in months to commence physiotherapy.

### *Changes to PRI score*

The change to the pain experience with the PRI showed that the earlier the diagnosis, the greater the improvement of pain with: 1 month to diagnosis resulted in an improvement of 18 points; 2 months to diagnosis resulted in an improvement of 17 points; 3 or more months to diagnosis resulted in an improvement of 14 points.

The change of PRI with the months to commence physiotherapy showed an opposite effect, with a far larger reduction of pain experience by those who commenced their physiotherapy later. Those who started 3 or more months following their injury improved by 20 points.

Those who started 1 month later showed a change of 16 points; those who started physiotherapy 2 months later showed a change of 14 points. These are graphically shown in Figures 8.6-7.



*Figure 8.6. PRI change after 1 year and time in months to diagnosis.*

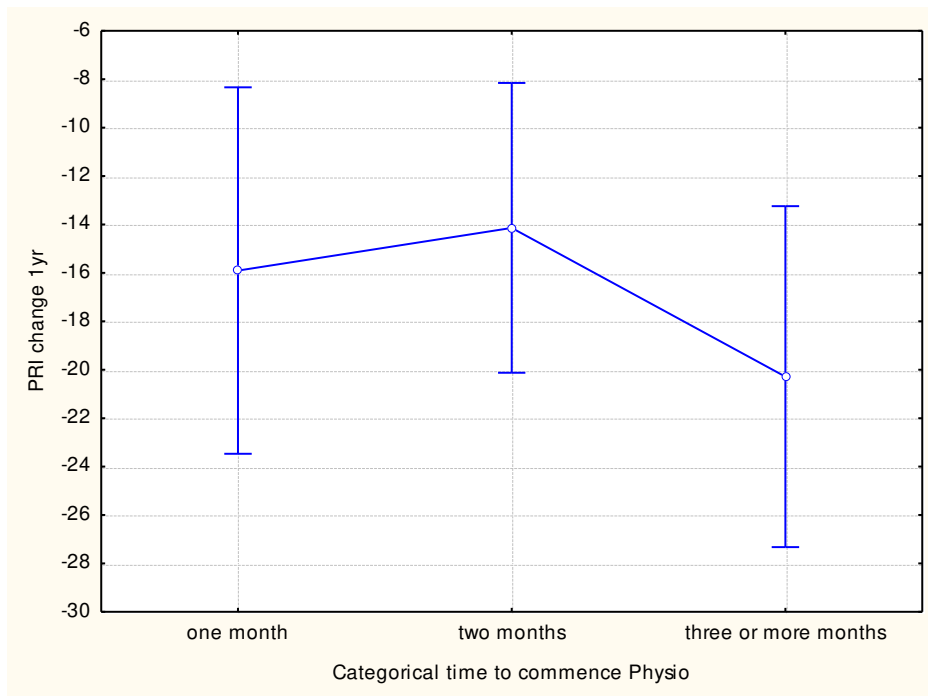


Figure 8.7. PRI change after 1 year and time in months to commence physiotherapy.

### 8.3.3 Logistic regression analysis continuous variables

Univariate logistic analysis was completed for independent continuous variables for categorical variables for a complete recovery. These results found small effects for the continuous variables of higher personality neuroticism, (OR=0.91, CI=0.84-0.98, Chi<sup>2</sup>=7.93, p=0.01); poorer baseline WHODAS2 function (OR=0.94, CI=0.89-1.00, Chi<sup>2</sup>=4.06, p=0.04); and poorer mental health (OR=0.94, CI= 0.83-0.97, Chi<sup>2</sup>=8.53, p=0.003) to be a predictor of a poor recovery. Higher personality extraversion showed a strong effect as a predictor for complete recovery (OR=1.12, CI= 1.04-1.21, Chi<sup>2</sup>=12.42, p=0.002).

These results are displayed in Tables 8.3.

Table 8.3. Univariate analysis of continuous independent variables.

Univariate analysis of continuous variables for a complete recovery, N=53				
	OR	95% CI	Chi <sup>2</sup>	p
Age	1.02	0.98-1.05	0.91	0.34
Fear avoidance: TSK	1.00	0.95-1.05	>0.01	0.93
Health anxiety: HAI	1.01	0.96-1.07	0.25	0.62
Baseline PRI	1.05	0.98-1.12	2.19	0.14
Personality: high score EPQE	<b>1.12</b>	<b>1.04-1.21</b>	<b>12.42</b>	<b>0.002*</b>
Personality: high score EPQN	<b>0.91</b>	<b>0.84-0.98</b>	<b>7.93</b>	<b>0.01*</b>
Poor Mental Health: Kessler10	<b>0.94</b>	<b>0.83-0.97</b>	<b>8.53</b>	<b>0.003*</b>
Baseline WHODAS 2	<b>0.94</b>	<b>0.89-1.00</b>	<b>4.06</b>	<b>0.04*</b>

PRI - Short form McGill Pain Questionnaire Pain Rating Index

WHODAS2 - World Health Organisation (WHO) Disability Assessment Schedule 2.0

TSK – Tampa Scale for Kinesiophobia

HAI – Health Anxiety Index

Kessler10 – Ten item psychological distress Kessler

EPQE - Eysenck Personality Questionnaire Extraversion

EPQN - Eysenck Personality Questionnaire Neuroticism

Significance\* p<0.05

Univariate analysis of categorical variables showed with strong effect that the anti-convulsant prescription of gabapentin or pregabalin along with physiotherapy was associated with a complete recovery, (OR=6.66, CI= 1.98-22.43, Chi<sup>2</sup>=10.5, p=0.002). Psychological intervention with a psychologist concurrent with physiotherapy was also associated with a strong effect for poor recovery, where psychological support showed a significant association with a poorer recovery (OR=0.20, CI= 0.04-0.83, Chi<sup>2</sup>=5.73, p=0.02). These data are shown in Table 8.4.

Table 8.4. Univariate analysis of categorical independent variables.

Univariate logistic analysis of categorical predictors for complete recovery, N=53				
	OR	95% CI	Chi <sup>2</sup>	p
<b>CRPS</b> Type 1 N=57 Type 2 N=9	0.57	0.09-3.41	0.39	0.54
<b>Injury:</b> Fracture N=28 No Fracture N=38	1.61	0.53-4.87	0.71	0.40
<b>Baseline allodynia</b> Yes N=32 No N= 34	0.93	0.32-2.75	0.02	0.90
<b>Prescription of anti-convulsion secondary analgesia concurrent with physiotherapy</b> Yes N=34 No N=32	<b>6.66</b>	<b>1.98-22.43</b>	<b>10.5</b>	<b>0.002*</b>
<b>Prescription of tricyclic secondary analgesia concurrent with physiotherapy</b> Yes N=39 No N=27	1.14	0.37-3.52	0.05	0.82
<b>Psychological support concurrent with physiotherapy</b> Yes N=19 No N=47	<b>0.20</b>	<b>0.04-0.83</b>	<b>5.73</b>	<b>0.02*</b>

Significance\* p<0.05

Multivariate logistic analysis was used to account for potential reverse causality or confounding in the univariate analyses. This may occur when a third variable becomes causally associated with an outcome/dependent variable but is not causally associated with the intervention/independent variable, so that the direction of cause and effect may be misidentified. In this analysis, the association of psychological support being associated with a poorer recovery may exhibit reverse causality as the intervention may be applied to a participant with greater distress, hence requiring a greater intensity or duration of input that those with less distress. On the other hand, confounding is a potential problem with a baseline measure which for those who score worse (in this sample for example, those with poorer

mental health or quality of life) also require a longer duration or greater number of interventions to achieve the same result as those with a better baseline score.

Multivariate analysis for continuous independent variables showed that the strong effect of personality extraversion as a predictor for a full recovery remained (OR=1.01, CI=1.01-1.21, Chi<sup>2</sup>=11.483, p=0.04), but that the small effects for higher personality neuroticism, poorer baseline WHODAS2 function and poorer mental health were diluted so that they could no longer be considered important as predictors for a poor recovery. These data are shown in Table 8.5.

*Table 8.5. Multivariate analysis of continuous independent variables.*

<b>Multivariate analysis of continuous variables for a complete recovery, N=53</b>				
	<b>OR</b>	<b>95% CI</b>	<b>Chi<sup>2</sup></b>	<b>p</b>
<b>Age</b>	1.00	0.95-1.05	0.91	0.98
<b>Fear avoidance: TSK</b>	1.03	0.95-1.12	0.23	0.44
<b>Health Anxiety: HAI</b>	1.06	0.94-1.19	0.51	0.34
<b>Baseline PRI</b>	0.99	0.90-1.09	1.74	0.80
<b>Personality: high score EPQE- Extraversion</b>	<b>1.10</b>	<b>1.01-1.21</b>	<b>11.48</b>	<b>0.04*</b>
<b>Personality: high score EPQN- Neuroticism</b>	0.93	0.84-1.04	2.62	0.20
<b>Poor Mental Health: Kessler10</b>	0.93	0.85-1.01	2.91	0.10
<b>Baseline poor function and quality of life: WHODAS 2</b>	0.94	0.85-1.03	1.94	0.18

PRI - Short form McGill Pain Questionnaire Pain Rating Index

WHODAS2 - World Health Organisation (WHO) Disability Assessment Schedule 2.0

TSK – Tampa Scale for Kinesiophobia

HAI – Health Anxiety Index

Kessler10 – Ten item psychological distress Kessler

EPQE - Eysenck Personality Questionnaire Extraversion

EPQN - Eysenck Personality Questionnaire Neuroticism

Significance\* p<0.05

Multivariate analysis for categorical predictors also showed that the effect of no psychological support being associated with a full recovery was diluted; but that the concurrent prescriptions of the anticonvulsant secondary analgesics, Gabapentin or Pregabalin, maintained their strong effect to predict a full recovery (OR=6.67, CI= 1.71-26.01, Chi<sup>2</sup>=8.41, p=0.006). These data are shown in Table 8.6.

Table 8.6. Multivariate logistic regression for categorical independent variables.

Multivariate logistic analysis of categorical predictors for complete recovery, N=53				
	OR	95% CI	Chi <sup>2</sup>	p
<b>CRPS</b> Type 1 N=27 Type 2 N=9	1.69	0.22-12.93	0.25	0.61
<b>Injury:</b> Fracture N=28 No Fracture N=38	0.87	0.22-3.38	0.04	0.84
<b>Baseline allodynia</b> Yes N=32 No N= 34	0.86	0.24-3.13	0.05	0.82
<b>Prescription of anti-convulsion secondary analgesia concurrent with physiotherapy</b> Yes N=34 No N=32	<b>6.67</b>	<b>1.71-26.01</b>	<b>8.41</b>	<b>0.006*</b> <b>Complete recovery</b>
<b>Prescription of tricyclic secondary analgesia concurrent with physiotherapy</b> Yes N=39 No N=27	1.02	0.27-3.83	0.00	0.97
<b>Psychological support concurrent with physiotherapy</b> Yes N=19 No N=47	0.23	0.04-1.10	3.78	0.06

Significance\* p<0.05

### 8.3.4 Logistic regression analysis of the timing to diagnosis and to commencement of physiotherapy

Univariate logistic regression analyses showed that diagnosis timing as well as timing to commencement of physiotherapy in months had no effect in predicting a complete recovery.

Analyses included individual months to avoid potential co-linearity. These data are shown in Tables 8.7-8.

*Table 8.7. Univariate logistic analysis of diagnosis timing and recovery*

Category of diagnosis timing	OR	95% CI	Chi <sup>2</sup>	P
One month only	0.86	0.40-1.84	1.19	0.69
2 to less than 3 months	0.75	0.27- 2.11	1.19	0.58
3 months or more	0.80	0.43-1.50	1.19	0.49

Significance\* p<0.05

*Table 8.8. Univariate logistic analysis of physiotherapy timing and recovery.*

Category of physiotherapy timing	OR	95% CI	Chi <sup>2</sup>	P
One month only	1.31	0.60-2.28	3.12	0.69
2 to less than 3 months	0.48	0.20-1.40	3.12	0.58
3 months or more	0.76	0.43-1.35	3.12	0.35

Significance\* p<0.05

#### **8.4 The hypothesis test 1.2**

The primary hypothesis 1.2 proposed that a positive outcome for CRPS would associated with an early diagnosis. These results showed no association between the timing of diagnosis and the outcome for CRPS. However, the null hypothesis that time until diagnosis is not associated with CRPS outcomes cannot be rejected with this cohort. This is because the baseline measures were not influenced by the time of diagnosis to affect this test and because the sample size may have been too small to detect such an association. However, it is possible that this assumption reflects a Type 2 error of an incorrect refute of the null hypothesis.

It was observed with these results, that the CRPS diagnosis could be made in different ways. Diagnosis could be made by a treating Physiotherapist who would start the appropriate management immediately. Other patients were specifically referred to physiotherapy for management of their CRPS after diagnosis was made by a Medical Practitioner, and they had



received no prior physiotherapy intervention for their inciting injury, or had experienced delays to treatment due to time spent excluding other possible diagnoses to explain their symptoms.

#### *Explanation for hypothesis 1.2 finding*

A plausible reason not to reject the null hypothesis is that due to the low prevalence of CRPS, the large geographical area of the South Island, the financial, enrolment, and logistic constraints, it was not possible to further extend data collection beyond the allocated time. The candidate had arranged trips each year across the region to every centre inviting participation from Physiotherapists to ensure the best possible cohort sample size. It was neither possible nor feasible to have recruited a larger sample size over the 3 year period. CRPS prevalence is low and obtaining large sample sizes can be difficult, as others have reported [390].

Another possible reason may be considered for this finding. It is possible that the complex presentations of those with an early or delayed diagnosis were addressed by the different Physiotherapists across this wide region in an individualised, tailored approach for each respective CRPS presentation. This approach was effective (regardless of the diagnosis timing or the commencement of physiotherapy), since 45% of this cohort made a complete recovery. It has been reported in both the graded and pain exposure literature that long-standing CRPS function can be improved and pain also resolved [100, 117]. Although the evidence is not strong, recovery does occur with either of these methods. It is plausible that either method may be effective in a specific CRPS presentation or that both are effective at different phases of the CRPS recovery trajectory.

Another argument is that these results, and that of other studies, show that recovery is still possible if the diagnosis is not detected early. Early diagnosis was shown to be effective to reduce the incidence of CRPS to zero after fracture of the distal radius with the early detection and aggressive management of any signs or symptoms that were warning signs of the possibility of CRPS [76]. These present results showed that almost half the patients made a complete recovery and all showed significant, clinically relevant improvement. Hence, it would be reasonable to imply that the CRPS trajectory could be directed towards recovery at any stage by the treating Physiotherapists irrespective of the time since the inciting injury.

It would be common sense, good practice, and could also reduce suffering to identify CRPS signs and symptoms early. Furthermore, to apply intervention as early as possible, and hence,

improve efficiency associated with potentially lost or wasted time, and any potential litigation issue associated with the diagnosis being ignored. Overlooking the diagnosis has been recently reported be a problem for CRPS patients N=12, [44], in the courts of the United States [391], and involving a Psychiatrist in court to verify a CRPS patient's good mental health [392]. Even if the diagnosis is delayed as other possible causes are ruled out, hope remains for the CRPS patient, Clinician or Physiotherapist and it is suggested that intervention commences in a constructive manner.

In summary, there are four plausible explanations: 1) the null hypothesis is not rejected; 2) a Type 2 error of an incorrect refute of the null hypothesis; 3) individualised, tailored physiotherapy applied by skilled Physiotherapists contributes to a good recovery, regardless of how long the time to diagnosis has taken; 4) recovery is possible regardless of diagnosis timing or intervention and hope remains an appropriate message.

## **8.5 Discussion**

These results showed with univariate variable logistic regression analyses of poorer outcomes to be diluted with multivariate analysis other than the concurrent prescription of anticonvulsant medication. These diluted variables were: poorer mental health; poorer quality of life and functional ability at baseline level; higher scores of neuroticism; concurrent psychological support. This does not mean that psychology input implies a poor outcome. It is possible that the univariate effect of the concurrent psychological support was a consequence of reverse causality and that poorer baseline mental health, poorer quality of life, and higher neuroticism were associated with a poorer outcome due to confounding. Hence it may be that those who present with poorer function or mental health have a greater proportion of change to achieve, than those who present with better baseline function or mental health, in the measured time to recovery. They either require more treatment in the same time period or require more intense intervention to achieve the same result as those who commenced at the same time.

Psychosocial factors were not shown in the literature summarised in Chapter 2 to be predictors for the onset of CRPS. However, some studies did show allodynia or anxiety to be a predictor of poorer outcomes with small effect sizes. The literature was mixed about the

relationship of anxiety, depression or catastrophising for CRPS risk, trajectory or outcomes. Multiple studies and meta-analyses did not provide strong evidence [92, 93].

Personality and its relationship with CRPS outcomes is not known. These results provided a novel contribution to the literature that extraversion scores and CRPS outcomes are intertwined. The finding that the univariate effect of extraversion personality trait was associated with a better outcome has been reported for other conditions [359, 360]. Alternatively, extraversion's positive effect could be interpreted that personality has an interactive effect in the therapeutic relationship, as it has been reported to influence behaviour [393]. The candidate also speculates about the possibility that the paradigm of physiotherapy care may facilitate recovery for those CRPS patients with higher scores of this trait at the expense of those who have lower scores. This may warrant further investigation.

It is also speculated that the interactive effect of personality extraversion trait may be associated in a positive way with the therapeutic relationship. The psychotherapy literature has shown the therapeutic relationship to be an essential ingredient in the model of care [293, 383]. A successful therapeutic relationship may be an important ingredient in complete recovery from CRPS.

Poor mental health is possibly a factor involved with the CRPS scenario from multiple aspects. These results show weak evidence for mental health to be associated with a poorer outcome. The patient with CRPS may develop poor mental health resulting from the stress associated with not being able to work, accompanied by severe pain and frustration with the functional disability. However, there are others who at the time of their injury, are maybe experiencing a transient time of poorer mental health, experiencing unforeseen stresses beyond their ability to cope. There are those who may have always experienced poorer mental health, so that the usual burdens of life overwhelm them; their CRPS is simply another part of the puzzle of life that they need to make sense of and fit into their reality.

The concurrent prescription of tricyclic antidepressants showed a higher baseline pain experience, with greater health anxiety and poorer quality of life and functional ability. The concurrent prescription of anticonvulsants group showed a different scenario, with greater fear avoidance and personality neuroticism. These differences were beyond the scope of this project. It may be that the anticonvulsant group is effective for a sub-group of patients.

### *Implication for clinical practice*

In clinical practice, the heterogeneous presentation and trajectory for each CRPS patient's recovery requires that the physiotherapist uses skill, patience and flexibility to develop an individualised management plan. Anticonvulsants, gabapentin or pregabalin, prescription may be considered and future robust trials are necessary to test for their effect. It cannot be suggested with strong evidence that this prescription is the guarantee for complete recovery. However, it may have a place for a trial in a new CRPS patient who shows fear avoidance and tendencies towards personality neuroticism.

For several reasons, best practice could be early detection of a possible diagnosis of CRPS. However, currently, there is no algorithm available to show the signs and symptoms that constitute a likely CRPS diagnosis when the Budapest criteria are not yet fulfilled. There is no standard forecast method. There is no recognised trajectory pathway, whereby the Budapest criteria signs and symptoms can be suspected to escalate towards meeting the diagnosis.

When diagnosis has been delayed, suggesting that there is no hope would potentially be detrimental for the CRPS patient [44]. Nevertheless, it would be also reasonable to recommend a realistic, open and flexible management approach, with adequate explanation of the trajectory of CRPS and the potential outcomes. It is shown in Chapter 2 that not all CRPS patients make a complete recovery, despite early detection and standard intervention. Hence, this approach would be recommended to avoid disappointment from the unrealistic, optimistic guarantee of a definite recovery, which subsequently may not eventuate.

These results showed no likely trajectory or predictive baseline factors, hence it is suggested that Physiotherapists treating CRPS may have to optimise a fine balance. This balance is between the personal awareness of their own experiences, strengths, weaknesses, personality traits, understanding of the law, and the integration of best knowledge with available evidence. It is suggested that effective management also considers the context of each individual patient's personality, beliefs, social context, culture and expectations.

Hence, it is suggested that it may be important for the management of CRPS to cultivate an effective therapeutic relationship. It is also plausible to suggest that an individually tailored approach together with an effective therapeutic relationship form ingredients in promoting complete recovery from CRPS.

### *Implications for research*

These results may imply confounding associated with the timing for diagnosis, and timing to commence with physiotherapy, and reverse causality with psychological support. There may be complex interactive effects between baseline variables, intervention and other factors not measured with this study which were also associated with outcomes. These were beyond the scope of this study.

Confounding or reverse causality effects may be reduced by the application of a randomisation methodology. This was not possible with this study. It was reported to be difficult to implement an RCT for CRPS in a clinical setting [114] and would potentially be more challenging in multiple clinical setting across a region. The cluster RCT method could also be considered, especially if analysis applied an intention to treat approach [394].

It would also be recommended that the differences in responses with the secondary analgesia tricyclic and/or anti-convulsant groups be further investigated. The relationship of physiotherapy timing, duration and intensity with these prescriptions would be recommended for future research.

Practicing clinicians are in a void regarding evidence-based guidelines or validated pathways. There is no clear model of care in the literature. While the research methods have rigour, the intrinsic variability of the CRPS condition makes it extraordinarily difficult for statistical analyses to find sufficiently strong evidence to identify causal links. The clinical reality is that Physiotherapists do see CRPS patients and as showed in Chapter 3, some will see 2-3 new CRPS patients each month. They have a duty of care to provide treatment. It is suggested, as a priority, that a conceptual clinical model be proposed with the limited available evidence and subsequently tested for validation with future CRPS research.

## CHAPTER NINE

### **The relationships between physiotherapy applied and complete recovery**

#### **9.1 Introduction**

This chapter presents a) the findings about the relationships that the physiotherapy intensity; the categories of intervention modalities applied; the prescribed homework, and participant adherence had on the respective CRPS patients' outcomes a year later b) the tests for objective 2.1. A complete recovery from CRPS (Chapter 8) is determined as a full recovery of function on the WHODAS2 score and full resolution of pain on the PRI score.

#### **9.2 Method**

The analysis used inferential statistics to determine: the effects of physiotherapy intensity; the categories of intervention applied; the prescribed homework; how the prescribed homework was rated for reduction of the pain experience on the outcome measures; and adherence with the route of formal discharge by the treating Physiotherapist, self-discharge by participant or ongoing physiotherapy 1 year later.

##### *Analytic approach*

The approach with inferential statistics was to use student-t tests or univariate and multivariate logistic regression with Odds Ratios (OR), Confidence interval (CI) and Chi squared ( $\chi^2$ ) statistics to determine effect with  $p < 0.05$  for significance.

#### **9.3 Results**

##### **9.3.1. Physiotherapy intensity relationship with a complete recovery from CRPS**

The total number of physiotherapy sessions attended, the total number of weeks attended, the number of hours as a proportion of the number of weeks attending physiotherapy, as well as number of sessions as a proportion over the number of weeks, were calculated. These data show that the greater the number of physiotherapy sessions attended and the greater the number of weeks attending, the poorer the outcomes (OR=0.92, CI=0.87-0.97). It is possible to explain this finding as confounding: those who required more treatment in the same time period or required more intense intervention to achieve the same result as those who

commenced at the same time as them, required a greater number of sessions and consequently a greater number of weeks. However, this effect was weak as it was not seen when converted to the proportional intensity of hours per week or contact sessions per week. These data are shown in Table 9.1.

*Table 9.1. Physiotherapy category of intervention dose and relationship with complete recovery.*

<b>Univariate analysis complete recovery after 1 year N=66</b>				
	<b>OR</b>	<b>95% CI</b>	<b>Chi<sup>2</sup></b>	<b>p</b>
<b>Total N of physiotherapy sessions attended</b>	<b>0.92</b>	<b>0.87-0.97</b>	<b>13.8</b>	<b>0.002*</b>
<b>Total duration of weeks of physiotherapy</b>	<b>0.93</b>	<b>0.89-0.97</b>	<b>12.8</b>	<b>0.004*</b>
<b>N hours/weeks proportion of physiotherapy intensity</b>	0.54	0.1-2.1*	2.2	0.1
<b>N contact session/weeks proportion for physiotherapy intensity</b>	0.39	0.09-1.6	2.2	0.3

Significance\* p<0.05

*Univariate and multivariate logistic regression analysis of all physiotherapy intervention categories effect for a complete recovery*

Physiotherapy intervention was categorised as treatment interventions for pain (TIP), for function (TIF), for education (Educ), for immobilisation (TII), or for passive movement (Pass). Weekly averages were calculated for each outcome measure interview interval, at 6 weeks, 6 months, and 1 year.

Neither univariate nor multivariate analyses showed any weekly average for category of intervention to have an effect on a complete recovery. Data obtained from TII and Pass interventions were too small a quantity for logistic regression analysis. These data are shown in Table 9.2-3.

Table 9.2. Univariate analyses for physiotherapy treatment intervention categories averages on complete recovery.

Univariate analysis for complete recovery after 1year N=53				
	OR	CI	Chi <sup>2</sup>	p
<b>6-week average TIP</b>	0.97	0.82-1.15	0.10	0.76
<b>6-month average TIP</b>	0.79	0.58-1.07	2.78	0.13
<b>6-week average TIF</b>	0.86	0.62-1.17	0.98	0.33
<b>6-month average TIF</b>	0.60	0.36-1.01	4.52	0.06
<b>6-week average Educ</b>	0.96	0.36-2.57	0.01	0.94
<b>6-month average Educ</b>	0.41	0.07-2.34	1.04	0.31
<b>6-week average Pass</b>	Sample N too small to compute with logistic regression			
<b>6-month average Pass</b>	Sample N too small to compute with logistic regression			
<b>6-week average TII</b>	Sample N too small to compute with logistic regression			
<b>6-month average TII</b>	Sample N too small to compute with logistic regression			

Significance\* p<0.05

TIP: Physiotherapy treatment interventions for pain modulation;

TIF: Physiotherapy treatment interventions for functional restoration,

TII: Physiotherapy treatment interventions for immobilisation,

Educ: Physiotherapy treatment interventions for education.

Pass: Passive Physiotherapy treatment interventions.



Table 9.3. Multivariate analyses for physiotherapy intervention categories averages.

Univariate analysis for complete recovery after 1year N=53				
	OR	CI	Chi <sup>2</sup>	p
6-week average TIP	1.15	0.86-1.55	0.10	0.35
6-month average TIP	0.71	0.42-1.19	3.30	0.19
6-week average TIF	1.00	0.52-1.91	1.77	1.00
6-month average TIF	0.40	0.11-1.49	1.33	0.17
6-week average Educ	0.78	0.06-10.67	0.50	0.86
6-month average Educ	Sample N too small to compute with logistic regression			
6-week average Pass	Sample N too small to compute with logistic regression			
6-month average Pass	Sample N too small to compute with logistic regression			
6-week average TII	Sample N too small to compute with logistic regression			
6-month average TII	Sample N too small to compute with logistic regression			

Significance\* p<0.05

TIP: Physiotherapy treatment interventions for pain modulation;

TIF: Physiotherapy treatment interventions for functional restoration,

TII: Physiotherapy treatment interventions for immobilisation,

Educ: Physiotherapy treatment interventions for education.

Pass: Passive Physiotherapy treatment interventions.

### 9.3.2. The effect of individual TIP interventions

The individual TIP physiotherapy interventions were analysed in more detail as categorical variables against the outcome variable of complete recovery. This was in order to explore the hypothesis 2.1. This hypothesis suggested that *physiotherapy intervention specifically aimed at central processes has a positive effect on CRPS outcomes*. In order to explore this hypothesis, univariate and multivariate logistic regression analyses were completed for each modality of intervention listed as fulfilling the category of TIP. These were: graded motor imagery (GMI); sensory motor training (SMI); pool based primary exercise; (POOL) (vs. gym based); relaxation training; mirror exercise; deep breathing exercise (DBE); graded exposure (GEXP); cognitive techniques; or the prescription of Transcutaneous Electrical Nerve Stimulation (TENS).

This analysis for each individual intervention method showed no tentative findings or significant effect on a complete recovery. Second order multivariate analysis showed that sample numbers were too small for further analyses. These data are shown in Table 9.4.

Table 9.4. Univariate analyses of treatment interventions for pain modulation.

Univariate analysis for complete recovery after 1-year N=53				
Applied vs Not applied	OR	CI	Chi <sup>2</sup>	p
Graded Motor Imagery	1.93	0.64-5.8	1.40	0.23
Sensory Motor Training	0.45	0.14-1.44	1.85	0.17
POOL primary exercise	1.72	0.57-5.13	0.96	0.33
Relaxation training	1.20	0.27-5.41	0.56	0.81
Mirror exercise	0.83	0.23-3.04	0.08	0.77
Deep Breathing Exercises	1.25	0.27-5.63	0.08	0.77
Graded Exposure	1.38	0.46-4.15	0.3	0.34
Cognitive techniques	0.37	0.11-1.28	2.61	0.12
Transcutaneous Electrical Nerve Stimulation	0.53	0.14-2.02	2.61	0.35
Graded Motor Imagery + POOL+ Sensory Motor Training	Sample N too small to compute			
Relaxation training + Mirror exercise + Deep Breathing Exercises	Sample N too small to compute			
Graded Exposure + Cognitive techniques + Transcutaneous Electrical Nerve Stimulation	Sample N too small to compute			

Significance\* p<0.05

### 9.3.3. The effects of prescribed homework exercises

The frequency of homework adherence during the day or the week, as well as the rating of how much the CRPS participant felt the prescribed homework was helpful in reducing the pain experience, was determined at 6 weeks and 6 months for its effect on a complete

recovery. Univariate logistic regression analyses were applied. These data showed no effect for a complete recovery and are shown in Table 9.5.

*Table 9.5. Univariate analysis of prescribed homework and its rating on complete recovery.*

Univariate analysis for complete recovery after 1 year N=66				
	OR	CI	Chi <sup>2</sup>	P
Homework daily frequency at 6 weeks	0.6	0.1-2.6	0.1	0.53
Homework daily frequency at 6 months	1.2	0.9-1.5	3.2	0.07
Homework weekly frequency at 6 weeks	0.9	0.2-4.0	<0.1	0.92
Homework weekly frequency at 6 months	1.2	0.9-1.6	2.4	0.14
Rating of prescribed homework to reduce pain at 6 weeks	0.9	0.6-1.3	0.3	0.63
Rating of prescribed homework to reduce pain at 6 months	0.9	0.6-1.3	0.5	0.52

Significance\* p<0.05

## 9.4 The objective test 2.1

The secondary objective 2.1 explored if physiotherapy interventions specifically aimed at cortical processes positively affected outcomes. These data showed that treatment interventions categorised for pain modulation (TIP) had no effect on complete recovery.

### *Explanation for objective 2.1 finding*

In this study pain modulation interventions (TIP) were categorised to include mirror exercises, GMI, TENS, GEXP, SMT, relaxation training, breathing control exercise, and cognitive techniques. Although reviews and literature support these interventions, evidence is low as shown in Chapter 2, due to poor quality, low sample sizes, a high level of bias and low reproducibility of those studies. The present study objective finding confirms poor support for these interventions.

The logistic regression analyses were important to expose the potential for confounding. Hence, it is plausible that these results could support either of two interpretations: a) PM is effective or b) PEXP is effective. The TIP category was inclusive of PM and exclusive of PEXP methods. The observation with these results is that both methods were used and contributed to a positive outcome. It is suggested that either method of PM or PEXP as

potentially beneficial to overcome fear avoidance and facilitate recovery, but each for different reasons. These reasons follow.

### **9.5. The objective test 2.2**

The objective 2.2 explored if different physiotherapy treatment modalities have dissimilar effects for the outcomes for CRPS. These data suggested that a complete recovery from CRPS involved different intervention methods or in different combinations to achieve a complete recovery when it was obtained. However, since there was no randomising or no control group, this support for this objective was weak with a risk of bias.

#### *Explanation for hypothesis 2.2 finding*

Pain modulation intervention is focused around central processing. The principle of TIP intervention is not to increase the pain experience, but to reduce it through the restoration of tactile acuity and body perception disturbances associated with what is theorised to be associated with aberrant cortical changes. In contrast, the motivation for PEXP is a focus on functional restoration with no attention to the pain experience.

It was suggested that doing nothing has a potentially detrimental effect [383]. Likewise, simply applying any method randomly may also be unfavourable [395]. While this may appear to be a situation of equifinality, where complete recovery is an open state and any modality would potentially be able achieve recovery [395, 396], we cannot exclude the possibility that there may be other factors that are not yet known. This concept that different intervention methods all show positive and similar effect is also reported for other conditions in psychology [241] and pharmacology [206], where the reasons for this are not yet understood.

The literature in Chapter 2 showed that PM or PEXP were both helpful. However, neither showed strong evidence. These results showed that neither categories of TIP nor TIF intervention methods had a strong effect in predicting a complete recovery. Since each intervention category or individual method showed a different effect, and none were significant, their benefit is suggested to be indicated for different contexts or CRPS presentations.

## 9.6 Discussion

Spontaneous recovery was shown to occur for a small group (5%) in the first epidemiological study which examined the incidence and outcomes for CRPS [69]. These results show that some patients require little if any intervention and recover well. Recovery can also occur over different periods of time. Recovery appeared to be irrespective of the intensity of intervention. This is confirmed by recent review findings [201] where the explanations for the different responses to intervention intensity are not yet fully understood.

On the other hand, these results showed poor recovery for a small group despite all interventions across the medical or allied health disciplines. These data also showed that although a complete recovery was not made, they were still better off with reduced pain and improved functional ability albeit not to their pre-injury/pre CRPS level.

The potential confounding observed may possibly also be explained by dependence of the patient on the care of the physiotherapist for other reasons than CRPS or for many other possible beliefs beyond the scope of this project.

### *Implications for clinical practice*

It is suggested that professional judgement remains a vital ingredient in the therapeutic relationship. What intervention method could a Physiotherapist use when starting with a new CRPS patient? It is suggested that a clinician uses skill to choose appropriately from the choice of interventions that can be applied according to two opposing methods. It requires expert judgement to know which intervention to apply when treatment is commenced. It is not suggested that a standard protocol follows in a fixed sequential order of application. Instead, astute judgement is called for as each new subsequent session starts at a new beginning from where the last intervention's effect wore off, was not effective, or was effective. It is the ability of an experienced clinician to customise a dynamic approach with one or more intervention methods to start the process of recovery from the first and each subsequent point of contact. It is proposed that a tailored approach be adopted for physiotherapy CRPS care.

It can become difficult in any busy clinical setting (with the constraints of time pressures and the potential misunderstandings that some CRPS patients bring with them about their diagnosis), to establish an effective patient relationship using the intervention. There are many potential hindrances that influence the education, reassurance and provision of

interventions. It may be necessary to help alleviate the distress a CRPS patient might have with their potential aberrant cortical processing, inflammation, peripheral or central sensitisation.

The participants understanding about CRPS and cure was assessed in this project. The satisfaction with care questionnaire asked the questions: ‘Do you feel you have had an adequate explanation about your CRPS?’; ‘Did your Physiotherapist spend enough time with you?’ and, ‘Do you feel your Physiotherapist understood what was bothering you?’ These data showed that the results for these questions were overwhelmingly positive (Chapter 6), hence, it is reasonable to assume that potential hindrances or distress were satisfactorily addressed.

Hence, it may be that despite not showing strong evidence for physiotherapy treatment interventions, it still becomes important to apply them. It would be important to apply them in a sensible manner with a coherent plan, and in collaboration with the patient. This is in keeping with an effective therapeutic relationship [298] and the ethic legislation supporting patient’s choices about their preferences [397].

It is suggested that vigilant observation of contexts, the ongoing objective, and subjective evaluation of the intervention is communicated between treating Physiotherapist and the CRPS patient. This is a relationship where there is no place for judgement or blame, instead, there should be objective, open, flexible, and mutual communication about what is helpful and what is not. For any condition requiring physiotherapy care, communication is also shown to be an integral component of the ongoing therapeutic relationship [295]. This is an ongoing process. It creates a safe place for both treating Physiotherapist and CRPS patient and is reported to involve the combination of clinical expertise and the context, culture and preferences of the patient [383], such as: the provision of emotional support as well as mutual collaboration with a patient centred focus [295]; the contextual understanding of the patient to facilitate placebo and avoid nocebo responses [294]; and the appreciation of other interpersonal issues affecting the patient [398]. Furthermore, patients were reported to appreciate an individualised approach from their treating Physiotherapist where the therapeutic relationship was shown to be key to behavioural change [243]. Effective strategies that assisted self-efficacy and fear avoidance were shown to be more useful to reduce disability than usual physiotherapy care [297]. These data would suggest that these are also important factors when communicating with a CRPS patient in physiotherapy care.

### *Implications for further research*

There are no other prospective studies reflecting regional clinical practice, hence, it is proposed that future research explore other regions, and also include evaluation of potential factors with their interactive effects on the therapeutic relationship.

There is potential to also examine the effect of the communication process on both the therapeutic relationship with CRPS and for a complete recovery. It is possible that communication is a mediator for either a positive relationship or for a complete recovery. It may be that there are specific ingredients necessary for this communication process with a CRPS patient that support a complete recovery trajectory for CRPS.

Since no data in any CRPS literature showed any strong effect for any intervention method, it is important not to ignore the relationships that do exist as these potentially provide a platform for future exploration. The questions that are illuminated as the research process evolves, raise possibilities about new or alternative ideas. These tentative ideas also provide the substance to support or alternatively, challenge what is applied in clinical practice and assumed to provide benefit.

The following Chapter 10 integrates the findings from the previous Chapters, the literature, and the previously suggested models or pathways in order to propose a tentative conceptual clinical model for physiotherapy CRPS management.

## CHAPTER TEN

### Development of a conceptual clinical model

#### 10.1 Introduction

Aspects of this Chapter have been published as [399] and can be found in Appendix A.

No evidence based, relevant clinical model was available for the physiotherapy management of CRPS when this project commenced. There are a number of possible reasons: the low prevalence of CRPS contributes to difficulty with research evidence; no accurate gold standard for diagnosis; uncertainty about a likely CRPS trajectory; weak evidence for risks or prognostic factors; controversy about physiotherapy management methods with pain modulation in juxtaposition with a pain exposure approach; and poor evidence for the current physiotherapy interventions applied in CRPS management for any method.

The historical account and evaluation outlined in Chapter 2 showed that all previous published models or pathways had not yet been validated. The expert panel's model proposed in 2002 [33] was challenged in 2009 as needing to be updated in the context of the current knowledge base and a call was made for a new model to be developed [107]. However, no such models have been forthcoming.

The observation of clinical practice across a region as shown with these results, revealed no strong evidence for any significant relationships with physiotherapy intervention methods and CRPS outcomes. Although this dashed the hope that a robust prospective approach may have provided some guidance about effective management, with evidence to support it, this finding is consistent with the literature reviews which reported that there were no specific interventions to have a strong predictive effect for a good outcome [71, 201, 311].

Despite this poor evidence, it has continued to be a consistent theme that physiotherapy is essential. The initial model in 1998 had a central focus of physiotherapy management [23]. In the previous Chapters the results showed a complete recovery for 24 (45%) participants; a better proportion of complete recovery for those with lower limb CRPS, but all the cohort showing significant improvement. The active ingredient of physiotherapy intervention was not found and due to ethical constraints, it was not possible to withhold treatment. It was also



not possible to determine those who had experienced a spontaneous recovery without physiotherapy treatment during their CRPS journey.

Since these data examined both upper and lower limb CRPS it is proposed that it is valid for both presentations. This Chapter presents a clinical conceptual model that seeks to: address the need identified in 2009; provide a holistic approach; be clinically relevant; assimilate the limited evidence; and incorporate the key features of previous models.

## **10.2 Method**

The method for developing this proposed conceptual model involved merging a proposal from: a) a Spearman correlation of these data which provided a summary of all the associations of variance together, for all continuous or categorical variables, with a complete recovery for CRPS; b) the limited evidence from the literature; c) the limited findings from these results in the previous Chapters; and d) incorporating the essence of the previous models.

## **10.3 Results**

### *a) Spearman correlation matrices and models*

A Spearman correlation matrix was computed to determine the relationships of variance between categorical and continuous variables, and complete recovery. The Spearman correlation assesses non-linear relationships with a significance of  $p \leq 0.05$  and provides a measure for the strength of this correlation. A stronger Spearman correlation is a numeral closer to 1, while a weaker correlation is closer to zero. A number closer to negative 1 shows the correlation coefficient to be a strong negative relationship.

This Spearman correlation matrix was also analysed for correlations between the TIP or TIF and their relationships with each other, and with complete recovery. Since this was a longitudinal study, the direction of effect with these correlations, between variables or the outcome, could be determined. These correlations could be in one direction, or could be bidirectional.

The Spearman correlations enabled the simultaneous evaluation of the association of all variables with a complete recovery. These data are shown in Table 10.1 with significant correlations showed in bold.

VARIABLE	Spearman Correlation coefficient with complete recovery	Spearman Correlation coefficient with TIP 6-week, weekly average	Spearman Correlation coefficient with TIF 6-week, weekly average
Age	-0.12	<b>-0.25*</b>	0.12
Gender, female	-0.19	-0.08	<b>-0.25*</b>
Time to commence physiotherapy	0.08	0.02	<b>-0.34*</b>
Time to diagnosis	0.16	-0.01	<b>-0.29*</b>
Time to Pain Specialist Doctor	-0.17	-0.21	<b>-0.28*</b>
Tampa Scale for Kinesiophobia	-0.02	<b>0.26*</b>	0.00
Health Anxiety Index	-0.06	<b>0.27*</b>	-0.16
Kessler 10	<b>-0.42*</b>	0.13	0.04
Eysenck Personality Questionnaire Extraversion	<b>0.47*</b>	-0.12	-0.17
Eysenck Personality Questionnaire Neuroticism	<b>-0.35*</b>	0.17	-0.11
Pain Rating Index (McGill Pain Questionnaire) Baseline	-0.21	-0.00	0.01
World Health Organisation Disability Assessment Schedule 2 Baseline	<b>-0.31*</b>	0.09	0.10
Homework weekly average 6 months	-0.22	-0.05	0.04
Homework daily average 6 months	-0.24	-0.14	0.01
Homework rating for pain relief 6 months	0.11	0.05	0.07
Panadol prescription	0.12	-0.06	0.10
Non-Steroidal Anti-inflammatory prescription	-0.09	-0.21	-0.04
TOTAL duration physio WEEKS	<b>-0.46*</b>	0.12	0.23
TOTAL physio Intensity N divided by weeks	0.09	0.07	<b>0.29*</b>
TIP 6-week interval, weekly average	-0.03	1.00	0.23

TIP weekly average over one year	0.12	<b>0.68*</b>	0.04
TIP 6-month interval, weekly average	-0.19	<b>0.57*</b>	0.06
TIF 6-week interval, weekly average	-0.22	0.23	1.00
TIF weekly average over one year	0.04	0.13	<b>0.59*</b>
TIF 6-month interval, weekly average	<b>-0.32*</b>	<b>0.27*</b>	<b>0.69*</b>
EDUC 6-week interval, weekly average	-0.03	<b>0.57*</b>	<b>0.60*</b>
EDUC weekly average over one year	<b>0.36*</b>	<b>0.24*</b>	<b>0.27*</b>
EDUC 6-month interval, weekly average	-0.12	<b>0.44*</b>	<b>0.43*</b>
TII 6-week interval, weekly average	-0.07	-0.15	<b>0.38*</b>
TII weekly average over one year	0.02	-0.13	<b>0.26*</b>
TII 6-month interval, weekly average	-0.09	-0.14	<b>0.28*</b>
Primary analgesia prescription yes	0.14	0.17	0.02
Prescription any secondary analgesia yes	0.14	0.17	0.02
Morphine derivatives prescription yes	0.25	-0.07	-0.07
Tricyclic prescription yes	0.03	0.15	0.11
Gabapentin or preGablin yes	<b>0.44*</b>	0.18	0.03
Psychological support yes	<b>-0.32*</b>	<b>0.27*</b>	0.01
POOL Physiotherapy intervention yes	0.13	<b>0.42*</b>	0.06
Graded Motor Imagery intervention yes	0.16	<b>0.38*</b>	-0.02
Categorised Education level	0.01	0.10	0.11
Ethnicity Māori yes	<b>-0.33*</b>	0.04	0.04
Acupuncture yes	0.24	-0.07	-0.23
SMT yes	-0.19	<b>0.37*</b>	-0.01

<b>Skin sensory changes Baseline yes</b>	-0.02	<b>0.29*</b>	0.12
<b>Complete recovery</b>	1.00	-0.03	-0.22

Significance\*  $p > 0.05$

TIP: Physiotherapy treatment interventions for pain modulation,

TIF: Physiotherapy treatment interventions for functional restoration,

TII: Physiotherapy treatment interventions for immobilisation,

EDUC: Physiotherapy treatment interventions for education.

*Table 10.1. Spearman correlation coefficient matrix: TIF and TIP 6-week, weekly averages and complete recovery.*

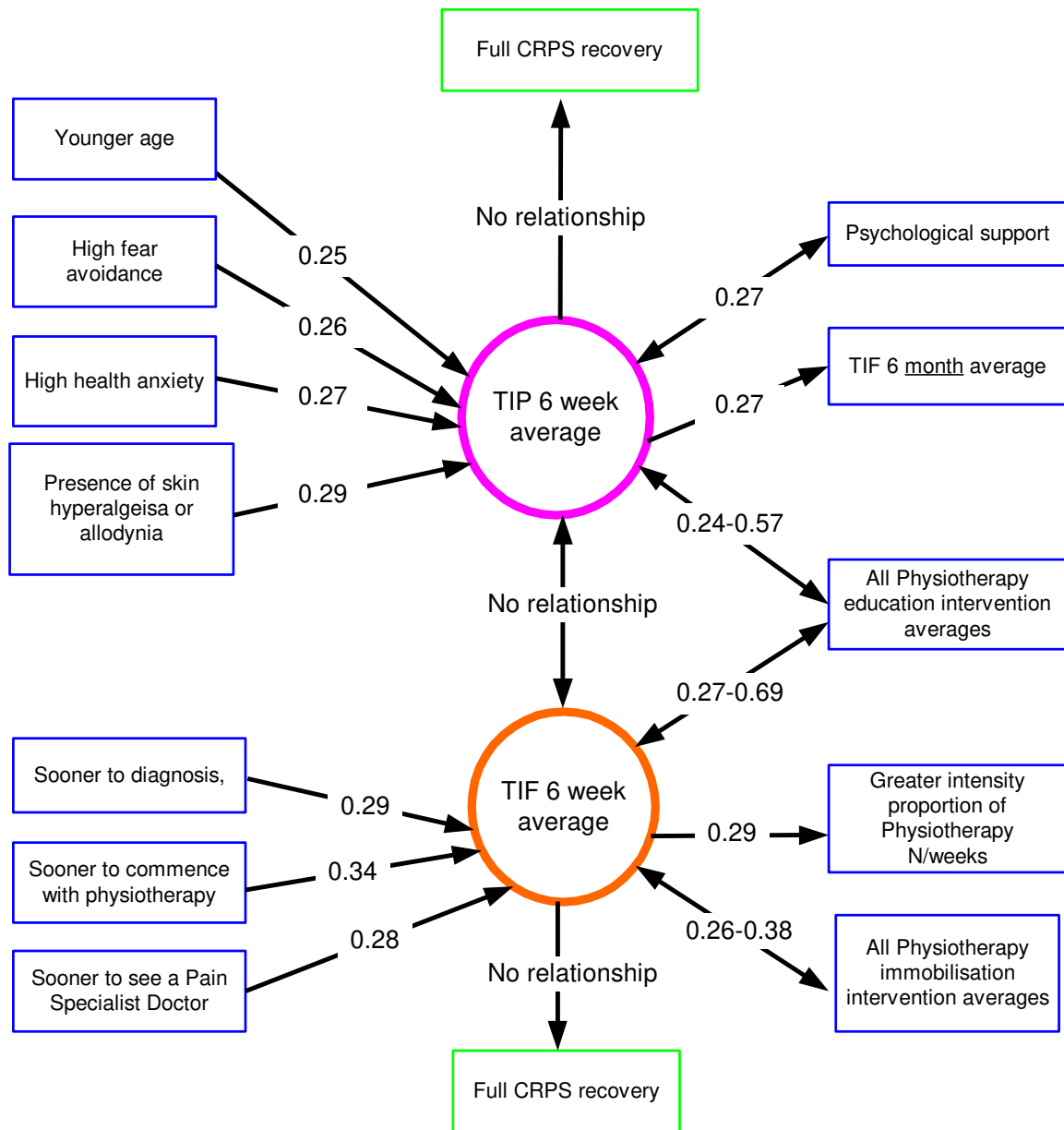
#### *The relationships of TIP and TIF with each other and complete CRPS recovery*

The significant TIP 6 week average had bidirectional associations with psychological support (0.27). Bidirectional in this context means that psychological support commences at the same time as physiotherapy or subsequently so its effect is potentially prospective and retrospective. The TIP 6-week average had an interactive relationship with all education intervention weekly averages: 6 weeks (0.57); 6 months (0.44); 1 year (0.24); and the TIF 6-month weekly average (0.27). It was determined by its relationships with higher health anxiety (0.27), higher fear avoidance (0.26), the presence of skin hyperalgesia or allodynia (0.29), and with a younger age (0.25).

The significant TIF 6-week average showed that it had an interactive association with all the educational physiotherapy intervention weekly averages: 6 weeks (0.60), 6 months (0.69), 1 year (0.27); with all the immobilisation intervention weekly averages: 6 weeks (0.38), 6 months (0.28), 1 year (0.26); and that it determined the greater intensity proportion of number of physio sessions divided by the number of weeks (0.29). This TIF 6-week average was associated with a shorter time to diagnosis (0.29), a shorter time to commence with physiotherapy (0.34), and a shorter time to have seen a Pain Medical Specialist Doctor (0.28).

The 6-week average used for each of these categories of intervention methods showed that neither TIP nor TIF had any relationship with complete recovery nor did they show any relationship with each other. It is interesting to note that the factors contributing to TIP are not the same as those for TIF. There is no commonality between factors other than education intervention. From this it is inferred that TIP and TIF are independent of each other and neither are associated with complete recovery.

The relationships for TIP and TIP with all categorical or continuous variables as well as with each other, and a CRPS complete recovery are shown with the arrow directions representing the directions of the associations, in Figure 10.1.



TIP: Physiotherapy treatment interventions for pain modulation,

TIF: Physiotherapy treatment interventions for functional restoration,

Figure 10.1. Spearman Correlation model for relationships between physiotherapy interventions TIP and TIF 6-week, weekly averages and full recovery,  $p < 0.05$ .

These results are interesting. Consider the mono-directional associations that contributed to TIP or TIF. For those situations where the treating Physiotherapist used pain modulation (TIP), there are a cluster of factors that preceded this intervention method. These factors, e.g.

high fear avoidance etc., may be broadly categorised as *personal distress factors*. It would appear that when a patient presented with these distress factors, the Physiotherapist made an effort to accommodate the pain in the treatment strategy, hence a choice to have used TIP.

This TIP also had a bidirectional relationship with psychological support. This meant that there were those who had already commenced their psychological support at baseline, while others had it introduced later. It would be considered plausible to infer, that these distress factors are associated with the need of psychological support in conjunction with their physiotherapy.

These personal distress factors did not precede the use of intervention for function (TIF). Likewise, the TIF factors did not precede TIP. Hence, these two intervention methods, TIP and TIF did not share the same preceding contributing factors. The only factor they shared in common was the education intervention which had a bidirectional association.

For the situations where functional interventions were used, a different cluster of factors were apparent. These were time based, where the time to diagnosis, commence with physiotherapy, and see a Pain Medical Specialist had been earlier, potentially without lengthy delays or difficulties around determining either diagnosis or management. It could be speculated that this shorter time provided clarity and reassurance so that distress factors were curtailed. The Physiotherapist may have been in a position to emphasise functional restoration, hence the choice to have used TIF.

Alternatively, it may also be speculated that TIF is associated with those patients who were more demanding, or perhaps even threatening, insisting on attention to their problems. Their distress or threat may have been alleviated with the prompt responses from all involved with their care, not only the treating Physiotherapist, and a focus on functional restoration ensued.

There is the possibility of a more positive alternative, and that is that the factors that precede TIF may reflect a situation where the patient is able to accept their diagnosis and make the necessary adjustment. Since education is a factor that is common to both TIF and TIP, it may be that these patients may have been able to embrace the education about their responsibility to take a proactive approach to their own self-management. The focus on function made sense to them.

*The relationships of continuous or categorical variables and a complete CRPS recovery*

As shown above neither TIP nor TIF 6-weekly averages were associated with a complete recovery. The significant Spearman correlation associations showed three groups of factors to be associated with a complete recovery. These were firstly baseline measure factors: better mental health (0.42); higher score of personality extraversion (0.47); a lower score of personality neuroticism (0.35); better functional ability and quality of life (0.31); and non-Māori ethnicity (0.36).

The second group of associations with a complete recovery were the physiotherapy intervention and were shown to be: a higher yearly weekly average of physiotherapy education intervention (0.36); a lower duration of weeks with physiotherapy care (0.46); and a lower intensity of 6-monthly treatment interventions for function (TIF), (0.32).

The third group were the other concurrent interventions with physiotherapy and were shown to be; no psychological support (0.32); and medical prescription of anticonvulsant medications (0.44). These associations are represented in Figure 10.2 with the arrows showing the direction of the association and the green dashed lines around each group of associations.

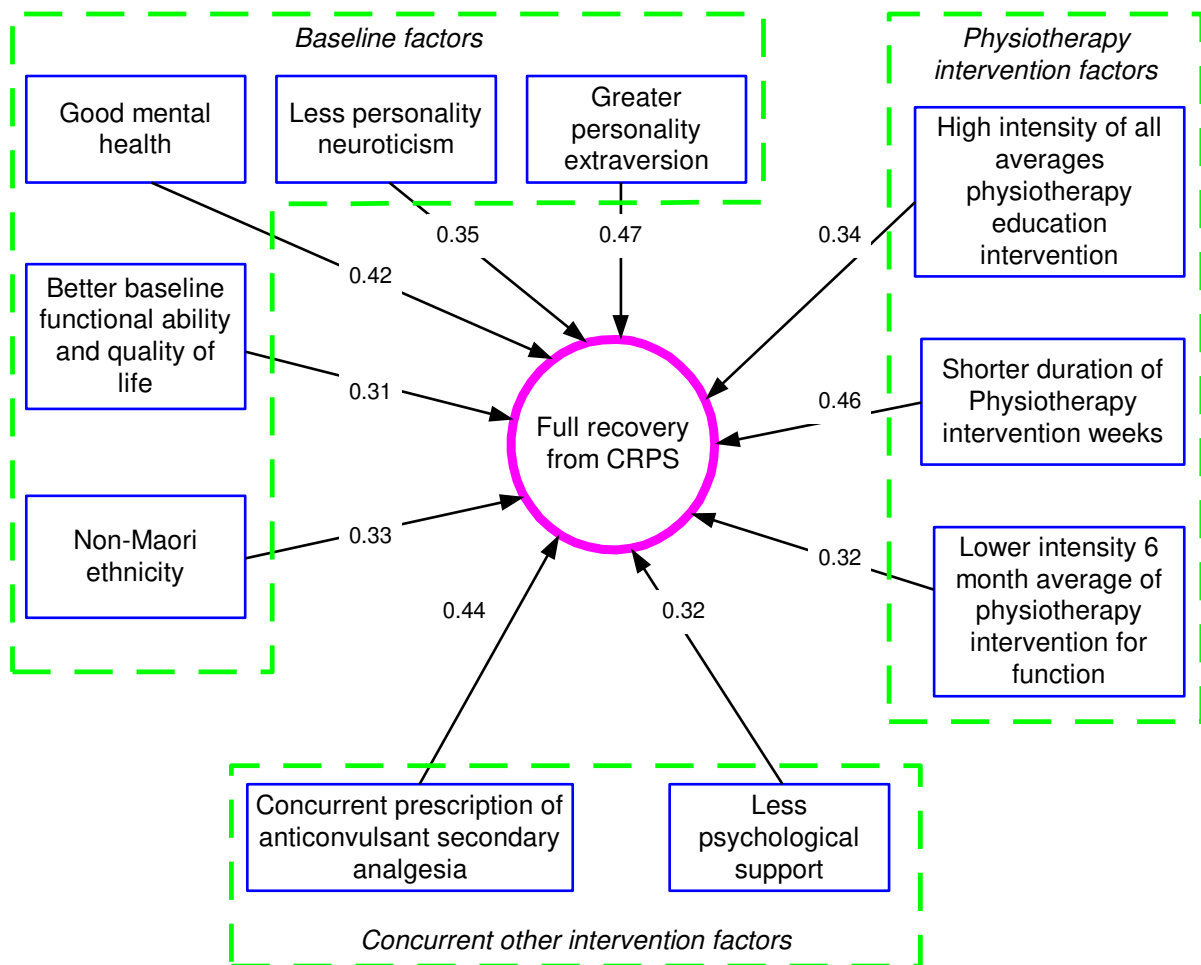


Figure 10.2. Model with Spearman correlation factors for complete CRPS recovery,  $p < 0.05$ .

There may be an interaction between the intervention and the baseline groups. The concurrent prescription of the secondary analgesia of the anti-convulsant group was shown to be the singular prescription to be associated with complete recovery despite that other prescriptions were also recorded with this cohort.

Those of non-Maori ethnicity showed disadvantage to this recovery for reasons unknown and it may be that cultural sensitivity for CRPS physiotherapy management needs further consideration. There may also be further sociological questions behind this finding.

These results showed that better baseline mental health, functional ability and quality of life preceded full recovery. These patients may have already been living with less CRPS related



disability. Hence, they may have been able to progress more rapidly and this is evident with a lower intensity of functional restoration interventions, and shorter duration of physiotherapy weeks. They may be more responsive to their education intervention and possibly their better mental health contributed to them to be open, flexible and receptive to their education intervention. Subsequently, they may have needed less psychological support.

Alternatively, an interpretation could be that the South Island Physiotherapists may show more confidence with management strategies, therapeutic relationships and certain patients' personalities. Those patients who have less CRPS related disability and also showed more extraverted traits achieved better outcomes.

It would also be plausible to infer that the paradigm of physiotherapy facilitates a complete recovery with those patients who may present with less pain related disability, versus those who present with greater needs are simply placed in a too hard basket. Hence, the above factors may be contributing to *intervention tolerance*.

*b) A summary of the literature towards a proposed conceptual model*

Chapter 2 showed that no proposed clinical models have been validated and all suggest a central focus with physiotherapy management in a step-wise approach. Medical and psychological support are suggested to be incorporated and the models are focused around the concept of optimising the patient outcomes. No models in the literature include the prevention of CRPS or the mental health and well-being of either the medical or allied health professional or the CRPS patient other than the therapeutic relationship being considered an essential ingredient. The literature also suggested limited evidence for both the pain modulation and pain exposure approaches.

It is plausible to assume that this dichotomy reflects that intervention tolerance is a factor to consider for CRPS physiotherapy intervention. The literature shows that there are CRPS patients who are able to tolerate intervention to restore function without analgesia through progressive loading with pain exposure; whilst the opposite is shown to be effective with intervention that does not provoke the pain and instead, the affected limb's cortical representation is re-organised, sensory-motor input is reconciled and tactile acuity is normalised so that tolerance for function is gradually facilitated.

*c) A summary of these data towards a proposed conceptual model*

The data from the previous Chapters show that over half of CRPS sufferers on the South Island will recover around 6 months with either a complete recovery, or significantly improved outcomes so that that discharge from physiotherapy ensues. Those who do not make a complete recovery still show significant improvement, but half the gains when compared with those who had complete recovery or were discharged by their treating physiotherapist. The interventions applied show that pain modulation was used more often in the first 6 weeks, whilst functional restoration interventions were used more often for the next 18 weeks.

When Physiotherapists were interviewed about their usual intervention methods, education was their priority intervention. However, their clinical notes did not reflect this. It may be that education was being applied, but simply not recorded. It is plausible to assume the combination of pain modulation in the first six weeks, coupled with functional restoration later, and supplemented with education at all stages contributed to the positive outcomes reflected with these results.

*d) A summary of the essence of previous models towards a proposed conceptual model*

All previous models described in Chapter 2 consistently suggested that physiotherapy is the central key in the process to improve a CRPS patient's outcome. Earlier models did not accommodate a fluctuating trajectory with flare ups of pain or deteriorating function and the 2002 model recognised this and attempted to accommodate it [33].

The essence of all previous models was a step-wise approach towards optimising an outcome for function and pain reduction as well as the ability of the CRPS patient to be able to cope. The models suggested that more invasive medical intervention was necessary if the step-wise approach did not obtain optimal function or improved pain control.

## **10.4 A proposed conceptual clinical model for CRPS management**

The candidate proposes a clinical conceptual model for the physiotherapy management of CRPS. This is tentatively designed to have a patient centred focus with a rotational, concurrent approach which either gains or slows momentum accordingly and appropriately with physiotherapy intervention, unlike the step wise process shown in previous models.

This proposed conceptual model has attempted to address the missing ingredients of the previous models to include a) prevention of CRPS and b) the mental health for both patient and clinician alike. This is because effective prevention was reported as a realistic option [76, 311] and the recent adoption that medical professionals also promote their own mental health and well-being [299] as an urgent issue needing to be addressed [300-302] and likewise for a CRPS patient [370].

The proposed model is developed further around these two principles (*securing foundations*) and is represented with four clinical intervention approaches (*pillars*), and the application of four physiotherapy intervention methods (*mainstays*). Each description in detail follows and the representation is shown in Figure 10.3.

#### **10.4.1 The two foundations**

The conceptual model is proposed to be secured on the two foundations. The first is *the prevention of CRPS* and the other *the promotion of good mental health*. The reason for this is that if CRPS can be prevented, then the management will not be necessary, hence it is a highest priority. A study showed an eight-step fracture clinic algorithm to be effective at reducing the incidence of CRPS to zero [76]. This finding supported the first concept of the prevention of CRPS, as a realistic objective to fulfil. It would indeed be a radical health transformation if the elusive problems of CRPS could be prevented from ever gaining a foothold by applying effective prevention strategies in all health facilities.

The second securing and foundation pillar is the promotion of well-being and good mental health. Mental health is defined by the WHO as the ability to realise one's full potential, to be able to cope with everyday life stresses, and to work productively and fruitfully, as well as make a positive contributions to the local or broader community [400]. This would apply to both clinician and patient. CRPS is not necessarily a straightforward condition to manage [143]. These results showed that poorer mental health was a potential contributor to a poorer outcome, albeit with a weak effect (Chapter 7).

#### **10.4.2 The four pillars**

The four pillars are summarised as: 1) physiotherapy effective therapeutic relationship; 2) tailored physiotherapy intervention; 3) medical involvement; and 4) psychological support.

The concept of the four pillars suggests that CRPS management involves physiotherapy intervention as the central feature with two separate complementary pillars, alongside the

medical involvement of prescriptions or procedures and psychological support. The centrality of the physiotherapy contribution is also a fundamental concept in all the previous models shown in Chapter 2. The literature also showed that not all CRPS patients will adhere to or find benefit from their medical intervention and evidence for its effect on positive CRPS outcomes is also moderate at best. Not all CRPS patients require psychological support and neither is there strong evidence for psychological interventions that predict a good CRPS outcome.

*Pillar one: An effective therapeutic relationship*

Pillar one is an effective therapeutic relationship is proposed to involve four components: agreement on mutual goals; therapist listening skills; competence and communication; and motivation and encouragement. These ingredients are supported in the literature [295]. The effective therapeutic relationship is one where both parties can agree on goals, and there is clarity of information from both parties. Patients need to feel comfortable about the information. It has been suggested that it is important for the information and mutual goals be valued in the same way between the Physiotherapist and the patient [293]. Furthermore, the literature showed that active listening skills, health provider competence with motivation, and encouragement are important ingredients for an effective therapeutic relationship [401].

Previous Chapters showed that it could be plausible that a positive therapeutic relationship was intertwined with a better CRPS outcome, and furthermore, that medical prescriptions were variables that contributed to the complete recovery or significant improvement. How the therapeutic relationship, medical, psychological or physiotherapy support interacted was not determined, but it was shown that the combination contributed to the positive outcome for the 45% of the cohort who showed complete recovery.

These results showed no intervention method to be superior to another. The Spearman correlations here, in Figure 12.1 show that neither the weekly averages of TIF or TIP, as individual intervention methods, have a positive relationship with complete recovery from CRPS. Hence, it would be credible to suggest that the positive changes to CRPS outcomes are associated with a *combination* of ingredients with physiotherapy, medical and psychological intervention and that for each participant, there was a different, tailored approach. Since the satisfaction with care questionnaire results in Chapter 6 show overwhelming satisfaction, it appears that an effective therapeutic relationship was in place

within the cohort studied here. In other countries, contexts or cultures this may be different and may require further evaluation.

*Pillar two: Individually tailored physiotherapy*

Pillar two is the individually tailored physiotherapy: a customised management plan with application of multiple complementing intervention methods. The four components of this individually tailored method are: 1) that it is systematic and be in accordance with competent physiotherapy standards of practice; 2) that it is multimodal, i.e. several different interventions; 3) that intervention methods are applied concurrently; 4) and that assessment of progress is a continuous activity where management is adapted rather than adhering to a fixed strategy.

These cohort results, the Spearman correlation, and the literature showed several interventions that potentially contributed to recovery. The interventions aimed at reducing pain are proposed to include education and the development of resilience, as excessive focus on pain at the expense of function is potentially detrimental as suggested by the PEXP advocates [115]. Likewise, interventions that severely heighten pain and potentially aggravate the central or peripheral sensitisation mechanisms, were the reason pain modulation interventions like mirror exercises and GMI were established [148, 402], and were shown to be alternatives to facilitate movement and activity without the distress associated with incapacitating pain.

The two other pillars suggested are the *Medical involvement* and the *Psychologist's support*, since these are shown with these data and the literature to be involved with CRPS management. Neither are mandatory, but both are recommended when indicated.

*Pillar three: Medical care*

The pillar of Medical care contributes with the prescription of appropriate primary or secondary analgesics helping to avoid the use of strong opioids [311]. A referral to a Specialist Pain Medicine Physician may also result in the prescription of further secondary analgesics, peripheral, plexus and neuraxial neural blockade that would facilitate the physiotherapy mainstay of exercise intervention [33]. A referral for peripheral or spinal cord neuromodulation may be necessary for recalcitrant CRPS cases [403]. A patient with mild CRPS may not need input from a Specialist Pain Medicine Physician [311], and these results

showed that the prescription of anticonvulsant medications may be beneficial to complete recovery.

#### *Pillar four: Psychological support*

The Psychologist's input helps the patient to understand their thoughts, feelings and behaviours associated with their pain related disability, and to discover psychological flexibility that enables and cultivates effective coping strategies [241]. These results in earlier chapters showed that absence of psychological support was not a hindrance to complete recovery. However, these data with the Spearman correlations show a possible interactive effect with other variables and psychological support with a CRPS recovery. These potential interactive effects were beyond the scope of this study. The support from the Clinical Psychologist with assistance about understanding central mechanisms of pain and facilitating resilience are tentatively suggested to be ingredients of this conceptual model and are also supported with the historical account of previous pathways outlined in Chapter 2.

#### **10.4.3 The four physiotherapy intervention mainstays**

This conceptual model proposes that these four pillars described above support four prescribed physiotherapy interventions. Four physiotherapy intervention *mainstays* are proposed as the central feature for intervention. These are proposed to progress in a cycle emphasising that they have a congruent effect on one another. The intention is to facilitate momentum for recovery. This recovery becomes an evolving cycle accommodating flare ups rather than a linear trajectory.

The proposed four mainstays are: *pain modulation intervention; education about intervention; functional intervention, and tolerance for prescribed intervention*. These four mainstays are proposed since these results showed that TIP and TIF were the larger proportion of modalities applied. Hence, pain modulation is suggested to form the starting point. Education about the exercise follows with functional exercise promoted in the context of the tolerance for the exercise intervention as essential. This is especially important since the Geneva Convention states that it is a basic human right not to experience pain [404]. Furthermore, the literature reported that the intervention methods aimed to managing aberrant cortical changes associated with CRPS were potentially aggravated by exercise or intervention methods that heightened the pain experience [140]. Although this has been

challenged by the pain exposure supporters [117], the evidence for this challenge is also weak.

The autonomic signs and symptoms can potentially be intimidating for some CRPS patients. The reassurance provided by competent health providers via education is suggested to be important about what CRPS is and what it is not. The literature, as outlined in Chapter 2, showed that education was an important component for effective health care, and also showed that myths about CRPS existed. Since CRPS has a low prevalence, it may possibly not be commonly understood by the public or even by those who are employed in health care. Education was also shown with these data to be the most important intervention that South Island Physiotherapists considered using most often, in the survey for usual CRPS clinical practice described in Chapter 3.

It is proposed that a *revolving cycle* follows for these interventions, at a tempo that the patient tolerates, and in an evolving recovery process. The concept proposes that if progress towards the goals is not made, or that there are flare ups of the pain experience, that either a slower or a quicker revolving of the cycle should ensue. The slower tempo could indicate the potential for psychological or medical involvement. This is also in accordance with the first proposed pathway in 1998 as outlined in the literature of Chapter 2.

These proposed mainstays of effective physiotherapy intervention are:

- 1) *Pain modulation intervention* emphasises a purpose about the ability to change the pain experience to less intensity or less interfering as a reduced sensory or emotional experience. It includes: graded motor imagery; mirror exercises; pool exercises; transcutaneous electrical nerve stimulation; cognitive behavioural therapy; acceptance and commitment to therapy; problem solving; relaxation and breathing; sensory–motor training including tactile acuity training, sensory mapping, and discrimination and desensitising; lymphoedema management; ergonomic modifiers; and pain contingent homework as prescribed.
- 2) *Education about intervention* emphasises the purpose, meaning or understanding of the exercise which is directed to the mutually collaborated patient-centred goals. Education may also extend to information about the diagnosis, trajectory, outcomes or understanding of CRPS.
- 3) *Functional restoration intervention* emphasises the purpose of functional gain toward normal activity associated with patient centred activities of daily living or exercise. It

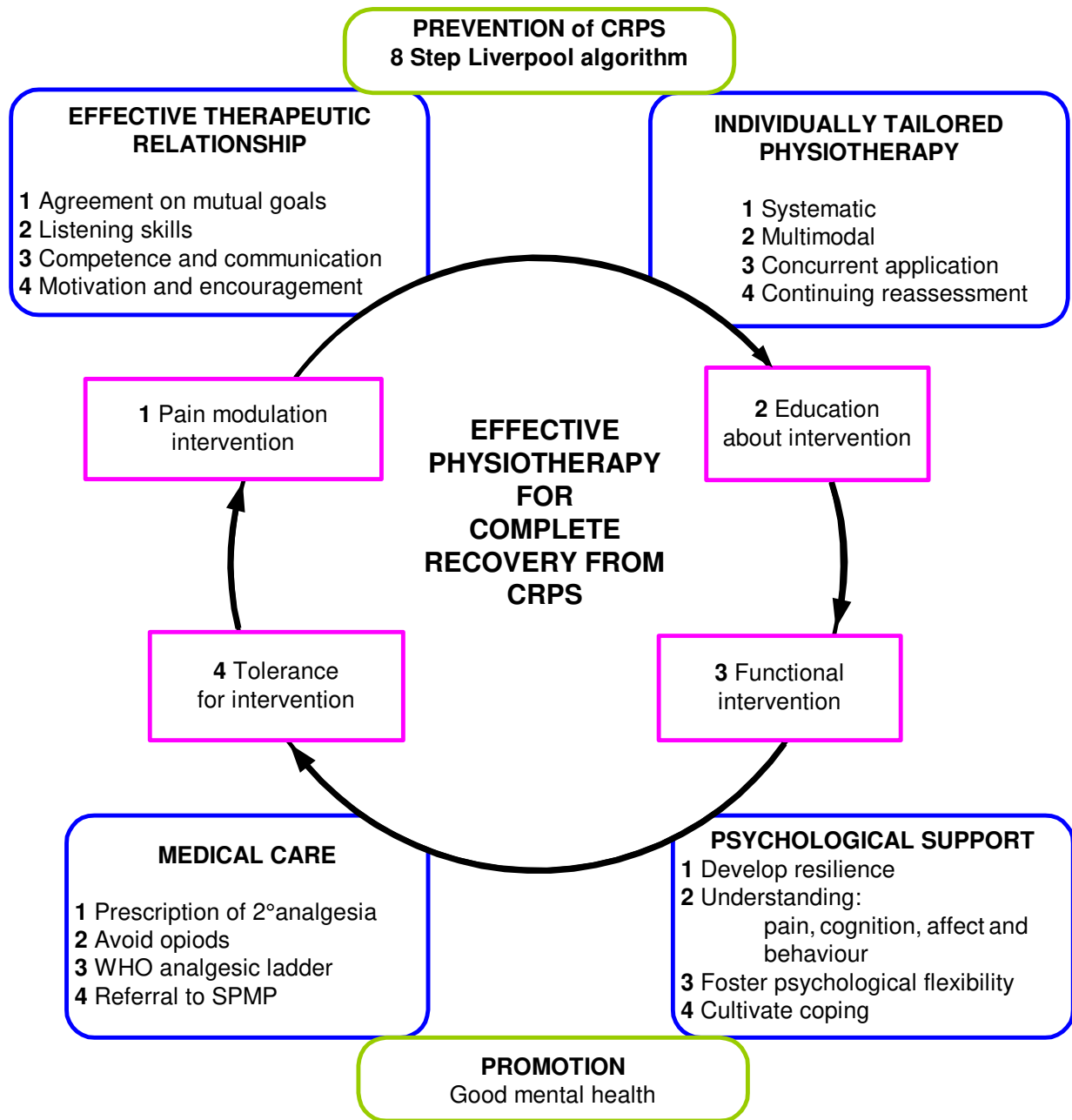
includes exercises, such as active, passive, resisted, balance and proprioceptive land-based exercise, together with exercise for lymphoedema management and time contingent homework as prescribed.

- 4) *Tolerance for intervention* emphasises the prescription of intervention intensity as strictly within the CRPS patient's physical, emotional and cognitive tolerance ability. Importantly, it is flexible to accommodate different tolerance abilities. Some may tolerate different exercise intervention modalities (intensity, duration, frequency, acceleration or deceleration) better than others, so that pain exposure or graded exposure are applied appropriately as tolerated.

It is also suggested that if an intervention helps to reduce pain, adherence by the patient will potentially be facilitated towards positive reinforcement with the immediate reward of pain reduction, and thus contribute towards functional gains. As functional ability improves, it is proposed that confidence with exercise develops which provides the necessary tolerance for the further progression towards the mutually agreed rehabilitation goals. It is shown in the literature that beliefs affect functional ability [405] and that confidence is intertwined with this relationship.

This proposed conceptual model is represented in Figure 10.3.





*Figure 10.3. A proposed conceptual model of effective physiotherapy for complete recovery from CRPS with four pillars, four revolving physiotherapy mainstays secured on a foundation of prevention and the promotion of good mental health.*

## 10.5 Discussion

There are no validated clinical models in the literature to show a reliable pathway guaranteeing an effective recovery with CRPS. An array of medical, psychological and physiotherapy intervention methods show weak benefit and the biopsychosocial model is suggested but there has been no RCT to date to validate it. The historical account showed models or algorithms with the central focus on physiotherapy management.

The above proposed conceptual model offers a tentative contribution to the broader knowledge for CRPS physiotherapy management as it integrates the literature evidence with these cohort data as well as addressing previously missed concepts. The model also considers both clinician as well as patient in the context of the more recent ethical challenge of shared decision making with patient centred management [406], which aligns with current competencies [312]. The concept addresses the prevention of CRPS, as reported to reduce the incidence of CRPS with distal radial fractures [76].

The conceptual model proposes that important factors are mental health or well-being, quality of life and interpersonal communication styles. This was supported by the literature [293, 295] as well as recent ethical requirements [397]. Hence, this model incorporates the components of mental health, well-being, quality of life and interpersonal communication styles with the focus of physiotherapy towards an effective therapeutic relationship, ongoing communication and reassessment around mutually agreed goals.

The candidate suggests from the Spearman correlation and logistic regression analyses that physiotherapy interventions for pain (TIP) and function (TIF) each serve separate purposes; that they complimentary; and that furthermore they are ineffective without each other. It is proposed that the complete recovery was facilitated by both intervention categories. It is also conjectured to make clinical sense in the context of the therapeutic relationship, that outcomes for functional gain and pain resolution would involve both pain modulation and functional restoration and that they are mutually inclusive for the management of CRPS.

Since CRPS patients may interact with several Medical or Allied Health Professionals it is also proposed that it may be important that this therapeutic relationship be upheld by all involved in the team who provide care, as a valuable contribution towards an effective recovery. The proposed conceptual model for physiotherapy management for CRPS suggests that there is flexibility with the evolving interventions for the treating Physiotherapist as well

as the individually tailored approach about which interventions to apply. By implication there would be flexibility in the interaction with medical or psychological support.

The strengths of this model are the integration of these current results with the existing body of knowledge, and the development of holistic framework to apply in physiotherapy clinical practice. Another strength the inclusion of factors that are important in recent competency and ethical requirements and clinician and patient mental health. This has not been achieved before.

Limitation of this model are that there is no strong evidence to support all aspects of it and that it has not yet been validated. It could be argued that the stepwise algorithm is more effective than a concurrent cycle of interventions with a variable tempo of momentum. The model also does not include those who might make a spontaneous recovery from CRPS without ever having engaged with physiotherapy treatment.

Furthermore, although similar to these Spearman correlations, the data in the previous chapters do show significance, but with weak effect sizes. The model does not include the patient's perspective about CRPS management in general, but did include how the patients viewed their satisfaction with care. These are considered two separate issues.

## **10.6 Summary**

This model proposes a holistic approach to facilitate a complete CRPS recovery. The proposal has at its centre, four treatment interventions which are surrounded by four principles, each with four components and secured with two foundations. These foundations are that the prevention CRPS is seen as a priority, and the promotion of good mental health and well-being for all clinicians involved and their CRPS patients. These are novel concepts not included in previous models. This proposed model integrated the limited evidence and the historical account to ensure that the intent and spirit of the past suggestions were also incorporated.

# CHAPTER ELEVEN

## Discussion

### 11.1 Synopsis

The purpose of this project was to answer questions, in a clinical setting, about outcomes and the associations that contributed to effective physiotherapy management of CRPS across a region. These questions were formulated into aims which established the project structure designed to answer them. These aims were achieved. An account of each Chapter follows.

Chapter 1 described the background to the syndrome and brought to attention the poor evidence for understanding and physiotherapy management for CRPS. The project aims were to provide information that would be applicable to everyday physiotherapy clinical practice and: described the characteristics of CRPS patients living in the South Island of New Zealand; observed changes over time/natural history; documented and categorised physiotherapy interventional methods; documented physiotherapy beliefs; measured and identified associations with patient outcomes; determined the risks for the onset of CRPS; explored the Māori journey; as well as to suggest a conceptual clinical model for physiotherapy CRPS management.

Chapter 2 expounded the literature and reported the lack of understanding or evidence across all aspects of CRPS. The diagnosis, pathophysiology, trajectory, intervention, and management showed inconclusive evidence and is complicated by CRPS low prevalence. An historical account of proposed models for physiotherapy management showed pathways that had neither evidence nor validation. A call was made in 2009 for an evidence-based model to be recommended [107].

Chapter 3 reported the beliefs that Physiotherapists across the South Island had about their CRPS management as well as documented what they reported for their usual practice. The beliefs showed division that were speculated to also reflect the dichotomy seen in the literature about two opposing methods for physiotherapy management. One method proposed that exacerbating the pain may be detrimental [119], while the other method proposed that the attention to accommodate the pain facilitated disuse with functional deterioration [116, 117]. Hence, it was conjectured that Physiotherapists were divided about how much pain they perceived was inevitable with CRPS management; and whether pain was indicated to be

provoked with their intervention, and if pain was provoked, to what extent it was necessary so that a good outcome could be expected.

Chapter 4 described the method to examine the research questions and proposed four hypotheses to be explored in order to fulfil the aims. This project sought to accomplish the aims by using clinical observation, in a prospective method to assess CRPS management and respective outcomes across the South Island region. Robust statistical research methods included a significance of  $p < 0.05$  applied to student-t tests, ANOVA, Mann Whitney U tests and logistic regression. Confidence intervals were applied to reduce errors associated with confounding. Analyses were proposed as the opportunity to view the status quo of current physiotherapy practice and to offer evidence about its effect on CRPS recovery over one year for this region. The outcome measures were obtained through independent telephone interviews following baseline when physiotherapy commenced at the 6-week, 6-month and 1-year intervals.

Chapter 5 illustrates the baseline characteristics for this cohort. The characteristics showed a cohort that closely matched the two other epidemiological studies available [69, 70]. Baseline variables also showed similarity to other studies for pain [89, 114, 141, 148]. Fear of movement was shown to be greater [255] and, conversely, lower when compared with other studies [100]. The upper limb disability scores were higher than other reported studies [196, 377, 378]. No literature was available for comparison of the lower limb function, personality, health anxiety and quality of life.

Chapter 6 reported the five aspects of the physiotherapy explored and the medical and psychology interventions as applied by Practitioners across the South Island for CRPS. The differences between those who received this adjunct support were evaluated so that the effect of potential confounding variables could be accounted for with the logistic regression analysis which followed later in Chapter 8. Physiotherapy intervention was evaluated for duration, intensity, prescribed homework adherence, and satisfaction of care. Interventions applied were categorised and weekly averages were calculated for each interval. The greatest proportion of interventions were shown to be exercise for functional restoration followed closely by interventions at reducing the experience of pain. Satisfaction with care was overwhelming positive for all of the nine-item Diehl-and-Deyo questions despite that prescribed homework was rated by most as, seldom, rarely, or never helpful for pain reduction. Fifty nine percent of the cohort were discharged around 6 months after starting their physiotherapy care.

Chapter 7 provided the account for changes of outcome measures over the year, and the analysis to determine significance. All participants showed significant improvement and a positive association was shown between the completion of physiotherapy intervention with outcomes vs. those who self-discharged with less contact time and intervention. Common factors were conjectured as having been ingredients which, together with the interaction of Clinician's expertise and the specific factors of the best available evidence, resulted in this more effective outcome [243, 294, 295, 383, 398]. Hence the null hypothesis for Hypothesis test 1.1 was rejected. This hypothesis was that physiotherapy positively contributes to CRPS recovery.

Chapter 8 outlined the associations that continuous and categorical factors had on the participant's outcome measures with a complete recovery. Complete recovery was defined as a zero PRI pain score from their MPQ-SF, and full restoration of their function on the WHODAS score following physiotherapy. Confounding was shown to potentially influence the effect of diagnosis timing on complete recovery for Hypothesis test 1.2, so that there was the possibility of an incorrect refute of the null hypothesis. This hypothesis was that an earlier diagnosis contributes to better CRPS outcomes. It was plausible to imply that the tailored physiotherapy applied by skilled Physiotherapists may have contributed to a complete recovery, regardless of how long the time was to diagnosis.

Strong effects were shown for complete recovery with the higher scores for extraversion and the concurrent prescription of the anticonvulsant medication group; while weak effects were shown for lower scores of neuroticism personality trait, better scores for baseline mental health, higher scores for better function and quality of life. Reverse causality was also shown to interact with concurrent psychological support.

Chapter 9 presented the associations between outcomes one year later with the physiotherapy intensity, the categories of intervention modalities applied, and the prescribed homework adherence. These data revealed that no intervention method was associated with a complete recovery. The Hypothesis 2.1 tested if treatment interventions for pain modulation (TIP) were associated with a positive outcome and showed no effect. Hence, for this hypothesis, the null hypothesis was not rejected. The Hypothesis 2.2 tested if different treatment interventions had different effects on CRPS and this hypothesis was tentatively supported. The candidate conjectured that a complete recovery from CRPS involved different intervention methods or in different combinations to achieve a complete recovery when it was obtained. However, this support was weak since there was no randomisation or control group.

Chapter 10 proposed a clinical conceptual model for physiotherapy management. This was to respond to a call made earlier in the literature about the lack of a suggested or validated physiotherapy management model [107]. Since these data examined both upper and lower limb CRPS, it was implied that it may be valid for both presentations. This proposed clinical conceptual model was integrated from the limited evidence in the literature; a Spearman correlation to summarise relationships from these data; the essence of previous models or pathways outlined in the literature. It was recognised that the proposed model is yet to be validated and that the evidence to support it is weak.

## **11.2 Deliberation**

It is suggested that the use of education as an intervention by Physiotherapists (as acquired through the initial survey), was actually the case. This was despite education being seldom recorded in the clinical records. It was categorised as only 6.2% of all interventions applied. This was in stark contrast to Physiotherapists' report in the initial survey that it was mostly used, 83%. The effect of this specific variable as an ingredient in the recovery was not able to be determined; but by implication it needed to be recognised as an active ingredient. This recognition was important as education about exercise was proposed as a component of the conceptual clinical model since it is recognised in the literature as important [243, 293-297] and in physiotherapy registration competencies [312].

It was also speculated that since these data showed a higher score for baseline upper limb disability with the Quick DASH scores when compared with other studies, that this would possibly explain their poorer outcomes when compared with the lower-limb affected group. The reasons for this cohort showing these higher baseline scores is not known. This upper limb group was larger than those affected by a lower limb CRPS (49% vs.17%), and these data showed that 38% of this upper limb affected group achieved complete recovery. This is in contrast to the greater percentage of 63% of those with the lower limb affected CRPS who made a complete recovery.

It is also plausible to imply that physiotherapy management is an effective ingredient the complete recovery from CRPS. Furthermore, this is consistent with the recent literature which reported that although a complete understanding or evidence about intervention methods for CRPS are lacking, outcomes have become more optimistic than those of the past [91, 240]. However, it is not apparent if this optimism applies to either upper or lower-limb

affected CRPS patients. These data supported that outcomes are more optimistic for lower-limb affected CRPS patients.

Intervention methods applied were categorised in order to provide a structure around which they could be assessed according to the two opposing approaches viz. PEXP or PM for their effect on outcomes. This was important as it helped to verify and compare the purpose of an intervention method, rather than simply being documented or assessed as an intervention for its own sake. It was also speculated from these data that the possibility of the physiotherapy management across the South Island with the multimodal approach of 20.4% TIF; 15.9% TIP; 6.2% Educ; 8.0% Pass; and 3.5% TII was effective. Furthermore, it was suggested that the combination of the greater proportions of TIP and TIF (34.5%) may have contributed to recovery. This was including the implication above that education had also taken place in conjunction with these interventions, despite not being documented accurately.

This suggestion was speculative as the data showed no strong evidence consistent with the literature for both the PM or PEXP methods. PM prevents the pain escalating, so that functional activity or exercise was not inhibited by the unbearable flare up of the pain associated with usual exercise or with PEXP [100, 110, 120, 121, 407]. PEXP focussed on functional goals and not on fear avoidance [115-117]. There was dichotomy in the literature showing that persistent pain can be aggravated by activation due to temporal summation [408]. On the other hand, the population who exercised regularly experienced less persistent pain than those who did not [409, 410]. Hence, the candidate would suggest that both PM or PEXP may have an appropriate place to be used in conjunction in the physiotherapy management for CRPS.

These data also showed that 59% had been discharged at 6 months. The gains made with functional ability at the 6-month interval were maintained at the 1-year interval, except that the upper limb function had decreased slightly when compared with lower limb function. The lower limb function was shown to continue to improve over the last 6-month period. The reasons for these differences were unable to be determined and may be worth pursuing.

These data showed accordance with other studies where recovery or improvement can occur within 6 months [88, 89, 91], and that the greatest intensity of weekly averages for attendance and intervention methods was in the first 6 weeks. The reliability and validity to the outcomes were potentially strengthened as independent interviewing reduced the risk of bias associated with outcome measure assessment and its report [72]. The outcome measures used were



chosen as most relevant for clinical practice. At the time of starting this project, the CRPS severity score had not yet been published [343]. These data about physiotherapy intervention also supported the recent literature to show that CRPS outcomes can be positive [91].

Another aim for this project was to explore the Māori narrative. It had been reported in other health conditions in New Zealand that Māori have poorer life expectancy with dialysis treatment [411] and poorer outcomes to aortic aneurysm repairs [412]. However, this ethnic disparity is not apparent with cancer survival rates [413]. These are the first data to evaluate the Māori who have a recent CRPS. The Spearman correlation showed effect for their poorer outcome, but logistic regression did not. Hence the effect was weak and the sample extremely small with  $N = 6$  (9%). It is suggested that this merits further investigation.

These data showed no significant relationship between diagnosis timing and the time to starting physiotherapy (after injury), to be associated with outcomes. The literature suggests weak evidence that early diagnosis was associated with better outcomes [91, 94-96, 414]. Furthermore that detection of early warning signs significantly reduced the incidence of CRPS [76]. It could be postulated that physiotherapy across this region was effective with the tailored and creative approach used for each individual patient. These data reflected a highly variable approach to intervention methods, to intensity and to duration of physiotherapy and that a delayed diagnosis or time to commence with physiotherapy was not detrimental to recovery.

However, these suggestions are speculative. As this sample was small, the relationship around both the diagnosis timing and time to commence with physiotherapy may not have been possible to be detected accurately. It is recognised with CRPS research that since prevalence is low [415], it was extremely difficult to arrange large samples for longitudinal studies, due to time constraints as well as logistics. The literature remains inconclusive with no strong evidence for factors that contribute to a poor outcome [93, 255].

These results showed that higher personality extraversion was associated with a better outcome with a strong effect. This personality trait was reported in mental health research as a positive attribute towards a better health outcome or a protective factor [359, 360]. It was also worthwhile noting that patients with chronic regional pain (not CRPS) are shown to have normal personality traits when compared with those who suffer widespread body pain [356]. The results of the current study possibly reflected that the interaction of personality traits with

CRPS or with the therapeutic relationship may have been influencing factors, as reported in other health studies [243, 293-297].

Since present results reflected an overwhelming positive satisfaction with care across all nine items of the DDS questionnaire, it was difficult to determine any individual effect. It was plausible to suggest that this positive affirmation of physiotherapy care reflected amicable therapeutic relationships for all participants. However, since most publications assessed this relationship from the patient's perspective [298], it was not possible with these data to extract how patient extraversion potentially may have interacted with the treating Physiotherapist's perspective of the therapeutic relationship.

This therapeutic relationship was documented in the earliest model, as the first important ingredient in the algorithm of CRPS management [23] with the Physiotherapist at its centre. However, this construct was not assessed in either of the two systematic reviews [107, 108] on the evidence for interventions for CRPS. This is a limitation, as the first stepwise algorithm for CRPS management stated that to establish a therapeutic relationship was the first and foremost priority [23]. Furthermore, this concept has also been raised in the literature by the PEXP supporters [115]. Here those authors noted that a particular Physiotherapist facilitated good outcomes with an approach of intervention that ignored the complaints from the patients about pain. At the same time, the approach did not seem to perplex, disrupt or cause the patients' distress to escalate. Patients neither formally complained nor self-discharged. In fact, these patients showed outstanding progress and good outcomes.

In a similar trend, those same authors and others [141, 416] also noted that the GMI original publications involved a single clinician in a single setting. Subsequent RCT's that showed evidence for GMI, were also limited by involving a single research group [107]. The other GMI publications involving multi-centre or several clinicians showed that GMI is not effective [141]. The involvement of the positive association of GMI with a single clinician in a single setting is suggested to have an influence on the positive outcome which is not replicated in larger settings. It had been poorly understood and documented in CRPS research that a smaller sub-group do not improve as much as the others [44, 161, 417, 418], and it is possibly that this improvement may be a consequence of the effective single therapeutic relationship. Perhaps this is reflected with the positive effect reported in the single setting GMI trials.

Hence, the therapeutic relationship was proposed to be included as a pillar in the conceptual model. This is in keeping with all the previous pathways or models. This model also attempted to integrate a holistic approach to include the prevention of CRPS and the mental health or well-being of both practitioner and patient alike as an integral component, since the promotion of clinician mental health was shown to be an urgent issue to address [300, 301]. The complementary nature of the clinical management with prevention and mental health had not been suggested before and were proposed as being important to be included.

This proposed conceptual model also offered flexibility for the treating Physiotherapist to use an individually tailored approach. This, alongside the therapeutic relationship, complemented the cycle of: pain modulation exercise; education about exercise; functional restoring exercise, and tolerance for exercise.

These four interventions were suggested to be a cycle which may gain momentum in order to facilitate a complete recovery, and are integrated with the four pillars around it. This was suggested in order to provide an integrated and evolving approach of a multi-modal management that may accommodate inevitable flare ups and the fluctuating nature of the recovery trajectory. This is in contrast to the stepwise sequential algorithm.

### **11.3 Implications for practitioners**

It is proposed that these results showed categories of physiotherapy interventions each to have served specific, separate purposes which complemented one another, and were ineffective without one another. Robust analysis of this cohort showed no strong predictive effect for any intervention method and all outcome measures showed significant improvement.

This implied that a competent Physiotherapist has an array of intervention method choices to apply. These results did not suggest that an array of different and potentially opposing categories of intervention methods should simply be applied on an ad hoc basis, or in a sequential stepwise manner. What these data did suggest was an integrated approach with careful and thorough assessment of the context for each patient's presentation. Patients with higher fear avoidance and health anxiety displayed a greater intensity of intervention methods associated with TIP. The opposite is shown for health anxiety with a greater intensity of intervention methods associated with TIF. Neither TIP nor TIF intensity were associated with a complete recovery. It suggested that the combination of both categories provides a successful ingredient for a complete recovery. Furthermore, these two main ingredients were

supplemented with the smaller components of education, treatment interventions for immobilisation, and passive interventions.

Another aspect that was suggested as important for physiotherapy was the therapeutic relationship. It was outlined above as important aspect for clinical practice with New Zealand Physiotherapy Board competency standards [312]. The therapeutic relationship is suggested to be a significant factor contributing to a complete recovery. The candidate suggests the reason for this is that a therapeutic relationship is a bi-directional, dynamic, and also possibly a fragile, dynamic entity. Both the patient and the Physiotherapist should be 100% involved, and not 50:50 each; the Physiotherapist should communicate understanding of what CRPS is and what it is not, with competent explanations. Appropriate concurrent intervention methods should be applied, according to how the patient interacted with their Physiotherapist. This creates trust, compliance and open, flexible communication and these principles are in keeping with the research evidence about an effective therapeutic relationship for other conditions [243, 293-297]. These present results showed that a complete recovery was possible for 45%, regardless of how long it took to diagnose, or how long the duration of the CRPS had been and that satisfaction of care was overwhelmingly positive.

To start physiotherapy management with a patient with a delayed diagnosis of CRPS may not be in vain. These data supported showed that a diagnosis of greater than 4 months was not associated with a poorer outcome which is consistent with some literature [92, 93]. It is suggested that it is important to provide a message of hope with support for those who suffer a long duration of CRPS or protracted delays to their diagnosis being made. This message was also a component of the principles of trust for an effective therapeutic relationship [243].

It has been suggested that it was also important for Physiotherapists to understand the role of the Family Doctor, the Specialist Pain Medicine Physician and the Psychologist [233, 236, 249, 419]. Their contribution to the complete recovery for CRPS was shown in these present results and the strong effect was showed with the concurrent prescription of the anticonvulsant medications. The proposed conceptual model suggested that these two roles are important pillars alongside the tailored physiotherapy and therapeutic relationship.

The therapeutic relationship was also suggested not to be exclusively between a Physiotherapist and patient, but to also include the Family Doctor, Specialist Pain Medicine Physician or Clinical Psychologist. It is proposed that a competent Physiotherapist would be

able to integrate effective communication between all members of the team involved, as well as facilitate appropriate referral.

#### **11.4 Strengths**

There are multiple strengths with this project. As a prospective, observational, longitudinal study across a region, it was the first contribution about the CRPS trajectory and outcomes over a year, associated with the categories of physiotherapy intervention methods used in current clinical practice. Analysis of clinical records obtained over the year provided a foundation of evidence about the status quo, and how this affected outcomes.

The longitudinal, observational, prospective research design used with this project was useful in providing the evidence for the *direction of effect* found within the data. This would be unable to be provided by the cross-sectional method which can identify a relationship, but not the direction of this relationship's effect [405]. A time period of 1 year to observe the trajectory for a CRPS was also considered an important strength. It was necessary to determine how the effect of physiotherapy management potentially continued beyond the initial treatment phase over a full year, beyond earlier discharge [72]. This is in contrast to studies which only describe the outcome at discharge and are not able to provide evidence about how any benefit was maintained.

Furthermore, this longitudinal design was applied across a region. It was important to evaluate a region, as the potential bias to local prevalence is reduced. This reduced the risk of bias associated with either the localised clinical diagnostic or practice methods or with CRPS prevalence [72].

Potential bias was addressed with the use of an independent interviewer. Reliability was improved with strict adherence to the Budapest criteria for the diagnosis of CRPS for the inclusion criteria, the statistical approach of using the significance,  $p < 0.05$ , as well as logistic regression with confidence intervals. This robust method contributed to the reliability and validity of the findings. The interference with usual clinical practice was minimised with the candidate giving clear instructions to all Physiotherapists, such as: 'Please continue with your CRPS management as usual; the independent interviewer was impartial about the physiotherapy applied, has a doctorate herself and was familiar with research processes'. Furthermore, it was an explicit priority for the candidate not to inconvenience or influence the usual everyday clinical practice of Physiotherapists across the region.

This sample matched well with another epidemiological study and another prospective study in New Zealand [69, 70]. The application of robust statistical analysis confirmed valid and reliable evidence [255]. The use of self-reporting questionnaires is also reported to be a valid measure [420].

An additional strength was the potential education about Budapest CRPS diagnostic criteria for practicing Physiotherapists to enable more accurate diagnosis to take place beyond the time frame for this project. Furthermore, the platform for the potential narrative and outcomes of Māori patients with CRPS to be explored is tentatively laid. This small sub-group have no literature to date about their CRPS experiences, trajectories or outcomes.

The aims of the project were achieved. The project has contributed to both physiotherapy and to clinical practice for CRPS management as well as to the international published literature. These strengths lay a firm foundation for the further debate and research about physiotherapy management for CRPS.

## **11.5 Limitations**

A prospective study can be thwart with problems like participant recruitment or subsequent attrition. There was the relatively small sample size of Physiotherapists, with potential bias being represented by the 57% response rate for the questions (that reported their usual clinical practice and beliefs about what was important for CRPS management). The influence of reverse causality may have occurred. This is when the direction of cause and effect may have been misidentified, where another third variable becomes causally associated with an outcome/dependent variable but is not causally associated with the intervention/independent variable. This may have arisen in the analysis with concurrent psychological support to be associated with a poorer CRPS outcome. Since this research was not a clinical trial, intention to treat was not possible to determine.

CRPS research was recognised as difficult due to its low prevalence in any population [203, 421]. Longitudinal attrition contributed to 13 (19%) CRPS participants lost to the follow-up interviews 1 year later. Despite the full cohort of physiotherapy intervention data being available, this study's findings need to be interpreted in the context of its limitations. The complete data set with its sample size of 66 participants, despite being similar to some studies, is considered small. It was not possible to determine if other potential participants declined to participate with the recruitment process. Physiotherapists were requested personally by the candidate to report a declined participant on their invitation, no such reports

were received. The sample size may also have been reduced by Physiotherapists forgetting to invite their CRPS patients to participate, or feeling vulnerable to having their clinical records scrutinised.

Another issue contributing to potential weakness is the representation of this cohort as a sample of the population with a new CRPS diagnosis from December 2013-2017. The enquiry to the relevant national health departments showed that no database exists for the record of all new patients listed with a CRPS diagnosis in New Zealand. A document provided by the predominant health insurer showed no record of new diagnoses for CRPS being kept each year and that it was described with a diagnosis of Sudeck's atrophy, a diagnostic term outdated by more than 50 years. Hence, it was not possible to determine what proportion of the CRPS population of the South Island of New Zealand was represented by this cohort.

Furthermore, it was not possible to determine those CRPS patients who did not present to physiotherapy, or presented to other health care providers, or who simply self-managed their problem without interacting with any health service. The first epidemiological publication on CRPS noted that 93% of the CRPS population attended physiotherapy and 87% reported about physiotherapy being efficacious [69]. The effect of attending physiotherapy, or not, is yet to be explained [69, 70, 74, 231, 422, 423].

Since there are no data about the beliefs for physiotherapy CRPS management, a weakness of this study is the novel questions about beliefs for the management of CRPS that have been raised have no valid or reliable tools to be measured with.

Another weakness of this study was that it could also be argued that the categories of physiotherapy interventions may have been allotted differently with alternative results. There was no validated or reliable tool for accurately measuring frequencies or categories of the physiotherapy interventions. A potential weakness of this study was also the use of the Likert scale for measuring the frequency of the physiotherapy interventions as this is not formally validated.

As already noted, education as an intervention was seldom recorded; it may be that other interventions were not recorded as well, or that their details were not specific enough. This was not unusual in busy clinical practice; it was also a recognised issue in clinical research [424]. This was especially so in this project where the candidate had to rely on clinicians to provide information and obtain their patients' consent. At the same time, the candidate could

not interfere in order not to influence usual clinical practice or the information provided to the patient.

It was beyond the scope of this paper to explore the effect of referral to a Specialist Pain Medicine Physician which was applied for one third of the cohort. Prescription dose titrations, adherence, compliance, or the decline of the offers for the referral to a Specialist Pain Medicine Physician were not possible to determine in this study and contributed to another limitation. Literature shows secondary analgesic medication to have a moderate effect for CRPS outcomes [425]. Medical interventions for CRPS can have questionable evidence [108].

It was beyond the scope of this project to explore the clinical presentation of each participant when discharged by the treating Physiotherapist. The assumption that discharge meant a satisfactory result may not have been the case.

The exploratory nature of this project without the structure of a clinical trial which would include randomisation and a control group may have led to potential bias which is addressed in the next section.

### **11.6 Identifying bias with the Quality in Prognostic study (QUIP) tool**

It is reported that clinical trial prognostic studies may have 6 areas of potential bias [426]. These are 1) representative study participation, 2) participant attrition, 3) appropriate prognostic measurement, 4) appropriate outcome measurement, 5) potential confounding, and 6) statistical approach. This project was not designed as a clinical trial as this was not possible to implement and was not the scope of the aims. The primary aim was evaluate the associations between physiotherapy interventions and CRPS patients' outcomes.

Nonetheless, it is important to identify potential bias. It was determined for this project that:

- 1) There was a low risk of bias with representative study participation, as participants were included with Budapest criteria for their CRPS diagnosis and all participating Physiotherapists were trained by the researcher about these criteria as shown in Chapter 4.
- 2) There was a low risk of bias with participant attrition as those who were lost to follow up 1 year later showed no statistically significant difference to baseline variables than those who participated as shown in Chapter 5.



- 3) There was a moderate risk of bias with the categories of physiotherapy intervention. These could be categorised differently as is addressed earlier in this Chapter.
- 4) There was a low risk of bias with the outcome measurement instruments as these were validated and reliable questionnaires.
- 5) There was a high risk of potential confounding due to the lack of randomisation or a control group. This is identified in Chapter 8.
- 6) There was a low risk of bias with statistical approach attributed to the strict adherence of associations with the complete recovery being supported by logistic regression analysis.

### **11.7 Implications for future research**

The willingness of the South Island Physiotherapists to engage with this project with their referrals and the consent process was encouraging. There has been no regional study to evaluate physiotherapy for CRPS with a longitudinal study before. However, the refusal of two managers in one District Health Board was discouraging to the candidate as outlined in Chapter 4. Upon further reflection, it is suggested that these negative responses potentially reflect that physiotherapy research was not active in this particular health board and that it was not encouraged, in fact, it was actively discouraged. It was not possible to investigate the reasons for this and it was prudent for the candidate to comply and not interfere or question this refusal. It stands to reason that an important area for research would be the barriers associated with District Health Board's ability to support their staff to engage in the research to generate evidence-based practice and evaluate their clinical practice.

There are many other areas shown with this project that potentially would benefit from further research. Since usual or standard physiotherapy is often not described with clinical trials, future research about regional standard physiotherapy practice for CRPS management would be helpful. Potentially this may contribute to cluster randomised control trial research method to evaluate the effect of physiotherapy intervention methods.

There is also potential benefit from further investigation to explore the differences in beliefs about what is important for the management of CRPS. This would be for both physiotherapists and CRPS patients alike, and how these beliefs interact with intervention methods or outcomes. These data illuminated differences between physiotherapists who saw CRPS patients more often than those who did not. The possible factors influencing this may

provide further insight about ingredients that potentially interact with the therapeutic relationship, intervention methods used or the patient outcomes.

The possible factors of the therapeutic relationship that are specific to assist with CRPS recovery have not yet been reported [427, 428]. This project was exclusively patient focused with validated and reliable outcome measures showing significant improvement, despite timing of diagnosis or methods of intervention. It is suggested that what is effective for CRPS may be reflected in the interaction between Physiotherapist and patient, especially around the construct of personality extraversion trait. It could be that the paradigm of physiotherapy mediates recovery for extraversion personality traits to the detriment of those without this trait. This warrants further scrutiny.

It is also suggested that further research could investigate the qualities of the Physiotherapist in terms of confidence, experience, competence, knowledge and method of tailored intervention that is associated with good outcomes. Hence, it is suggested that there may be a need to be a change in the focus of what is being measured from exclusively patient focussed to also include being therapist focussed. This may provide further insight into potential interactive effects between factors affecting the therapist or patient, and how factors potentially change over time.

In a therapeutic relationship, education is considered an essential ingredient [429] and is also important for the management of persistent pain [261]. Perhaps the good outcomes seen across the year with this data were due to the diligent education provided by the Physiotherapists. Spearman correlation showed similar associations of 6-week, weekly averages of TIP and TIF with all education weekly averages. Physiotherapists were possibly taking for granted a normal part of their responsibility despite that they may not have actually documented it in the clinical record for their patients. Another question is that when education is documented, to what extent is this documentation an important aspect of the therapeutic relationship? Would it provide the evidence for the positive change for an outcome? In these data the effect of education was not strong enough to be detected with logistic regression (possibly since it was not recorded), rather than being an intervention with no significant effect. This needs further investigation and also in the context of the therapeutic relationship.

It would be useful to investigate the effect of prescribed homework on outcomes, the therapeutic relationship and the CRPS trajectory. These results showed that despite

homework being rated poorly to relieve pain, satisfaction of care was consistently positive. The reasons for this would be potentially useful to offer scope for further understanding about the interactive effects of homework for pain relief, adherence, outcomes, and satisfaction.

Future research to determine interactive effects and the ingredients of psychological support concurrent with physiotherapy for CRPS is necessary. This is since these results showed with logistic regression analysis that psychological support was associated with a poorer CRPS recovery; however, psychological support was potentially interacting with other variables to show an alternative and interactive result or was affected by reverse causality.

On the other hand, perhaps there is a subgroup of CRPS patients who are going to recover spontaneously without any intervention. Intervening is speculated to possibly contribute to a poorer recovery for such a group if patient autonomy is not upheld [406]. It is important to note that the first epidemiological study showed that a small group recovered well without any intervention [69]. Future research about the factors that contribute to spontaneous recovery is an area that has no research and would potentially be beneficial to the broader understanding about CRPS management.

Future research also needs to evaluate the effect of physiotherapy across other regions and it is suggested that this would mean data collection for a larger cohort, over longer periods, with larger sample sizes. Potentially, cluster randomisation across a region may be possible to implement. Data possibly needs to be collected across other large regions or with a high population densities and in many countries. Multi-centre studies across many regions can make use of the global technology with the Internet and World Wide Web to access CRPS participants or access to physiotherapy clinical records. Larger sample sizes potentially contribute to better validity and reliability; especially as the effect of a single clinician is eliminated.

Furthermore, the interaction of international collaboration with local everyday clinical practice provides a stage for stronger relationships between researchers and clinicians which would prove mutually beneficial. Further exploration about the relationship between CRPS outcomes with culture and ethnic groups, in particular, the narrative for the Māori in keeping with the Treaty of Waitangi [37, 38, 430] is important for New Zealand.

As these data relate to CRPS of less than 1-year duration, it was not possible to examine recalcitrant CRPS or CRPS of long duration. Both these conditions have been shown in the literature to be managed effectively with graded exposure *in vivo* and spinal cord stimulation,

respectively [100, 101, 431]. The longer duration of CRPS outcomes with or without physiotherapy would benefit from further investigation.

It is also proposed that future research tests all the aspects of the tentatively suggested conceptual model for the physiotherapy management of CRPS. This model was a tentative proposal, and as such, there is no other current model for comparison to be tested.

# CHAPTER TWELVE

## Conclusions

The purpose of this project was to determine outcomes and relationships associated with physiotherapy interventional methods used for CRPS patients in a clinical setting across the region of the South Island of New Zealand.

These aims were to:

- Document and categorise the physiotherapy beliefs and usual practice in the treatment of CRPS;
- describe the characteristics of CRPS patients living in the South Island of New Zealand;
- determine the risks for the onset of CRPS in the literature;
- measure patient outcomes and changes over time/natural history for one year after commencing physiotherapy for patients presenting to physiotherapy;
- document and categorise the physiotherapy interventional methods received;
- identify potential predictors of outcomes;
- investigate the efficacy of the current physiotherapy intervention applied;
- and propose a conceptual model for physiotherapy CRPS management.

The longitudinal, observational method over one year following a CRPS diagnosis provided the findings for evidence and direction of effect. The aims were achieved by the strict inclusion of the Budapest criteria for the diagnosis of CRPS to improve reliability.

A robust statistical approach was used with evidence found through Spearman correlation, and logistic regression applied to a significance of  $p < 0.05$ . The outcomes for CRPS patients attending outpatient physiotherapy clinics across the entire South Island of New Zealand between December 2013 and 2017 were examined for the relationships between outcomes and the intervention methods applied by Physiotherapists.

The findings were explored with 75 CRPS patients who signed consent to be interviewed and had their physiotherapy clinical records accessed. Other characteristics were 52 females and 14 males who participated with ages ranging from 11 to 77 years (mean 46 years) of predominantly New Zealand Europeans; 57 (86%) had a CRPS Type 1 and 9 (14%) had a CRPS Type 2 diagnosis; fractures were the inciting event for 28 (42%); followed by soft

tissue injury 24 (36%), and surgery 14 (21%); the upper limb was more frequently affected than the lower limb with 49 (74%), and 17 (26%). An equal proportion had their diagnosis made within 1 month, or within 2-4 months. A third of participants attended physiotherapy within 1-2 months following inciting injury.

This cohort's characteristics closely resembled epidemiological data from other large studies. Thirteen participants were lost to follow up at the final interview for outcome measures one year later. However, a full data set for all physiotherapy interventions was obtained. Potential bias was reduced through the use of an independent interviewer for outcome measures. Outcome measures were obtained through telephonic interview when commencing physiotherapy, at 6 weeks, at 6 months and at 1 year later.

All participants showed significant improvement in their outcomes measures of pain, function, and quality of life. Satisfaction with physiotherapy care was overwhelmingly positive. Twenty-four (45%) participants showed a complete recovery with complete resolution from pain, and with full restoration of function within the year. Physiotherapy interventions were categorised into: treatment interventions for pain modulation; function; immobilisation; passive movements; and education. They demonstrated a high level of variability across all dependent continuous or categorical variables. Physiotherapy had a median of 16 contact sessions (IQR= 9–33) over a period close to 6 months (IQR= 3-9). Using logistic regression multivariate analysis, it was shown that complete recovery was not predicted by: time to diagnosis; time to the commencement of physiotherapy; baseline variables; psychological interventions; physiotherapy interventions (method, category, or intensity). Complete recovery was associated with the concurrent prescription of the secondary analgesia anti-convulsant medication group and the extraversion personality trait

Four hypotheses were tested. The primary Hypothesis 1 that physiotherapy management positively affected outcomes in CRPS was accepted. The primary Hypothesis 2, an early diagnosis was not found to positively affect the outcomes for CRPS, and the null hypothesis not rejected. The secondary objective 1 that physiotherapy intervention specifically aimed at cortical process positively affected the outcomes in CRPS was shown to be untrue and the null hypothesis not rejected. The secondary objective 2 that treatment interventions have dissimilar effects on CRPS outcomes was accepted.

These data were further scrutinised using Spearman correlations. A proposed conceptual clinical model was developed by integrating the current limited evidence in the literature with

these cohort's data and the intent of previously published models or pathways. This model proposed two securing foundations; the prevention of CRPS, and the mental health of both the clinician and patient alike. These foundations then integrated with four pillars: the effective therapeutic relationship; individually tailored physiotherapy, medical and psychological support. Four physiotherapy interventions revolved to facilitate recovery: pain modulation intervention; education about intervention; functional restoring intervention, and tolerance for intervention as a suggested pathway to a complete recovery for CRPS. Future research is needed to validate this proposed conceptual clinical model.

Future research is suggested to include other regional prospective studies which interview the treating Physiotherapist, evaluate of the beliefs that patients and clinicians have, how these beliefs may change over time and how beliefs about CRPS management interact with interventions and outcomes. Large international collaborations or cluster randomised controlled trials may be necessary for the larger sample sizes required to establish more robust evidence about effective interventions and factors that predict a complete recovery.

In conclusion, this project's aims were achieved. The findings were disseminated through conference presentations and publications in local and international settings. The novel contributions to the broader body of knowledge were:

- the description of CRPS patients for the South Island of New Zealand and their trajectory with the associated outcomes;
- the first regional prospective study of standard physiotherapy management for CRPS with the direction for the effect for intervention;
- the account of the status quo of current physiotherapy practice on the South Island of New Zealand;
- the outcomes for Māori CRPS patients were identified;
- evidence that physiotherapy interventions as whole may be associated with a complete CRPS recovery;
- showing that no particular physiotherapy intervention method was more effective;
- that diagnosis timing was not associated with complete recovery with this regional practice;
- that the personality extraversion trait has a strong effect with a complete recovery;
- that a concurrent prescription of the anticonvulsant group medication has a strong effect on a complete recovery;

- and a clinical conceptual model was proposed which also incorporated the current ethical and competency requirements and the essence of previous models or pathways.

The challenges did not prevent the achievement of the aims. These difficulties were the low prevalence of CRPS, participant attrition, the widespread South Island region with its geographical challenges of steep mountain ranges and long travelling distances, and the lengthy process of arranging locality authorisation from each of the four South Island District Health Boards. The successful achievement of these aims was considered not to be an end in itself, but rather another golden thread in the broader international tapestry towards a better clinical understanding about the physiotherapy management for CRPS.

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# Appendix A

## PUBLICATIONS

### Peer reviewed publications:

1. Pons, T., Shipton, E.A., Williman, J., and Mulder, R.T., *Potential Risk Factors for the Onset of Complex Regional Pain Syndrome Type 1: A Systematic Literature Review*. *Anesthesiology Research and Practice*, 2015. **2015**(956539): p. 1-15.
2. Pons, T. and Shipton, E.A., *Physiotherapy and the management of complex regional pain syndrome*. *Pain Management*, 2016. **6**(6): p. 515-518.  
<http://www.futuremedicine.com/doi/full/10.2217/pmt-2016-0037>
3. Pons, T., Shipton, E.A., and Mulder, R., *Beliefs and Clinical Practice for Complex Regional Pain Syndrome (CRPS) Managed by Physiotherapists on the South Island of New Zealand*. *International Journal of Clinical Medicine*, 2017. **8**: p. 42-54.
4. Pons, T., Shipton, E.A., Williman, J., and Mulder, R., *Physiotherapy interventions and the outcomes for Complex Regional Pain Syndrome (CRPS) Type 1 on the South Island of New Zealand – a longitudinal, prospective case series*. *The Open Pain Journal*, 2017. **10**: p. 5-13.
5. Pons T, Shipton EA, Williman J, Mulder RT. *A proposed clinical conceptual model for the physiotherapy management of Complex Regional Pain Syndrome (CRPS)*. *Musculoskeletal Science and Practice* 2018; 38(December):15-22.

### Publications in submission to peer reviewed journals:

1. Pons, T., Shipton, E.A., Williman, J., and Mulder, R., *Standard Physiotherapy for Complex Regional Pain Syndrome (CRPS): ingredients for recovery; a prospective cohort, longitudinal study*.

**Poster presentations to local and international conferences:**

1. Poster: Potential Risk Factors for the Onset of Complex Regional Pain Syndrome Type 1: A Systematic Literature Review. *41<sup>st</sup> Annual New Zealand Pain Society Scientific meeting*. April 2016. New Plymouth.
2. Poster: Physiotherapy management for Complex Regional Pain Syndrome (CRPS) on the South Island of New Zealand – a 6 month case series. *37<sup>th</sup> Annual Australian combined Society Scientific meeting*. April 2017. Adelaide.
3. Poster: Recovery for Complex Regional Pain Syndrome (CRPS) with Physiotherapy across the South Island region of New Zealand. *43<sup>rd</sup> Annual New Zealand Pain and Australian combined Society Scientific meeting*. April 2018. Sydney.
4. Poster: How Physiotherapists manage Complex Regional Pain Syndrome (CRPS) across the South Island region of New Zealand. *43<sup>rd</sup> Annual New Zealand Pain and Australian combined Society Scientific meeting*. April 2018. Sydney.



## Review Article

# Potential Risk Factors for the Onset of Complex Regional Pain Syndrome Type 1: A Systematic Literature Review

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Anaesthetists in the acute and chronic pain teams are often involved in treating Complex Regional Pain Syndromes. Current literature about the risk factors for the onset of Complex Regional Pain Syndrome Type 1 (CRPS 1) remains sparse. This syndrome has a low prevalence, a highly variable presentation, and no gold standard for diagnosis. In the research setting, the pathogenesis of the syndrome continues to be elusive. There is a growing body of literature that addresses efficacy of a wide range of interventions as well as the likely mechanisms that contribute to the onset of CRPS 1. The objective for this systematic search of the literature focuses on determining the potential risk factors for the onset of CRPS 1. Eligible articles were analysed, dated 1996 to April 2014, and potential risk factors for the onset of CRPS 1 were identified from 10 prospective and 6 retrospective studies. Potential risk factors for the onset of CRPS 1 were found to include being female, particularly postmenopausal female, ankle dislocation or intra-articular fracture, immobilisation, and a report of higher than usual levels of pain in the early phases of trauma. It is not possible to draw definite conclusions as this evidence is heterogeneous and of mixed quality, relevance, and weighting strength against bias and has not been confirmed across multiple trials or in homogenous studies.

## 1. Introduction

There is a growing body of literature addressing a variety of disorders known as Complex Regional Pain Syndrome (CRPS). It is a condition that presents with a pain experience that is severe and disproportionate to the inciting event and is accompanied by highly variable signs and symptoms of inflammatory, sensory, autonomic, trophic, or motor features. Anaesthetists in the acute and chronic pain teams are often involved in treating Complex Regional Pain Syndromes. The onset of CRPS can follow injuries ranging from minor injuries to fracture(s), from lesions of the central nervous system, or from surgery [1–3]. Its prevalence is low, ranging from 5.46 to 26.2 per 100 000 [4, 5]. This low prevalence has led to difficulty in research where robust statistical analysis necessitates larger sample sizes [6, 7].

Furthermore, CRPS nomenclature continues to be debated and remains controversial [8–11]. Research had shown that this condition is not wholly a problem of the sympathetic nervous system. The old terms “reflex sympathetic dystrophy” and “causalgia” needed to be changed [12]. In 1994, the committee for taxonomy of the International Association for the Study of Pain (IASP) identified specific diagnostic criteria for this syndrome that were termed the IASP criteria. This IASP committee changed the name to Complex Regional Pain Syndrome or CRPS. The term CRPS Type 1 (CRPS 1) applies, if there is no nerve damage, or CRPS Type II, if the nerve is physically and permanently damaged, and this nomenclature replaced the terms “reflex sympathetic dystrophy” and “causalgia,” respectively [13]. Other diagnostic criteria developed were the Veldman [14] and Harden/Bruehl [15] criteria that

continue to be used in clinical practice and research. The Harden/Bruehl criteria became known as “The Budapest Criteria” with minor modifications. Though published in an IASP-sanctioned book, the Harden/Bruehl criteria have not been officially endorsed by the IASP. The “Budapest Criteria” are used in clinical diagnosis. Here a report of at least one symptom in 3 or 4 categories (sensory, vasomotor, sudomotor/oedema, motor/trophic) with at least one sign at time of evaluation in 2 or more of the categories (sensory, vasomotor, sudomotor/oedema, motor/trophic) confirms a clinical CRPS diagnosis. There must be no other diagnosis that better explains the signs and symptoms. Budapest Clinical Criteria have retained sensitivity almost identical to the IASP criteria but with much improved specificity.

In the “Budapest Research Criteria,” diagnostic decision rule is at least one symptom in all four symptom categories and at least one sign (observed at evaluation) in two or more sign categories. The intent of the Budapest Research Criteria was to maximize specificity (minimize false positives) at the expense of sensitivity. They have a high specificity but a low sensitivity [16, 17]. This systematic review explores the literature since 1999. It therefore includes a level of variation for diagnostic criteria.

CRPS 1 is considered by most to be overdiagnosed [6, 18, 19]. There are a few, however, who still consider it underdiagnosed [20]. The precise pathophysiological mechanisms and predictive factors underlying CRPS 1 or subsets of CRPS 1 remain unknown [6, 21–23]. A standard diagnostic test is unavailable and the absence of a gold standard makes the validation of diagnostic criteria difficult [6, 24, 25]. Effective treatment strategies (in both the research and clinical fields) have moderate evidence [26–29]. A variety of medical and physiotherapy interventions and a multidisciplinary approach to the management of CRPS 1 continue to be widely used [23, 30, 31]. These factors contribute to the difficulty in determining potential risk factors for CRPS 1 in a reliable and statistically valid way.

There has been no systematic review of risk factors which may contribute to the onset of CRPS 1. This is the first systematic review to address factors posing as possible risk factors for the onset of CRPS 1. This paper selects from the current literature to systematically describe factors which expose a potential risk factor for a possible relationship to the onset of CRPS 1. This paper defines a risk factor as a factor contributing to a likely association of the onset of CRPS 1. This association is not necessarily causal.

## 2. Materials and Methods

**2.1. Study Selection.** Key words for CRPS (such as diagnosis, epidemiology, aetiology, genetics, history, pathophysiology, rehabilitation, risks, fractures, osteoporosis, or predictors) were combined in searches of Web of Science and OVID Medline for articles dated 1996 to April 2014. All abstracts were screened. Inclusion criteria for data extraction were articles written in English with reference to risks or predictors associated with the onset of CRPS 1. Exclusion criteria included articles written in other languages or no mention of CRPS 1 risks for either onset or outcomes or prognosis. A

TABLE 1: Search terms for Web of Science CRPS 1 risks.

Database	Search statement (1996 to April 2014)	Results
Web of Science	CRPS and risks	128

TABLE 2: Search terms for OVID Medline(R) CRPS 1 risks.

Number	Search statement	Results
1	OVID Medline(R) < 1996 to April 2014 Complex Regional Pain Syndromes (diagnosis, epidemiology, aetiology, genetics, history, physiopathology, and rehabilitation)	617
1	OVID Medline(R) < 1996 to April 2014 *Complex Regional Pain Syndromes/ep, et (Epidemiology, Aetiology)	104
2	crps.tw.	1122
3	Complex Regional Pain Syndrome* .tw.	1515
4	1 or 2 or 3	1823
5	*Epidemiology/	2325
6	epidemiology.tw.	63875
7	aetiology.tw.	22487
8	etiology.tw.	75941
9	5 or 6 or 7 or 8	159810
10	*Risk Factors/	592
11	*Risk/	1573
12	risk* .tw.	990294
13	10 or 11 or 12	990691
14	4 and 9 and 13	9
15	4 and 9	80
1	OVID Medline(R) < 1996 to April 2014 Complex Regional Pain Syndromes/or Reflex Sympathetic Dystrophy/	2054
2	Fractures, Bone/or Osteoporotic Fractures/or Ulna Fractures/or Tibial Fractures/or Radius Fractures	31463
3	1 and 2	117

\* Before the word indicates focussing the subject heading. This means the results that have been retrieved have that subject heading as a major topic in the article, rather than something more minor.

\* After the word refers to truncation. This means searching for all words have the same start, but different endings. In this case, for search 12 e.g. risk\* .tw would look for risk, risks, risky, and anything else that starts with risk.

total of 969 abstracts were screened according to the study selection inclusion and exclusion criteria. Forty-one abstracts were included, and 928 abstracts were excluded. Search terms are outlined in Table 1 (Web of Science search) and Table 2 (Groups of OVID Medline searches).

**2.2. Data Extraction.** The methodology of the 41 articles included through the study selection was screened for data extraction with these inclusion criteria being randomised controlled trials, prospective and retrospective studies for

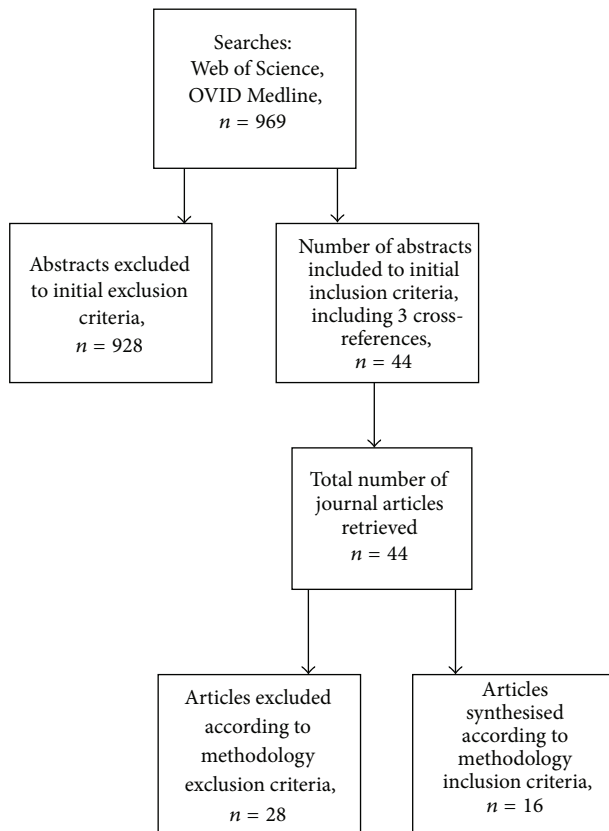


FIGURE 1: Summary of data extraction.

CRPS 1. Exclusion criteria incorporated CRPS Type 11, methodology used in animal studies, case studies, and case control studies or cross-sectional studies. Sixteen articles met these inclusion criteria (10 prospective studies, 6 retrospective studies). Twenty-five articles were excluded due to the direction of effect not being able to be determined. These inclusion and exclusion criteria were used to determine evidence for a direction of the effect specific for the likelihood or not for the potential risk for the onset of CRPS 1. A prospective or retrospective study can provide evidence for the likelihood (or not) of a risk towards the onset of a disease by determining a direction of effect. Animal studies, case studies, case control studies, and cross-sectional studies provide evidence of a relationship. They are not able to determine the direction of effect of this relationship over a period of time. Longitudinal, prospective, or retrospective studies by nature of their design are more able to determine this necessary direction of effect to reveal the potential risks for the onset of disease [7]. Figure 1 summarises the data extraction.

### 3. Results

**3.1. Data Synthesis.** No randomised controlled trials (RCTs) were found describing either possible risk or predictive factors for the onset of CRPS 1. Ten prospective studies and six retrospective studies (total of 16) were included for the data synthesis. These data were synthesised from the following

patient samples: 77 patients after knee replacement surgery; 1976 patients after distal fractures of the radius; 748 patients after wrist or ankle fractures; 168 CRPS male patients from the Turkish armed forces; 1639 CRPS 1 male and female patients with duration of disease for <1 year; and 453 male and female CRPS 1 patients with duration of disease >1 year. Four hundred and sixty patients were lost to follow-up; 21 eligible fracture patients were lost due to administrative errors; 216 patients refused to participate; there were 1052 controls (male and female). The human populations from which the patient epidemiological studies were sourced consisted of a total of 297,372 people. Eight studies used the IASP criteria for diagnosis. Six studies used a variation between the Veldman and Harden/Bruehl criteria. One study did not define their criteria stating their use of “standard criteria.” Criteria were not stated at all in one study. In the prospective studies, follow-up time varied from 3 months to 2 years. In the retrospective studies, follow-up time varied from 3 to 10 years. Table 3 describes the data from the literature synthesised from prospective studies. Table 4 describes the data from the literature synthesised from retrospective studies.

**3.2. Data Analysis.** The data show a high level of heterogeneity. There are no particular variables consistent across these studies with evidence strong enough to comprise a risk factor. Rating criteria for quality and relevance and weighted strength against bias were based on published recommendations [7, 62, 63]. Quality and relevance criteria used included the following: the sample had to be representative of the CRPS 1 population; an adequate control group was needed; study attrition rate was required; adequate description of study and measurements used were necessary (to identify a potential risk factor); the statistical analysis needed to be appropriate.

The data were analysed for a weighted strength against the risk of possible bias. The criteria used included bias risk in sample selection, study design, funding provision, detection, and measurement. Two authors (Tracey Pons, Roger T. Mulder) independently assessed each paper for quality, relevance, and weighted strength against potential bias. Any disagreement was discussed and resolved by consensus. Where a disagreement could not be resolved by consensus, the two other authors (Edward A. Shipton, Jonathan Williman) arbitrated disagreement and facilitated consensus amongst all four authors. Observer expectancy was considered to be reduced since 2 authors’ (Roger T. Mulder, Jonathan Williman) expertise is outside the pain management field; hence, no external observer was included as they were considered objective enough with no historical or current involvement with CRPS 1 diagnosis or management.

Quality and relevance were measured against six factors. Ratings were graded as poor, adequate, or good with the following algorithm: good = five or six factors rated as yes; adequate = three or four factors rated as yes; and poor = less than two factors rated as yes. The weighting against bias was measured against five factors. Ratings were graded as weak, acceptable, or strong with the following algorithm: strong = all five factors rated as no risk; acceptable = three or four factors rated as no risk; and weak = two or less factors rated as no risk.

TABLE 3: Characteristics of the prospective data literature synthesized.

Author	Number of initial sample	Outcome measure listed in <i>italics</i> followed by instrument used	Result for risk towards the onset of CRPS 1	Diagnostic criteria used for CRPS 1 diagnosis	Number in sample lost to follow-up, declined to participate, or study attrition (%)	Follow-up period
Harden et al. 2003 [32]	77 patients for total knee replacement	<i>Pain intensity</i> : McGill Pain Questionnaire <i>Depression</i> : Beck Depressive Inventory <i>Anxiety</i> : trait form of the State Trait Anxiety Inventory	CRPS 1-like symptoms following total knee replacement were not predicted by preoperative psychological distress or pain levels	IASP	26 (33.7%)	6 months
Schürmann et al. 2000 [33]	27 distal radial fracture patients	<i>Oedema</i> : Likert scale <i>Active ROM</i> : Likert scale <i>Sympathetic function</i> : laser Doppler flowmetry, inspiratory gasp test, and contralateral cooling test Age or gender is NOT included in analyses	Failure of the sympathetic nervous system predicted those who developed CRPS 1 in the early stages of patients who had radial fractures and also possibly suffer from a systemic sympathetic dysfunction that is not limited to the affected limb	IASP	None	12 weeks
Puchalski and Zyluk 2005 [34]	121 distal radial fractures Population group: postmenopausal women, retired, or disability pensioners	<i>Personality traits</i> : Eysenck Personality Questionnaire <i>Depression</i> : Beck Depressive Inventory if <60 years of age or Yesavages Geriatric Depression Scale <i>CRPS I severity</i> : Zyluk scoring system	In 62 patients with distal radial fractures, 18% developed CRPS 1 (8 females, one male) Their psychological behaviour patterns or depression did not differ with those who had not developed CRPS 1	Veldman and Zyluk CRPS 1 scoring system	59 (48.7%) refuse permission for psychological examination Of 62 patients included, 12 (19.4%) were lost to follow-up	20 months
Beerthuisen et al. 2012 [35]	748 wrist or ankle fractures	<i>Health related quality of life</i> : SF-36 survey <i>Medical fracture details</i> : type, location of fracture with type of fracture and treatment or number of weeks in plaster	Of 596 patients with wrist or ankle fractures, 7% developed CRPS 1; wrist or ankle fracture dislocation and intra-articular fracture contributed significantly to the likelihood of the development of CRPS 1; one year following the fracture, no CRPS 1 patient was pain-free; the highest majority of patients were females (73%); the highest incidence was between 61 and 70 years of age; early reporting of high levels of pain and other musculoskeletal comorbidities made the risk of CRPS 1 more likely	3 sets of criteria: Veldman, IASP, and Harden/Bruehl as well as confirmation with experienced clinician	152 (20.3%) decline consent 46 (18.6%) are lost to follow-up	1 year

TABLE 3: Continued.

Author	Number of initial sample	Outcome measure listed in italics followed by instrument used	Result for risk towards the onset of CRPS 1	Diagnostic criteria used for CRPS 1 diagnosis	Number in sample lost to follow-up, declined to participate, or study attrition (%)	Follow-up period
Dijkstra et al. 2003 [36]	91 distal radius fractures	<i>Pain: Visual Analogue Scale</i> <i>Stressful events before fracture: Social Readjustment Rating Scale</i>	Only one female patient (age 69 years) developed CRPS 1 after a follow-up of 88 patients	IASP	3 are lost to follow-up	1 year
Dilek et al. 2012 [37]	74 with distal radius fractures treated with closed reduction and plaster casts	<i>Psychological assessment: Anxiety Sensitivity Index, Toronto Alexithymia Scale-20, State Trait Anxiety Inventory, and Beck Depression Inventory</i>	In 50 patients, a high risk for developing CRPS 1 was found in those with a high anxiety personality trait score; of the 50 patients, 26% (13/50) developed CRPS 1; 34% of the females (age 62.38 ± 10.8) developed CRPS; 11% of the males developed CRPS 1	IASP	13 (17.6%) refuse permission for psychological examination; 4 (5%) are excluded due to needing surgery; 7 (9%) are lost to follow-up	16 months
Jellad et al. 2014 [38]	121 consecutive patients with fractures of the distal radius treated conservatively	<i>Pain: Visual Analogue Scale</i> <i>Active range of motion: Goniometer and Kapandji distance</i> <i>Hand and wrist function: Patient Related Wrist Evaluation</i> <i>Depression or Anxiety: Arabic adaption of Hospital Anxiety and Depression scale</i> <i>Quality of Life: Arabic adaption of SF-36</i>	CRPS 1 occurred in 32.2% of patients, mostly females (age 52.9 ± 13.2) [odds ratio 5.774 95% CI 1.391–23.966]; these also reported severe pain and impairment of quality of life where the CRPS 1 onset occurred in the third and fourth week after cast removal	Veldman	31 (25.6%) excluded as treated operatively or other problems	9 months
Goris et al. 2007 [39]	114 distal radius fractures 95 females, 19 males, mean age of 62 years (range 22–82 years)	<i>Medical fracture details: type, location of fracture with type of fracture and treatment or number of weeks in plaster</i> <i>Skin temperature: infrared ear thermometer and ThermoCAM E2 infrared camera</i> <i>Oedema: custom made device for measuring accurate finger circumference</i> <i>Active range of motion: Goniometer</i> <i>Skin colour: subjective Likert scale</i> <i>Grip strength: dynamometer</i> <i>Blood analysis: venous blood samples for lactate and oxygen saturation</i>	CRPS 1 onset was associated with an increased regional inflammatory score (sensitivity 100%, specificity 16%); it was not associated with raised inflammatory markers in the blood; age and gender not included in published analyses	IASP and Harden/Bruehl criteria	25 (21.9%) are lost to follow-up	1 year

TABLE 3: Continued.

Author	Number of initial sample	Outcome measure listed in italics followed by instrument used	Result for risk towards the onset of CRPS 1	Diagnostic criteria used for CRPS 1 diagnosis	Number in sample lost to follow-up, declined to participate, or study attrition (%)	Follow-up period
Gratl and Schürmann 2005 [40]	10 CRPS patients, 4 males and 6 females, age 53–79 years with average age of 62 years	<i>Sympathetic function</i> : laser Doppler flowmetry, inspiratory gasp test, and contralateral cooling test	Dysfunction of the sympathetic nervous system evident in the early stage of CRPS 1 was measured in this German study; this dysfunction was transitory; it normalised over the course of the syndrome; the diagnosis of CRPS 1 was able to be made 46 to 72 days following an injury	Harden/Bruehl	None	3 months
Moseley et al. 2014 [41]	1549 near consecutive patients with radial fractures across 3 hospital out-patients	<i>Pain</i> : NRS <i>Reaction time</i> : seconds <i>Dysynchiria</i> : absent or present <i>Swelling</i> : affected thumb and first 3 fingers' circumference as a proportion of unaffected hand <i>Catastrophising</i> : Pain Catastrophising Scale	A pain score of $\geq 5$ in the first week of fracture is shown to be predictive and should be considered a "red flag" risk for the likely onset of CRPS 1; 55 patients have developed CRPS 1 at evaluation 112 days after fracture; age and gender were not predictive of CRPS 1 onset	Referred to as "established criteria" without formal reference	21 likely CRPS 1 patients lost due to administrative error; 93.3% of all fractures eligible for inclusion and 94.5% agree to participate; 97.2% contacted for follow-up; no numbers of patients given, only percentages	Sequential cohort over 2 years

TABLE 4: Characteristics of the retrospective data literature synthesized.

Author	Number of initial sample	Outcome measure listed other than age and gender	Risk factor towards the onset of CRPS 1	Diagnostic criteria used for CRPS 1 diagnosis	Period time for inspection
Allen et al. 1999 [42]	134 CRPS patients; 70% female, 30% male Mean group age at evaluation 41.8 (18–71) years	Inciting injury Location Job related occupation Legal and worker compensation issues Season Bone scans Treatment, medical and allied Immobilisation Myofascial component	A diagnostic bone scan was not predictive of a CRPS 1 diagnosis The inciting event was sprains in 29%, surgical procedures in 24%, and fractures in 16%; since physician imposed immobilisation in either a cast or splint involved 47% of the sample, the possibility of immobilisation is raised as a possible risk factor as well	IASP	1992–1997 [5 years]
de Mos et al. 2007 [5]	Source population 190 902 assessed from 46 general medical practices	Sensory Vasomotor Sudomotor Motor/trophic Neurologic Complaints Alternative diagnoses	Postmenopausal female gender and having a fracture; upper limb affected more frequently than the lower limb	3 sets of criteria Veldman, IASP, and Harden/Bruehl	1996–2005 [9 years]
Sandroni et al. 2003 [4]	Source population 106 470 with unified access to all patient records	Clinical characteristics Signs and symptoms Laboratory tests Response to treatment	Risks for onset of CRPS 1 were identified as female gender or suffering an upper limb fracture	IASP	1989–1999 [10 years]
Duman et al. 2007 [43]	168 males in Turkish military hospitals	Inciting injury Location Hospitalisation	Inciting event for onset of RSD was fracture in 55.3%, incisive trauma in 16.7%, and soft tissue sprains/strains in 28%	IASP and three-phase bone scan	2003–2006 [3 years]
van Rijn et al. 2007 [22]	Neurology outpatient clinic study of 185 patients with CRPS 1, 86.5% females, mean age at onset of CRPS 37.5 ± 15.4 years, 91% of whom developed dystonia	Clinical and temporal characteristics	Earlier onset of dystonia (<1 year) to be possibly related to the same mechanism and that delayed onset dystonia was related to another mechanism; 86.5% of participants were female; the inciting injury for CRPS 1 was soft tissue in 49.7%, fracture in 25.9%, and surgery in 24.3	IASP	1998–2004 [6 years]
Anderson and Fallat 1999 [44]	33 patients with lower limb CRPS 1 or sympathetically maintained pain; 60% were female; group average age 43.5 ± 12.6 years	Clinical characteristics Type of injury or surgery Time to diagnosis Signs and symptoms Treatment	Fracture was the most common cause for injury (45%); trauma accounted for 73%	Not given other than being confirmed by an anaesthesiologist at the pain management centre	1990–1997 [7 years]

TABLE 5: Results presenting quality and relevance of data extraction for onset of CRPS 1 from prospective studies.

Prospective studies	Population sample representative	Adequate control group	Study attrition described	Risk/predictor outcome adequately defined	Risk/predictor outcome adequately measured	Analysis statistically appropriate	Quality
Harden et al. 2003 [32]	No	No	Yes	Yes	Yes	Yes	Adequate
Schürmann et al. 2000 [33]	No	No	No	Yes	Yes	No	Poor
Puchalski and Zyluk. 2005 [34]	No	No	Yes	Partly	Yes	Yes	Poor
Beerthuizen et al. 2012 [35]	Yes	Yes	Yes	Yes	Yes	Yes	Good
Dijkstra et al. 2003 [36, 46]	No	Yes	Yes	Partly	No	No	Poor
Dilek et al. 2012 [37]	No	No	Yes	Yes	Yes	No	Adequate
Jellad et al. 2014 [38]	No	Yes	Yes	Yes	No	Yes	Adequate
Goris et al. 2007 [39]	No	Yes	Yes	Yes	Yes	Yes	Good
Gradl and Schürmann 2005 [40]	Partly	No	No	Yes	Yes	No	Poor
Moseley et al. 2014 [41]	Yes	Yes	Partly	Yes	No	Yes	Adequate

TABLE 6: Results presenting quality and relevance of data extraction for onset of CRPS 1 from retrospective studies.

Retrospective studies	Population sample representative	Adequate control group	Study attrition described	Risk/predictor outcome adequately defined	Risk/predictor outcome adequately measured	Analysis statistically appropriate	Quality
Allen et al. 1999 [42]	No	No	No	Yes	Yes	Yes	Adequate
de Mos et al. 2007 [5]	Yes	Yes	No	Yes	Yes	Yes	Good
Sandroni et al. 2003 [4]	Yes	No	Yes	Yes	Yes	Yes	Good
Duman et al. 2007 [43]	No	No	No	Yes	No	No	Poor
van Rijn et al. 2007 [22]	Yes	No	No	Yes	Yes	Yes	Good
Anderson and Fallat 1999 [44]	Yes	No	No	No	Yes	Yes	Poor

These data provide a broad and heterogeneous research platform towards probing for possible risk factors for the onset of CRPS 1. In this systematic review, 2 prospective studies and 3 retrospective studies were rated as good (total of 5). Four prospective studies and 1 retrospective study were rated as adequate (total of 5). Four prospective studies and 2 retrospective studies were rated as poor (total of 6). For the weighted strength against bias, 7 prospective studies were weak, 2 were acceptable, and 1 was strong. In the retrospective studies, 3 were weak, 2 were acceptable, and 1 was strong. In summary for the weighted strength against bias, 10 were weak, 4 were acceptable, and 2 were strong. However, these findings should be treated with caution as their statistical reliability and consistency have not been established across multiple or homogeneous studies.

The quality and relevance data are outlined in Table 5 for prospective studies and in Table 6 for retrospective studies. The weighting strength against bias data is illustrated in Table 7 for prospective studies and in Table 8 for retrospective studies.

The following are shown *not* to be risk factors for the onset of CRPS 1: namely, preoperative psychological distress; preoperative pain levels (with poor quality, poor relevance, and weak weighting against bias); psychological behaviour and depression (with adequate quality and relevance but with weak weighting against bias); and a diagnostic bone scan (with adequate quality and relevance but with weak weighting against bias). The factors not considered to be risk factors for the onset of CRPS 1 are summarised in Table 9.

The potential risk factors identified with a strong weighting against bias as well as good quality and relevance are being female (particularly postmenopausal), a fracture of the distal radius, and dislocation or an intra-articular fracture of the ankle. The factors presenting as possible risks for the onset of CRPS 1 are summarised in Table 10.

#### 4. Discussion

Potential risk factors identified (strong weighting against bias, good quality, and relevance) across the 16 papers



TABLE 7: Results showing weighted strength against possible bias risk for prospective studies' analyses with risk rating in bold italics.

Authors	Population sample selection bias risk	Study design bias risk	Funding provision bias risk	Detection bias risk	Measurement bias risk	Weighted strength across the five factors
Harden et al. 2003 [32]	77 participants, 61.6% female, awaiting TKR in single centre setting	16 develop CRPS 1 by 1 month and 7 by 6 months after TKR Mixed within/between designs	No mention of funding or conflict of interests	All samples assessed by the same physician	Point-biserial correlations due to small sample of CRPS	
	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>Weak</b>
Schürmann et al. 2000 [33]	27 participants, gender percentages not given, all with distal radial fractures in single centre setting	4 out of 27 develop CRPS 1 and two are identified as borderline	Acknowledgment is given to funder support, potential conflict of interests is not mentioned	Consensus between examiners only for oedema, reliable Doppler perfusion monitor	Regression analysis	
	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>No</b>	<b>Weak</b>
Puchalski and Zyluk 2005 [34]	121 patients, gender percentages not given, approached with distal displaced radial fractures, the day after fixation of the fracture in single centre setting	59 refuse to participate in psychological examination; 49.5% of the sample group is available for analysis	No mention of funding or conflict of interests	Sample assessed by "we," but clarity about authors assessment for agreement is not mentioned	A Mann-Whitney <i>U</i> -test for determining statistical relationships	
	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>No</b>	<b>Weak</b>
Beerthuis et al. 2012 [35]	Multicentre setting of 3 hospitals in single city, telephonic interview of 748 patients, 63.6% female, with single fracture of wrist, scaphoid, ankle, or metatarsal	596 participate (80%) and 18.1% of those who developed possible CRPS signs refused or were unable to attend	Acknowledgment is given to 2 sources of funding and neither funders are involved with design, conduct, preparation, review, or approval of the manuscript	Routine examination followed up by single experienced pain specialist clinician to confirm CRPS 1 diagnosis	A Mann-Whitney <i>U</i> -test due to skewed distribution of variables, binary logistic regression analysis using SPSS	
	<b>No</b>	<b>Yes</b>	<b>No</b>	<b>Yes</b>	<b>No</b>	<b>Acceptable</b>
Dijkstra et al. 2003 [36]	All patients, gender percentages not given, with fracture of distal radius who visit a single setting approached the day after the fracture	91 participants, 3 drop-outs; only 1 female develops CRPS 1	No funding acknowledged and hospital staff thanked for cooperation	Only researchers given as assessors for CRPS 1, no other confirmation of diagnosis	Descriptive statistics used and analysis not possible with only one CRPS 1 subject	
	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>Weak</b>
Dilek et al. 2012 [37]	All patients, 64% female, presenting to single setting with fractures of distal radius asked to participate in psychological assessment 2 days after cast application	74 participants with 24 drop-outs	No conflict of interests identified and no funders acknowledged, thanks given to patients who participated	No confirmation validation given for CRPS 1 diagnosis other than fulfillment of IASP criteria	Comparative statistics described with <i>P</i> value for significance but no statistical approach described	
	<b>No</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>Weak</b>

TABLE 7: Continued.

Authors	Population sample selection bias risk	Study design bias risk	Funding provision bias risk	Detection bias risk	Measurement bias risk	Weighted strength across the five factors
Jellad et al. 2014 [38]	All patients, 62.2% female, presenting to single setting with closed fractures of distal radius referred by orthopaedic surgeons for rehabilitation <b>Yes</b>	90 participants with zero drop-outs. <b>Yes</b>	No mention of funding or conflict of interests <b>Yes</b>	No confirmation validation given for CRPS 1 diagnosis other than fulfillment of Veldman criteria <b>Yes</b>	Logistic regression analysis using SPSS <b>No</b>	<b>Weak</b>
Goris et al. 2007 [39]	Multicentre setting of 3 hospitals in 2 cities, 83.3% female <b>No</b>	114 participants with 6 drop-outs 1 year later <b>No</b>	No benefit of any form is declared <b>No</b>	Confirmation of diagnosis using 2 criteria as well as assessment by 2 investigators and blinding to results at a year's follow-up <b>No</b>	Mann-Whitney <i>U</i> -test for paired data, Kruskal-Wallis test for nonparametric data, Gunni's multiple comparison test with regression coefficient for change of regional inflammation score <b>No</b>	<b>Strong</b>
Gradl and Schürmann 2005 [40]	All consecutive patients, 60% female, who develop CRPS 1 following trauma in single centre setting <b>Yes</b>	10 participants <b>Yes</b>	No mention of funding or conflict of interests <b>Yes</b>	Confirmation of diagnosis using Harden/Bruehl criteria by 2 independent surgeons and pain specialist investigators and blinding to results at a year's follow-up <b>No</b>	Repeated measures every 10 days for 3 months with result of measures graphically presented but no statistical approach described <b>Yes</b>	<b>Weak</b>
Moseley et al. 2014 [41]	1661 patients, 51.5% female presenting to multicentre (3) hospital settings with fractures of distal radius not needing surgical fixation; no city(s) mentioned <b>No</b>	1549 participants, 21 drop-outs due to administrative error, only mentioned as percentages <b>No</b>	No mention of funding or conflict of interests <b>Yes</b>	Routine examination by single experienced pain specialist clinician to confirm CRPS 1 diagnosis made by "standard criteria" listed in an appendix <b>Yes</b>	A predictive model was developed using logistic regression, likelihood ratio test, with bootstrap sampling and goodness of fit with Hosmer-Lemeshow test <b>No</b>	<b>Acceptable</b>

TABLE 8: Results showing weighted strength against possible bias risk for retrospective studies' analyses with risk rating in bold italics.

Authors	Population sample selection bias risk	Study design bias risk	Funding provision bias risk	Detection bias risk	Measurement bias risk	Weighted strength
Allen et al. 1999 [42]	Medical records of all consecutive CRPS 1 patients, 70% female, who were referred to a single setting multidiscipline pain centre <b>No</b>	134 consecutive CRPS 1 patients <b>Yes</b>	No mention of funding or conflict of interests <b>Yes</b>	Independent review of medical records <b>No</b>	Result of measures listed with <i>P</i> values for significance but no statistical approach described <b>Yes</b>	<b>Weak</b>
de Mos et al. 2007 [5]	Electronic medical records of one country, population gender mix not given <b>No</b>	Estimation of CRPS 1 incidence from data of 600 000 patients; control groups are those who do not develop CRPS 1 <b>No</b>	Acknowledgment of funding provided through TREND, a Dutch government research grant; no mention of conflict of interests <b>No</b>	Potentially overstrict retrospective application of 3 sets of criteria: Veldman, IASP, and Harden/Bruehl, to electronic records by independent reviewers with <i>k</i> statistics for agreement <b>No</b>	Poisson distribution, logistic regression, chi-square, and Student's <i>t</i> -tests using SPSS software <b>No</b>	<b>Strong</b>
Sandroni et al. 2003 [4]	Electronic medical records of one region, population gender mix not given <b>No</b>	Estimation of CRPS 1 incidence from data of 70 745 patients <b>No</b>	Acknowledgment of funding provided through two sources, no conflict of interests mentioned <b>No</b>	Potentially lenient retrospective application of IASP criteria to electronic records by one reviewer with 10% random independent assessment and 93.4% agreement <b>Yes</b>	Chi-square, Fisher's exact, and Wilcoxon rank sum tests with no software described <b>No</b>	<b>Acceptable</b>
Duman et al. 2007 [43]	Medical records of two tertiary military hospitals in one country, all male <b>Yes</b>	168 CRPS 1 patients <b>Yes</b>	No mention of funding or conflict of interests <b>Yes</b>	Author review with no independent assessment using IASP criteria and three-phase bone scan <b>Yes</b>	Descriptive statistics only using SPSS <b>Yes</b>	<b>Weak</b>
van Rijn et al. 2007 [22]	Medical records of all CRPS patients, 86.5% female, who were referred to a single setting movement disorder centre <b>No</b>	121 CRPS 1 patients <b>Yes</b>	Acknowledgment of funding provided through TREND, a Dutch government research grant; no mention of conflict of interests <b>No</b>	Author review with no independent assessment using IASP criteria <b>Yes</b>	A multivariate analysis using Cox's proportional hazards model, Mann-Whitney <i>U</i> -test, chi-square tests, and Student's <i>t</i> -tests using SPSS software <b>No</b>	<b>Acceptable</b>
Anderson and Fallat 1999 [44]	Medical records of all CRPS patients, 61% female, seen in a single setting foot and ankle trauma clinic <b>Yes</b>	33 CRPS 1 patients <b>Yes</b>	No funding mentioned and acknowledgment of assistance with statistical analysis and illustrations <b>Yes</b>	CRPS 1 diagnosis confirmed in records by medical specialist at pain management centre <b>Yes</b>	Regression analysis, unpaired <i>t</i> -test, paired <i>t</i> -test, and Pearson's correlation using SPSS <b>No</b>	<b>Weak</b>

TABLE 9: Results summary showing factors examined and not found to be risk factors for the onset of CRPS 1 with weighting bias strength and quality and relevance.

Not a risk factor for CRPS onset	Evidence source	Weighting bias strength	Quality and relevance of data extraction
Preoperative psychological distress or pain levels	Puchalski and Zyluk 2005 [34]	Weak	Poor
Diagnostic bone scan	Allen et al. 1999 [42]	Weak	Adequate
Psychological behaviour: depression	Harden et al. 2003 [32]	Weak	Adequate

TABLE 10: Results summary showing possible risk factors for the onset of CRPS 1 with weighting bias strength and quality and relevance.

Risk factors for CRPS onset	Evidence source	Weighting strength against bias	Quality and relevance of data extraction
Female gender	Puchalski and Zyluk 2005 [34]	Weak	Poor
	Dijkstra et al. 2003 [36, 46]	Weak	Poor
	Dilek et al. 2012 [37]	Weak	Adequate
	Sandroni et al. 2003 [4]	Acceptable	Good
	Allen et al. 1999 [42]	Weak	Adequate
Postmenopausal female gender	van Rijn et al. 2007 [22]	Acceptable	Good
	Beerthuizen et al. 2012 [35]	Acceptable	Good
	Jellad et al. 2014 [38]	Weak	Adequate
	de Mos et al. 2007 [5]	Strong	Good
Fracture of distal radius or an ankle dislocation or intra-articular fracture	Sandroni et al. 2003 [4]	Acceptable	Good
	Beerthuizen et al. 2012 [35]	Acceptable	Good
	de Mos et al. 2007 [5]	Strong	Good
	Duman et al. 2007 [43]	Weak	Poor
Immobilisation	Anderson and Fallat 1999 [44]	Weak	Poor
	Allen et al. 1999 [42]	Weak	Adequate
Report of higher than usual levels of pain in early phase of trauma	Beerthuizen et al. 2012 [35]	Acceptable	Good
	Jellad et al. 2014 [38]	Weak	Adequate
	Moseley et al. 2014 [41]	Acceptable	Adequate

are as follows: being female (particularly postmenopausal); obtaining a fracture of the distal radius; suffering an ankle dislocation or intra-articular fracture; and reports of higher than usual levels of pain in the early phases after trauma. The findings of this systematic review should be treated with caution as their statistical reliability and consistency have not yet been established across multiple or homogeneous studies and diagnostic criteria were mixed with Budapest Criteria not being used.

Age was accounted for in most studies. Age as a consistent potential risk factor for the onset of CRPS 1 could not be identified. This is shown in the population studies by Sandroni et al. [4], Moseley et al. [41], and de Mos et al. [5], as well as in the study by van Rijn et al. [22]. Although most of these data show that the risk increases in postmenopausal women [5, 34–38, 40], the retrospective studies by Allen et al. [42] and by Anderson and Fallat [44] show a lower age. This might be due to average age of the group sample with the inclusion of both genders. The average age of the female sample groups is, unfortunately, not provided in either of these studies. Females at any age pose a higher risk for the

onset of CRPS 1. However, the study of males in the armed forces by Duman et al. [43] shows that males are vulnerable as well. This systematic review shows that the onset of CRPS Type 1 is higher in females than in males in the mixed gender studies.

The data show the cause of the inciting event to be mixed. It can be related to surgery, fractures, or soft tissue injuries. The presence of other comorbidities is neither predictive nor a risk factor for the onset of CRPS 1. Reports of higher than usual levels of pain in early phase of trauma were cited as strong evidence of a risk factor by Beerthuizen et al. [35] but as weak evidence by Jellad et al. [38].

Psychosocial factors are weakly weighted as a risk factor for the onset of CRPS 1. Moseley et al. find catastrophising not to be predictive for the onset of CRPS [41]. This is confirmed by other reviews and studies investigating psychological influences on the onset and progression of CRPS [58, 59, 64–66]. Psychological behaviour, depression, and preoperative psychological distress or pain levels are not predictive of the onset of CRPS. The earlier literature described the “Sudeck A personality,” a personality of high anxiety, as a likely risk

factor towards the onset of CRPS 1 [61]. A high anxiety personality trait was identified by this systematic review as only a weak potential risk [37]. In other persistent pain conditions, these complex interactions between the onset of the pathogenesis of CRPS 1 and psychological factors are predictive of level of function [45, 60]. Their interaction in CRPS 1 continues to be investigated by clinicians and researchers [5, 64].

These data show that a positive diagnostic bone scan is not a risk factor for the onset of CRPS 1 [46] and has been confirmed by other studies [42, 47, 48]. Interobserver consistency with interpretation of bone scans appears to be variable [49]. However, a diagnostic bone scan has been found to be helpful towards a diagnosis of CRPS 1 in some observations [50, 51], but since recovery of bone mass following ankle fractures remains variable, it is not necessarily indicative of CRPS 1 [52].

Two recent systematic reviews have collated the prognostic findings about CRPS 1 [53, 67]. Both agreed that the quality of evidence is poor. Our systematic review has confirmed this regarding the risks of onset of CRPS 1. One review retrieved 1648 relevant papers of which twelve were robust enough for qualitative analysis [53]. Prognostic factors for poor outcomes were grouped within 7 clinical clusters as follows: (1) gender, where two studies show the male gender and one study shows the female gender; (2) age, where there is a high variation in age of onset affecting prognosis; (3) inciting event, such as polytrauma, inciting event other than fracture, severe initial injury, and distal articular location; (4) localisation site, either upper or lower extremity; (5) clinical features, such as exercised induced pain, sensory disturbances, initial cold skin temperature, complications of infection, skin ulcers, chronic oedema, dystonia or myoclonus, algodystrophy score > 7 out to 10, low SF-36 general health score, disease duration > 1 year, and coexistence of misdiagnosed nerve injury and compression; (6) associated comorbidities included alcoholism and psychological background in nontraumatic CRPS 1; and (7) diagnosis where a delay of >2 months after inciting event was shown to be associated with poorer outcomes. The other review found that many CRPS 1 patients recover in 6–13 months but that a significant number continue to experience persistent pain and disability [67].

**4.1. Implications for Research.** This systematic review highlights potential risk factors that will contribute to future exploration about the onset of CRPS 1. Identifying risk factors associated with a poor prognosis is important as well. Risk factors for the onset of CRPS 1 identified in this systematic review may or may not be associated with a poor prognosis. The low prevalence of CRPS 1, its heterogeneous presentation, and its lack of highly specific or sensitive diagnostic criteria as well as the lack of clarity around consensus for these criteria create challenges in carrying out research [4, 6, 21, 42, 54, 55]. In CRPS 1, more trials across different settings are needed. The cross-sectional and case control studies excluded from this systematic review may still offer insight into the development of future longitudinal studies to determine direction and strength of the effects.

**4.2. Implications for Clinical Practice.** No specific or sensitive clinical sign or clinical symptom was shown in this review to pose a risk factor for the onset of CRPS 1. Clarity around the sensitivity and specificity of laboratory and imaging testing is needed [42, 47, 48, 51, 52]. This review confirms the importance of maintaining clinician awareness and of being aware of potential risk factors to enable the early diagnosis of CRPS 1 [56]. Evaluation by experienced clinicians hastens the diagnosis [36, 57]. Early diagnosis and referral to pain management specialists and physiotherapists are related to better outcomes [53, 68, 69]. Moseley et al. [41] suggested that a pain score of  $\geq 5$  in the first week of fracture could be considered a “red flag” risk for the likely onset of CRPS 1.

## 5. Conclusion

This systematic review shows that the accurate potential risk factors for the onset of CRPS 1 remain elusive. Studies remain heterogeneous, of mixed quality and relevance, and with varied weighting against the risks of bias. The low prevalence of CRPS 1 accompanied by a lack of a gold standard for diagnosis contributes to the difficulties around determining potential risk factors for the onset of CRPS 1.

Potential risk factors identified with strong weighting against bias and good quality and relevance are summarised as follows: being female (particularly postmenopausal); obtaining a fracture of the distal radius; suffering an ankle dislocation or intra-articular fracture; and reports of higher than usual levels of pain in the early phases after trauma. Potential risk factors with much weaker weighting against bias and poorer quality and relevance include immobilisation, psychosocial barriers, and a positive diagnostic bone scan. Definite conclusions cannot be drawn as evidence remains inconsistent across multiple trials or in homogenous studies.

## Conflict of Interests

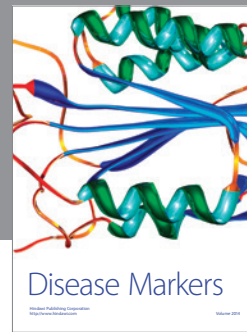
The authors declare no conflict of interests regarding the publication of this paper.

## References

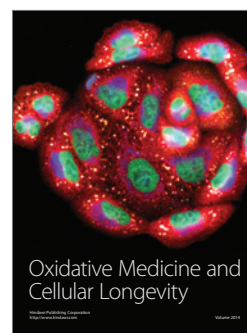
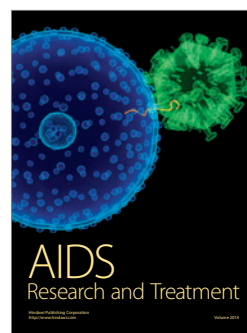
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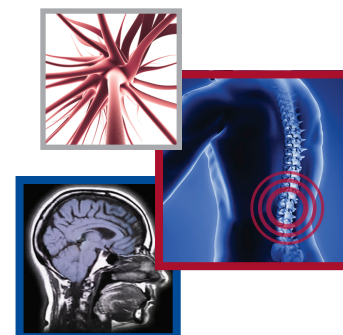
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# Physiotherapy and the management of complex regional pain syndrome



“It is imperative to reduce the risk of developing complex regional pain syndrome following an injury, and of preventing a recurrence.”

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Physiotherapy is recognized in the literature as an essential element in the management of complex regional pain syndrome (CRPS) [1,2]. Recently, the outcomes have been more optimistic for this syndrome [3,4]. This is despite an incomplete understanding of its precise etiology, progression, its heterogeneous presentation and lack of a gold standard for diagnosis or management. At times, it can be mistakenly referred to in publications as Chronic Regional Pain Syndrome. Previous nomenclature assumed aberrant sympathetic activity for etiology and diagnosis, but this has also been shown not to be the case [5]. CRPS type I has signs and symptoms with no overt neural pathology while CRPS type II has an actual neural injury as well. Fortunately, not all neural injuries develop CRPS type II.

Sensitivity and specificity of the signs and symptoms associated with CRPS have been found to be more accurate with the use of the Budapest criteria [6]. A diagnostic algorithm seems easier to apply. However, guidelines for a sequential approach to

management, especially physiotherapy management remain elusive.

Publications frequently refer to standard physiotherapy as being important or affecting outcomes. What this involves is often not described [7]. Standard physiotherapy assumptions remain unwarranted due to the high variability of presentation of CRPS patients. It is unlikely that individual physiotherapists would follow a similar algorithm. It is unlikely as well that physiotherapy would be the only modality considered in the management of CRPS. Pharmacological interventions, physical interventions (such as neural blockade or bisphosphonate infusions) and psychological interventions provide additional considerations. It has been shown that a multimodal or biopsychosocial rehabilitative approach is likely to be more beneficial than a single biomedical approach [8,9]. Controlling the pain experience using psychological interventions can be added to physiotherapy management [10]. Recognized psychological interventions include acceptance and

## KEYWORDS

- chronic pain • complex regional pain syndrome • neuropathic pain
- pain management • persistent pain
- physiotherapy • psychology

“Physiotherapy is recognized in the literature as an essential element in the management of complex regional pain syndrome.”

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commitment therapy, cognitive–behavioral therapy and mindfulness. Acceptance and commitment therapy aims at accepting the pain experience and committing to the fulfilling activities that have been neglected. Cognitive–behavioral therapy focuses on modifying behavior, so that the pain experience is minimized and is less interfering with activity. Mindfulness aims at the experience of the present moment, so that awareness of self in the present is not interrupted by the pain experience.

Physiotherapy research on CRPS in both the clinical and laboratory settings remains vibrant. This is despite the controversy and debate that continues across disciplines researching this syndrome. This research explores prevention of CRPS following injury or fracture as well as studying efficacies of known or of novel interventions.

Physiotherapy interventions for CRPS aim to reduce the risk of onset, to reduce complications or poor outcomes, to control the pain experience and to improve the functional ability of the affected limb. Functional goals include the following: to restore the active range of motion of joints; to restore the strength, flexibility and endurance of muscle or soft tissue; to normalize posture and movement patterns; to improve motor control; to cultivate patient self-efficacy and to provide education on the syndrome [11].

The relationship between functional ability and pain continues to be debated. A yet to be answered question for CRPS is how pain experiences associated with physiotherapy interventions affect functional abilities or outcomes? There are two contrasting hypotheses associated with physiotherapy interventions. One hypothesis focuses primarily on pain modulation. This is based on the theory that the pain experience is associated with cortical reorganization. Pain may be controlled by accessing premotor cortical activity using the visual pathway. This can be used to modulate the sensory–motor input due to the plasticity of neural networks. The clinical interventions supporting this hypothesis are aimed primarily at acknowledging the pain experience and trying to minimize it, while working toward improving functional abilities. These include mirror exercises, graded motor imagery and sensorimotor training [9].

With mirror exercises [11], the unaffected limb is exercised and the reflected image of the movement is watched in the mirror. This reflected image looks exactly like the affected

limb (before the CRPS), so that movement is visualized as occurring normally in the affected limb. Mirrored postures or movements that do not provoke pain are initiated first. These are followed by gradually incremented increases in postures or movements as tolerated. On progression, the affected limb behind the mirror is included to accompany the movement of the unaffected limb.

Graded motor imagery takes place sequentially over 6 weeks. The first 2 weeks are spent looking at photographs of limb postures. This then progresses toward laterality training (the ability to correctly identify left from right). This is followed by imagined movements (imagining the posture or movement viewed in a photograph), and then finally by mirror exercises as described above. The photographs can be used, so that the unaffected limb follows the posture or movement of the photograph to be viewed in the mirror.

Since a strong relationship has been shown between images of posture and pain, it is thought that by activating the premotor cortex, sensory input can be reconciled with the motor output. Disrupted body schema and altered cortical representation are slowly corrected by extinguishing the guarding that inhibits the motor intent and planning. Researching the use of prisms for body perception exercises allows the affected limb's perceived location in space or body side to be altered. This reduces pain, resulting in the activity of the affected limb being better tolerated [12]. Prisms are yet to be used routinely in this way in a clinical setting.

Sensorimotor training [13] makes use of different textures and objects touching the affected limb. This in turn can be used for desensitization, training in two-point discrimination or for sensory mapping (locations in which one or two points/textures are felt). The use of functional MRI has shown pain to be linked with somatosensory cortical representation [14]. The restoration of cortical maps (in which the sensory input in the sensory–motor cortex is spatially represented) has shown a reduction in pain intensity as well. As motor function improves with pain reduction, the sensory and proprioceptive feedback mechanisms are reconciled. Correct representations are thereby reinforced, so that functional ability is restored.

The results obtained from these interventions with their primary focus on pain reduction contrast with the recent results shown by

“An individually tailored approach should be taken in the management of complex regional pain syndrome.”

pain exposure physiotherapy (PEXP). PEXP focuses exclusively on disuse of the affected limb. The hypothesis of this method is that the disuse fuels the cycle of pain through neglect of the limb and attention to pain. A recent randomized controlled trial showed five sessions of PEXP physiotherapy to be as effective as usual physiotherapy [15]. It was less costly or time consuming, due to the shorter time demand on the physiotherapist. In this setting, pain is ignored as a false warning signal and analgesia not applied during the progressive use of the affected limb.

The evidence for the use of PEXP or pain modulation for this purpose is low or at best moderate [11]. It is important that both pain exposure or pain modulation hypotheses are tested in multiple trials and across different settings. This is key as other medical, pharmacological or physical interventions for CRPS are all shown to have limited effect [1]. However, the multidisciplinary approach to the management of CRPS is still promoted.

It is imperative to reduce the risk of developing CRPS following an injury, and of preventing a recurrence. A recent case series written up by Hand Therapists demonstrated an extremely simple eight-step algorithm that markedly reduced the onset of CRPS following conservative management for fracture of the distal radius [16]. Immobilization has been shown to be a risk factor for the onset of CRPS [17] or in the development of neuropathic pain [18]. In a recent systematic review on predicting risk for the onset of CRPS, the following risk factors were shown:

being female (particularly being a postmenopausal female); having a fracture of the distal radius or intra-articular fracture of the ankle and having a higher than usual (>5/10 Numerical Rating Scale) following trauma [19]. All medical or allied health practitioners should be aware of these risks, so that early referral is expedited. Early detection, diagnosis and referral for appropriate management have been shown to improve outcomes [20].

An individually tailored approach should be taken in the management of CRPS. Recent publications show more positive outcomes for CRPS [3,4]. Health practitioners are becoming more aware of this syndrome, resulting in earlier referral. They seem better equipped to manage it. Future research should focus more on the prevention of CRPS. It should concentrate on educating health providers about its detection. Contrasting hypotheses for physiotherapy interventions should be further delineated as well. All these future measures are necessary to improve the outcomes of those suffering from CRPS.

#### Financial & competing interests disclosure

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# Beliefs and Clinical Practice for Complex Regional Pain Syndrome (CRPS) Managed by Physiotherapists on the South Island of New Zealand

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## Abstract

On the South Island of New Zealand, Anaesthetists and other Medical Professionals, frequently refer their patients with Complex Regional Pain Syndrome (CRPS) for physiotherapy management. Beliefs about what is important for the management of patients with CRPS are lacking across all medical and allied health disciplines. Difficulties are no gold standard for diagnosis and evidence for intervention methods is moderate or can be conflicting. This paper explores what Physiotherapists believe to be important in a clinical setting for their management of CRPS, as well as documenting and evaluating their interventional methods used in everyday clinical practice across the region of the South Island of New Zealand. This has not been recorded before. Eighty-one Physiotherapists replied to questions on their usual treatment interventions for the management of CRPS, their frequency of use of these treatment interventions, and what they believed to be important in the management of pain and improvement of function. The results demonstrated that CRPS is not a common condition seen regularly by Physiotherapists; that there is a high level of variation between the physiotherapy interventions used and that Physiotherapists' beliefs regarding interventions used for pain management and functional restoration differ. Education was reported as the most frequently used intervention method. Those physiotherapists seeing CRPS patients more frequently are more likely to use evidence based intervention methods like graded motor imagery or sensory motor training.

## Keywords

Physiotherapy, Anaesthetists in Pain Management, Complex Regional Pain Syndrome (CRPS), Beliefs, Management, Intervention Methods, Outcomes

## 1. Introduction

Complex Regional Pain Syndrome (CRPS) is a persistent pain syndrome with a low prevalence [1] [2] which exhibits abnormal sensory, motor, sudomotor, vasomotor, and/or trophic findings and shows variable progression over time [3] [4] [5] [6]. It is evaluated by anaesthetists in Pain Management or by physiotherapists. It can be argued that it is both under-diagnosed [7] and over-diagnosed [8] [9]. Early diagnosis and referral by anaesthetists in Pain Management or by other medical disciplines to physiotherapists is regarded as essential [10]. Unresolved issues remain. There is no gold standard for the management of CRPS. Contrasting interventional methods exist in the literature around improving functional ability or controlling the pain experience. Beliefs about what is important or not for the management of CRPS remain unknown.

In other domains, beliefs held by Medical Practitioners and Allied Health Professionals are shown to affect practice, for example, as follows: the pain experienced in the elderly can be minimised [11]; physiotherapists will continue to treat low back despite any evidence of improvement [12]; and beliefs about opioid medication affect prescription practice [13] [14].

Amongst physiotherapists two opposing beliefs exist regarding pain modulation or pain exposure. Pain modulation is supported by the evidence for Graded Motor Imagery (GMI) [15] [16], mirror exercise [17], Sensory-Motor Training (SMT) [18], Graded Exposure (GEXP) [19], relaxation [20], psychological techniques [21] and Transcutaneous Nerve Stimulation (TENS) [22]. Pain Exposure (PEXP) is supported by the evidence for progressive exercise loading without analgesia moving towards restoration of function [15] [23] [24]. The beliefs of Medical Practitioners or Allied Health Professionals on the management of CRPS are not documented.

## 2. Purpose

Beliefs about what Physiotherapists in a clinical setting regard as important for their management of CRPS, as well as their beliefs about the interventional methods used in everyday clinical practice across the region of the South Island of New Zealand were evaluated.

## 3. Method

There are 150 private practices and hospital outpatient departments listed across the South Island of New Zealand by the New Zealand Physiotherapy Society (PNZ). Physiotherapy staff numbers in these practices or clinics vary from solo practitioners to those with high staff numbers. Each individual practice or clinic was contacted to find out whether they accepted CRPS patients or not. Those accepting CRPS patients were asked to fill in a paper-based questionnaire about their usual physiotherapy management for CRPS, and what they believed to be important in the management of pain and for the function in these patients. Ethical approval for this study was provided by the University of Otago Ethics

committee (Reference number H13/103). Inclusion criteria were a registered Physiotherapist currently working in any setting on the South Island of New Zealand who also accepted treating CRPS patients. Exclusion criteria were a registered Physiotherapist who never saw CRPS patients.

The questionnaire given to the Physiotherapist contained four sections. The first section asked how frequently CRPS patients were treated by them. A Likert Scale containing the following information was used: never; seldom (2 - 5 times per year); occasionally (5 - 10 times a year); regularly (2 - 3 times per month); or often (more than 5 times per month. The second section asked about the precise interventions carried out and their frequency of use. A Likert scale containing the following information was used, such as: never use this; occasionally use this; often use this; or most often use this. The third section enquired about what unlisted interventions the Physiotherapist used and their frequency of use. The fourth section looked at the beliefs the Physiotherapist held about the management of CRPS. The belief choice was as follows: reducing the pain is essential to improve the function; improving the function is essential to reduce the pain; exercising and increasing pain is contra-indicated; and exercising and increasing pain is indicated.

#### 4. Statistical Analysis

Standard descriptive statistics (Statistica 7, Microsoft Excel for windows PC) was used to compare categorical variables. Data analysis used ANOVA tests for significance between categorical variables and frequency of consultations with Physiotherapists.

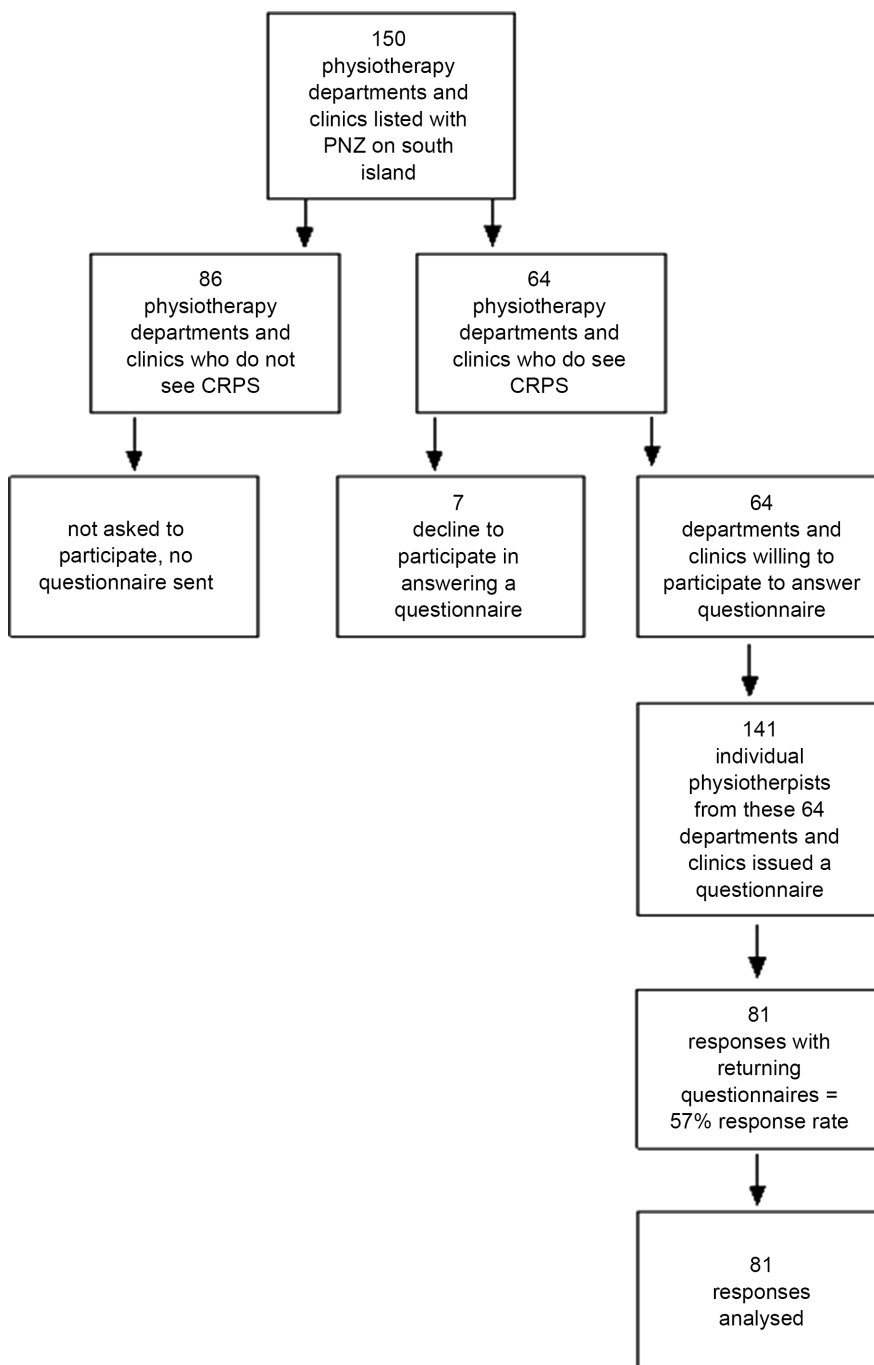
#### 5. Results

The 64 clinics and hospital outpatient departments who accepted patients with CRPS employed a total of 141 Physiotherapists. The 84 clinics and hospital outpatient departments who did not accept CRPS patients were excluded from the sample. Questionnaires were posted in self-addressed and pre-stamped envelopes (one for each Physiotherapist), or personally delivered. Eighty-one Physiotherapists answered the questionnaire and returned it either personally (n = 5) or by mail (n = 76). This provided a response rate of 57%. Participation rate in the physiotherapy intervention questionnaire is shown in **Figure 1**.

Eighty six (57.3%) of the 150 physiotherapy practices or outpatient clinics contacted never accepted any CRPS patients and were not asked to participate in the study. The 81 Physiotherapists who treated patients with CRPS came from 64 (or 43%) of the clinics and hospital outpatient departments across the South Island of New Zealand. Seven (or 4%) of the 150 clinics contacted accepted patients with CRPS declined to answer the questionnaire. Reasons given were as follows: no reason given (n = 1); about to retire (n = 1); staff shortages (n = 1); unwilling to have practice scrutinised (n = 2); too busy (n = 1); or an assessment only service (n = 1).

Sixty-three per cent of this sample of Physiotherapists on the South Island

who accepted patients with CRPS treated them infrequently (2 to 5 times annually). Twenty per cent treated 5 to 10 CRPS patients annually. Only 1% of Physiotherapists treated more than 5 CRPS patients in a month; 9% of Physiotherapists treated 2 - 3 CRPS patients each month. These data were simplified into two categories. Ninety per cent of Physiotherapists were categorised as seldom treating CRPS patients (less than 2 CRPS patients per month). Ten per cent of Physiotherapists were categorised as more frequently treating CRPS patients (more than 2 CRPS patients per month).



**Figure 1.** Participation with the physiotherapy intervention questionnaire.



The routine physiotherapy interventions examined were as follows: active exercises within pain limits; active exercises despite pain; resisted exercises despite pain; eccentric exercises; pain exposure exercises; graded exposure exercises; education; passive exercises within pain limits; passive exercises despite pain; pool exercises; neural stretches; tendon glides; balance exercises; proprioceptive exercises; lymphoedema massage; oedema massage; prescribed homework; scheduled as time contingent or pain contingent; sensory mapping training; discrimination training; desensitising training; GMI in classic order; GMI in ad hoc order; mirror exercises; prism exercises; relaxation exercises; breathing control; cognitive techniques for pain control; problem solving techniques for pain control; cognitive behavioural therapy (CBT); acceptance and commitment therapy (ACT); iontophoresis; soft tissue mobilisation; trigger point release; and other interventions (not listed). Fifteen Physiotherapists used acupuncture.

Education was the modality most commonly used as an intervention for CRPS (83% of Physiotherapists). Proprioceptive training and desensitising were often used (58% of the Physiotherapists). Forty nine percent of physiotherapists applied active exercise despite pain occasionally; active and resisted exercises within pain limits were used by 41% and 42% of the Physiotherapists, respectively. The types of interventions listed as occasionally used by the largest groups were trigger points release (53%), active exercise despite pain (49%), pool exercise (44%), and soft tissue mobilisation (41%). On the other hand, Physiotherapists (88%) seldom used iontophoresis, acupuncture (81%), prism exercise (78%), or acceptance and commitment therapy (70%).

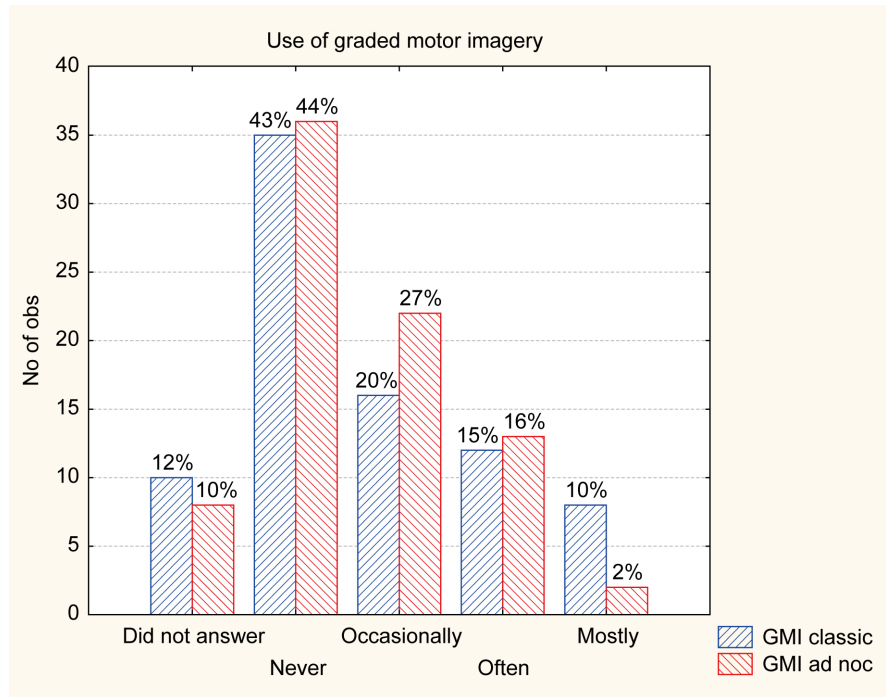
The frequency of use of all interventions used is listed in **Table 1**.

In the group who mostly used GMI, 10% used it in the classic order versus 2% who used it in an ad hoc sequence. However, 43% never used a GMI classic sequence at all. Twenty per cent occasionally used the GMI classic sequence. Fifteen percent of the GMI users often applied the classic sequence. Ten percent of Physiotherapists used the classic sequence of GMI as the most common intervention. Those who used the ad hoc sequence showed similar figures. This is shown in **Figure 2**.

These data were further analysed using ANOVA tests for significance to determine if the frequency of seeing CRPS patients affected the type of intervention used. The more frequently a Physiotherapist evaluated CRPS patients, the following occurred, namely: 1) they used GMI more often rather than occasionally in the classic order of the 3 phases,  $p = 0.017$ ; 2) the more they used relaxation techniques often rather than occasionally,  $p = 0.021$ ; 3) the more likely they were to use SMT, and sensory mapping or discrimination occasionally rather than never,  $p < 0.001$  and; 4) the more often they used oedema massage rather than seldom,  $p = 0.029$ . **Table 2** outlines the significant differences between those Physiotherapists who evaluated CRPS patients frequently compared to those who seldom saw CRPS patients.

**Table 1.** Physiotherapy interventions for CRPS and frequency of use.

Intervention method	Answered question	Frequency of use by Physiotherapist (% valid answers)			
	N (%)	Never	Occasionally	Often	Mostly
Active exercise within pain limit	77 (95%)	0%	14%	41%	41%
Active exercise despite pain	76 (94%)	20%	49%	20%	5%
Resisted exercise within pain limit	74 (91%)	2%	33%	42%	14%
Resisted exercise despite pain	73 (89%)	38%	40%	11%	0%
Eccentric exercise	72 (89%)	38%	40%	11%	0%
Pain exposure exercise	65 (80%)	30%	32%	11%	7%
Graded exposure exercise	69 (85%)	11%	20%	33%	21%
Education	79 (98%)	0%	1%	14%	83%
Passive exercise within pain limits	71 (88%)	9%	32%	30%	17%
Passive exercise despite pain	71 (88%)	36%	37%	11%	2%
Pool exercise	76 (94%)	22%	44%	20%	7%
Neural stretches	72 (91%)	11%	43%	33%	4%
Tendon glides	72 (91%)	19%	36%	32%	2%
Balance exercise	73 (89%)	9%	22%	51%	9%
Proprioceptive Exc	86 (94%)	2%	20%	58%	14%
Lymphoedema massage	73 (90%)	48%	36%	5%	1%
Oedema massage	86 (95%)	25%	42%	20%	9%
Prescribed Homework: Scheduled as time contingent	85 (93%)	6%	22%	48%	16%
Prescribed Homework: Scheduled as pain contingent	85 (93%)	25%	36%	19%	14%
Sensory mapping training	70 (86%)	42%	32%	12%	1%
Discrimination training	74 (91%)	40%	28%	19%	5%
Desensitising training	76 (94%)	2%	20%	58%	14%
Graded Motor Imagery (GMI) in classic order	71 (90%)	43%	20%	15%	10%
GMI in your own order or ad hoc	73 (90%)	44%	27%	16%	2%
Mirror exercise	78 (96%)	21%	31%	35%	10%
Prism exercise	69 (85%)	78%	7%	0%	0%
Relaxation exercises	73 (90%)	11%	33%	33%	12%
Breathing control	75 (93%)	12%	33%	33%	14%
Cognitive techniques for pain control	73 (90%)	22%	33%	26%	9%
Problem solving techniques for pain control	74 (91%)	20%	31%	25%	16%
Cognitive Behavioural Therapy (CBT)	72 (89%)	48%	15%	22%	4%
Acceptance and Commitment Therapy (ACT)	68 (84%)	70%	9%	4%	1%
Transcutaneous Electrical Nerve Stimulation (TENS)	73 (90%)	21%	44%	23%	1%
Iontophoresis	71 (90%)	86%	0%	1%	0%
Soft tissue mobilisation	74 (91%)	9%	41%	37%	5%
Trigger point release	73 (90%)	11%	53%	26%	0%
Acupuncture	81 (100%)	81%	9%	11%	0%



**Figure 2.** Use of graded motor imagery in clinical physiotherapy practice.

**Table 2.** Significant differences between those Physiotherapists who saw CRPS seldom versus those who saw CRPS patients often.

Physiotherapy intervention method more likely to be used by the physio who sees CRPS patients more often	Frequency of use more likely	P value
Graded Motor Imagery (GMI)	From occasional to often	0.017
Relaxation techniques	From occasional to often	0.021
Sensory-Motor training (SMT)		
• Sensory mapping	• From never to occasional	0.007
• Discrimination	• From never to occasional	0.007
• Desensitising	• From occasional to often	0.007
Oedema massage	From seldom to often	0.029

Beliefs about what was considered most effective for the management of CRPS patients proved highly variable. Physiotherapists were almost equally divided about whether or not reducing the pain experience was essential to improve the functioning (51% and 43%, respectively). This is shown in **Figure 3**.

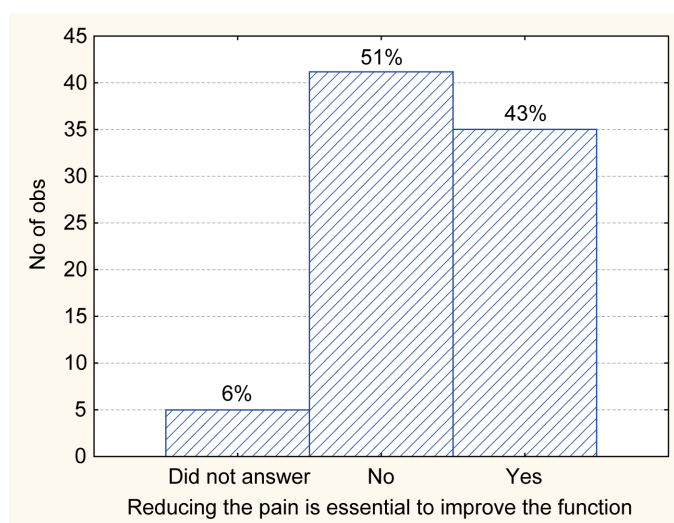
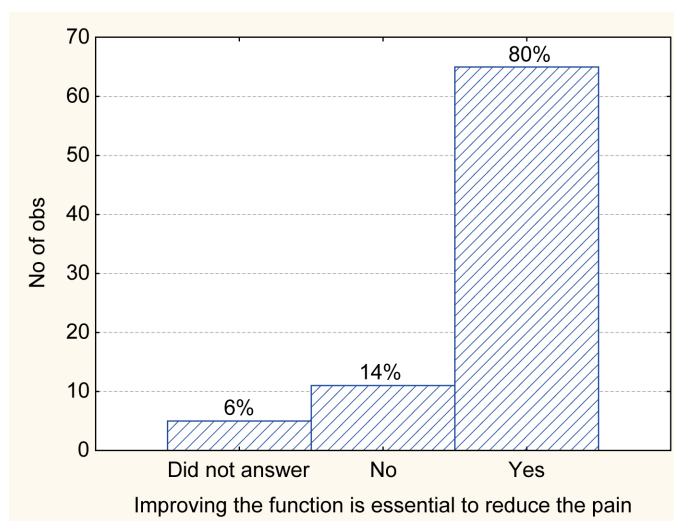
Eighty per cent believed that improving the function was essential to reduce pain; 14% believed that it was not essential. This is shown in **Figure 4**.

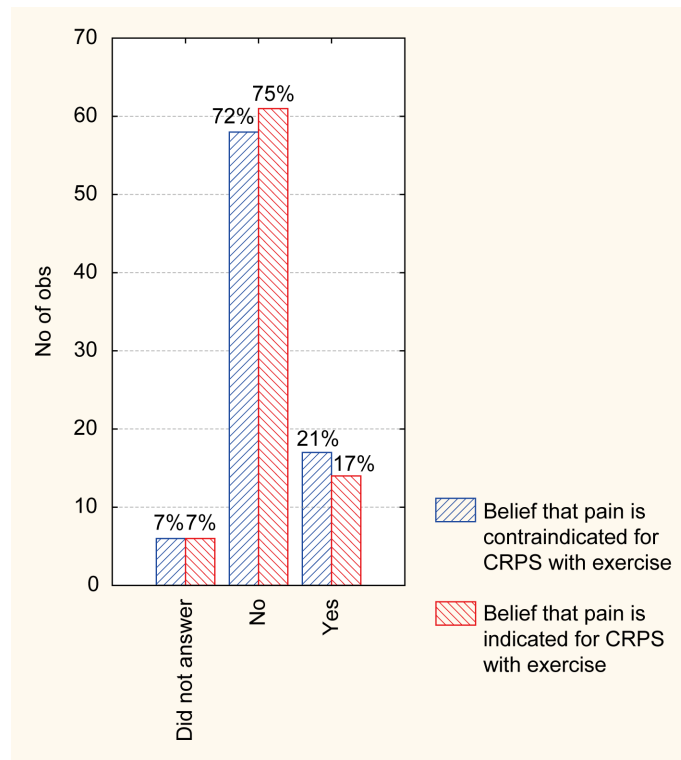
Physiotherapists were equally divided on their beliefs about exercise and pain being either indicated or contraindicated in CRPS. These beliefs are shown in **Figure 5**.

The beliefs were summarised and are represented in **Table 3**.

**Table 3.** Summary of Physiotherapist beliefs about what is best for CRPS intervention method.

Physiotherapist beliefs about what is best for CRPS intervention method			
	Did not answer	Yes	No
	n (%)	n (%)	n (%)
Reducing the pain is essential to improve the function	5 (6%)	35 (43%)	41 (52%)
Improving the function is essential to reduce the pain	5 (6%)	65 (80%)	11 (14%)
Exercising and increasing the pain is contraindicated	6 (7%)	17 (21%)	58 (72%)
Exercising and increasing the pain is indicated	6 (7%)	14 (17%)	61 (75%)

**Figure 3.** The belief about reducing the pain being essential in CRPS to improve the functioning.**Figure 4.** Improving the function is essential in order to reduce the pain experience.



**Figure 5.** Beliefs about exercise and increasing pain being indicated or not for CRPS.

## 6. Discussion

These data provide the first contribution to literature about a systematic survey of physiotherapy and CRPS management in everyday clinical practice. Half of all New Zealand South Island physiotherapy practices do not manage CRPS patients. Only 10% of the Physiotherapists that manage CRPS patients treat more than two CRPS patients per month. Education was most often used as an intervention for CRPS. This was recorded by 83% of the Physiotherapists who together with Anaesthetists play an important role in education as CRPS patients possess a sub-minimum standard of basic knowledge about the syndrome [25]. Similar to diseases like diabetes, education enables behavioural change as well [26].

The data showed that the more frequently Physiotherapists evaluated CRPS patients, the more likely they were to use interventions with moderate based evidence, such as GMI and SMT. However, GMI and SMT were not used by many other Physiotherapists who evaluate CRPS patients less frequently. It is not possible to determine the reasons for these differences. This clearly needs further investigation. It has been suggested that physiotherapy management for CRPS needs to be specifically personalised [27]. This can be particularly difficult, as CRPS presentations, progression and outcome are variable. There is little specific evidence about what intervention to apply and when [28]?

These data illuminated the inconsistency with which physiotherapy interventions (other than education that is mostly used) are practised by those managing CRPS patients. A third of the sample often used cognitive techniques and

breathing control with relaxation techniques; another third used them occasionally. Those treating more CRPS patients are more likely to use the above technique rather than occasionally. Less than 15% are most likely to use these techniques. Eighty per cent are familiar with these interventions but do not apply them regularly.

Beliefs were divided about pain reduction being essential or not for improving the function of the affected CRPS limb. Eighty per cent believed that by improving function, the pain is reduced. Exercising and increasing the pain was a belief supported by 17%. It was found that 49% applied active exercises despite pain, but then only occasionally. When asked whether pain was contra-indicated or not for CRPS exercises, the groups were almost equally divided. Half believed that it was inevitable to have some pain with exercise; only 17% of this group believed that pain with exercise was really necessary.

Holding different beliefs influences the interventional modalities chosen for pain reduction or improvement in function for the treatment of CRPS patients. It influences the relationship the Physiotherapist has with the referring Anaesthetist. Applying any intervention by one half of Physiotherapists can become potentially difficult, if pain exacerbation is thought to be contraindicated, as pain forms the hallmark of CRPS. There are CRPS patients who present with reasonable function, but suffer severe pain [29]. The clinical presentation of CRPS remains inconsistent [1] [2] [30] [31] [32] [33]. Resolving how beliefs influence CRPS management is essential.

A weakness of the study is the relatively small sample size with potential bias being represented by the 57% response rate. Another weakness of the study is the use of Likert scale for measuring the frequency of the physiotherapy interventions that is not formally validated.

The strength is that this study provides the first evidence to represent data across a region, about Physiotherapist beliefs and usual interventions for CRPS patients. The use of self-reporting questionnaires as a valid measure is supported [34]. Future studies should be undertaken to develop validated questionnaires about beliefs around CRPS for Anaesthetists in Pain Management, Physiotherapists, and other health care providers, as well as for patients suffering from CRPS. It is important to determine how these beliefs influence referral, intervention method(s) and patient outcomes.

## 7. Conclusion

CRPS is not common on the South Island of New Zealand. Usual physiotherapy interventions vary widely. Different beliefs exist about the importance of managing the pain experience and the importance of improving function. These reflect the dichotomy seen in current evidence. Education is the most commonly used intervention. Those treating more CRPS patients are more likely to use interventions such as GMI and SMT often (rather than seldom, or not at all). How Anaesthetists in Pain Management and Physiotherapy beliefs about pain management and functional restoration affect CRPS outcomes requires closer scrutiny.

## Conflict of Interest

The authors declare no conflict of interests regarding the publication of this paper. No funding contribution was received towards selection, extraction or analysis of the data from any source.

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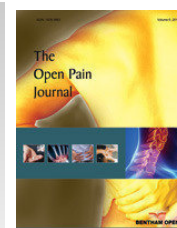
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## RESEARCH ARTICLE

# Physiotherapy Interventions and the Outcomes for Complex Regional Pain Syndrome (CRPS) Type 1 on the South Island of New Zealand – A Longitudinal, Prospective Case Series

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**Abstract:** Physiotherapy is considered in pain medicine to be a key element in the management of Complex Regional Pain Syndrome (CRPS). This is the first paper to document and categorise all physiotherapy intervention methods used as well as evaluate the outcomes of a case series of 18 CRPS patients attending physiotherapy in a prospective, longitudinal study across a region. Outcomes were measured across the region of the South Island of New Zealand over 1 year through independent telephonic interviewing of the pain experience with the McGill Pain Questionnaire-short form, function with Foot Function Index for the lower limb or Disability of the Arm Shoulder and Hand for the upper limb, and quality of life with the World Health Organisation Disability Schedule. Clinical records were accessed for each CRPS participant following discharge from physiotherapy to categorise the intervention methods used. Seventeen participants received intervention for both functional restoration with pain modulation and only one participant received functional restoration with no pain modulation; 12 also received immobilisation with 10 receiving passive interventions. All outcome measures improved significantly by 6 months and were maintained at 1 year. Eighty five percent had their diagnosis of CRPS confirmed within 3 months of their injury; half had fracture as the precipitating injury for their onset of CRPS with a third following soft tissue injury and 11% following surgery. Physiotherapists showed a high variation with the intervention methods used and showed a greater proportion of intervention methods focusing on functional restoration followed by pain modulating interventions. Future research is necessary to define what physiotherapy interventions are efficacious in the management of CRPS.

**Keywords:** Physiotherapy, Complex Regional Pain Syndrome (CRPS), Case series, Prospective, Longitudinal study, Outcomes, Intervention methods.

## INTRODUCTION

Complex Regional Pain Syndrome (CRPS) is an uncommon pain syndrome characterized by persistent regional pain that is disproportionate in time or degree to the usual course of any known trauma or other lesion [1]. CRPS may occur at the time of an injury, subsequent to an injury or occur spontaneously [2]. A distal predominance affecting the limbs with abnormal sensory, motor, sudomotor, vasomotor, and/or trophic findings is usual, with the syndrome showing variable progression over time [2 - 5]. The Budapest criteria are the most accepted criteria for the diagnosis of CRPS, where Type 1 is defined as no definitive nerve lesion and Type 2 as associated with a nerve lesion [6, 7].

It has been suggested that physiotherapy is an essential element in the management of CRPS [1, 4, 8 - 10]. Despite this, there is little research detailing the mechanisms how physiotherapy contributes to the recovery from CRPS [10], nor strong evidence for the safety or effectiveness of physiotherapy management of CRPS in clinical practice.

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Unfortunately, reference in the published literature to “usual physiotherapy” of CRPS patients seldom contains details about intervention methods used [10 - 12].

The aims of this paper were to describe the natural history of 18 CRPS Type 1 patients living in the South Island of New Zealand (population ~ 1 million, area 150 437 km<sup>2</sup>) [13] for one year after starting physiotherapy; to document; categorise the physiotherapy interventional methods that they received and measure the patient outcomes.

## **METHODS**

### **Participants and Recruitment**

There are 150 private practices and hospital outpatient departments listed across the South Island of New Zealand as members of the New Zealand Physiotherapy Society (PNZ) or indexed in the telephone directory. Each practice was contacted to find out whether they accepted CRPS patients and would be willing to enrol any patients identified between February 2014 and February 2016 into the study. Treating physiotherapists were asked to;

- Assess patient eligibility and conduct informed written consent for the researcher to interview the patient and access to their clinical record (written consent was provided by a parent or guardian if patient was younger than 18 years),
- Provide the researcher access to their clinical notes to extract and categorise intervention methods used,
- List the autonomic changes observed and reported,
- Continue treatment as normal.

Participant inclusion criteria were a confirmed diagnosis by either General practitioner, Medical Specialist or Physiotherapist of CRPS according to the Budapest criteria [6] within one year of presenting to the treating physiotherapist. Potential participants were excluded if their CRPS diagnosis had been longer than 1 year; they had a terminal co-morbid condition; were blind (sight was necessary for graded motor imagery); or were unable to communicate in English or Maori (including deafness and cognitive impairment). Ethical approval for this study was provided by the University of Otago Ethics committee (Reference number H13/103, and ethical approval was granted from each individual South Island regional District Health Board.

### **Procedures**

Upon receipt of signed consent, the researcher contacted each participant by telephone, explained the project, confirmed eligibility, and commenced the baseline measures. Baseline measures included age, gender and ethnicity as defined by Statistics New Zealand [14], as well as details about the initial event precipitating injury or pain, and time from first experience of pain to; (i) CRPS diagnosis; (ii) first physiotherapy intervention; and (iii) first pain medical specialist consultation.

The following outcome measures were also assessed at baseline and by independent interviewer at 6 weeks, 6 months and at 1 year. Pain intensity was measured using the Short form McGill Pain Questionnaire (SF-MPQ), an easy to administer scale [15, 16] widely used in CRPS research [17]. The SF-MPQ consists of 15 items that sum to form the Pain Rating Index (PRI), one item that measures Present Pain Intensity (PPI), and an 11-point Numerical Rating Scale (NRS). Functional ability was assessed using the 11-item Quick Disability of the Arm, Shoulder, Hand questionnaire (QuickDASH) [18 - 20] for those with CRPS of the upper limb, and the 23-item Foot Function Index (FFI) [21, 22] for those with CRPS of the lower limb. Quality of life associated with disability was assessed using the 12-item World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2) [23], which was chosen as appropriate for both upper and lower extremities.

Following the last interview, the treating physiotherapist(s) were contacted and clinical notes were accessed by the researcher to determine the type, frequency, and duration of interventions administered as well as clinic non-attendance. Physiotherapy treatment interventions were categorised into one of five by an experienced Physiotherapist and a Pain Specialist Physician according to the “target” of the intervention; where functional restorative target active joint range of motion, muscle strength, balance and proprioceptive exercise; pain modulation target central processing; immobilisation restricts or inhibits any active activity and passive interventions require no active engagement of the participant with the intervention:

- Functional restorative interventions (TIF): active, passive, resisted, balance or proprioceptive land based exercise with time contingent homework prescribed.
- Pain modulation interventions (TIP): Graded Motor Imagery (GMI), mirror exercise, pool exercise, Transcutaneous Electrical Nerve Stimulation (TENS), Cognitive Behavioural Therapy (CBT), acceptance and commitment therapy (ACT), problem solving, relaxation and breathing, Sensori-motor Training (SMT) including sensory mapping, and discrimination and desensitising with pain contingent homework prescribed.
- Education: a written record of “education”.
- Immobilising interventions (TII): bracing, splinting or taping.
- Passive interventions(TIP): massage (scar tissue, lymphoedema or oedema), acupuncture, ultrasound, and application of heat or wax bath.

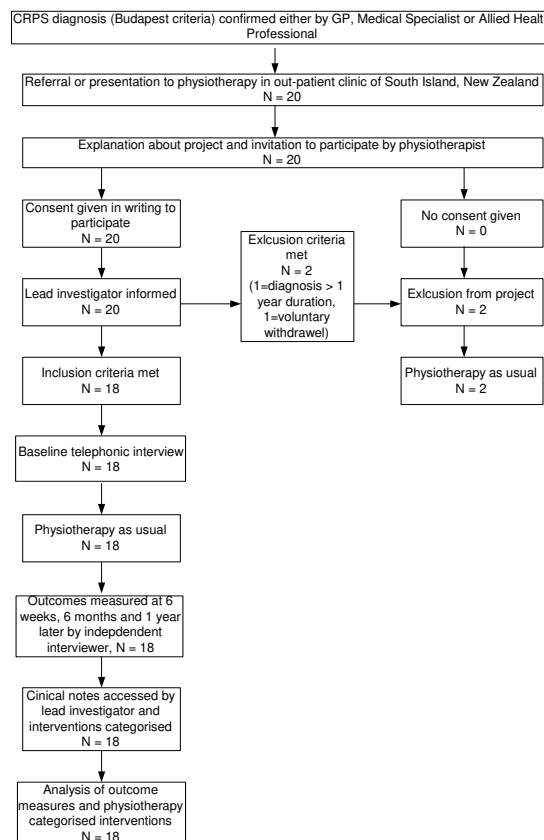
Other interventions, both medical prescriptions or procedures and other allied or alternative health interventions were recorded from the participant’s interviews and verified with the clinical physiotherapy notes.

**Statistical Analysis**

Participant baseline characteristics and outcome measures were summarised using standard descriptive statistics. Paired student-t tests were used to test statistical significance (using a significance level of  $p < 0.05$ ) of changes in outcome measures from baseline to one year. Analysis was performed using Statistica 7 and Microsoft Excel for windows PC.

**RESULTS**

Sixty-four (43%) of the 150 physiotherapy practices or outpatient clinics contacted reported that they accepted CRPS patients, and fifty seven of these (89%) indicated they were willing to recruit patients into the study. Twenty CRPS patients signed consent to participate, but one was excluded due to their duration of CRPS greater than one year at consent and one withdrew for personal reasons. All follow up measures were completed for all participants. Fig. (1) represents the flow chart of recruitment for participants and clinical records for this project.



**Fig. (1).** Flow chart for recruitment of CRPS participants.

Participants were predominantly New Zealand European (Pakeha) female with a wide age range (11 to 72 years); from mid and north Canterbury where the greatest population density lives; the education equivalent of completed school years; half with a fracture injury which precipitated their CRPS; the upper limb affected more often (68%) than the lower limb and most (85%) had been diagnosed within the past three months. Participant baseline demographic and clinical details are reported in Table 1.

**Table 1. Demographic and clinical characteristics of CRPS participants.**

Characteristics	N (%)
Age in years, Mean (SD) [range]	43.9 (19.5) [11 to 72]
Gender Female Male	16 (88%) 2 (12%)
Ethnicity New Zealand European (Pakeha) Maori Pacific Other	15 (82) 1 (6) 1 (6) 1 (6)
Education number of years, Mean (SD)	13.5 (3.3)
Region, from south to north Southland Otago Mid and North Canterbury South Canterbury Nelson/Marlborough	2 (11) 2 (11) 12 (68) 1 (5) 1 (5)
CRPS precipitating event Fractures Soft tissue injury Surgery	9 (53) 7 (37) 2 (11)
Affected limb Upper limb Lower limb	13 (68) 5 (32)
Laterality Right center	10 (53) 8 (47)
Time to diagnosis from injury 1-3 months 3-7 months	16 (85) 2 (15)

### Physiotherapy Interventions

The eighteen participants summed a total of 365 physiotherapy sessions (median = 16.5 sessions, IQR = 8-33), involving 274 contact hours (median = 13, IQR = 4.3 - 19.4). Participants on average attended physiotherapy for median 20 weeks with Physiotherapy interventions had been completed by 6 months for 10 participants' (55%) and three (17%) had self-discharged by this time. One more participant was discharged by their one year interview leaving 4 (22%) engaged with ongoing Physiotherapy. The number of physiotherapy sessions attended and number of contact hours with the Physiotherapist had large interquartile ranges from their respective medians, namely 20 (14) and 15 (13), respectively. These are shown in Table 2.

**Table 2. Summary of physiotherapy delivered.**

	Self-discharge	Discharge by Physio	On-going Physio	Whole Sample
	N = 3	N = 13	N = 2	N=18
Total no of physio sessions attended, median (IQR)	7.0 (3-17)	16.0 (8-30)	42.0 (39-45)	16.5 (8-33)
Total no of contact hours with physiotherapist hours, median (IQR)	4.3 (2-17)	12 (4.5-17))	36.2 (33.4-39)	13 (4.3-19.4)
Total duration of weeks of physiotherapy, median (IQR)	12 (4-16)	20 (16-32)	38 (32-44)	20 (16-32)

\*IQR = interquartile range

Physiotherapy categorised interventions for participants were collated. Seventeen participants received intervention for both functional restoration with pain modulation contributing to 55% of all interventions applied and only one participant received functional restoration with no pain modulation intervention; 12 received immobilisation and 10 received passive interventions. Data at 6 weeks showed a slightly greater use of pain modulation than functional restoration intervention but by one year it showed the total percentage of modalities focused around improving function (42%) was greater than the percentage of interventions focusing on modalities for pain modulation (34%). All received a record of education but this was documented at most only once a week. The average weekly numbers of interventions for each category tended to decrease over time. Data is shown in Table 3.

**Table 3. Summary of categorised physiotherapy interventions over intervals across one year.**

Category of Intervention	Intervention total N, mean (SD) Interventions per week, mean (SD)				Percent of all Interventions
	6 weeks	6 months	1 year	Total	
Functional Restoration N= 18	22 (13) 3.7 (2.1)	44 (43) 2.4 (2.4)	8 (15) 0.4 (0.6)	74 (60) 1.4 (1.2)	42
Pain Modulation N= 17	24 (28) 4 (5)	27 (38) 1.5 (2.1)	7 (15) 0.3 (0.6)	59 (73) 1.1 (1.4)	33
Functional Restoration and Pain Modulation N=17	46 (32)	71 (70)	15 (29)	97 (68)	55
Education N= 18	6 (4) 1.1 (0.7)	8(8) 0.5 (0.5)	2 (3) 0.08 (0.1)	16 (13) 0.3 (0.2)	9

(Table 3) contd.....

Category of Intervention	Intervention total N, mean (SD) Interventions per week, mean (SD)				Percent of all Interventions
	6 weeks	6 months	1 year	Total	
<b>Immobilisation</b> N=12	5 (8) 0.8 (1.3)	9 (18) 0.5 (1.1)	1 (5) 0.05 (1.2)	15 (29) 0.3 (0.6)	9
<b>Passive</b> N=10	4 (8) 0.7 (1.3)	8 (14) 0.4 (0.7)	0.7 (1.8) 0.03 (0.08)	13 (18) 0.3 (0.4)	7

**Outcome Measures**

Mean scores for the outcome measures of the SF-MPQ, WHODAS, FFI, and QuickDASH all showed significant improvement with a clinically important change with the reduction by half the baseline score at 6 months. A statistically significant improvement is shown to be maintained at 1 year but FFI was the only scale to show continued improvement after six months Table 4.

**Table 4. Mean (SD) scores for primary outcome measures changes at 6 weeks, 6 months and 1 year.**

Outcome dependent variable (Score range, clinically important change)	Baseline score, mean (sd) N = 18	Change at 6 weeks, mean (sd) N = 18	Change at 6 months, mean (sd) N = 18	Change at 1 year, mean (sd) N = 18	t-test P (change at 1yr)
<b>SF-MPQ PRI</b> (0 to 45, >5)	21.8 (8.1)	-9.4 (9.9)	-15.6 (10.7)	-15.6 (12.2)	<0.001
<b>SF-MPQ NRS</b> (0 to 10, > 3)	6.4 (1.6)	-3.0 (2.6)	-4.4 (2.8)	-4.6 (2.8)	<0.001
<b>WHODAS</b> (0 to 60, > 15)	80 (22.5)	-27.3 (28.1)	-47.3 (26.7)	-47.1 (34.8)	<0.001
	N = 5	N = 5	N = 5	N = 5	
<b>FFI</b> (0 to 100, >10)	47.6 (12.1)	-20.47 (13.0)	-29.5 (14.2)	-39.9 (21.1)	0.02
	N= 13	N= 13	N= 13	N= 13	
<b>QuickDASH</b> (0 to 100, >15)	60.0 (18.5)	-31.3 (25.6)	-43.4 (21.2)	-39.7 (21.0)	<0.001

**DISCUSSION**

These data provide the first contribution to the literature about physiotherapy interventions used for management of CRPS in clinical practices across a region. The characteristics of this case series sample show a predominantly female Pakeha (New Zealand European) group with an age range from 11 to 72 years. CRPS is shown to affect all age groups with the greatest risk being the post-menopausal female [24]. The average education level was 13 years, involving completion of an equivalent schooling qualification. Almost seventy percent were from the region of the greatest population density, mid/north Canterbury. Half had fracture as the precipitating injury for their onset of CRPS with a further third following soft tissue injury and a small group of 11% following surgery. Laterality of affected limb was almost equally shared between left and right sides and most (68%) had their upper limb affected.

This case series shows 85% to have had their diagnosis of CRPS confirmed within 3 months of their injury and that all outcome measures improved significantly by 6 months and were maintained at 1 year. This supports the evidence that early diagnosis can improve outcomes [9, 25]. Clinically important changes are represented in the QuickDASH as a change of 15 points [26]; WHODAS as 15 [27]; MPQ PRI as 5 with NRS as 3 [28]; FFI as 10 [21]. This sample shows significant clinical improvement across all measures 6 months after commencing physiotherapy. The FFI shows continued improvement between 6 months and 1 year while the QuickDASH deteriorated slightly despite still maintaining significant improvement from baseline measure. Fifty-five per cent had completed their physiotherapy intervention by 6 months later with a good outcome. Only 2 required ongoing physiotherapy care and their outcomes were also improved by this time. However, three patients self-discharged from physiotherapy and chose alternative therapies (2 chose Neuro-linguistic programming and 1 would not disclose his intervention) and their outcomes improved despite their non-attendance. It is shown that CRPS can resolve spontaneously for a small sub group [29].

This sample shows that the outcome measure improvement is despite a widely varied duration or category of physiotherapy intervention(s) used. It supports the optimistic outcomes with tailored intervention [30 - 32], yet it is also possible that the improvement seen with this case series is simply regression to the mean. Other publications [33 - 36] document physiotherapy and that the CRPS problems improve, but this is the first to record and categorise every physiotherapy intervention used across a region and evaluate the respective outcomes. The outcomes measures all show

a significant improvement with reduction by at least half the baseline score which is shown to be a clinically meaningful change. The sample size is, however, too small to make any definite conclusions regarding the efficacy of any specific intervention used. It is noted that for this sample a slightly greater percentage of interventions focussed on both functional restoration as well as pain modulation. The effect is not possible to determine with this small sample size. It is also possible the different physiotherapy interventions could be categorised differently. Furthermore, it is not possible to determine those CRPS patients who did not present for physiotherapy, or presented to other health care providers, or who simply self-managed their problem without interacting with any health service. The first epidemiological publication on CRPS noted that 93% of the CRPS population did attend physiotherapy and 87% reported about physiotherapy being efficacious [29]. The effect of attending physiotherapy, or not, is yet to be explained [29, 37 - 41].

These data illuminate a possible conflict that influences the physiotherapist's management of CRPS patients. A dichotomy exists in the literature showing that persistent pain can be aggravated by activation due to temporal summation [42]; yet the population who exercise more regularly experience less persistent pain [43, 44]. Many CRPS patients present with reasonable functioning, but continue to experience severe pain despite persevering with exercise [45]. Management for CRPS remains difficult; the clinical presentation of CRPS remains highly variable [46]. Hence, to simply normalise function does not necessarily reciprocally reduce the pain experience or vice-versa. Ethically, it is not possible to deny treatment, and which intervention method and at what dose is urgently needed to be determined for the different presentations of CRPS. Importantly also, to explore why some self-discharge or do not attend physiotherapy and what constitutes their subsequent improvement is crucial. There is at present no algorithm for what physiotherapy intervention(s) are essential for the physiotherapy management of CRPS. Despite these difficulties, physiotherapy is recognised as an essential part in reducing pain and improving function in the management of CRPS [4, 8, 11, 47 - 50]. Other data report favourable outcomes for a sub group of CRPS patients [25, 38, 51, 52] which is consistent with this case series. However, it is reported that others recover poorly resulting in poor health and function [38, 45, 53 - 55].

A weakness of the study was its small sample size allowing potential bias to occur from both CRPS participants and five per cent of Physiotherapists who do manage CRPS patients did not engage with this study reflecting a possible skew reflection of usual physiotherapy applied for CRPS. The clinical notes of intervention accuracy are problematic, *e.g.* education is an integral part of the Physiotherapist's conversation with any patient, yet the intervention of "education" was only recorded at most once a week. To obtain independent recorders of physiotherapy interventions was not possible for this study since it covered an area 150437 km<sup>2</sup>. Another potential recognised weakness of the study is the use of Likert scales for accurate statistical analysis of continuous variables.

This study's strength is its originality to document and report data across a region for physiotherapy interventions with respective outcomes, minimal interviewer bias and valid self-reporting questionnaires [56]. There is a lack of good evidence as well as disagreement about which physiotherapy interventions are effective in managing the diverse presentations of CRPS. Future research is needed to determine a robust evidence based model for the physiotherapy management of CRPS and this paper is the first to provide a platform for comparison across a region.

## CONCLUSION

This is the first record of physiotherapy for CRPS management and patient outcomes across a region. CRPS is not a common problem presenting to health professionals and this case series showed all outcome measures to show significant improvement after 1 year with intervention methods focusing primarily on functional restoration and pain modulation. There is a lack of strong evidence to determine which interventions are effective in a clinical setting for the diverse presentations of CRPS. Future research should define what physiotherapy interventions are efficacious in the management of CRPS.

## CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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## IN SUBMISSION

Standard physiotherapy for complex regional pain syndrome (CRPS): ingredients for recovery; a prospective, longitudinal, cohort study.

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# Standard physiotherapy for complex regional pain syndrome (CRPS): ingredients for recovery; a prospective, longitudinal, cohort study.

## **Summary (123 words)**

No specific physiotherapy intervention influenced a complete recovery in a longitudinal, prospective, study across the region of the South Island of New Zealand for CRPS.

## **Abstract (248 words)**

Standard Physiotherapy CRPS management has been shown to be equally beneficial to pain exposure, more beneficial than graded motor imagery alone, and is considered to be essential for an optimal outcome. This is the first evaluation of the efficacy of regional standard physiotherapy intervention for recently diagnosed CRPS and involved the South Island of New Zealand. Patient outcomes, changes over time for one year after commencing physiotherapy, medical or psychological concurrent intervention and the respective physiotherapy applied were evaluated. Informed, written consent was obtained, and pre and post outcome measures followed baseline (using an independent telephonic interviewer) at 6 weeks, 6 months and at 1 year after commencing physiotherapy. Outcome measures used were: pain intensity; functional ability; quality of life and satisfaction of care. Novel potential predictors included the Health Anxiety Index, the Extraversion and Neuroticism scale of the brief-version Eysenck Personality Questionnaire, and the ten-item psychological distress Kessler questionnaires. Statistical analysis used standard descriptive statistics and logistic regression to determine predictive effects with an alpha of 0.05. Fifty-two females and 14 males participated, aged 11 to 77 years (mean 46 years) between December 2013 and 2018. Results showed that all participants obtained improvement. No specific physiotherapy intervention significantly influenced recovery. Full recovery correlated with the extraversion personality measure and the concurrent prescription of secondary anticonvulsant analgesia. The novel factor of personality extraversion warrants further investigation, and a clinical conceptual model which integrates the limited evidence for the physiotherapy management of CRPS should be considered in future research.

## **Key words**

Physiotherapy, Complex Regional Pain Syndrome (CRPS), observational cohort longitudinal study, outpatient, region, outcomes, intervention methods, intervention categories, telephonic interviewing, independent interviewing, logistic regression, odds ratio, confidence interval.

## **1. Introduction (6520)**

Complex Regional Pain Syndrome (CRPS) remains an enigma,[39] and it can be difficult in a clinical setting for a Physiotherapist to know where to start in managing a recently diagnosed patient. There is debate about classifying it as a neuropathic pain condition [29]. Its aetiology is not fully understood [44]. There is no gold standard for its diagnosis. Although the Budapest criteria have improved the sensitivity and specificity of diagnosis [40], yet members of one hand team were reported to interpret CRPS clinical signs differently [27]. Physiotherapists' beliefs about what is important for the management of CRPS remain diverse [59].

Determining the course of treatment is not straight forward, and standard physiotherapy referred to in clinical trials is often not described in detail; neither has standard physiotherapy across a region been evaluated. Furthermore, since the presentation and trajectory of CRPS over time is variable [11; 38; 52], outcomes are shown to be heterogeneous [3; 76], its prevalence is low [21; 64], and robust statistical analysis is difficult to determine strong effects for intervention methods for CRPS.

A recent case series first documented the data about standard physiotherapy applied across a region in respect to CRPS outcomes [60]. The type of physiotherapy used was categorised. A high variation of intervention intensity and methods used were reported. All outcome measures showed significant improvements 6 months later that were maintained at the 1 year mark. In order to establish what standard physiotherapy across a region involved and its effect, the aims of this study were as follows: a) to measure patient outcomes and changes over time for one year after commencing physiotherapy; b) to document and categorise the physiotherapy interventional methods received; c) to identify predictors of patient outcomes, and; d) to investigate the efficacy of current physiotherapy interventions for CRPS across a region.

## **2. Method**

### **2.1. Participants, recruitment and outcome measures**

A prospective cohort of 66 CRPS patients, observed between December 2013 and December 2017 in the South Island of New Zealand, was used to investigate associations between physiotherapy interventions and patient outcomes.

The recruitment process, the inclusion/exclusion criteria, the quantitative outcome measure instruments, and the physiotherapy interventions evaluated were described in a case series [60]. In summary, outcome measures taken at baseline (at the start of physiotherapy after the diagnosis of CRPS), at 6 weeks, at 6 months and at 1 year were measured using the following: quality of life with the World Health Organisation (WHO) Disability Assessment Schedule 2.0 (WHODAS 2) [34; 72; 77]; functional ability of the upper limb with the Quick Disability of the arm, shoulder and hand (QuickDASH) [4-6; 69]; functional ability of the lower limb with the Foot Function Index (FFI) [12; 13]; pain with both the Short Form-MPQ Questionnaire [41; 50] and the single measurement 11-point numerical rating scale (NRS-11 [31] which is sensitive and specific to evaluate the experience of pain [78]; satisfaction of care with the Deyo and Diehl Satisfaction (DDS) Questionnaire [26] .

### **2.2. Physiotherapy intervention**

Physiotherapy interventions were categorised by TP and ES as treatment interventions for: pain (TIP); function (TIF); education (Educ); immobilisation (TII); or were passive (Pass). The weekly averages calculated for each outcome measure interview interval (6-weeks, 6-months and 1 year) and individual TIP physiotherapy interventions were analysed further as categorical variables against the outcome variables of complete CRPS recovery. TIP interventions included were: graded motor imagery (GMI), sensory motor training (SMI), pool based primary exercise, (POOL) (vs. gym based), relaxation training, mirror exercise, deep breathing exercise (DBE), graded exposure (GEXP), cognitive techniques, or the prescription of Transcutaneous Electrical Nerve Stimulation (TENS).

The time to diagnosis; the time to commence with physiotherapy and concurrent medical or psychological support data were documented as well. Psychosocial measures like catastrophising, anxiety or depression have been shown to have mixed evidence associated with CRPS outcomes [2; 61]. Health anxiety, a specific facet of anxiety associated with body

sensations and physical health, was chosen as a novel measure of contributing to understanding about CRPS. This was measured using the Health Anxiety Index (HAI) [63]. Furthermore, the ten item Kessler (Kessler 10) was chosen to measure psychological distress [43; 49].

Personality and CRPS were also explored as potential novel factors with the Eysenck Personality Questionnaire Extroversion and Neuroticism scale, brief version (EPQ-BV) [28] The Tampa scale for Kinesiophobia (TSK) [74] has also been used in CRPS research before to evaluate the fear of movement (kinesiophobia) [19].

### **3. Analysis**

Quantitative statistical methods were used. Data from the physiotherapy clinical record data were collated using Microsoft Excel for windows for personal computers. Standard descriptive statistics were used to review patient characteristics. Analysis used statistical software Statistica 7.1 and 7.13 ®. The primary analyses looked at changes to outcome between pre and post outcome measures. Secondary analyses compared baseline variables and demographic data. Those who made a *complete recovery* for the analyses obtained a zero PRI pain score from their MPQ-SF, and obtained full restoration of their function on the WHODAS score. The DASH or FFI outcome scores were not included since the division between QuickDASH (upper limb CRPS) and FFI (lower limb CRPS) contributed to samples too small for robust statistical testing. Relationships between continuous and categorical variables that included categories or intensity of physiotherapy intervention associated with outcome measures were analysed using logistic regression models to provide evidence for the strength of the effect size. To assess statistical significance, an  $\alpha$  (alpha) of 0.05 was used.

### **4. Results**

#### **4.1. Descriptive characteristics**

Seventy-five CRPS patients were assessed for inclusion. Nine participants were excluded for the following reasons: one due to their duration of CRPS being greater than a year; two due to diagnoses not being CRPS; one due to the language barrier with interviewing; two were not able to be contacted for baseline interview; one withdrew with no reason given, and; two withdrew for personal reasons. Thirteen were lost to follow up at the final interview for outcome measures one year later. A total of 66 participants were included in the analyses for

categories of physiotherapy interventions applied, and 53 participants were analysed for outcome measures one year later. Their physiotherapy intervention data was available. The participation process is shown in the Flow chart (Figure 1).



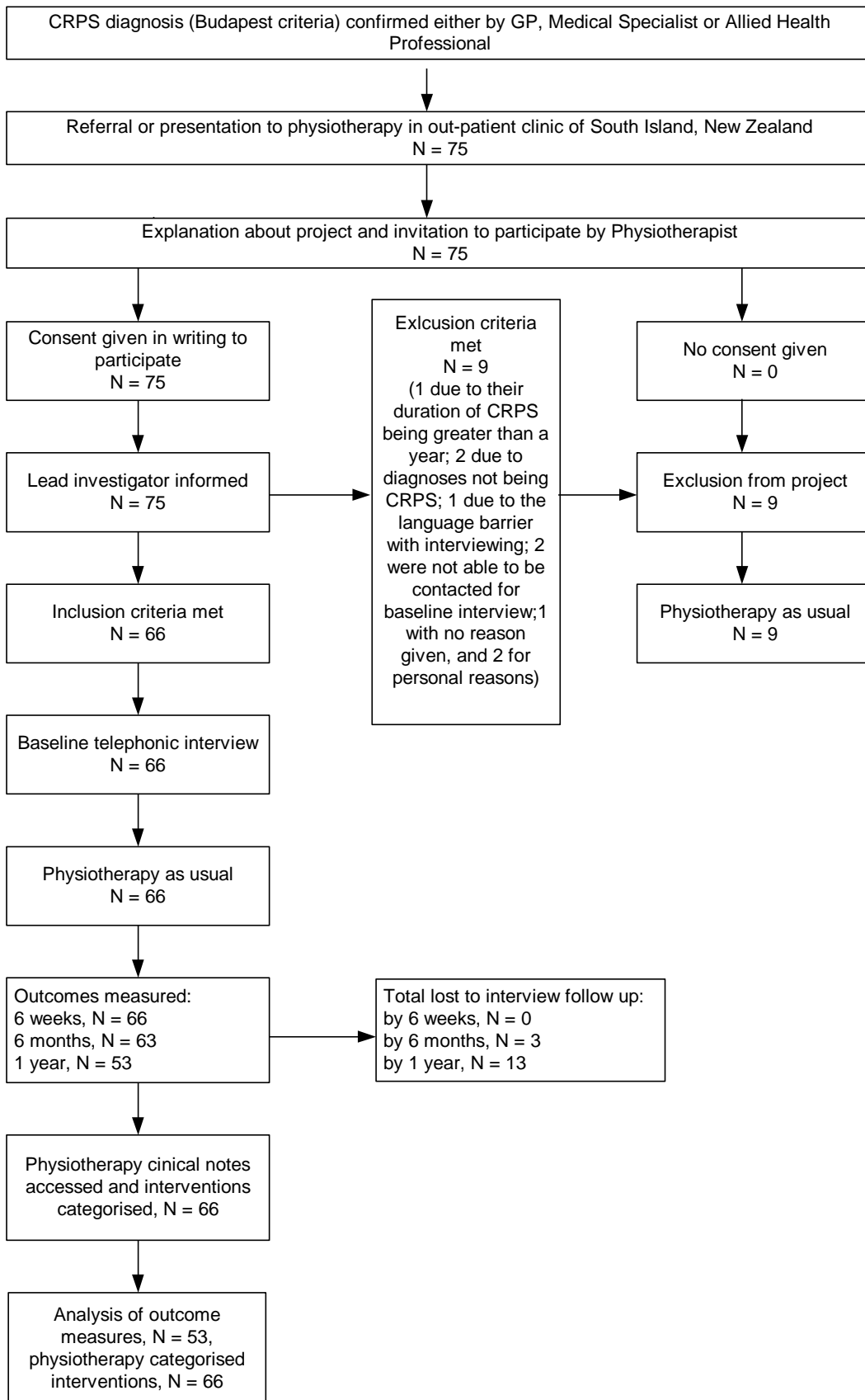


Figure 1. Flow chart of participation

Fifty-two females and 14 males participated with ages ranging from 11 to 77 years (mean 46 years). New Zealand Europeans formed the predominant ethnic group; fifty-seven or 86% of participants were diagnosed as CRPS Type 1, and 9 or 14% were diagnosed as CRPS type 2. Fractures were the inciting event for 28 or 42% of participants, followed by soft tissue injury in 24 or 36% of participants, and surgery in 14 or 21% of participants. The upper limb was more frequently affected than the lower limb in 49 or 74% and 17 or 26% of participants, respectively.

The Nelson/Marlborough and West coast regions were represented in this sample by one participant each, and the other South Island regions were represented proportionally to their population densities. The largest sample of 37 or 56% of participants came from mid and north Canterbury the area supporting Christchurch, the largest South Island city. Fourteen or 21% of participants came from South Canterbury; 9 or 14% of participants came from Southland, and 4 or 6% of participants came from Otago.

Twenty-six or 40% of participants were employed. Twenty or 30% of participants were not employed due to their CRPS; 7 or 11% were scholars or tertiary students; 6 or 9% were already retired; 4 or 6% were staying at home to care for family; 2 or 3% were not working for other reasons, and; 1 or 2% was a non-paid volunteer.

#### **4.2. Timing to diagnosis and the start of physiotherapy**

There was an equal number of participants ( $n = 28$ , 42%) with time taken from the inciting injury to diagnosis of 1 month, and from the inciting injury to diagnosis at 2 – 4 months. In 10 or 15% of participants their diagnosis took longer than 4 months to be made. The mean time to diagnosis in this cohort was 2.4 months (with a SD of 1.87). These data are shown in Table 1.

Table 1. Baseline descriptive statistics

DESCRIPTION	N (%)
<i>Time to diagnosis from injury</i>	
1 month	28 (42)
2 - 4 months	28 (42)
≥ 4 months	10 (15)
<i>Time taken to physiotherapy from injury</i>	
Less than 1 month	20 (30)
1-2 months	21 (31)
2 and < 3 months	9 (13)
3 and <6 months	10 (14)
≥ 6 months	7 (10)
<i>Referred to a Medical Pain Specialist (MPS)</i>	
Yes	45 (68)
No	21 (32)
<i>Time taken to see the MPS from injury</i>	
1 month - up to 3 months	17 (26)
3 months – up to 6 months	11 (17)
≥ 6 months (SD)	18 (27)

The time taken to start physiotherapy was similar as within 1 month for 20 (30%), and within 2 months for 21 (31%). Nine (13%) started physiotherapy within 3 months. Ten (14%) took 4 to 6 months to start; seven (10%) waited for more than 6 months before they started physiotherapy. The mean times to diagnosis, the commencement of physiotherapy and to see a Medical Pain Specialist are shown in Table 2.

Table 2. Baseline months to diagnosis, physiotherapy and Pain Medical Specialist

MONTHS	N	Mean	SD	Median	Lower Quartile	Upper Quartile
<b>Time to diagnosis</b>	66	2.4	1.9	2.0	1.0	3.0
<b>Time to commence physiotherapy</b>	66	1.9	0.9	2.0	1.0	3.0
<b>Time to see Pain Medical Specialist</b>	53	4.4	4.4	3.0	1.0	6.0

Abbreviation: SD – Standard Deviation

### 4.3. Potential predictor scores

The higher the score for the TSK, Kessler 10, HAI and EPQ reflect a greater extent of the construct being measured, namely; TSK, higher fear avoidance; Kessler 10, higher mental distress; HAI, higher health anxiety; EPQE, greater personality extraversion trait, and EPQN, greater personality neuroticism trait. These measures were applied once only. These data are shown in Table 3.

*Table 3. Baseline predictor variable descriptive statistics*

<b>Predictor measure</b>	<b>N</b>	<b>Mean</b>	<b>SD</b>	<b>Median</b>	<b>Lower Quartile</b>	<b>Upper Quartile</b>
<b>TSK</b>	66	37.0	10.7	38.0	29.0	45.0
<b>Kessler10</b>	65	10.5	8.9	9.0	3.0	17.0
<b>HAI</b>	66	30.5	10.4	28.0	21.0	40.0
<b>EPQE</b>	64	39.6	9.0	41.0	33.0	47.0
<b>EPQN</b>	64	38.3	10.4	39.5	31.0	46.0

### 4.4. Outcome measure baseline scores

Each outcome measure score for pain, PRI and NRS11 produced a higher score to represent higher/worse pain experience. Each functional measure, the WHODAS2, DASH and FFI scored greater disability with a higher score. These data baseline measures are shown in Table 4.

*Table 4. Outcome measures at baseline: mean, standard deviation median, upper and lower quartiles*

<b>Outcome measure</b>	<b>N</b>	<b>Mean</b>	<b>Std Dev</b>	<b>Median</b>	<b>Lower Quartile</b>	<b>Upper Quartile</b>
<b>PRI</b>	66	26.1	8.4	26.0	20.0	33.0
<b>NRS11</b>	66	6.2	1.7	6.0	5.0	7.0
<b>WHODAS2</b>	66	31.3	9.6	33.5	23.0	40.0
<b>FFI</b>	17	45.9	16.5	45.3	31.2	55.9
<b>DASH</b>	49	69.2	14.9	72.7	59.1	79.5

Those lost to follow up showed no differences from the responders with baseline categorical or continuous variables (using Student-t tests). These data are shown in Table 5.

*Table 5. Student-t tests for differences between baseline categorical and continuous variables of lost to follow up and responders*

	<b>N</b> <b>Baseline</b>	<b>Mean</b>	<b>SD</b>	<b>N</b> <b>Lost to follow up</b>	<b>Mean</b>	<b>SD</b>	<b>t-value</b>	<b>p</b>
<b>TSK</b>	54	36.1	11.2	12	40.8	7.3	-1.4	0.13
<b>HAI</b>	54	30.4	10.1	12	31.1	12.2	-0.2	0.35
<b>EPQE</b>	54	38.6	9.9	10	36.3	12.8	0.7	0.25
<b>EPQN</b>	54	23.5	8.7	10	25.2	10.7	-0.5	0.34
<b>PRI</b>	54	25.5	8.9	12	28.5	5.2	-1.1	0.06
<b>NRS11</b>	54	6.2	1.7	12	6.0	1.9	0.4	0.65
<b>FFI</b>	16	45.4	16.9	1	54.1	0.0	-0.5	1.00
<b>QuickDASH</b>	38	68.2	15.5	11	72.7	12.5	-0.9	0.48
<b>Kessler 10</b>	54	10.2	9.0	11	11.5	9.0	-0.4	1.00

#### 4.5. Medical and psychological intervention

Data was collated for medical and psychological support over the year and is shown in Table 6.

*Table 6. Medical and psychological support applied.*

<b>Management</b>	<b>Description</b>	<b>N of full sample (%)</b>
Medical	Pamidronate infusion	5 (7)
	Neural blockade	3 (3)
	Prescription of non-steroidal, anti-inflammatory	12 (21)
	Prescription of oral cortisone	2 (4)
	Prescription of any oral morphine derivatives	12 (21)
	Prescription of tricyclic secondary analgesia	39 (58)
	Prescription of gabapentin or pregablin secondary analgesia	34 (51)

	Over the counter or prescribed paracetamol	27 (41)
Psychology	Individual sessions	19 (28)

#### 4.6. Physiotherapy intervention

Satisfaction with care was found to be overwhelmingly positive with the DDS Questionnaire. This uniform response seen across all intervals limited analysis for any potential effect. The number of days in physiotherapy care was documented as well. Thirty-nine participants (59%) were discharged by 200 days with 16 (24%) of these discharged earlier by 12 weeks; a further fifteen (22%) were discharged by 300 days (just short of 10 months). Thirteen (19%) were seen up to one year. One participant was seen only once and self-discharged following the initial physiotherapy contact.

The mean and median number of weekly sessions attended with their treating Physiotherapist was calculated for each outcome measure interval. The intervals are: baseline to 6 weeks; 6 weeks to 6 months (a total of 18 weeks), and 6 months to one year (a total of 24 weeks). These data showed that for the first six weeks, most were seen approximately weekly with 1.1 times per week and subsequently less frequently from 6 weeks to 6 months. These data are shown in Table 7.

*Table 7. Mean and median number of physiotherapy sessions, attended per week, for each interval.*

No of physiotherapy sessions per week	Attending physiotherapy N	Discharged N	Mean	SD	Median	Min	Max	Lower quartile	Upper quartile
<b>Baseline to 6 weeks</b>	66	0	1.1	0.5	1.1	0.2	3.0	0.8	1.5
<b>6 weeks to 6 months</b>	60	6	0.5	0.3	0.4	0.0	1.3	0.2	0.7
<b>6 months to 1 year</b>	26	40	0.4	0.3	0.3	0.0	1.3	0.2	0.6

A total of thirty nine participants (59%) were discharged by 200 days or just over 6 months; a further fifteen (22%) were discharged by 300 days or just short of 10 months. Thirteen (19%) were seen up to one year. One participant was seen only once and self-discharged following the initial physiotherapy contact. The route for discharge was documented. Forty-seven (71%) participants were discharged by their physiotherapist. Small and similar groups, 9 (14%) and 10 (15%), respectively, either self-discharged (they chose to discontinue their physiotherapy despite follow up being arranged), or required ongoing care beyond the year.

The time at discharge showed the trend of an almost linear gradual reduction in the number of weeks attending physiotherapy before discharge. This was for those who self-discharged or were formally discharged by their treating physiotherapist. There was no apparent difference between these two groups regarding the time at which discharge occurred.

The weekly average for each category of intervention was calculated by each outcome measure interview interval, at 6-weeks 6-months and at 1 year. These categories were TIP, TIF, TII, Educ, or Pass. The weekly averages showed that TIP interventions were similar and slightly greater than TIF at 6 weeks. TIF had dropped to less than TIP by 6 months. These data are shown in Table 8.

*Table 8. Categorized physiotherapy interventions weekly means*

Category of Physiotherapy intervention	Mutually exclusive interventions per week, Mean (SD)				Percent proportion of Physiotherapy interventions
	Baseline to 6 weeks N = 66	6 weeks to 6 months N = 66	6 months to 1 year N=63	Baseline to 1 year N = 66	
<b>Functional restoration (TIF)</b> N yes = 66 (100%)	2.3 (1.8)	1.4 (1.6)	0.3 (0.6)	2.3 (2.8)	20.4
<b>Pain Modulation (TIP)</b> N yes = 64 (96%) N no = 2 (4%)	2.5 (3.1)	1.1. (1.5)	0.3 (0.7)	1.8 (1.8)	15.9
<b>Education (Educ)</b> N yes = 66 (100%)	0.9 (0.6)	0.4 (0.4)	0.07 (0.1)	0.7 (0.9)	6.2

<b>Immobilisation</b> <b>(TII)</b> <b>N yes = 43 (64%)</b> <b>N no = 23 (36%)</b>	0.8 (1.2)	0.3 (0.8)	0.03 (0.1)	0.4 (0.5)	3.5
<b>Passive interventions</b> <b>(Pass)</b> <b>N yes = 46 (69%)</b> <b>N no = 20 (31%)</b>	1.2 (0.9)	0.7 (0.9)	0.2 (0.5)	0.9 (0.8)	8.0

#### 4.7. Outcome measure changes

All changes in outcome measures showed a similar trend with most of the positive changes occurring in the first six weeks, followed by an estimated half as many positive changes occurring by six months. The trend for positive changes slowed between six months and 1 year for pain reduction, and remained stagnant for further gains of both functional ability using the QuickDASH and quality of life and function using the WHODAS2. However, further functional gain did gradually continue for those with lower limb CRPS as reflected with further improvement in the FFI score. Each outcome measure score for pain or for function is represented with a higher score for a worse pain experience, or for a worse functional disability. Hence, a change towards recovery is attributed as a negative number. These data are shown in Table 9.



Table 9. Changes to outcome measures at each interval

<b>Outcome dependent variable (Score range, clinically important change)</b>	<b>Baseline score, mean (SD) N = 66</b>	<b>Change at 6 weeks, mean (SD) N = 66</b>	<b>Change at 6 months, mean (SD) N = 63</b>	<b>Change at 1 year, mean (SD) N = 53</b>
<b>SF-MPQ PRI (0 to 45, &gt;10)</b>	26.0 (8.4)	-11.2 (10.9)	-15.4 (11.4)	-17.1 (11.3)
<b>NRS-11 (0 to 10, &gt; 3)</b>	6.2 (1.7)	-2.3 (2.2)	-3.5 (2.6)	-3.8 (3.1)
<b>WHODAS2 (1 to 60, &gt; 10)</b>	33.5 (9.5)	-8.1 (7.9)	-11.0 (9.1)	-10.7 (11.9)
	<b>N = 17</b>	<b>N = 17</b>	<b>N = 15</b>	<b>N = 15</b>
<b>FFI (0 to 100, &gt;10)</b>	45.8 (16.5)	-20.5 (13.2)	- 23.9 (15.8)	- 31.6 (18.5)
	<b>N = 49</b>	<b>N = 49</b>	<b>N = 48</b>	<b>N = 38</b>
<b>QuickDASH (1 to 100, &gt;15)</b>	69.2 (14.9)	-22.2 (19.6)	-34.6 (23.8)	-36.9 (24.7)

#### 4.8. Logistic regression analysis for independent variables effect for a complete recovery

Full resolution from all pain and full restoration of function are considered the best outcomes when treating a CRPS patient. These data showed 24 participants (45%) obtained full recovery. A smaller proportion of 14 (38%) with upper limb affected CRPS showed full recovery versus 10 (63%) with lower limb affected CRPS. Univariate logistic analysis found small effects for the continuous variables of higher personality neuroticism, poorer baseline WHODAS2 function and poorer mental health to predict a poorer outcome. Higher personality extraversion predicted a better outcome. These data are displayed in Table 10.

Table 10. Univariate analysis of continuous independent variables.

Univariate analysis of continuous variables for a complete recovery, N=53				
	OR	95% CI	Chi <sup>2</sup>	p
Age	1.02	0.98-1.05	0.91	0.34
Fear avoidance: TSK	1.00	0.95-1.05	>0.01	0.93
Health Anxiety: HAI	1.01	0.96-1.07	0.25	0.62
Baseline PRI	1.05	0.98-1.12	2.19	0.14
Personality: high score EPQ Extraversion	<b>1.12</b>	<b>1.04-1.21</b>	<b>12.42</b>	<b>0.002*</b>
Personality: high score EPQ Neuroticism	<b>0.91</b>	<b>0.84-0.98</b>	<b>7.93</b>	<b>0.005*</b>
Poor Mental Health: Kessler-10	<b>0.09</b>	<b>0.83-0.97</b>	<b>8.53</b>	<b>0.003*</b>
Baseline WHODAS 2	<b>0.94</b>	<b>0.89-1.00</b>	<b>4.06</b>	<b>0.04*</b>

Significance\* p > 0.05

Univariate analysis of categorical variables showed (with strong effects) that the prescription of the anticonvulsant secondary analgesics, gabapentin or pregabalin concurrent with physiotherapy was associated with a complete recovery. These data are shown in Table 11.

Table 11. Univariate analysis of categorical independent variables

Univariate logistic analysis of categorical predictors for complete recovery, N=53				
	OR	95% CI	Chi <sup>2</sup>	p
CRPS Type 1 N=27 Type 2 N=9	0.57	0.09-3.41	0.39	0.54
Injury: Fracture N=28 No Fracture N=38	1.61	0.53-4.87	0.71	0.40
Baseline allodynia Yes N=32 No N= 34	0.93	0.32-2.75	0.02	0.90
Prescription of anti-convulsion secondary analgesia concurrent with physiotherapy Yes N=34 No N=32	<b>6.66</b>	<b>1.98-22.43</b>	<b>10.5</b>	<b>0.002*</b>
Prescription of tricyclic secondary analgesia concurrent with physiotherapy Yes N=39 No N=27	1.14	0.37-3.52	0.05	0.82
Psychological support concurrent with Physiotherapy Yes N=19 No N=47	<b>0.20</b>	<b>0.04-0.83</b>	<b>5.73</b>	<b>0.02*</b>

Significance\* p > 0.05

Multivariate analysis showed that the effect of no psychological support being associated with a full recovery was diluted, but that the concurrent prescription of the anticonvulsant secondary analgesics, gabapentin or pregabalin showed a strong effect. These data are shown in Table 12.

Table 12. Multivariate logistic regression for categorical independent variables.

Multivariate logistic analysis of categorical predictors for complete recovery, N=53				
	OR	95% CI	Chi <sup>2</sup>	p
<b>CRPS</b> Type 1 N=27 Type 2 N=9	1.69	0.22-12.93	0.25	0.61
<b>Injury:</b> Fracture N=28 No Fracture N=38	0.87	0.22-3.38	0.04	0.84
<b>Baseline allodynia</b> Yes N=32 No N= 34	0.86	0.24-3.13	0.05	0.82
<b>Prescription of anti-convulsion secondary analgesia concurrent with physiotherapy</b> Yes N=34 No N=32	<b>6.67</b>	<b>1.71-26.01</b>	<b>8.41</b>	<b>0.006*</b>
<b>Prescription of tricyclic secondary analgesia concurrent with physiotherapy</b> Yes N=39 No N=27	1.02	0.27-3.83	0.00	0.97
<b>Psychological support concurrent with Physiotherapy</b> Yes N=19 No N=47	0.23	0.04-1.10	3.78	0.06

Significance\* p > 0.05

Univariate logistic regression analyses showed that diagnosis timing as well as timing to commencement of physiotherapy in months had no effect in predicting a complete recovery. Analyses included individual months to avoid potential co-linearity. These data are shown in Tables 13-14.

Table 13. Univariate logistic analysis of diagnosis timing and recovery.

Category of diagnosis timing	OR	95% CI	Chi <sup>2</sup>	P
<b>One month only</b>	0.86	0.40-1.84	1.19	0.69
<b>Two to less than 3 months</b>	0.75	0.27- 2.11	1.19	0.58
<b>3 months or more</b>	0.80	0.43-1.50	1.19	0.49

Significance = p<0.05

Table 14. Univariate logistic analysis of physiotherapy timing and recovery.

Category of physiotherapy timing	OR	95% CI	Chi <sup>2</sup>	P
One month only	1.31	0.60-2.28	3.12	0.69
Two to less than 3 months	0.48	0.20-1.40	3.12	0.58
3 months or more	0.76	0.43-1.35	3.12	0.35

Significance =  $p < 0.05$

#### 4.9. Logistic regression analysis for dependent variables effect for a complete recovery

Neither univariate nor multivariate analyses showed any weekly average for category of physiotherapy intervention to have an effect on a complete recovery. Data obtained from TII and Pass interventions were too small for logistic regression analysis. The 6 month average TIF shown to have a detrimental effect was not strong with the CI that spans 1. It is plausible that this finding can be explained by reverse causality. These data are shown in Table 15-16.

Table 15. Univariate analyses for physiotherapy treatment intervention categories averages on complete recovery.

Univariate analysis for complete recovery after 1year N=53				
	OR	95% CI	Chi <sup>2</sup>	p
6 week average TIP	1.03	0.87-1.22	0.09	0.76
6 month average TIP	1.39	0.91-2.13	2.78	0.09
6 week average TIF	1.17	0.85-1.60	0.97	0.32
6 month average TIF	<b>1.58</b>	<b>0.99-2.52</b>	<b>4.93</b>	<b>0.03*</b>
6 week average Educ	1.04	0.39-2.77	0.005	0.94
6 month average Educ	2.45	0.43-14.08	1.04	0.31
6 week average Pass	Sample N too small to compute with logistic regression			
6 month average Pass	Sample N too small to compute with logistic regression			
6 week average TII	Sample N too small to compute with logistic regression			
6 month average TII	Sample N too small to compute with logistic regression			

Significance\*  $p < 0.05$

Table 16. Multivariate analyses for physiotherapy treatment intervention categories averages on complete recovery.

Multivariate analysis for complete recovery after 1year N=53				
	Chi <sup>2</sup>	OR	95% CI	p
6 week average TIP	0.87	0.87	0.64-1.17	0.35
6 month average TIP	1.92	1.41	0.84-2.36	0.17
6 week average TIF	0.00	1.00	0.52-1.91	1.00
6 month average TIF	2.21	2.50	0.67-9.31	0.14
6 week average Educ	0.03	1.27	0.09-17.34	0.86
6 month average Educ	0.77	0.10	0.00-19.36	0.38

The analysis for each individual TIP intervention method showed no tentative findings or significant effect on a complete recovery. Second order multivariate analysis showed that sample numbers were too small for further analyses. These data are shown in Table 17.

Table 17. Univariate analysis of treatment interventions for pain modulation.

Univariate analysis for complete recovery after 1year N=66				
Applied vs Not applied	OR	95% CI	Chi <sup>2</sup>	p
GMI	1.93	0.64-5.83	1.40	0.23
SMT	0.45	0.14-1.44	1.85	0.17
POOL primary exercise	1.72	0.57-5.13	0.96	0.33
Relaxation training	1.20	0.27-5.41	0.56	0.81
Mirror exercise	0.83	0.23-3.04	0.08	0.77
DBE	1.25	0.27-5.63	0.08	0.77
GEXP	1.38	0.46-4.15	0.3	0.34
Cognitive techniques	0.37	0.11-1.28	2.61	0.12
TENS	0.53	0.14-2.02	2.61	0.35
GMI + POOL+ SMT	Sample N too small to compute			
Relaxation training + Mirror exercise + DBE	Sample N too small to compute			
GEXP + Cognitive techniques + TENS	Sample N too small to compute			

Significance\*;  $p \leq 0.05$

## 5. Discussion

These cohort data closely represented other large epidemiological studies [21; 22; 64; 66] as well as a single New Zealand North Island region study [1]. The data showed that CRPS was predominantly found in female Europeans, with a ratio of 1 male to 4 females, with a mean age of 46 years, and with a fracture as the precipitating injury in 44% of them. Fractures have been identified as potential risks for the onset of CRPS [61], as well as being the most common precipitant for the injury that subsequently developed into CRPS [21; 22; 64; 66]. These data also showed that the upper limb was more frequently affected than the lower limb, in keeping with literature [21; 51; 64], but that CRPS of the lower limb was reported to be frequently excluded in research trials [18]. One large cross sectional web-based study, N = 875, reported a higher incidence affecting the lower limb [66]. The reasons for this discrepancy are not known. The data showed the affected laterality to be of similar proportions on the left or on the right. This is in keeping with other studies [30; 62].

These data showed participants' baseline pain to be within the range of other CRPS studies [1; 14; 25; 42]. Fear of movement with the TSK was shown to be greater when compared

with a North Island study (N= 59, mean TSK=28,6) [2], but lower when compared to a sample who had CRPS for more than 2 years (N=8 with a mean score of 54.5) [20]. The QuickDASH score mean was higher than reported in two French studies [N=20, as 62.8 [47] and N=8 as 40.8 [45], respectively], and in a Turkish study [N=36 as 55.3 [65]. These data also showed that those affected with lower limb CRPS had better recovery than those with upper limb affected CRPS. This is perhaps explained by the higher scores of disability measured in this cohort's QuickDASH baseline scores when compared to these other three studies.

These data showed that recovery is still possible if the diagnosis is not detected early. Early diagnosis has been shown to be effective in reducing the incidence of CRPS to zero, such as that occurring after a fracture of the distal radius with early detection and aggressive management of any warning signs or symptoms of the possibility of CRPS [36]. In this cohort, CRPS was not effectively prevented. Yet, almost half the patients made a complete recovery, and all showed significant, clinically relevant improvements. It would be reasonable to imply that the CRPS trajectory could be directed towards recovery at any stage, by the application of similar resources and efforts applied by treating Physiotherapists, irrespective of the time since the inciting injury. It would be tentatively ventured that early identification of CRPS signs and symptoms would be common sense, good practice, and could potentially reduce suffering. Interventions should be applied as early as possible, thereby potentially improving efficiency associated with lost or wasted time, and avoiding any potential litigation issue associated with the diagnosis being ignored. Litigation has recently been reported be a problem for CRPS patients N=12, [46]. This occurred in the courts of the United States [35]. It can even involve the use of a Psychiatrist in court to verify a CRPS patient's mental health [54]. Even if the diagnosis is delayed whilst other possible causes are ruled out, hope can persist for the CRPS patient, Clinician or Physiotherapist. Support remains for early constructive intervention [7].

A positive outcome was also related with a strong effect to the concurrent use of gabapentin or pregabalin with physiotherapy. A randomised controlled trial (RCT) (N = 58, with differences outlined in Mann-Whitney U scores but no effect size given) showed that gabapentin potentially had a small benefit when compared to placebo [73]. A controlled clinical trial showed that gabapentin in combination with a specific graded exercise programme supervised by a physiotherapist significantly decreased pain in early CRPS, but did not improve function [70]. Both amitriptyline and gabapentin were helpful for sleep and

for reducing pain in paediatric CRPS; N = 34; t-tests showed significant improvement in pain (no co-efficient, odds ratio or confidence intervals were given to reflect the effect size) [10].

An innovative contribution was made with the evaluation of personality extraversion. Its strong effect observed with this study suggests that this warrants further investigation. The relationship of personality extraversion to CRPS outcomes is not known, and is not suggested as a measure in the recent COMPACT core outcome measures [38]. These data provide a fresh contribution to the literature in that extraversion scores and CRPS outcomes may be associated. The finding that personality extraversion trait's univariate effect was associated with a better outcome has been reported in other conditions [16; 55]. The positive effect of extraversion could suggest that personality has an interactive mediating effect in the therapeutic relationship, as it has been reported to influence behaviour [15]. It would be credible to raise the question about the paradigm of physiotherapy practice as a potential contributor to CRPS recovery when a CRPS patient presented with the personality extraversion trait. It is conjectured that this factor plays a role in facilitating the therapeutic relationship, since an effective therapeutic relationship is reported as an essential ingredient in the model of care in the psychotherapy literature [48; 53].

Furthermore, the novel application of the Kessler 10 and WHODAS2 allow for comparison to other diseases or syndromes associated with disability. Since there was no literature for WHODAS2 for CRPS populations, these baseline data were compared with a healthy Australian population sample [32], and were shown to have a greater disability and poorer quality of life. The literature is mixed about the relationship of anxiety, depression or catastrophising in association with CRPS risk, trajectory, and outcomes. Multiple studies and meta-analyses have not confirmed an association of psychosocial risks with either the onset of CRPS or its prognosis [3; 75].

These data showed that full recovery was possible for 24 participants (45%) with no pain or functional disability. Thirty-nine participants (59%) were already discharged close to 6 months following commencing with physiotherapy. Poor recovery (although still an improvement from baseline measures) affected 10 participants (19%) who had not yet been discharged from physiotherapy care 1 year later. It remains an enigma that despite all interventions, a sub group of CRPS patients do not show a good recovery [23]. It has been suggested that potential biomarkers [7] be developed as tools towards improved management for the diverse subgroups.

It is speculated that recovery seen with these data may be attributed to the application of a combination of physiotherapy categories of intervention. This combination (as outlined in Table 6) showed that in the first 6 weeks a greater proportion of pain modulation interventions were applied. This was reversed in the following 18 weeks, where functional restorative interventions formed a greater proportion. However, since there was no randomisation with a control group, this support remained weak. These data would support the systematic reviews that showed there to be no strong evidence for pain modulation interventions. These were categorised in this observation to include mirror exercises, GMI, TENS, GEXP, SMT, mirror exercise, relaxation training, breathing control exercise, and cognitive techniques. Although some reviews and literature supported these interventions, their quality of evidence was low [18; 56; 68].

It is implied that in the group who made a complete recovery or were discharged, that physiotherapy management was an effective ingredient. This would be tentatively supported by the support recent suggestions that although a complete understanding or evidence about intervention methods for CRPS is lacking, outcomes have become more optimistic than those of the past [9; 57]. It is not apparent if this optimism applies to both upper or lower limb affected CRPS. These data support that outcomes are more optimistic for lower limb affected CRPS. Furthermore, it would be plausible to question whether or not CRPS should be referred to in the literature as a *chronic* condition, since this is not the case for the larger proportion of this cohort. It is suggested that it would be more sensible to refer to it being *chronic in only a subgroup*. This suggestion promotes sensible practice in that potential catastrophising about a CRPS trajectory, by either a clinician or patient, may be avoided.

### **5.1. Implication for clinical practice**

The heterogeneous presentation and trajectory of each CRPS patient's recovery is highly variable as reflected in these data. It is suggested in clinical practice that skill, patience and flexibility may optimise a physiotherapy management plan. Despite similar interventions, there were those who showed a poorer recovery. Using logistic regression, these data showed a predictive positive effect with concurrent anticonvulsive medication prescription for a complete recovery. A larger group were prescribed tricyclic antidepressants (N=39) than those prescribed anticonvulsants (N=34), yet did not show the same recovery. It would be prudent to consider that anticonvulsants might prove helpful in facilitating CRPS recovery.



However, the evidence from these data was weak. Robust evidence for pharmaceutical prescriptions enabling CRPS recovery is still lacking [33].

Following fracture of the distal radius, early detection and management to reduce the onset of CRPS has been suggested as best practice [36]. When the Budapest criteria are not yet fulfilled, there is no method available to forecast the signs and symptoms that constitute a possible CRPS diagnosis. These data showed that diagnostic timing did not influence outcomes. In contrast, it is suggested that a delayed CRPS diagnosis is reported to be detrimental [46]. To avoid inappropriate optimism or information, it is reasonable to recommend a realistic, open and flexible management approach, with adequate explanation of the trajectory of CRPS and its potential outcomes.

These data showed no specific trajectory or predictive baseline factors. It is suggested that physiotherapy management involves the integration of best evidence-based knowledge and mutual engagement, in order to reach towards goals consistent with each individual patient's personality, beliefs, social context, culture and expectations. This is in keeping with the competency requirements and ingredients of the therapeutic relationship [48; 58; 71]. Such a relationship has been shown to have a moderate effect ( $r = 0.22$ ) on influencing outcomes, regardless of the instrument or outcome measure used [48]. Mental health research reported that it is not simply the conversation or communication about information that is important for an effective therapeutic relationship, but that mutual engagement and understanding are facilitated [79].

## **5.2 Implications for research**

There is no clear model of care for CRPS in the literature, leaving practicing clinicians without clear guidelines or suggested pathways. A recommendation was made in 2009 to update the management model as it was out of date with current evidence [18]. The clinical reality is that Physiotherapists do see CRPS patients. Some Physiotherapists on the South island of New Zealand will see 2-3 new CRPS patients each month [59]. Further research is necessary to evaluate standard physiotherapy practice in other regions. Current evidence needs to be collected and integrated into developing a conceptual clinical model for physiotherapy CRPS management that can be subsequently tested.

The recent Core Outcome Measures for use in CRPS Clinical Trials (COMPACT) recommended core consistent outcome measures, so that collaborative research and meta-

analyses can be facilitated in future research [38]. This core was not available at the time this project commenced. It is advocated that this project's method be replicated using COMPACT in other regions. Evaluating personality extraversion warrants future investigation about its effects on outcomes, effects on the paradigm of physiotherapy management and effects on the therapeutic relationship.

It is suggested that there is a subgroup of CRPS patients who are going to recover spontaneously without any intervention. Should patient autonomy not be upheld, intervening would possibly contribute to a poorer recovery in such a group [67]. Of note is that the first epidemiological study showed that a small group recovered well without any intervention [64]. Future research is needed about the factors that contribute to spontaneous recovery. This would be beneficial to the broader understanding of CRPS management.

### **5.3. Strengths and limitations**

The strength of this study is to offer novel contributions to the literature, namely: 1) it describes the standard physiotherapy practice used in treating CRPS over a wide region, and evaluates its effects; 2) it presents the possibility of personality extraversion influencing CRPS outcomes. Since the interviews were undertaken by an independent interviewer, it is reasonable to assume that the outcome measures were less likely to be influenced by bias from either the treating physiotherapist or the researcher. Potential bias associated with local prevalence of intervention methods was reduced with this large, regional evaluation. The diagnosis of CRPS was strictly fulfilled with the Budapest criteria; this together with robust logistic regression analysis in a longitudinal study design provided support for these effects.

The limitations identified were as follows: the adherence or titrations of the concurrent prescribed secondary analgesia was beyond the scope of this study; the application of CRPS severity score was not possible due to the necessity of telephonic outcome measures over the large region area 150 437 km<sup>2</sup> [37]; the reliability of these results were limited by participant attrition, where 13 participants (20%) were lost to follow up a year later; reverse causality could potentially have influenced intervention intensity, and the finding that concurrent psychological support was associated with a poorer outcome in the univariate analysis. Confounding may also have influenced outcome measure result, especially as it was neither possible nor ethical to deny treatment, and; randomisation with the use of a control group for

comparison of baseline measures was not possible to implement. It has been reported that it would be difficult to implement an RCT for CRPS in a clinical setting [25] and that it would also potentially be more challenging in multiple clinical settings across a wide region.

Other limitations were as follows: it was not possible to evaluate CRPS patients who either did not present to physiotherapy or had declined any intervention, either medical or allied health, which potentially reduces the effect of attending physiotherapy; it could also be argued that the categories of physiotherapy interventions may have been allotted differently with alternative results. There was no validated or reliable tool for accurately measuring frequencies or categories of the physiotherapy interventions. The effect of attending physiotherapy is yet to be explained [8; 17; 21; 24; 39; 64] and remains important to determine.

## **6. Conclusion**

All participants showed improvement in their outcomes measures of pain, function, and quality of life 1 year after commencing physiotherapy with a recent diagnosis of CRPS. Over half the cohort made a full recovery or sufficient recovery to warrant discharge after 6 months of physiotherapy care. Full recovery was not associated with any particular physiotherapy intervention category. It was associated with the concurrent prescription of anticonvulsant secondary analgesia and the extrovert personality. Future research should evaluate the effect of standard physiotherapy interventions in other regions. Large international collaborations are needed so that larger sample sizes can be obtained assisting reliability and meta-analysis. It remains important that a clinical model for physiotherapy be developed.

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Original article

### A proposed clinical conceptual model for the physiotherapy management of Complex Regional Pain Syndrome (CRPS)



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# **A proposed clinical conceptual model for the Physiotherapy management of Complex Regional Pain Syndrome (CRPS).**

(3334 words)

## **1. Introduction**

The literature shows that clinical models for CRPS management remain sparse. None to date have been validated. The earliest model for CRPS management showed a stepwise management pathway [1]. It stated that physiotherapy management was essential. Around this same time, a Randomised Controlled Trial (RCT) showed that physiotherapy was superior to occupational therapy for the management of CRPS. However, no effect size for this finding was reported. All treatment interventions applied used a protocol of: ‘with pain, no gain’ [2]. The actual methods or categories of interventions applied were not given.

Steps towards functional restoration were proposed in 2001 [3]. A subsequent clinical pathway was proposed later in 2002 [4]. It was essentially unchanged with physiotherapy interventions as the fundamental component. A notable change with this pathway was the recognition that relapse may occur. In the same year, another review showed that the evidence for the treatment of CRPS remained limited for all treatment interventions [5].

In 2006, the Dutch Order of Medical Specialists proposed their evidence based guidelines for the management of CRPS in association with the Netherlands Association of Reflex Sympathetic Dystrophy patients [6]. No model was included with these guidelines. Standard physiotherapy was to be according to the protocol. The attempt to answer what physiotherapy proved effective was followed in 2009 with a systematic review about physiotherapy interventions for CRPS [7]. The authors also suggested that a model be developed following the findings of their review, as the evidence in this review contrasted sharply to previous pathways [7].

This suggestion was not heeded as demonstrated in the evidence based guidelines that were published in 2010 from systematic review findings [8]. ‘Standardised’ physiotherapy and occupational therapy was advised [8]. Neither was this call followed in 2011 when a comprehensive guideline for the medical diagnostic and interventional management for

CRPS was presented [9]. No detail is given about what constituted this physiotherapy rehabilitation, or of what it aimed to achieve.

It was a disappointment to find that the 4th publication of Practical Diagnostic and Treatment Guidelines (2013) [10] suggested a physiotherapy pathway unchanged from the publication of 2002. In the same year, the first Cochrane systematic review of CRPS management demonstrated poor evidence for all aspects of CRPS management [11]. Subsequently, in 2014, two comprehensive reviews were published [12, 13]. Neither offered any further evidence and both raised further questions. In 2016, a review reported evidence and potential answers to these questions about CRPS pathophysiology and known progression; no model was proposed. [14]. A recent masterclass suggests a functional restoration algorithm based on the model proposed in 2001, where goals of physiotherapy are proposed as to normalise abnormal movement patterns, help the patient understand the condition and address pain related fear [15].

In summary, this historical account of the literature showed that evidence for physiotherapy management was weak. There are several possible reasons: the low prevalence of CRPS contributes to difficulty in gathering research evidence [16-18]; no accurate gold standard for diagnosis [19-21]; uncertainty about likely CRPS trajectories and outcomes [22, 23]; weak evidence regarding risk factors [24]; controversy over physiotherapy management methods with pain modulation in juxtaposition with a pain exposure approach [25, 26].

The call in 2009 was for a proposal that addresses the previous missing gaps found within previous models. A new model is proposed in this paper. This is based on the insight from the past models; that gained from our recent, observational, multi-centre, prospective, longitudinal study across a region; and the integration of evidence found in the literature. This includes the novel aspects of a) effective prevention and b) the mental health for both patient and clinician alike in accordance with the recent adoption that by medical professionals of the need to care and promote their own mental health and well-being [27], as an urgent issue to be addressed [28-30], and likewise for that of a CRPS patient [31].

## **2. Method**

A prospective, observational, multi-centre, longitudinal study design was applied across the region of the South Island of New Zealand where the recruitment, inclusion and exclusion criteria, participation and outcomes of our initial published case series are described in detail

[32]. Ethical approval was provided by the University of Otago Ethics committee (H13/103). Since the recovery data examined both upper and lower limb CRPS it seemed valid for both presentations. Outcomes were obtained through an independent interview.

The method to develop this proposed model involved merging together of three components: a) significant Spearman correlations from this longitudinal data which provided a summary of all the associations of variance for all continuous or categorical variables with the separate categories of physiotherapy treatment interventions of either pain modulation or functional restoration, and the complete recovery from CRPS; b) integrating the limited evidence for interventions from the literature; c) incorporating the essence of which provided the motivation for the previous models.

### 3. Results

#### *Spearman Correlation matrices and models*

A Spearman correlation assesses non-linear relationships with a significance of  $p \leq 0.05$  and provides a measure for the strength of this correlation. Since this was a longitudinal study, the direction of the correlations between variables or the outcome could be determined between the categories of physiotherapy treatment interventions for pain modulation (TIP); or between treatment interventions for functional restoration (TIF); or between their relationships with each other or with complete CRPS recovery. These data are shown in Table 1 with significant correlations showed in bold.

VARIABLE	Spearman Correlation coefficient with complete recovery	Spearman Correlation coefficient with TIP 6-week, weekly average	Spearman Correlation coefficient with TIF 6-week, weekly average
Age	-0.12	<b>-0.25*</b>	0.12
Gender, female	-0.19	-0.08	<b>-0.25*</b>
Time to commence physiotherapy	0.08	0.02	<b>-0.34*</b>
Time to diagnosis	0.16	-0.01	<b>-0.29*</b>
Time to Pain Specialist Doctor	-0.17	-0.21	<b>-0.28*</b>
TSK	-0.02	<b>0.26*</b>	0.00
HAI	-0.06	<b>0.27*</b>	-0.16
Kessler 10	<b>-0.42*</b>	0.13	0.04

EPQE	<b>0.47*</b>	-0.12	-0.17
EPQN	<b>-0.35*</b>	0.17	-0.11
PRI Baseline	-0.21	-0.00	0.01
WHODAS2 Baseline	<b>-0.31*</b>	0.09	0.10
Homework weekly average 6 months	-0.22	-0.05	0.04
Homework daily average 6 months	-0.24	-0.14	0.01
Homework rating for pain relief 6 months	0.11	0.05	0.07
Panadol prescription	0.12	-0.06	0.10
NSAID prescription	-0.09	-0.21	-0.04
TOTAL dur physio WEEKS	<b>-0.46*</b>	0.12	0.23
TOTAL physio Intensity N div wks	0.09	0.07	<b>0.29*</b>
TIP6wkAVWK	-0.03	1.00	0.23
TIP GRD weekly AV	0.12	<b>0.68*</b>	0.04
TIP6moAVWK	-0.19	<b>0.57*</b>	0.06
TIF6wkAVWK	-0.22	0.23	1.00
TIF GRD weekly AV	0.04	0.13	<b>0.59*</b>
TIF 6m AVWK	<b>-0.32*</b>	<b>0.27*</b>	<b>0.69*</b>
Educ6wkAVWK	-0.03	<b>0.57*</b>	<b>0.60*</b>
EDUC GRD weekly AV	<b>0.36*</b>	<b>0.24*</b>	<b>0.27*</b>
Educ6moAVWK	-0.12	<b>0.44*</b>	<b>0.43*</b>
TIH6wkAVWK	-0.07	-0.15	<b>0.38*</b>
TIIGRD wkAV	0.02	-0.13	<b>0.26*</b>
TIH6moAVWK	-0.09	-0.14	<b>0.28*</b>
Primary analgesia prescription yes	0.14	0.17	0.02
Prescription any secondary analgesia yes	0.14	0.17	0.02
Morphine derivatives prescription yes	0.25	-0.07	-0.07
Tricyclic prescription yes	0.03	0.15	0.11
Gabapentin or preGablin yes	<b>0.44*</b>	0.18	0.03
Psychological support yes	<b>-0.32*</b>	<b>0.27*</b>	0.01
POOL Physiotherapy intervention yes	0.13	<b>0.42*</b>	0.06
GMI intervention yes	0.16	<b>0.38*</b>	-0.02

<b>Categorised Education level</b>	0.01	0.10	0.11
<b>Ethnicity Māori yes</b>	<b>-0.33*</b>	0.04	0.04
<b>Acupuncture yes</b>	0.24	-0.07	-0.23
<b>SMT yes</b>	-0.19	<b>0.37*</b>	-0.01
<b>Skin sensory changes Baseline yes</b>	-0.02	<b>0.29*</b>	0.12
<b>Complete recovery yes</b>	1.00	-0.03	-0.22

Significance\* p>0.05

*Table 1. Spearman Correlation coefficient, TIF and TIP 6-week, weekly averages and complete recovery.*

The relationships for TIP and TIP with all categorical or continuous variables as well as with each other, and a CRPS complete recovery showed that neither TIP nor TIP had any relationship with complete recovery, nor any relationship with each other. However, each showed that there were associations with different variables. These are shown, using the arrow directions to represent the directions of the associations, in Figure 1.



**Spearman Correlations for Phyiotherapy (TIP and TIF 6 week averages)  
relationships for CRPS management clinical model,  $p < 0.05$**

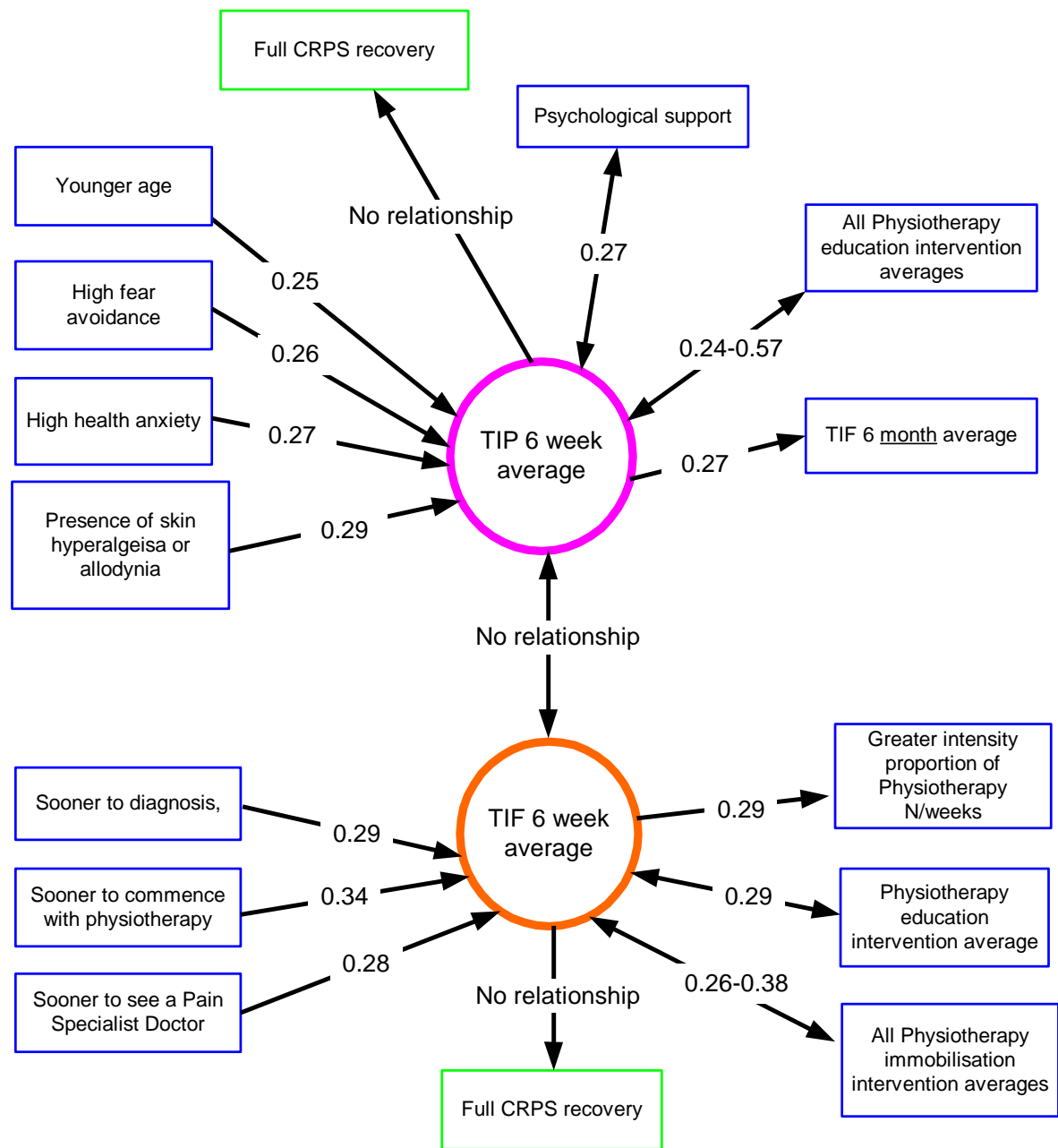
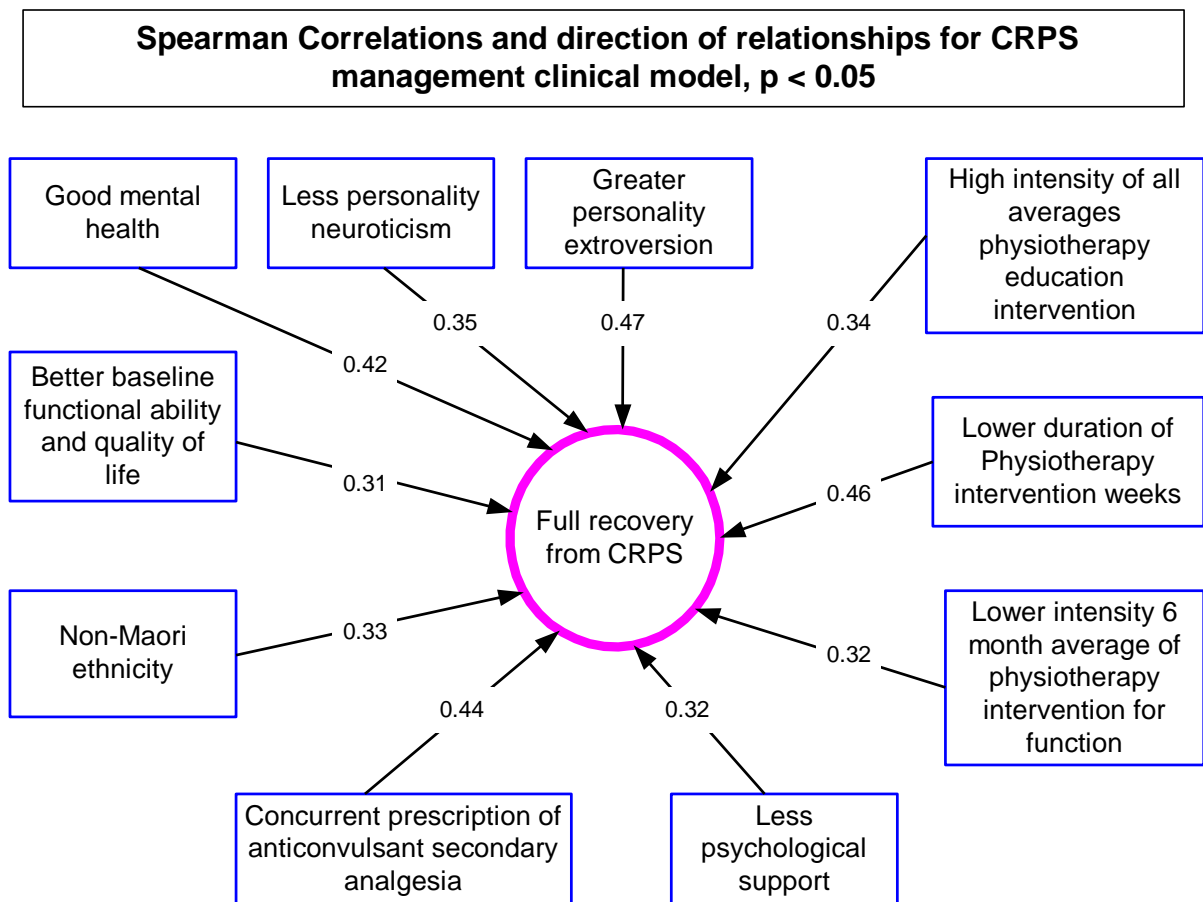


Figure 1. Spearman Correlation model for relationships between physiotherapy interventions at 6 weeks using TIP and TIF 6-week, weekly averages,  $p < 0.05$ .

The significant Spearman correlation relationships of baseline measures found to be associated with a complete recovery were: better mental health; higher score of personality extraversion; a lower score of personality neuroticism; better functional ability and quality of life; and non-Māori ethnicity. The positive associations of intervention for a full recovery were the higher intensity of physiotherapy education intervention (recorded in clinical notes as ‘education’ and calculated as a weekly average intensity for analysis) and the concurrent medical prescription of anticonvulsant medications. The association of lower duration of weeks with physiotherapy care, intensity of 6-monthly treatment interventions for function and no psychological support with a complete recovery possibly reflect reverse causality. These associations are represented in Figure 2.



*Figure 2. Model with Spearman Correlation with direction of relationships for complete CRPS recovery,  $p < 0.05$ .*

A proposed clinical conceptual model for the physiotherapy management of CRPS is developed around two securing foundations. It is represented with four pillars, each with four priority items, and held together by the revolving, concurrent interaction of four mainstays of physiotherapy interventions.

#### **4.1 The two foundations**

The entirety of this conceptual model is proposed to be secured on the two foundations. One is held visually above, *the prevention of CRPS*; and the other below, *the promotion of good mental health*. The reason for this is that if CRPS can be prevented, it is the highest priority. A study showed an eight-step fracture clinic algorithm to be effective at reducing the incidence of CRPS to zero [33]. The second securing and foundation pillar is the promotion of well-being or good mental health. Mental health is defined by the World Health Organisation (WHO) as the ability to realise one's full potential, to be able to cope with everyday life stresses, and to work productively and fruitfully, as well as make a positive contributions to the local or broader community [34]. This would apply to both clinician and patient [35]. This concept is not reflected in CRPS literature reviews, models or standard care protocol, despite systematic reviews identifying the negative impact of mental health stress affecting the Health Provider sector [36-39].

#### **4.2 The four pillars**

The four pillars are: 1) physiotherapy effective therapeutic relationship; 2) tailored physiotherapy intervention; 3) medical involvement; and 4) psychological support.

The pillar of an effective therapeutic relationship is tentatively proposed to involve four components, namely: agreement on mutual goals; listening skills; competence and communication, and motivation and encouragement [40, 41]. Furthermore, the literature showed that active listening skills, health provider competence with motivation and encouragement are important ingredients for an effective therapeutic relationship [42].

It is tentatively suggested using the pillar of the individually tailored physiotherapy has four components. The four components proposed are that this plan is systematic (be in accordance with competent physiotherapy standards of practice) [43], multimodal, that intervention methods are applied concurrently and that assessment is a continuum and not an end in itself.

The pillar of Medical care contributes with the prescription of appropriate primary or secondary analgesics helping to avoid the use of strong opioids [13]. A referral to a Specialist Pain Medicine Physician may also result in the prescription of further secondary analgesics, peripheral, plexus and neuraxial neural blockade that would facilitate the physiotherapy mainstay of exercise intervention [4]. A referral for peripheral or spinal cord neuromodulation may be necessary for recalcitrant CRPS cases [44]. A patient with mild CRPS may not need input from a Specialist Pain Medicine Physician [13], and these data showed that the prescription of anticonvulsant medications may be beneficial to complete recovery.

The pillar of a Psychologist's input is proposed to help the patient to develop resilience, to understand their thoughts, feelings and behaviours associated with their pain related disability, and to discover psychological flexibility that enables and cultivates effective coping strategies [45]. A subgroup of CRPS patients require psychological support and to determine what characterises those will benefit from this support vs. those who do not require it is not yet determined [46, 47]. The support from the Clinical Psychologist with assistance about understanding central mechanisms of pain is tentatively suggested to be an ingredient of this conceptual model and is also supported with the recent masterclass recommendations [15].

This conceptual model tentatively proposed that these four pillars may be the structure that supports the four mainstays of prescribed physiotherapy interventions.

### **4.3 The four physiotherapy intervention mainstays**

Four physiotherapy mainstays are the central feature for intervention and are tentatively proposed to revolve, emphasising that the four components of exercise intervention each contribute to one another; have a positive congruent effect on one another; that momentum for recovery is facilitated; and that recovery is evolving process accommodating flare ups, rather than a linear trajectory.

The proposed four mainstays are: *pain modulation intervention; education about intervention; functional intervention, and tolerance for prescribed intervention*. These four mainstays are proposed since both TIP and TIF were applied with these data. Pain modulation is proposed to form the starting point. Education about the exercise follows with functional exercise promoted in the context of the tolerance for the exercise intervention

since the literature suggested that the intervention methods aimed to managing aberrant cortical changes associated with CRPS were potentially aggravated by exercise or intervention methods that heightened the pain experience [26] . Although this has been challenged by the pain exposure supporters [48], evidence for both sides of this debate is weak.

The literature showed that education is an important component for effective health care, that myths about CRPS existed [49] and that most CRPS patients do not meet a minimum standard of basic knowledge about CRPS [50]. Since CRPS has a low prevalence, it is suggested that it may possibly not be commonly understood by the public nor even by those who are in the health care [18]. Education was also shown to be the most common intervention that South Island Physiotherapists used in a survey for usual CRPS clinical practice [51].

This revolving cycle is suggested to be harmonious and not juxtaposed in an evolving recovery process. The concept proposes that if progress towards the goals is not made, or there are flare ups of the pain experience, that either a slower or a quicker revolving of the cycle should ensue. This is also in accordance with the first proposed step-wise pathway in 1998. These tentatively proposed revolving mainstays of effective physiotherapy intervention are described in details as:

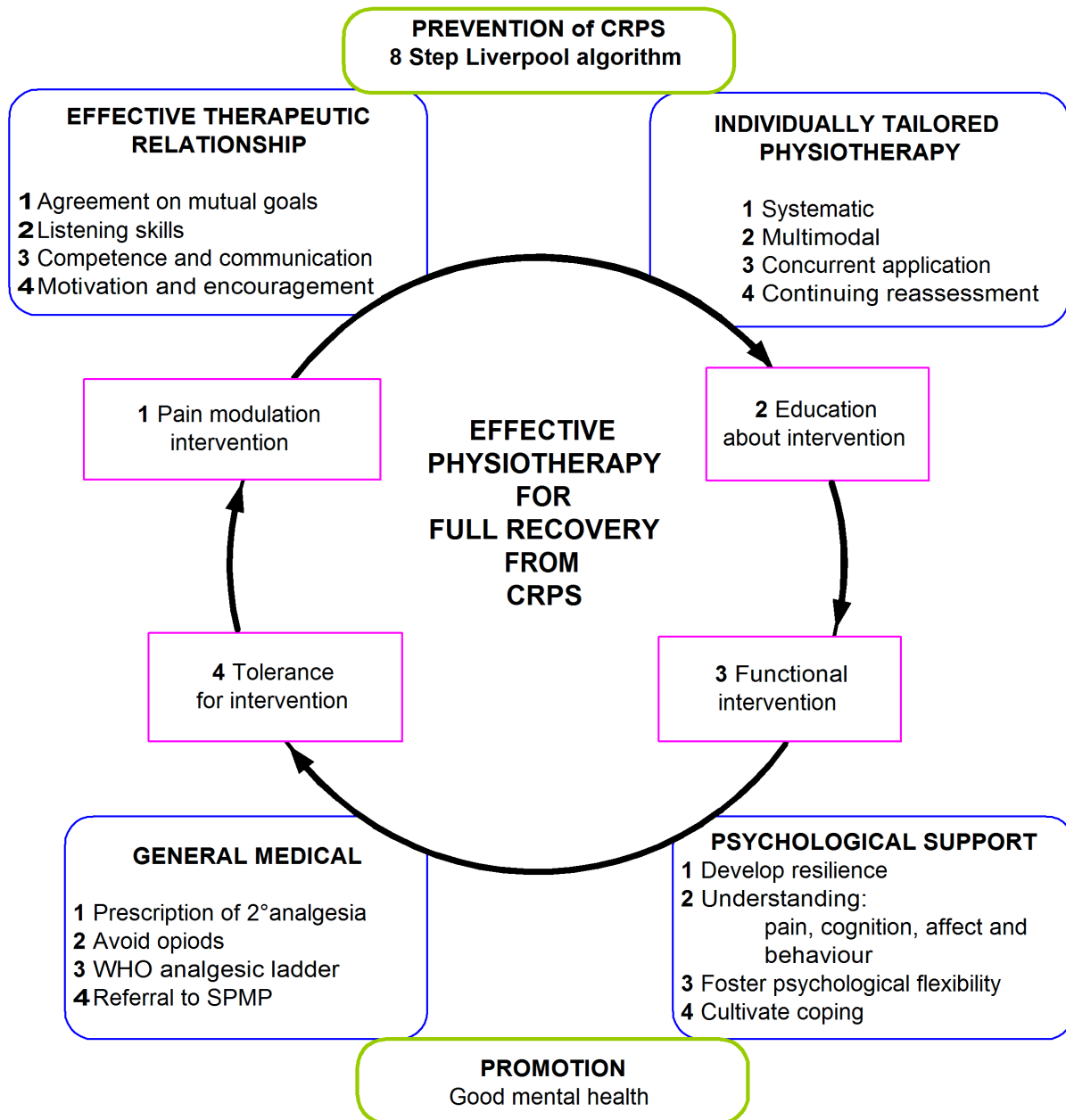
- 1) *Pain modulation intervention* emphasising a purpose about the ability to change the pain experience to less intensity or less interfering as a reduced sensory or emotional experience. It includes: graded motor imagery; mirror exercises; pool exercises; transcutaneous electrical nerve stimulation; cognitive behavioural therapy; acceptance and commitment to therapy; problem solving; relaxation and breathing; sensory–motor training including tactile acuity training, sensory mapping, and discrimination and desensitising; together with pain contingent homework as prescribed.
- 2) *Education about intervention* emphasising the purpose, meaning or understanding of the exercise which is directed to the mutually collaborated patient-centred goals. Education may also extend to information about the diagnosis, trajectory, outcomes or understanding of CRPS.
- 3) *Functional restoration intervention* emphasising the purpose of functional gain toward normal activity, associated with patient centred activities of daily living or exercise. It includes exercises, such as active, passive, resisted, balance and

proprioceptive land-based exercise, together with time contingent homework as prescribed. It also includes interventions for oedema management.

- 4) *Tolerance for intervention* emphasising the prescription of intervention intensity as strictly within the CRPS patient's physical, emotional and cognitive tolerance ability. Importantly, it is flexible to accommodate different tolerance abilities of either graded [52] or pain exposure [53, 54].

As pain reduces and functional ability improves, it is proposed that confidence with exercise develops which provides the necessary tolerance for the further progressions towards the mutually agreed rehabilitation goals. It is shown in the literature that beliefs affect functional ability [55] and that confidence is intertwined with this relationship.

This proposed conceptual model is represented in Figure 3.



*Figure 3. A proposed conceptual model of effective physiotherapy for complete recovery from CRPS with four pillars, four revolving physiotherapy mainstays secured on a foundation of prevention and the promotion of good mental health.*

#### 4. Discussion

The observation of clinical practice across a region revealed no strong evidence for any significant relationships with specific physiotherapy intervention methods and CRPS outcomes. This finding is consistent with the literature reviews which reported that there were no specific interventions to have a strong predictive effect for a good outcome [12-14]. The initial model in 1998 had a central focus of physiotherapy management [1].

This proposal also considers both clinician as well as patient in the context of the more recent ethical challenge of shared decision making with patient centred management [56], which aligns with current competencies [57] as well addresses the prevention of CRPS, as reported to reduce the incidence of CRPS with distal radial fractures [33]. It was considered necessary to include in a proposed model components that constitute mental health or well-being, quality of life and interpersonal communication styles as supported by the literature [40, 41] as well as recent ethical requirements [58].

The literature also suggests limited evidence for either the pain modulation or pain exposure approaches [15, 59]. It is reasonable to suggest this dichotomy reflects that intervention tolerance may be a factor to consider for CRPS physiotherapy intervention [60, 61], especially since the Geneva Convention states that it is a basic human right not to experience pain [62]. Furthermore, the literature shows that the intervention methods aimed to managing aberrant cortical changes associated with CRPS were potentially aggravated by exercise or intervention methods that heightened the pain experience [26]. Although this has been challenged by the pain exposure supporters [48], the evidence for this challenge is also weak. The literature showed that there are CRPS patients who are able to tolerate intervention to restore function without analgesia through progressive loading with pain exposure; whilst the opposite is shown to be effective with intervention that does not provoke the pain and instead, the affected limb's cortical representation is re-organised, sensory-motor input is reconciled and tactile acuity is normalised so that tolerance for function is gradually facilitated.

It is suggested from these Spearman Correlation data and the literature that physiotherapy interventions for pain (TIP) and function (TIF) each serve separate purposes. They are complimentary, and furthermore are ineffective without each other for the management of CRPS.



### *Strengths*

The strengths of this model are the first integration of clinical data from a region's standard, physiotherapy intervention methods and the respective CRPS patient outcomes towards the model design. Furthermore, these data are integrated with the existing body of knowledge towards a tentatively proposed, holistic, conceptual model to apply in physiotherapy clinical practice. Furthermore, it is also tentatively suggested that this attempt has an inherent strength with the inclusion of factors that are important in recent competencies and ethical requirements which have not been included in models to date.

### *Weaknesses*

Weaknesses of this model are that there is no strong evidence to support it and that it has not been tested. Furthermore, these Spearman correlations are limited with the reliability and validity of the relationships found. Ethical constraints of the longitudinal observation of clinical practice limited the ability to include a control group or to randomise the design and reverse causality potentially influenced intervention intensity. It was also not possible to determine the potential effect of a CRPS patient declining a physiotherapy referral, or participating in any other form of intervention, or to compare the choice for self-management without the support of any intervention. Neither does this model include the patient's perspective as per the recent proposal that a clinical model for CRPS management could involve the experience of the CRPS patients [63].

## **5. Conclusion**

It is acknowledged that: a) this is a proposed model; b) it requires further scrutiny and validation; c) there is no strong statistical evidence in any literature to date including these data for its confirmation. Nonetheless, it creates an answer to the call made in 2009 by integrating this longitudinal study's data with a comprehensive literature critique, and incorporates the intent and spirit of the previously proposed models. It is important for future research to test; validate; and compare the concurrent rotational approach with the stepwise algorithms, and include the patient's perspective as well.

### **Conflict of interest**

The authors have no conflict of interest to declare.

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## **POSTER PRESENTATIONS:**

1. Potential Risk Factors for the Onset of Complex Regional Pain Syndrome Type 1: A Systematic Literature Review. *41<sup>st</sup> Annual New Zealand Pain Society Scientific meeting*. April 2016. New Plymouth.
2. Physiotherapy management for Complex Regional Pain Syndrome (CRPS) on the South Island of New Zealand – a 6 month case series. *37<sup>th</sup> Annual Australian combined Society Scientific meeting*. April 2017. Adelaide.
3. Recovery for Complex Regional Pain Syndrome (CRPS) with Physiotherapy across the South Island region of New Zealand. *43<sup>rd</sup> Annual New Zealand Pain and Australian combined Society Scientific meeting*. April 2018. Sydney.
4. How Physiotherapists manage Complex Regional Pain Syndrome (CRPS) across the South Island region of New Zealand. *43<sup>rd</sup> Annual New Zealand Pain and Australian combined Society Scientific meeting*. April 2018. Sydney.

## Potential risk factors for the onset of Complex Regional Pain Syndrome type 1 (CRPS 1):

### A systematic literature review

This is the **first** systematic review to determine the potential risk factors for the onset of CRPS 1. Eligible articles were analysed dated 1996 to April 2014. Potential risk factors for the onset of CRPS 1 were identified from 10 prospective and 6 retrospective studies.

**Early diagnosis improves CRPS 1 prognosis.** Clinicians are urged to take heed of potential risks and refer for appropriate pain management if:

- patient female, particularly post-menopausal;
- fracture of the distal radius
- ankle dislocation or intra-articular fracture
- report of higher than usual levels of pain in the early phases after trauma.

Pons, T., et al., Potential Risk Factors for the Onset of Complex Regional Pain Syndrome Type 1: A Systematic Literature Review. *Anesthesiology Research and Practice*, 2015. doi:10.1155/2015/956539. p. 15 pages.

Potential risk factors for CRPS 1 onset	Evidence source	Weighted strength against bias	Quality and relevance of data extraction
Post-menopausal female gender	Beerthuis A., et al. 2012; De Mos, M. et al., 2007 Sandroni, P., et al., 2003	Strong; Strong; Acceptable	Good; Good; Good
Fracture of distal radius or an ankle dislocation or intra-articular fracture	Beerthuis A., et al., 2012; Sandroni, P., et al., 2003; De Mos, M. et al., 2007	Acceptable; Acceptable; Strong	Good; Good; Good
Report of higher than usual levels of pain in early phase of trauma	Beerthuis A., et al., 2012; Mossley L., 2014	Strong; Acceptable	Good; Adequate
Female gender	Sandroni, P., et al., 2003; Allen, G.; Galer, B.; Schwartz, L., 1997; Van Rijn, M., et al., 2007	Acceptable; Weak; Acceptable	Good; Adequate; Good

See journal publication for full evidence. Potential risk factors with much weaker weighting against bias and poorer quality and relevance include immobilisation, psychosocial barriers, and a positive diagnostic bone scan.

This systematic review shows that the **accurate potential risk factors** for the onset of CRPS 1 **remain elusive**. Studies remain heterogeneous, of mixed quality and relevance, and with varied weighting against the risks of bias.

**The low prevalence of CRPS 1 accompanied by a lack of a gold standard for diagnosis contributes to the difficulties around determining potential risk factors for the onset of CRPS 1.**



## Physiotherapy management for Complex Regional Pain Syndrome (CRPS) on the South Island of New Zealand – a 6 month case series



UNIVERSITY  
**OTAGO**  
*Te Whare Wānanga o Ōtago*  
NEW ZEALAND

The aim was to document, categorise and analyse the physiotherapy interventions used with the respective CRPS patients' outcomes for a case series of CRPS Type 1 and Type 2 patients attending physiotherapy in a prospective, longitudinal study over the South Island of New Zealand.

Outcomes were measured through independent telephonic interviewing using validated and reliable questionnaires

*The pain experience, function, quality of life all showed significant improvement for 56 CRPS patients over 6 months from January 2014 to January 2016 where satisfaction with care was overwhelmingly positive.*

CONTINUOUS VARIABLE	N (%)
No of pain modulation modalities applied (% all interventions)	36 (31)
No of function focus modalities applied (% all interventions)	42 (37)
No of immobilisation modalities applied (% all interventions)	12 (10)
No of passive modalities applied (% all interventions)	12 (10)
Education recorded as a modality (% all interventions)	13 (11)
No of days per week doing physio prescribed exercises	6 (3)
No of times per day doing physio prescribed exercises	3 (2)
Participation	
Discharged by physio	20 (43)
with physiotherapy	
Discontinue (self)	7 (15)
discharged	
Ongoing physio other 6 months	20 (42)
Medication prescription	
Paracetamol	25 (51)
Tramadol	18 (33)
Secondary analgesia (TCAs, Gabapentin, Pregabalin)	25 (51)
Oral corticosteroids short-term dose	2 (4)
Medication procedures	
Neural blockade	2 (4)
Spinal cord	4 (8)

Physiotherapy prescribed exercises were helpful to reduce the pain experience



Pool exercise is significantly better than land based exercise at reducing the experience of pain measured with the Mc Gill Pain Rating Index (PRI),  $p=0.05$

Graded Motor Imagery (GMI) has a significant relationship with improved quality of life with the scores for the World Health Organisation Disability Assessment Schedule  $p=0.01$  and Foot Function Index,  $p=0.048$

Most saw their physiotherapist 17 times in 6 months

**Implications for practitioners from this case series:** Physiotherapy contributes to positive outcomes for CRPS Type 1 or 2 with interventions and exercise for both pain modulation as well as to improve function over 6 months.

A third of these patients did not find their physiotherapy function focused exercises helpful to reduce their pain experience.

A half of these patients were also prescribed secondary analgesia.

**Future research:** Determine a clinical model for exercise that improves function with effective pain modulation.

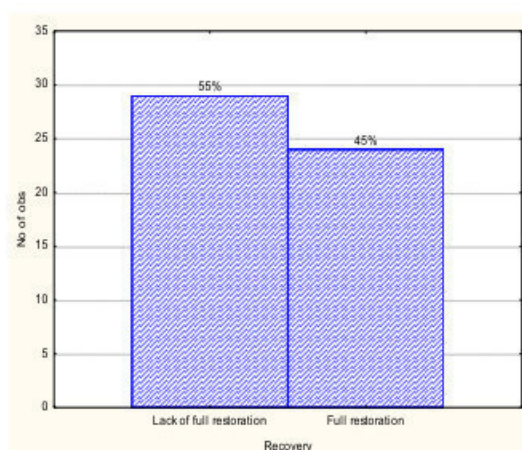
Tracey Pons, Edward Shipton, Jonathan Williman, Roger Mulder

Thanks are extended to the New Zealand Pain Society for their funding

# RECOVERY FOR COMPLEX REGIONAL PAIN SYNDROME (CRPS) WITH PHYSIOTHERAPY ACROSS THE SOUTH ISLAND REGION OF NEW ZEALAND



This paper describes the first observational, longitudinal clinical study across a region to determine the relationships of Physiotherapy categorical interventions for full recovery from CRPS across the South Island of New Zealand .

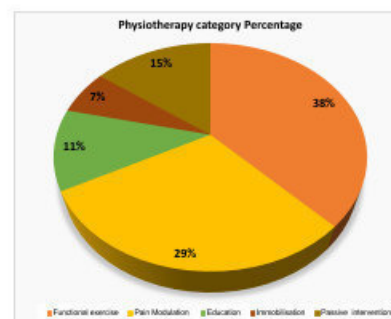


Category	Chi <sup>2</sup>	OR	CI	p
6 week average for PAIN MODULATION	0.1	0.9	0.6-0.4	0.8
6 month average for PAIN MODULATION	3.3	1.4	0.8-2.4	0.07
6 week average for FUNCTIONAL EXERCISE	1.8	0.9	0.5-1.9	0.18
6 month average for FUNCTIONAL EXERCISE	1.3	2.5	0.7-9.3	0.2
6 week average EDUCATION	0.5	1.3	0.1-17.3	0.5
6 month average EDUCATION	0.8	0.1	<0.1-19.3	0.4

No Physiotherapy intervention method shows any strong effect to predict a full recovery. Immobilisation showed a weak effect to contribute to poorer recovery of function,  $\beta=0.5$ ;  $p=0.02$

## OUTCOME MEASURES

- Pain intensity: Short form McGill Pain Questionnaire.
- Functional ability: Quick Disability of the Arm, Shoulder, Hand Questionnaire. (upper limb)  
Foot Function Index (lower limb)
- Quality of life: World Health Organisation Disability Assessment Schedule 2.0



## Implications for practitioners

A multimodal tailored approach is suggested using interventions for pain modulation as well as exercise for functional restoration.

**Future research:** Determine a Physiotherapy clinical model that improves function with effective pain modulation.

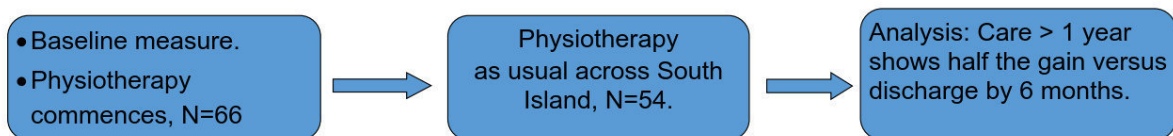
Tracey Pons, Edward Shipton, Jonathan Williman, Roger Mulder

Thanks are extended to the New Zealand Pain Society for their funding

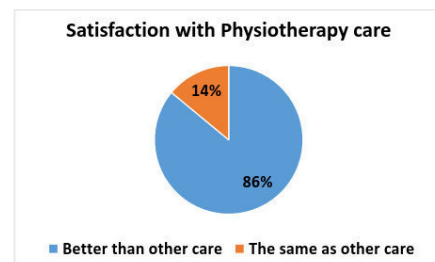
# HOW PHYSIOTHERAPISTS ARE SHOWN TO MANAGE COMPLEX REGIONAL PAIN SYNDROME (CRPS) BY ACROSS THE SOUTH ISLAND REGION OF NEW ZEALAND



This paper describes the first observational, longitudinal description Physiotherapy management for their CRPS patients across the South Island of New Zealand and the participant's respective outcomes



Category of Physiotherapy intervention	Interventions per week, Mean (SD)			
	6 weeks	6 months	1 year	Total
<b>Functional restoration</b> N = 66 (100%)	2.3 (1.8)	1.4 (1.6)	0.3 (0.6)	2.3 (2.8)
<b>Pain Modulation</b> N = 64 (96%)	2.5 (3.1)	1.1 (1.5)	0.3 (0.7)	1.8 (1.8)
<b>Education</b> N = 66 (100%)	0.9 (0.6)	0.4 (0.4)	0.07 (0.1)	0.7 (0.9)
<b>Immobilisation</b> N = 43 (64%)	0.8 (1.2)	0.3 (0.8)	0.03 (0.1)	0.4 (0.5)
<b>Passive interventions</b> N = 46 (69%)	1.2 (0.9)	0.7 (0.9)	0.2 (0.5)	0.9 (0.8)



Physiotherapy intensity showed a median of 16 sessions with an inter quartile range (IQR) of 9–33 over 1 year. Self-discharged or required ongoing care beyond one year = 10 (19% each), and the other 44 (81%) being discharged within six months. All showed significantly improvement across all outcome measures.

**Implications for practitioners**  
It is suggested that pain modulation interventions are applied concurrently with exercise for functional restoration.

**Future Research**  
Explore the ingredients for the effective Physiotherapy management with pain modulation and functional restoration for CRPS

**Tracey Pons, Edward Shipton, Jonathan Williman, Roger Mulder**  
Thanks are extended to the New Zealand Pain Society for their funding

## **Appendix B:**

### **Ethical approvals and Māori consultation**

#### **Information sheets and consent form**

# Confirmation from National Health Disability and Ethics committee



Health and Disability Ethics Committees  
1 The Terrace  
C/- MEDSAFE, Level 6, Deloitte House  
10 Brandon Street  
PO Box 5013  
Wellington  
6011

0800 4 ETHICS  
hdec@moh.govt.nz

12 November 2013

Mrs Tracey Pons  
118 Ohoka Rd  
Kaiapoi 7630

Dear Mrs Pons

Re:	<b>HDEC ref:</b>	<b>13/CEN/180</b>
	Study title:	Complex Regional Pain Syndrome (CRPS) physiotherapy management: A cohort longitudinal study across South Island New Zealand: a PhD proposal.

Thank you for submitting your application for HDEC review on 11 November 2013. The Secretariat has assessed the information provided in your application and supporting documents against the Standard Operating Procedures.

This application has not been validated, as on the basis of the information you have submitted, it does not appear to be within the scope of HDEC review. This scope is described in section three of the *Standard Operating Procedures for Health and Disability Ethics Committees*.

Participants will give informed consent for use of their data and consent to be followed up. Data will not be published in an identifiable form. There are no deviations from standard treatment. The risks for study involvement are no different from non-involvement. An observational study requires HDEC review only if the study involves more than minimal risk (that is, potential participants could reasonably be expected to regard the probability and magnitude of possible harms resulting from their participation in the study to be greater than those encountered in those aspects of their everyday life that relate to the study).

If you consider that our decision not to validate this application is in error please contact us as soon as possible giving reasons for this.

This letter does not constitute ethical approval or endorsement for the activity described in your application, but may be used as evidence that HDEC review is not required for it.

Please don't hesitate to contact us for further information.

Yours sincerely,



Nic Aagaard  
Administrator  
Health and Disability Ethics Committees  
hdec@moh.govt.nz

Encl: appendix A: documents submitted

**Appendix A**  
**Documents submitted**

<i>Document</i>	<i>Version</i>	<i>Date</i>
Covering Letter: Covering letter. word doc	version 1	02 November 2013
CV for CI	version 1	02 November 2013
Evidence of CI indemnity	version 1	02 November 2013
Survey/questionnaire: pdf	version 1	11 November 2013
Protocol: pdf file	version 1	11 November 2013
CVs for other Investigators: Prof Shipton pdfProf Mulder pdfDr Williman pdf	version 1	11 November 2013
Evidence of scientific review: Dr Turner pdf	version 1	11 November 2013
Maori consultation pdf	version 1	11 November 2013
PIS/CF: Consent form pdf	version 1	11 November 2013
Investigator's Brochure: Information sheets physios and participants	version 1	11 November 2013
Application	1	11 November 2013

## University of Otago Ethical approval and extension



H13/103

Academic Services  
Manager, Academic Committees, Mr Gary Witte

19 December 2013

Professor E Shipton  
Department of Anaesthesia (ChCh)  
Christchurch Hospital  
University of Otago, Christchurch

Dear Professor Shipton,

I am again writing to you concerning your proposal entitled "**Complex Regional Pain Syndrome (CRPS) physiotherapy management: A cohort longitudinal study across South Island New Zealand**", Ethics Committee reference number **H13/103**.

Thank you for your letter of 18th December 2013 addressing the issues raised by the Committee.

The Committee is grateful for the amendments made as requested. The Committee also thanks you for the inclusion of the Peer Review comments (table 3) made by Dr Hilda Mulligan and the action taken in response to those comments.

On the basis of this response, I am pleased to confirm that the proposal now has full ethical approval to proceed.

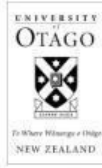
Approval is for up to three years from the date of this letter. If this project has not been completed within three years from the date of this letter, re-approval must be requested. If the nature, consent, location, procedures or personnel of your approved application change, please advise me in writing.

Yours sincerely,



Mr Gary Witte  
**Manager, Academic Committees**  
Tel: 479 8256  
Email: gary.witte@otago.ac.nz

c.c. Professor E A Shipton Head Department of Anaesthesia (ChCh)



H13/103

Academic Services  
Manager, Academic Committees, Mr Gary Witte

9 November 2016

Professor E Shipton  
Department of Anaesthesia (ChCh)  
Christchurch Hospital  
University of Otago Medical School  
University of Otago, Christchurch

Dear Professor Shipton,

I am again writing to you concerning your proposal entitled "**Complex Regional Pain Syndrome (CRPS) physiotherapy management: A cohort longitudinal study across South Island New Zealand**", Ethics Committee reference number **H13/103**.

Thank you for your letter of 3rd November 2016 requesting an extension of the ethical approval for the above study in order to extend the recruitment of participants.

The Committee accepts and approves the amendment and grants re-approval for a further 3 years from the date of this letter.

Your proposal continues to be fully approved by the Human Ethics Committee. If the nature, consent, location, procedures or personnel of your approved application change, please advise me in writing. I hope all goes well for you with your upcoming research.

Yours sincerely,

Mr Gary Witte  
**Manager, Academic Committees**  
Tel: 479 8256  
Email: gary.witte@otago.ac.nz

c.c. Professor E A Shipton Head Department of Anaesthesia (ChCh)



## Maori consultation

---



5 August 2013

Professor Edward Shipton & Tracey Pons  
Department of Medicine  
University of Otago, Christchurch

*Mā te rangahau Hauora e tautoko te whakapiki ake te Hauora Māori.  
All health research in Aotearoa New Zealand benefits the Hauora (health and wellbeing)  
of tangata whenua.*

Tēna kōrua,

Thank you for taking the time to meet with me at MIHI at the University of Otago, Christchurch on the 1<sup>st</sup> August 2013, to discuss your research study titled:

*Complex Regional Pain Syndrome (CRPS) Physiotherapy Management: A controlled trial of no-pain versus pain exposure management.*

I note that for this research project that you and Tracey Pons (PhD student) are the Principal Investigators for this study.

### **Commentary on Proposed Research Projects**

From my discussion with you, I have ascertained that the aim of this research project is to determine the efficacy of clinical interventions for the management of CRPS and in particular physiotherapy intervention for CRPS using a six week graded motor imagery programme versus standard physiotherapy. The study will be conducted with patients with a formal diagnosis of CRPS undergoing rehabilitation in private physiotherapy practices based in Christchurch and Dunedin. It is possible that this study may extend to include physiotherapy practices in the wider South Island region. This study aims to recruit 100 – 200\* participants over a 2 – 3 year period and measure patients before starting the rehabilitation programme and again at the end of the programme.

### **Māori Health Gain**

In terms of Māori health gain, your research application should highlight the direct benefits for Māori participants who participate in the studies and document the direct health benefits/gains for those individual Māori participants who consent to be part of this research. Furthermore, this project could be strengthened by including a clear epidemiological profile of current rates of Māori with CRPS (highlighting current disparities between Māori and non-Māori) nationally, which would provide an appropriate context to the importance of this research topic on future Māori health gain and the impact of this toward achieving Whānau Ora. We also discussed the importance of reviewing and including additional literature regarding the current rates of Māori using rehabilitative physiotherapy and providing a comparative account of those rates compared to non-Māori.

Research Office, Department of the Dean  
University of Otago, Christchurch  
PO Box 4345, Christchurch Mail Centre, Christchurch 8140, New Zealand  
Tel +64 3 364 0237 • Fax +64 3 364 1490 • Email [research.uoc@otago.ac.nz](mailto:research.uoc@otago.ac.nz)  
[www.uoc.otago.ac.nz](http://www.uoc.otago.ac.nz)

---

### **Ethnicity**

As your study may involve a number of Māori participants there is a need to acknowledge the issues pertaining to ethnicity and to consider how ethnicity data will be collected for this study. I understand that ethnicity data has already been collected from ACC, however it is recommended that ethnicity data is collected from each participant in accordance with the MOH guidelines, which involves the use of the Census 2006. Should a participant identify as Māori, but this is not recorded in their records, this should be reflected by ensuring the participant is correctly recorded as being Māori.

You have also indicated you will be undertaking a sub-analysis using ethnicity this may help to unmask some distinct diverges between ethnic groups in relation to specific trajectories in the study.

### **Partnership**

With regard to Māori involvement, you informed that Maria Sorenson (Māori Physiotherapist) would be providing cultural oversight to the study. Her involvement in the study may also allow you to consider what cultural aspects or considerations need to be taken into account regarding the incorporation of a Tikanga based framework for this research project. It is commended that Māori participants in your study will be given the opportunity to be interviewed by a Māori interviewer.

### **Potential Further Support Resources**

Further resources that you might want to access to strengthen your responsiveness to Maori within your research are: 1. *HRC's Ngā Pōu Rangahau Hauora Kia Whakapiki Ake Te Hauora Māori 2004-2008*, 2. *The Health Research Strategy to Improve Māori Health and Well Being 2004-2008*. The other reference that is available is 3. *Hauora Māori Standards of Health IV: A Study of the Years 2000-2005* by Bridget Robson and Ricci Harris, Māori Health Research Unit, Wellington School of Medicine, University of Otago, Wellington. All provide Maori specific information on a range of health issues.

The recent publication *Tātau Kahukura: Māori Health Chart Book 2010*, Ministry of Health, 2010 (2<sup>nd</sup> edition), is an update relating to the socio economic determinants of health, health status and service utilisation of the Māori population. Further references are available from the HRC's *Guidelines for Researchers on Health Research Involving Māori* (page 22), [www.hrc.govt.nz](http://www.hrc.govt.nz)

### **Dissemination of Results**

The HRC's *Guidelines for Researchers on Health Research Involving Māori*, is important in terms of how your research results may contribute to Māori health gain. This should occur not only in an academic forum, but also within the community from where data is drawn. Therefore the findings from this study should be further discussed with relevant Māori stakeholders. I would recommend that you utilise the Māori Researchers, Māori health professionals or Māori health experts involved in your study to assist you in the dissemination of your research to the appropriate Māori forums. These forums will allow an opportunity for the consideration of Māori community feedback into any discussion going forward. The Māori Research Advisor may also assist in facilitating this meeting.

---

**Ethics**

It is a requirement of the ethics approval process, that a final report be submitted when the research is complete. A copy of the report should also be supplied to me at that time, as findings from this project may contribute to the development of future research hypotheses or projects. It is therefore important that appropriate Māori organisations and Māori researchers are aware of your findings.

I wish you well in your research.

Nāku iti nei

A handwritten signature in blue ink, appearing to read 'Karen Keelan', written in a cursive style.

Karen Keelan  
Māori Research Advisor

## Email communication with Maori Women's Welfare League

On 23/10/2013 6:55 p.m., Maria Sorensen wrote:  
Hi again Tracey

I have had a chance to read your project and think it looks very comprehensive and well designed. It will be very helpful to have a clearer picture of what works best for CRPS patients. I support your project and I am happy to assist wherever I can.

I wondered if there was a reason why acupuncture was not included as a treatment intervention on the Physio questionnaire?

I will be in touch next year about the Maori Women's Welfare League meeting.

Kind regards  
Maria

---

----- Original Message ----- From: "Tracey Pons" <tracey@pons.ws>  
To: "Maria Sorensen" <maria@racecoursephysio.co.nz>  
Sent: Thursday, October 10, 2013 8:51 AM  
Subject: Re: Research project\_Tracey Pons

Hello Maria

Thank you very much, your time already is greatly appreciated and I understand how busy you are.

I have no specific deadlines at present and I will let you know if I find that I do have to have something from you. I am in the process of submitting my ethics application with the NHDEC and University Ethics committees. I have had the NHDEC inform me that since this project is simply observational with non identified individuals presented in the outcome analyses that their formal approval is not required as the project represents no potential threat to anyone's health/welfare. The formal confirmation of this is currently in process.

I have changed some the questionnaires I originally sent you. I managed to find some much shorter versions which make telephonic interviewing much easier. I really appreciate your word to me that you would be available for any potential Maori participant with my project who would prefer to have a specific Maori physio interviewer rather than the Pakeha physio, myself. Here attached please find my updated questionnaires. You will see that I have also included a flow chart for how the process works for a physio to refer a participant for the interviewing. I am also planning a brief interview with physios to help categorise how CRPS is generally treated.

I look forward to hearing form you about presenting Maori Women's Welfare League meeting in the New Year. I appreciate you being willing to arrange this at an appropriate time.

Kind regards and again, many thanks,

Tracey Pons

Uni Otago Student no: 1089539  
118 Ohoka Rd  
Kaiapoi, 7630  
Tel: 03 327 2359  
Fax: 03 327 2329  
Cell: 021 236 2111

---

On 10/10/2013 8:24 a.m., Maria Sorensen wrote:  
Hi Tracey

Just letting you know that I haven't forgotten you. I will get back to you once I have had a good read of your proposal so I hope there is no deadline that I may have missed. Let me know if you need anything from me urgently and I will get on with it sooner.

I had a Maori Women's Welfare League meeting last weekend and the tone was very much in preparation for the end of the year function so there was not alot of business on the agenda. I will raise the subject of your prposal with them at our first meeting early next year and take it from there.

Will be in touch soon.

Regards  
Maria

---

----- Original Message ----- From: "Tracey Pons" <tracey@pons.ws>  
To: <maria@racecoursephysio.co.nz>  
Sent: Monday, September 23, 2013 9:12 PM  
Subject: Research project\_Tracey Pons

Hello Maria

It was so nice to chat to you today. You are so encouraging and helpful - much appreciated by me!

Here is my proposal and the document which contains the information sheet, consent form and all the questionnaires. CRPS usually affects either the hand or the foot, not both. So a participant would answer either the QuickDash or the Functional Foot Index.

I look forward to hearing from you and engaging in a few month's time with your Women's Health Forum.  
Any comments about my proposal are most gratefully received - more heads are always better than one!

Warm wishes and many thanks,

Tracey Pons

## Locality authorisations: South Island District Health Boards

### *Canterbury and Southern District Health Boards*



## Authorisation report

<b>Study ref:</b>	
Study title:	A project to assess physiotherapy management of Complex Regional Pain Syndrome (CRPS)
Status:	Unable to get status.


This authorisation report was generated by Canterbury DHB Research Office CDHB Research Office on 11 Feb 2014

Authorisation Type	Authorisor	Date and time	Lead Investigator(s) at locality
Co-ordinating Investigator	Tracey Pons	11 Nov 2013, 05:08 PM	
Primary Contact Person	Tracey Pons	11 Nov 2013, 05:09 PM	
Locality	CDHB	11 Feb 2014, 03:18 PM	Tracy Pons Prof Edward Shipton Prof Roger Mulder Dr Jonathan Williman
Locality	Health Research South	22 Jan 2014, 09:41 AM	Prof Rob Walker


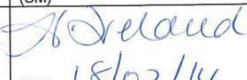
# South Canterbury District Health Board

## Research Application Checklist NEW

### SECTION 1.: To be completed by the applicant:

Title of Research Proposal	Physiotherapy for Complex Regional Pain Syndrome
Research Reference Number	
Name of key person accountable for research project	Tracey Pons
Name of SCDHB principal researcher	
Primary Service involved in research proposal	
Contact address	118 Onoka Rd Kaiapoi, 7630
Phone / email	03 329 2359 021 236 2111 tracey@pons.co.nz
Start date of research	Feb 2014 → End 2017
Finish date of research	End 2017
Name & signature of person making application	Tracey Pons 

### SECTION 2: To be completed by the applicant and confirmed by the designated SLT member prior to submission to the relevant Ethics Committee

Checklist for Approval Process	This column is to be initialled by the applicant to indicate requirement has been met:	This column is to be signed off and dated by the SLT member as indicated:
Requirement:	Comments / Proof attached Y or N	Signature & Date
A preliminary meeting with the service manager & clinical director, SCDHB has been held to outline overall scope and purpose of the research project including identifying any potential or expected changes in current practice	Preliminary meeting held with Clinical Leader and Senior Physiotherapist. Further discussions and information exchanges between Service Manager, Clinical Leader & Tracey Pons.	 25 Feb 14
Proof of consultation with relevant SCDHB clinicians who may become involved in the research is evidenced	Yes	 (SM) 18/02/14

An outline of any impact on the service delivery on other services including diagnostics, consumables, ALOS, follow up regime, staff time and practice	No cost, Minimal impact on physiotherapy department's current service delivery. purely observational (SM) <i>Luweck 25 Feb 14</i>
Financial details including a breakdown of costs associated with staff, facilities, equipment, computer access and access to clinical records is identified by SCDHB principal researcher	Printing, telephone costs are all provided by researcher. Consent forms are provided with stamped addressed envelope (GM SS)
Any funding issues related to the patients access to the study research at the conclusion of the study is evidenced and resolved	None (GM SS)
Proof of consultation with local Maori	see note Attached i) Sauterhqui Requires local sign off (GM Q&R) <i>Maori Health Forum</i>

**Next Steps:**

Consider if legal review required (? if this is really required if using national indemnity format)	No (GM SS)
Sign DHB indemnity form	(CEO)
Sign locality agreement	(GM SS)
Sign declaration form	(CMO)

**SECTION 3: To be presented by the applicant and sighted by the designated SLT member prior to CEO sign off**

Checklist for Approval Process	This column is to be initialised by the applicant to indicate requirement has been met:	This column is to be signed off and dated by the SLT member as indicated:
Requirement:	Comments / Proof attached	Signature & Date
Present ethics approval		(CMO)
Present national indemnity document		(GM Q&R)

**Next Steps:**

Approve research proposal	(CEO)
Advise applicant that approval has been granted	(GM Q&R)

Name *N. T. T. T.*

Designation: CEO

Signature *[Signature]*

Date *9/4/14*



# Nelson Marlborough District Health Board

04-07-14:09:39 : MEDICAL OUTPATIENTS

: +64 3 5461288 # 1 / 1



Nelson Marlborough  
District Health Board

Fax: 03 546 1288  
Phone: 03 546 1247

*Medical Outpatients  
Nelson Hospital*

Private Bag 18  
Nelson 7042  
New Zealand

03 July 2014

cc *Deidre Crichton, Team Leader Physiotherapy, Nelson*  
cc *Hilary Exton, Allied Health Advisor*  
cc *BBK*

Mrs Tracey Pons  
119 Ohaka Road  
Kaiapoi 7630

Fax 03 3272329

Dear Tracey

I am pleased to now be able to confirm successful completion of the approvals process via the NMDHB for your research proposal "Complex Regional Pain Syndrome Physiotherapy Management: A cohort longitudinal study across South Island New Zealand (ECRH Ethics Committee Referral Number H13/103).

We would be pleased to receive a notification at completion of your project and a copy of the final paper once completed. Please feel free to contact me if issues arise during his process.

Your sincerely

Dr Bruce King  
Clinical Director Medical Surgical Services  
BBK:SUE

## Information sheet to participating physiotherapist

PhD RESEARCH PROJECT:  
**Physiotherapy for CRPS: Oct-13**



### What is this project about?

Complex Regional Pain Syndrome (CRPS) management usually involves physiotherapy from the earliest stage of diagnosis. Physiotherapy is recognised as essential for the management of this extremely painful condition, but exactly how to manage it is controversial as well as poorly researched in the clinical field. This project seeks to find out:

1. How is CRPS currently being treated in the South Island of NZ
2. What are the possible factors that affect the outcomes of pain, function, quality of life and satisfaction with physiotherapy intervention?
3. Which factors of intervention make the biggest difference for improvement of function and decrease in pain experience
4. And finally develop a model from the data that can serve as a protocol for the management of CRPS in everyday clinical practice

### How can you be involved?

I am asking all physiotherapists who treat CRPS in the South Island of NZ to

- a. Contact me when a referral of CRPS is received. I am Tracey Pons on Tel 03 327 2359 or cell 021 236 2111 or email: [tracey@pons.ws](mailto:tracey@pons.ws)
- b. Explain the project to your patient. The following words may be helpful:  
*"This project is measuring how physiotherapy for your CRPS helps. The researcher is a physio with many years of experience treating CRPS. She is asking your permission to phone you when you start your physio with me, and then again 6 weeks, 6 months and 1 year later. When she phones you she will spend about 15 min each time asking you some questions about your pain, your everyday quality of life and ability, your dealings with your physio as well as some information about how you feel about yourself and life. Nothing about your treatment with me is going to be affected. What this project is trying to find out is what works the best for you and others who have CRPS."*
- c. Ask your patient for consent to participate by signing the form I give you. The following words may be helpful: *"Please would you sign this form to give Tracey, the researcher, your permission for her to phone you. You have no obligation to take part with this research and even if you do or don't sign today and change your mind later, that will not affect your treatment with me at all."* Please either fax the consent to me: 03 327 2329 or post it to 118 Ohoka Rd, Kaiapoi, 7630.
- d. Send me your clinical notes in whichever form you prefer, email, fax or post when you discharge your patient. I will contact you when I phone the patient to remind you.

If you would like to have any clarity regarding anything you are not sure about, please feel free to ask me. The University supervisors for this project are Prof's Ted Shipton and Roger Mulder. I can be contacted at any time for any queries you might have on 03 327 2359 or 021 236 2111 or email: [tracey@pons.ws](mailto:tracey@pons.ws)

**A very big thank you for helping me to gather data for this research project.**

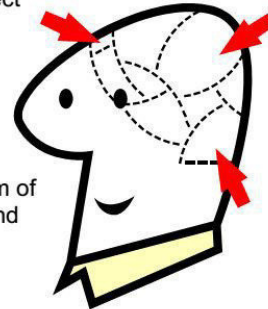
## Information sheet to participant

*PhD RESEARCH PROJECT: Physiotherapy for CRPS*  
**Information for patients**



### What is CRPS?

CRPS can be explained as a painful condition that can affect every aspect of your leg or arm. Medical scientists are still trying to get to a full understanding about why and when it happens. CRPS is a condition where the nerves involved with your limb send “amplified” signals to your brain; subsequently the brain becomes over-protective to processing any more nerve information coming from your limb. We know that your pain is real and intense. Your team of Physiotherapist, General Practitioner, Medical Specialist and sometimes a Psychologist or another Allied Health Professional can help you to manage it.



### How Physiotherapy solves this problem?



Since the brain is wonderfully adaptable, we treat both your brain and the problem limb. Physiotherapists look after your pain as well as help you to improve the function of your very painful limb. Your Physiotherapist will help your muscles get fitter and stronger using lots of specific exercises and other techniques to help your brain and nerve(s) calm down the pain. It is a normal part of CRPS that your limb may show changes in colour, swelling, hair growth, and temperature. Most likely, you will receive treatments from other medical staff such as medications.

**The best results** will be gained from your dedicated efforts and high repetition rate. “Go for it” by FREQUENTLY practising the “homework” given by your Physiotherapist.

If you would like to clarify anything you are unsure about, please feel free to ask your Physiotherapist, or telephone the Researcher (Tracey). Tracey can be telephoned regarding any queries on 03 327 2359 or 021 236 2111.

## Consent form for participant

*PhD RESEARCH PROJECT: Physiotherapy for CRPS*  
*Consent form information for patient: Page 1*



### **Information about this project with consent to participate**

Thank you for being willing to participate with this project. Physiotherapy for Complex Regional Pain Syndrome (CRPS) is what we are looking at. We want to find out what type of Physiotherapy works best. In order to answer this question we are collecting information about the treatment physiotherapists give to people, like you, who have developed CRPS. We also want to interview, by telephone or cell phone, each of these people, separately, at the start of physiotherapy treatment and then at 6 weeks, 6 months and 1 year after starting physiotherapy. The interview should take about 15 minutes each time and involves questions about your pain, function, quality of life and how you found your experience of treatment with your physiotherapist and your prescribed homework. I will also ask your physio about the details of the treatment you received.

This project is the first of its kind to be done anywhere in the world and has the potential to give us a lot of helpful information about how we can treat CRPS more effectively in the future. All the information we collect will be analysed anonymously, for both the physiotherapist and the person with CRPS. We may be able to keep the de-identified information for future research projects too. The information collected is designed to analyse what is the best Physiotherapy to treat CRPS. Since we need reliable information for the analysis, we need 160 people with CRPS all over the South Island of New Zealand to participate. Permission from the National Health and Disability Ethics Committee and University has been given for this project.

Please remember you do not have to participate with this project. You have no obligation to participate and whether you do or don't will not affect any of your treatment at all. If you would like to have any clarity regarding anything you are not sure about, please feel free to ask your physiotherapist or phone me. Tracey can be contacted for any queries you might have on 03 327 2359 or 021 236 2111. Tracey will call you soon after your signing this consent form.

There are no right or wrong answers and your personal answer is important to us.

This study has been approved by the University of Otago Health Ethics committee, reference no: H13/103. If you have any concerns about the ethical conduct of this research you may contact the Human Ethics committee administrator phone 03 4798256. Any issues you raise will be treated in confidence and investigated and you will be informed of the outcome.

Please keep this sheet of paper with you.



**Please give this signed form to your physiotherapist to send to the researcher.**

***I would like to participate in this project which is collecting information from my clinical notes about my physiotherapy and my CRPS progress. I am happy to be called about my progress, homework and physiotherapy. I understand that I need to give my name and phone number for the interviewing, and that all my information will be totally anonymous so that I am not able to be identified by anyone else.***

**Name:** \_\_\_\_\_

**Date:** \_\_\_\_\_

**Tel no:** \_\_\_\_\_

**Cell no:** \_\_\_\_\_

**Signature:** \_\_\_\_\_

## Appendix C

### Budapest criteria record for treating Physiotherapist

Adapted from: Harden RN, Bruehl S, Perez RS, Birklein F, Marinus J, Maihofner C, Lubenow T, Buvanendran A, Mackey S, Graciosa J, Mogilevski M, Ramsden C, Chont M, Vatine JJ. Validation of proposed diagnostic criteria (the "Budapest Criteria") for Complex Regional Pain Syndrome. *Pain* 2010;150(2):268-274.

#### General definition of the syndrome:

CRPS describes an array of painful conditions that are characterised by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor and/or trophic findings. The syndrome shows variable progression over time.

To make the CLINICAL diagnosis, the following criteria must be met:

1. Continuing pain which is disproportionate to any inciting event
2. Must report at least one symptom in 3 or 4 following categories:
  - **Sensory:** Reports of hyperaesthesia or allodynia
  - **Vasomotor:** Reports of temperature asymmetry or skin colour changes or skin colour asymmetry
  - **Sudomotor/Edema:** Reports of edema or sweating changes or sweating asymmetry
  - **Motor/Trophic:** Reports of decreased range of movement and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
3. Must display at least one sign at time of evaluation in 2 or more of following categories:
  - **Sensory:** Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch) and/or temperature sensation and/or deep somatic pressure and/or joint movement
  - **Vasomotor:** Evidence of temperature asymmetry  $>1^{\circ}\text{C}$  and/or skin colour changes or skin colour asymmetry
  - **Sudomotor/Edema:** Evidence of edema or sweating changes or sweating asymmetry
  - **Motor/Trophic:** Evidence of decreased range of movement and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
4. There is no other diagnosis that better explains the signs and symptoms

For RESEARCH PURPOSES; diagnostic decision rule should be at least one symptom **in all four categories** and at least one sign observed at evaluation in two or more sign categories.

**Table 1: CRPS sensory changes**

<b>Skin temperature</b>	A.1. Cold	A.2. Warm	A.3. Hot	A.4. Very hot		
<b>Skin colour</b>	B.1. Blue	B.2. Red	B.3. Pink	B.4. Blotchy	B.5. Bruising	B.5. Other
<b>Skin texture</b>	C.1. Glossy	C.2. Dry	C.3. Scaly			
<b>Lymph-oedema</b>	D. 1. Mild < 30%	D.2. Moderate 30-60%	D.3. Severe >60%			
<b>Skin sweating</b>	E.1. Mild: Feels slight clammy	E.2. Moderate: Feels wet	E.3. Severe: visible dripping of skin	E.4 No usual sweat or drier		
<b>Hair growth</b>	F.1. Absent	F.2. Increased				
<b>Nails</b>	G.1. Brittle and break easily	G.2. Whiter	G.3. More transparent	G.4. Other		
<b>Skin sensation</b>	H.1. Hyperalgesia (hypersensitive)	H.2. Allodynia (normal sensation like gentle soft touch is painful)	H.3. Hypoesthesia (Sensation loss)			

**Table 2. CRPS Motor Sudomotor changes.**

<b>Tremor</b>	Q. 1.  Mild: associated only with attempts of movement, but movement is still possible	Q2.  Moderate:  Visible at rest and increases with attempts of movement	Q3.  Severe  Visible at rest and prevents attempts of movement	Q4.  Dystonia. Use the UDRS to measure
<b>Clawing</b>	R. 1.  Mild: able to actively and passively correct to almost full ROM	R.2.  Moderate: able to actively and passively correct to half ROM	R.3.  Severe: Difficulty with active or passive correction to a quarter of ROM	R.4.  Contracture into claw hand
<b>Proprioception Problem</b>	S.1.  Mild: Difficulty with correct orientation of limb with eyes closed	S.2.  Moderate: Difficulty with correct orientation of limb with eyes open	S.3.  Severe: Great difficulty with correct orientation of limb with eyes open	S.4.  Proprioceptive loss:  Quite unable to orientate limb correctly for any movement.

Table 3. Outlines the medical investigations that can be used to confirm the CRPS diagnosis if the IASP criteria have also been met.

<b>DEXA Bone density scan</b>	Osteoporosis
<b>PET scan</b>	Hot spots

**PLEASE TICK THE APPROPRIATE BOX FOR YOUR CRPS PATIENT'S AUTONOMIC CHANGES AND SEND TOGETHER WITH THE CONSENT FORM.**



# Appendix D: Instruments

## McGill Pain Questionnaire, short form

Short form McGill Pain Questionnaire  
 Ronald Melzack © 1984

Please indicate with a tick [✓] the boxes that describe how your pain feels now:

	NONE	MILD	MODERATE	SEVERE
THROBBING				
SHOOTING				
STABBING				
SHARP				
CRAMPING				
GNAWING				
HOT-BURNING				
ACHING				
HEAVY				
TENDER				
SPLITTING				
TIRING-EXHAUSTING				
SICKENING				
FEARFUL				
PUNISHING-CRUEL				

Please mark on the line below where you would rate your pain now

NO PAIN |-----| WORST POSSIBLE PAIN

Please indicate with a tick [✓] in the box that describes how strong your pain intensity feels

NO PAIN	MILD	DISCOMFORTING	DISTRESSING	HORRIBLE	EXCRUCIATING
---------	------	---------------	-------------	----------	--------------

## WHODAS 2.0



# WHODAS 2.0

WORLD HEALTH ORGANIZATION  
DISABILITY ASSESSMENT SCHEDULE 2.0

## 12-item version, interviewer-administered

### Introduction

This instrument was developed by the WHO *Classification, Terminology and Standards* team, within the framework of the WHO/National Institutes of Health (NIH) Joint Project on Assessment and Classification of Disability.

Before using this instrument, interviewers must be trained using the manual *Measuring Health and Disability: Manual for WHO Disability Assessment Schedule – WHODAS 2.0* (WHO, 2010), which includes an interview guide and other training material.

The versions of the interview available are as follows:

- 36-item – Interviewer-administered<sup>a</sup>
- 36-item – Self-administered
- 36-item – Proxy-administered<sup>b</sup>
- 12-item – Interviewer-administered<sup>c</sup>
- 12-item – Self-administered
- 12-item – Proxy-administered
- 12+24-item – Interviewer-administered

<sup>a</sup> A computerized version of the interview (*iShell*) is available for computer-assisted interviews or for data entry

<sup>b</sup> Relatives, friends or caretakers

<sup>c</sup> The 12-item version explains 81% of the variance of the more detailed 36-item version

For more details of the versions please refer to the WHODAS 2.0 manual *Measuring Health and Disability: Manual for WHO Disability Assessment Schedule – WHODAS 2.0* (WHO, 2010).

Permission to translate this instrument into any language should be obtained from WHO, and all translations should be prepared according to the WHO translation guidelines, as detailed in the accompanying manual.

For additional information, please visit [www.who.int/whodas](http://www.who.int/whodas) or contact:

Dr T Bedirhan Üstün  
*Classification, Terminology and Standards*  
*Health Statistics and Informatics*  
*World Health Organization (WHO)*  
1211 Geneva 27  
Switzerland

Tel: + 41 22 791 3609  
E-mail: [ustunb@who.int](mailto:ustunb@who.int)



# WHODAS 2.0

WORLD HEALTH ORGANIZATION  
DISABILITY ASSESSMENT SCHEDULE 2.0

12
Interview

## Section 2 Demographic and background information

This interview has been developed by the World Health Organization (WHO) to better understand the difficulties people may have due to their health conditions. The information that you provide in this interview is confidential and will be used only for research. The interview will take 5–10 minutes to complete.

**For respondents from the general population (not the clinical population) say:**

Even if you are healthy and have no difficulties, I need to ask all of the questions so that the survey is complete.

I will start with some background questions.

A1	<b>Record sex as observed</b>	Female	1
		Male	2
A2	How old are you now?	_____ years	
A3	How many years in all did you spend <u>studying in school, college or university</u> ?	_____ years	
A4	<b>What is your <u>current marital status</u>? (Select the single best option)</b>	Never married	1
		Currently married	2
		Separated	3
		Divorced	4
		Widowed	5
		Cohabiting	6
A5	<b>Which describes your <u>main work status</u> best? (Select the single best option)</b>	Paid work	1
		Self-employed, such as own your business or farming	2
		Non-paid work, such as volunteer or charity	3
		Student	4
		Keeping house/ homemaker	5
		Retired	6
		Unemployed (health reasons)	7
		Unemployed (other reasons)	8
Other (specify) _____ _____	9		

Please continue to next page...



# WHODAS 2.0

WORLD HEALTH ORGANIZATION  
DISABILITY ASSESSMENT SCHEDULE 2.0

12

Interview

## Section 3 Preamble

### **Say to respondent:**

The interview is about difficulties people have because of health conditions.

### **Hand flashcard #1 to respondent**

By health condition I mean diseases or illnesses, or other health problems that may be short or long lasting; injuries; mental or emotional problems; and problems with alcohol or drugs.

Remember to keep all of your health problems in mind as you answer the questions. When I ask you about difficulties in doing an activity think about...

### **Point to flashcard #1**

- Increased effort
- Discomfort or pain
- Slowness
- Changes in the way you do the activity.

When answering, I'd like you to think back over the past 30 days. I would also like you to answer these questions thinking about how much difficulty you have had, on average, over the past 30 days, while doing the activity as you usually do it.

### **Hand flashcard #2 to respondent**

Use this scale when responding.

### **Read scale aloud:**

None, mild, moderate, severe, extreme or cannot do.

**Ensure that the respondent can easily see flashcards #1 and #2 throughout the interview**

**Please continue to next page...**



# **WHODAS 2.0**

WORLD HEALTH ORGANIZATION  
DISABILITY ASSESSMENT SCHEDULE 2.0

*Flashcard 1*

## **Health conditions:**

- **Diseases, illnesses or other health problems**
- **Injuries**
- **Mental or emotional problems**
- **Problems with alcohol**
- **Problems with drugs**

## **Having difficulty with an activity means:**

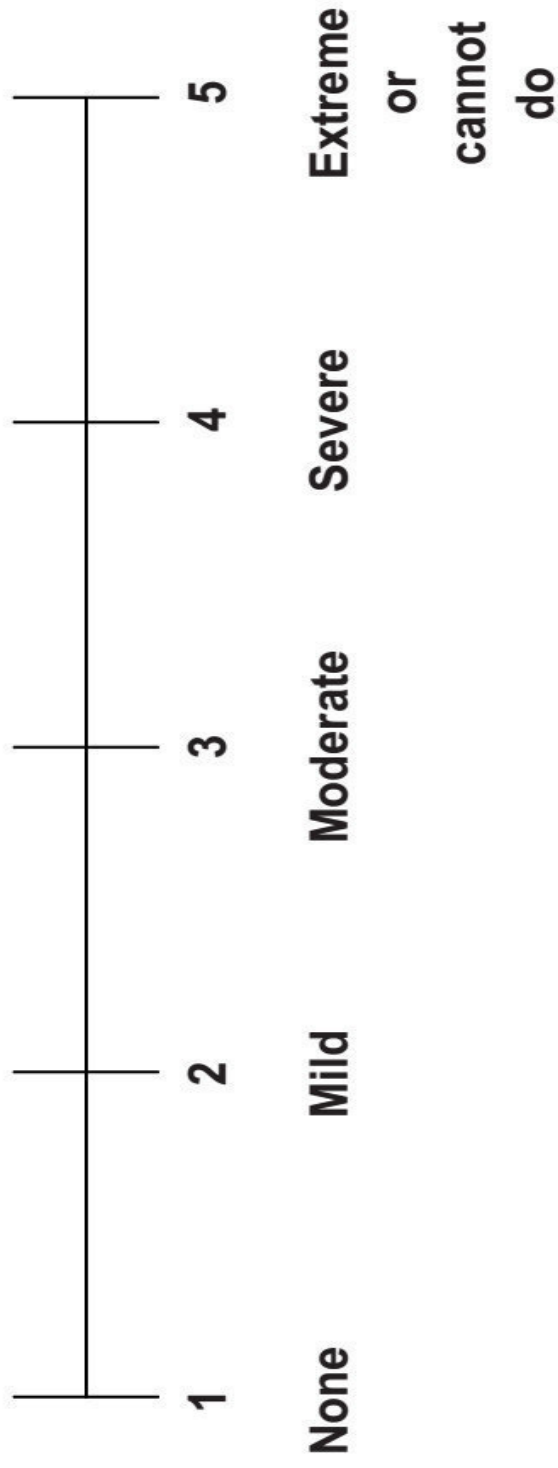
- **Increased effort**
- **Discomfort or pain**
- **Slowness**
- **Changes in the way you do the activity**

**Think about the past 30 days only.**

# WHODAS 2.0

WORLD HEALTH ORGANIZATION  
DISABILITY ASSESSMENT SCHEDULE 2.0

*Flashcard 2*





# WHODAS 2.0

WORLD HEALTH ORGANIZATION  
DISABILITY ASSESSMENT SCHEDULE 2.0

12
Interview

## Section 4 Core questions

### Show flashcard #2

In the past 30 days, how much difficulty did you have in:		None	Mild	Moderate	Severe	Extreme or cannot do
S1	Standing for long periods such as 30 minutes?	1	2	3	4	5
S2	Taking care of your household responsibilities?	1	2	3	4	5
S3	Learning a new task, for example, learning how to get to a new place?	1	2	3	4	5
S4	How much of a problem did you have joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can?	1	2	3	4	5
S5	How much have you been emotionally affected by your health problems?	1	2	3	4	5

In the past 30 days, how much difficulty did you have in:		None	Mild	Moderate	Severe	Extreme or cannot do
S6	Concentrating on doing something for ten minutes?	1	2	3	4	5
S7	Walking a long distance such as a kilometre [or equivalent]?	1	2	3	4	5
S8	Washing your whole body?	1	2	3	4	5
S9	Getting dressed?	1	2	3	4	5
S10	Dealing with people you do not know?	1	2	3	4	5
S11	Maintaining a friendship?	1	2	3	4	5
S12	Your day-to-day work/school?	1	2	3	4	5

H1	Overall, in the past 30 days, how many days were these difficulties present?	Record number of days ____
H2	In the past 30 days, for how many days were you totally unable to carry out your usual activities or work because of any health condition?	Record number of days ____
H3	In the past 30 days, not counting the days that you were totally unable, for how many days did you cut back or reduce your usual activities or work because of any health condition?	Record number of days ____

This concludes our interview. Thank you for participating.

## Quick Disability of the Arm, Shoulder, Hand questionnaire

# THE **QuickDASH**

OUTCOME MEASURE

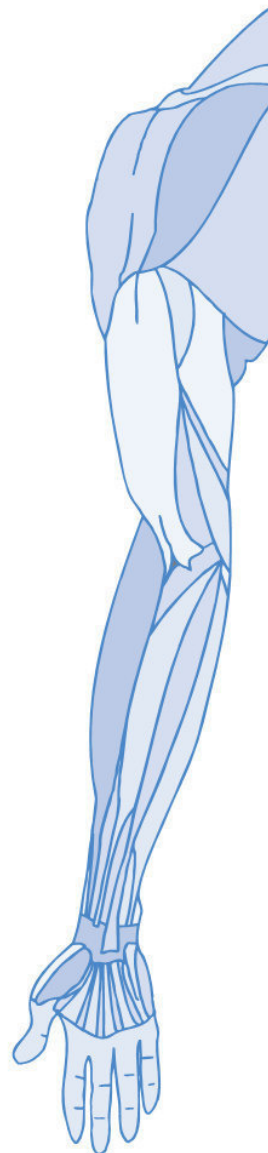
### INSTRUCTIONS

This questionnaire asks about your symptoms as well as your ability to perform certain activities.

Please answer *every question*, based on your condition in the last week, by circling the appropriate number.

If you did not have the opportunity to perform an activity in the past week, please make your *best estimate* of which response would be the most accurate.

It doesn't matter which hand or arm you use to perform the activity; please answer based on your ability regardless of how you perform the task.





## QuickDASH

Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. Open a tight or new jar.	1	2	3	4	5
2. Do heavy household chores (e.g., wash walls, floors).	1	2	3	4	5
3. Carry a shopping bag or briefcase.	1	2	3	4	5
4. Wash your back.	1	2	3	4	5
5. Use a knife to cut food.	1	2	3	4	5
6. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).	1	2	3	4	5

	NOT AT ALL	SLIGHTLY	MODERATELY	QUITE A BIT	EXTREMELY
7. During the past week, <i>to what extent</i> has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups?	1	2	3	4	5

	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
8. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem?	1	2	3	4	5

Please rate the severity of the following symptoms in the last week. (*circle number*)

	NONE	MILD	MODERATE	SEVERE	EXTREME
9. Arm, shoulder or hand pain.	1	2	3	4	5
10. Tingling (pins and needles) in your arm, shoulder or hand.	1	2	3	4	5

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
11. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? ( <i>circle number</i> )	1	2	3	4	5





## The Deyo and Diehl satisfaction questionnaire

### The Deyo and Diehl outpatient satisfaction questionnaire and demographic data

Please indicate with a tick [✓]....

<b>Dissatisfied/ No</b>	<b>Don't know</b>	<b>Satisfied/ yes</b>	
			1. Were you satisfied with your contact with your physiotherapist
			2. Did you have an adequate explanation of your CRPS
			3. Do you feel the physiotherapist was concerned about you
			4. Do you feel the physiotherapist understood what was bothering you
			5. Do you feel you understand what was wrong
			6. Did your physiotherapist spend enough time with you
			7. Would you like to see the same physiotherapist if you were to go back to that clinic/department
			8. Was your care with your physiotherapist for your CRPS better, worse or the same as your visits to your specialist or doctor
			9. Did you seek help from another doctor or allied health professional or hospital after your last visit with your physiotherapist? If yes, whom

## Ethnicity

### What ethnic group do you belong to?

1. New Zealand European	
2. Maori	
3. Samoan	
4. Cook Islands Maori	
5. Tongan	
6. Niuean	
7. Chinese	
8. Indian	
9. Other, please state: e.g. Dutch, Japanese, Tokelauan	
10.	

## Possible predictor: TSK

### Tampa Scale for Kinesiophobia

Please indicate your characteristics by circling one of the numbers on the right of each of the items.

	Strongly disagree 1	Disagree 2	Agree 3	Strongly agree 4
1. I am afraid I might injure myself if I exercise	1	2	3	4
2. If I were to try and overcome it, my pain would increase	1	2	3	4
3. My body is telling me I have something dangerously wrong	1	2	3	4
4. My pain would probably be relieved if I were to exercise	1	2	3	4
5. People aren't taking my medical condition seriously enough	1	2	3	4
6. My injury has put my body at risk for the rest of my life	1	2	3	4
7. Pain always means I have injured my body	1	2	3	4
8. Just because something aggravates my pain does not mean it is dangerous	1	2	3	4
9. I am afraid that I might injure myself accidentally	1	2	3	4
10. Simply being careful that I do not make any unnecessary movements is the safest thing I can do to prevent my pain from worsening	1	2	3	4
11. I wouldn't have this much pain if there weren't something potentially dangerous going on in my body	1	2	3	4
12. Although my condition is painful, I would be better off if I was physically active	1	2	3	4
13. Pain lets me know when to stop exercising so that I don't injure myself	1	2	3	4
14. It's really not safe for a person with a condition like mine to be physically active	1	2	3	4
15. I can't do all the things normal people do because it's too easy for me to get injured	1	2	3	4
16. Even though something is causing me a lot of pain, I don't think that it's actually dangerous	1	2	3	4
17. No one should have to exercise when he/she is in pain	1	2	3	4

# Possible predictor: Kessler 10

Binding margin

Date completed: \_\_\_ / \_\_\_ / \_\_\_\_\_

MENTAL HEALTH

MENTAL HEALTH

**Q2.** The last ten questions asked about feelings that might have occurred during the past 30 days. Taking them altogether, did these feelings occur More often in the past 30 days than is usual for you, about the same as usual, or less often than usual? (If you never have any of these feelings, circle response option "4.")

More often than usual			About the same as usual	Less often than usual		
A lot	Some	A little		A little	Some	A lot
1	2	3	4	5	6	7

The next few questions are about how these feelings may have affected you in the past 30 days. You need not answer these questions if you answered "None of the time" to **all** of the ten questions about your feelings.

Binding margin – do not write

**Q3.** During the past 30 days, how many days out of 30 were you totally unable to work or carry out your normal activities because of these feelings?

\_\_\_\_\_ (Number of days)

**Q4.** **Not counting the days you reported in response to Q3,** how many days in the past 30 were you able to do only half or less of what you would normally have been able to do, because of these feelings?

\_\_\_\_\_ (Number of days)

**Q5.** During the past 30 days, how many times did you see a doctor or other health professional about these feelings?

\_\_\_\_\_ (Number of times)

K10+ SELF-REPORT MEASURE (2 of 2)

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
<b>Q6.</b> During the past 30 days, how often have physical health problems been the main cause of these feelings?	1	2	3	4	5

K10+ SELF-REPORT MEASURE (1 of 2)

**Thank you for completing this questionnaire.**

## Possible predictor: EPQ-BV

### EPQ-BV

Please indicate your characteristics by circling one of the numbers on the right of each of the items.

Not at all 1	Slightly 2	Moderately 3	Very Much 4	Extremely 5	
1. Are you a talkative person?	1	2	3	4	5
2. Does your mood often go up and down?	1	2	3	4	5
3. Are you rather lively?	1	2	3	4	5
4. Do you ever feel miserable for no reason?	1	2	3	4	5
5. Do you enjoy meeting new people?	1	2	3	4	5
6. Are you an irritable person?	1	2	3	4	5
7. Can you usually let yourself go and enjoy yourself at a lively party?	1	2	3	4	5
8. Are your feelings easily hurt?	1	2	3	4	5
9. Do you normally take the initiative in making new friends?	1	2	3	4	5
10. Do you often feel "fed-up"?	1	2	3	4	5
11. Can you easily get some life into a rather dull party?	1	2	3	4	5
12. Would you call yourself a nervous person?	1	2	3	4	5
13. Do you tend to keep in the background on social occasions?	1	2	3	4	5
14. Are you a worrier?	1	2	3	4	5
15. Do you like mixing with people?	1	2	3	4	5
16. Would you call yourself tense or "highly-strung"?	1	2	3	4	5
17. Do you like plenty of action and excitement around you?	1	2	3	4	5
18. Do you worry to long after an embarrassing experience?	1	2	3	4	5
19. Are you mostly quiet when you are with other people?	1	2	3	4	5
20. Do you suffer from nerves?	1	2	3	4	5
21. Do other people think of you as being very lively?	1	2	3	4	5
22. Do you often feel lonely?	1	2	3	4	5
23. Can you get a party going?	1	2	3	4	5
24. Are you often troubled about feelings of guilt?	1	2	3	4	5

**Thank you very much for your cooperation!**



## Possible predictor: Health Anxiety Index-Short version

### Health Anxiety Index (short version)

Each question in this section consists of a group of four statements. Please read each group of statements.

Carefully and then select the one which best describes your feelings, over the past six months.

Identify the statement by ringing the letter next to it, i.e. if you think that statement (a) is correct, ring statement (a).

It may be that more than one statement applies, in which case, please ring any that are applicable.

1. (a) I do not worry about my health.  
(b) I occasionally worry about my health.  
(c) I spend much of my time worrying about my health.  
(d) I spend most of my time worrying about my health.
2. (a) I notice aches/pains less than most other people (of my age).  
(b) I notice aches/pains as much as most other people (of my age).  
(c) I notice aches/pains more than most other people (of my age).  
(d) I am aware of aches/pains in my body all the time.
3. (a) As a rule I am not aware of bodily sensations or changes.  
(b) Sometimes I am aware of bodily sensations or changes.  
(c) I am often aware of bodily sensations or changes.  
(d) I am constantly aware of bodily sensations or changes.
4. (a) Resisting thoughts of illness is never a problem.  
(b) Most of the time I can resist thoughts of illness.  
(c) I try to resist thoughts of illness but am often unable to do so.  
(d) Thoughts of illness are so strong that I no longer even try to resist them.
5. (a) As a rule I am not afraid that I have a serious illness.  
(b) I am sometimes afraid that I have a serious illness.  
(c) I am often afraid that I have a serious illness.  
(d) I am always afraid that I have a serious illness.
6. (a) I do not have images (mental pictures) of myself being ill.  
(b) I occasionally have images of myself being ill.  
(c) I frequently have images of myself being ill.  
(d) I constantly have images of myself being ill.

Please turn over to continue the questionnaire

7.
  - (a) I do not have any difficulty taking my mind off thoughts about my health.
  - (b) I sometimes have difficulty taking my mind off thoughts about my health.
  - (c) I often have difficulty in taking my mind off thoughts about my health.
  - (d) Nothing can take my mind off thoughts about my health.
8.
  - (a) I am lastingly relieved if my doctor tells me there is nothing wrong.
  - (b) I am initially relieved but the worries sometimes return later.
  - (c) I am initially relieved but the worries always return later.
  - (d) I am not relieved if my doctor tells me there is nothing wrong.
9.
  - (a) If I hear about an illness I never think I have it myself.
  - (b) If I hear about an illness I sometimes think I have it myself.
  - (c) If I hear about an illness I often think I have it myself.
  - (d) If I hear about an illness I always think I have it myself.
10.
  - (a) If I have a bodily sensation or change I rarely wonder what it means.
  - (b) If I have a bodily sensation or change I often wonder what it means.
  - (c) If I have a bodily sensation or change I always wonder what it means.
  - (d) If I have a bodily sensation or change I must know what it means.
11.
  - (a) I usually feel at very low risk for developing a serious illness.
  - (b) I usually feel at fairly low risk for developing a serious illness.
  - (c) I usually feel at moderate risk for developing a serious illness.
  - (d) I usually feel at high risk for developing a serious illness.
12.
  - (a) I never think I have a serious illness.
  - (b) I sometimes think I have a serious illness.
  - (c) I often think I have a serious illness.
  - (d) I usually think that I am seriously ill.
13.
  - (a) If I notice an unexplained bodily sensation I don't find it difficult to think about other things.
  - (b) If I notice an unexplained bodily sensation I sometimes find it difficult to think about other things
  - (c) If I notice an unexplained bodily sensation I often find it difficult to think about other things.
  - (d) If I notice an unexplained bodily sensation I always find it difficult to think about other things.
14.
  - (a) My family/friends would say I do not worry enough about my health.
  - (b) My family/friends would say I have a normal attitude to my health.
  - (c) My family/friends would say I worry too much about my health.
  - (d) My family/friends would say I am a hypochondriac.

Please turn over to continue the questionnaire

For the following questions, please think about what it might be like if you had a serious illness of a type which particularly concerns you (such as heart disease, cancer, multiple sclerosis and so on). Obviously you cannot know for definite what it would be like; please give your best estimate of what you think might happen, basing your estimate on what you know about yourself and serious illness in general.

15.
  - (a) If I had a serious illness I would still be able to enjoy things in my life quite a lot.
  - (b) If I had a serious illness I would still be able to enjoy things in my life a little.
  - (c) If I had a serious illness I would be almost completely unable to enjoy things in my life.
  - (d) If I had a serious illness I would be completely unable to enjoy life at all.
  
16.
  - (a) If I developed a serious illness there is a good chance that modern medicine would be able to cure me.
  - (b) If I developed a serious illness there is a moderate chance that modern medicine would be able to cure me.
  - (c) If I developed a serious illness there is a very small chance that modern medicine would be able to cure me.
  - (d) If I developed a serious illness there is no chance that modern medicine would be able to cure me.
  
17.
  - (a) A serious illness would ruin some aspects of my life.
  - (b) A serious illness would ruin many aspects of my life.
  - (c) A serious illness would ruin almost every aspect of my life.
  - (d) A serious illness would ruin every aspect of my life.
  
18.
  - (a) If I had a serious illness I would not feel that I had lost my dignity.
  - (b) If I had a serious illness I would feel that I had lost a little of my dignity.
  - (c) If I had a serious illness I would feel that I had lost quite a lot of my dignity.
  - (d) If I had a serious illness I would feel that I had totally lost my dignity.

# Outcome: Physiotherapy homework questionnaire

## Homework questionnaire

### SECTION 1

1. How often do you do your physiotherapy homework exercises in a week?

Never	Once	Twice	Three times	Four times	Five times	Six times	Every day

2. How often daily do your physiotherapy homework exercises in a day?

Never	Once	Twice	Three times	Four times	Five times	Every hour	More than every hour	Other

3. How would you rate how much your prescribed homework exercise helped to make your pain feel less?

Always	Almost always	Sometimes	Rarely	Never

4. What specific physiotherapy homework exercise helped you the most at home:  
 For pain \_\_\_\_\_  
 For being able to use your limb \_\_\_\_\_

### SECTION 2:

1. When did you first feel your pain *Date:* \_\_\_\_\_

2. When did you first have your CRPS diagnosis *Date:* \_\_\_\_\_

3. When did you first see a Pain Specialist doctor *Date:* \_\_\_\_\_

4. Have you had other treatments from doctors or pain specialists, if so what:  
 \_\_\_\_\_  
 \_\_\_\_\_

5. Have you had other medications prescribed from doctors or pain specialists, if so what  
 \_\_\_\_\_  
 \_\_\_\_\_

6. With all your treatment from physios and doctors and other health professionals what would say made the biggest difference to improving your pain and ability to use your limb  
 \_\_\_\_\_  
 \_\_\_\_\_

7. Would you like to have the study findings when it is completed? Oyes Ono

Thank you, this ends all my questions.

**Complex Regional Pain Syndrome (CRPS)**  
**physiotherapy management: A cohort longitudinal study**  
**across South Island New Zealand: a PhD proposal.**

Tracey Pons<sup>1</sup>

**Abstract**

Physiotherapy management for CRPS is considered to be essential. However, there is a lack of evidence-based valid treatment methods. There is controversy also between what treatment methods are safe or effective. It is proposed to assess physiotherapy intervention for patients with CRPS referred to all outpatient clinics in the South Island of New Zealand with an observational, cohort longitudinal study. This is to a) determine what treatment methods are currently being used by physiotherapists for the management of CRPS b) which treatment methods are more effective c) develop a clinical model for physiotherapy CRPS management d) potentially explore the Maori narrative about their experience with physiotherapy treatment methods for CRPS. This is

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the first known clinical observational study of physiotherapy for CRPS to be completed anywhere in the world. Ethical approval from University of Otago has been given, No: H13/103. Written consent from participants will be obtained. Pre and post outcome measures will be measured after 6 weeks of the intervention, at 6 months and at 1 year. Statistical analysis will compare pre and post outcome measures with a power of 0.8 and alpha of 0.05. Assuming an effect size of 0.2 a sample of 160 participants will be required.

**Key words**

Physiotherapy, Complex Regional Pain Syndrome (CRPS), Cohort longitudinal clinical study

## **1 Introduction**

Complex Regional Pain Syndrome (CRPS) is a persistent neuropathic pain condition that can follow any injury ranging from trivial to severe injury where the pain experience is severe and disproportionate to the inciting event [1-4]. The syndrome was identified in the American civil war [4] and was broadly named Sudeck's atrophy or algodystrophy. During World War 1 and 2 it was described as causalgia [5, 6]. Later, in 1953 two types of this syndrome were recognised and were named either "reflex sympathetic dystrophy" if the nerve was not damaged as it was thought to be a problem primarily associated with the sympathetic nervous system or "causalgia" if the nerve had been physically and permanently damaged [7, 8]. It was identified in 1970's that the problem involved the peripheral as well as central nervous system, but the mechanisms for the physiology involved remained inconclusive [7].

These broad diagnoses raised controversies [9] and the committee for taxonomy of the International Association for the Study of Pain (IASP) met in 1994 together with professionals publishing literature in this area and they identified specific diagnostic criteria for this syndrome. The controversy had been shown in research that this condition was not exclusively a problem of the parasympathetic nervous system so the terms "reflex sympathetic dystrophy and

causalgia” needed to be changed. This syndrome had been conclusively shown not to be a problem primarily related to the sympathetic nervous system [10]. This IASP committee changed the name to CRPS either Type 1 or Type 11 to replace the previous names of “reflex sympathetic dystrophy” and “causalgia” respectively [11].

CRPS and the IASP nomenclature continue to remain a complex problem. It was found that the diagnostic criteria decided upon by the IASP were not specific enough and were not used uniformly in clinical published research [8, 12]. Its diagnostic criteria have since this gathering in 1994 been debated and redefined again by the International Association for the Study of Pain (IASP) with the specialist Budapest committee in 2007 [8, 13]. These criteria are now considered the most likely to be reasonably accurate towards a clinical diagnosis as well as for research involving CRPS. Although these diagnostic criteria have been more robustly defined, the other difficulty is that the aetiology and development of the CRPS problem(s) are not yet fully understood [11-16]. Hence, effective treatment strategies in both the research and clinical fields are not yet fully developed. This project explores the current physiotherapy treatment for CRPS.



## 2 Literature

Physiotherapy management for CRPS is considered to be essential in the multi-disciplinary team approach despite few controlled studies [3, 4, 17-20]. The greater benefits of physiotherapy intervention for CRPS of the upper limb was confirmed in a randomised controlled trial (RCT) which compared physiotherapy and occupational therapy intervention [21]. It is also considered important that diagnosis is made as early as possible [1] and referral to physiotherapy is not delayed [1, 3, 20, 22]

A recent systematic literature review of different physiotherapy treatment methods suggested that graded motor imagery (GMI) was the most effective [23] to significantly reduce pain, swelling and improve function [17, 24-28]. GMI uses training to help patients who experience so much pain that they struggle to do any movement with the painful limb. The training involves firstly; to be able to recognise left from right, then to imagine doing the movement that hurts followed with mirroring the painful action with the reflection of the uninjured limb in the mirror.

However, the research protocol suggested with the GMI has been recently shown to be less effective in the clinical setting [29]. This is perhaps because

the intense approach applied in the research setting is difficult to replicate in the clinical setting and in a patient's everyday life. The research trials with functional magnetic resonance imaging (fMRI) showed central neuroplastic changes in CRPS whereby the somato-sensory cortex functioning of the affected limb was distorted [25-27]. These central changes are shown to be reversed through GMI intervention and maintained a year later. It is thought that GMI corrects the aberrant cortical reorganisation that is associated with CRPS when the pain and functional ability have improved [25, 28]. An interesting observation in these fMRI trials, is that where pain and functioning have not improved, despite the intervention, the somato-sensory cortex functioning has not changed either.<sup>2</sup>

There is also controversy between what other treatment methods are safe or effective. A case series of 106 patients showed that "pain exposure physiotherapy" was effective as a last resort for recalcitrant CRPS and a recent sample of 20 CRPS patients showed it to be beneficial [30, 31]. This physiotherapy treatment method allows as much pain provocation with exercise as the patient tolerates as the avoidance to using the limb is considered to be detrimental, despite the high experience of pain in using the limb. This approach has been questioned as possibly contributing to worsening the pain

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<sup>2</sup> This suggests that the entire problem is causally sustained in the cortex.

experience in CRPS [32]. It has also been questioned as there is not enough evidence to fully support it [17].

Pain exposure is quite different from graded exposure physiotherapy and the two terms may possibly be confused by practitioners. Fear avoidance has also been shown recently to be a problem for some CRPS patients [33] and graded exposure therapy has also been shown to be helpful for a small group of CRPS [34]. Graded exposure uses an approach where the experience of pain is not ignored, but rather exercise rehabilitation is allowed in a gently graded manner, sub-threshold to intolerable pain by constructing an exercise sequence into smaller tolerable actions. As tolerance is gradually improved the exercise sequence, larger actions and intensity is progressed.

There is also some evidence for mirror therapy supported with a robust clinical trial as well as further lower quality research [35, 36]. Mirror therapy is quite different from the interventions above where exposure to pain is either graded or ignored. The affected limb is not used initially while the unaffected limb performs the exercise rehabilitation of painful exercise and the patient views the unaffected limb in the mirror. Since the mirror reflects the image, the image looks like the affected limb performing the action. As pain experience is reduced through the viewing of the mirrored exercise, the affected limb is included in the exercising. Prism glasses were researched on the basis of mirror therapy and these small research trials showed some benefit [37, 38]. However,

the author found that it is not possible to acquire these prism glasses for use in the clinical field. The prism glasses are manufactured in the United Kingdom and the safety regulation procedures have not yet confirmed them safe for public use.

Other clinical research evidence is for the effect of transcutaneous neuromuscular stimulation (TENS) in reduction of the pain experience for CRPS. TENS has been investigated for many years and shown to be positive in early research of 1960's to be positive for all sorts of chronic pain conditions [39]. There is more recent evidence to support it, but this evidence is not very strong [40, 41].

It appears that there is a larger body of research trials for CRPS in the research setting, rather than the clinical setting. Further research trials show tactile discrimination to be a problem [25, 42] and that specific sensory discrimination training is effective to resolve the tactile discrimination problem as well as reduce the experience of pain and improve function for this problems [28, 43]. Body perception disturbances can sometimes also be seen with CRPS [44] and treatment aimed at activating cortical centres have also been shown to be helpful in the research setting for resolving the body perception disturbance [28, 45]. Virtual reality was tested in the research setting for 5 CRPS patients and shown to be helpful [46] as fMRI had shown previously that a reduction of the

pain can be produced from virtual reality through the modulating effect it has on the sensory and emotional central centres of the pain experience [47].

The management of CRPS remains, after all, a complex problem for both physiotherapy and medical management. Despite these controversies, physiotherapy management for CRPS continues to be widely accepted as a matter of course [3, 4, 18-20]. A wide variety of sometimes conflicting techniques are known by the author to be used in the clinical field. Further research is needed to explore all these physiotherapy modalities and this project is designed to determine what is actually happening in the clinical environment so that a clinical model for physiotherapy management can be developed.

### **3. Purpose of this project**

The purpose of this project is to determine the efficacy of the current standard physiotherapy intervention for CRPS. This will be determined from the outcomes of usual physiotherapy outpatient clinics across the South Island of New Zealand. The data collected will be analysed to determine the effect of the physiotherapy on the experience of pain and functional ability. The data will potentially also be used towards developing a clinical model towards the

physiotherapy management for CRPS. This model will then be open for further testing. This project will be assessing CRPS patients in all stages of the syndrome. This will be the first observational longitudinal study for all physiotherapy interventions used for CRPS in the clinical setting known to the author in the world. This is important to do as it will provide evidence towards the best practice for the physiotherapy management of CRPS.

It is proposed with this cohort longitudinal study to determine a) what treatment methods are currently being used by physiotherapists for the management of CRPS b) which treatment methods are more effective c) what are the likely prognostic factors that contribute to a better/worse outcome? These are important to examine as it may be that there are particular treatment methods being used that are shown to be ineffective or that there are other factors that influence the outcomes other than physiotherapy intervention itself. These are important to examine and the large cohort longitudinal study provide the evidence from which a model and protocol for the management of CRPS can be developed.

There is also currently no research that provides evidence for specific treatment methods in the clinical setting that are more effective than others or in which context. What is also not yet known is how patient compliance with physiotherapy treatment method, especially the homework component affects outcomes. Neither is it known which specific dose delivery of physiotherapy for

CRPS is more effective in terms of frequency of scheduled treatment method(s), appointments with the physiotherapist, duration of time of treatment method(s) or homework prescribed.

There is also no known research of how physiotherapy intervention in particular affects minority groups. In New Zealand this is particularly important to our Maori community. The treaty of Waitangi lays a foundation for mutual co-operation and understanding between the majority Pakeha and minority Maori ethnic groups in New Zealand [48-50]. This study will be the first to address the specific outcomes of the Maori population who are affected with CRPS and it lays a foundation where it may be possible to further explore the Maori narrative of their experience with CRPS and outpatient physiotherapy.

The effect of the other variables that will possibly also affect the pain experience and functioning of a patient being treated with physiotherapy with CRPS will also be explored. These are: ethnicity, duration of time with CRPS, frequency of physiotherapy intervention, length of time from first experience of pain to diagnosis, prescribed medication by medical intervention, all/any possible medical procedures also prescribed, age, gender, adherence to intervention programme, satisfaction with physiotherapy, anxiety, depression and neuroticism.

### **3. Hypotheses**

#### **3.1. Primary hypothesis**

The primary hypothesis is that is that a) the timing of diagnosis and b) the timing of the start of physiotherapy intervention after diagnosis affect the outcome for CRPS physiotherapy intervention.

#### **3.2. Secondary hypothesis**

The secondary hypothesis is that physiotherapy intervention a) specifically aimed at central processes and c) the specific sequence of physiotherapy treatment modality affect the outcome for CRPS physiotherapy intervention with the reduction of the experience of pain and improvement in functional ability for CRPS in the clinical environment

#### **3.2. Null hypothesis**

The null hypothesis is that any observed changes are due to chance.



## **4. Method**

### **4.1 Study design**

#### *4.11. Patient participation*

Patients with a diagnosis of CRPS referred to physiotherapy at outpatient clinics will be asked to participate. Participation is voluntary; no financial or other gain will be awarded for participation. The study will be undertaken across all physiotherapy outpatient clinics in the South Island, New Zealand.

Inclusion criteria:

- Formal diagnosis confirmed by GP or specialist for CRPS of upper limb
- No visual impairment
- Written informed consent will be obtained

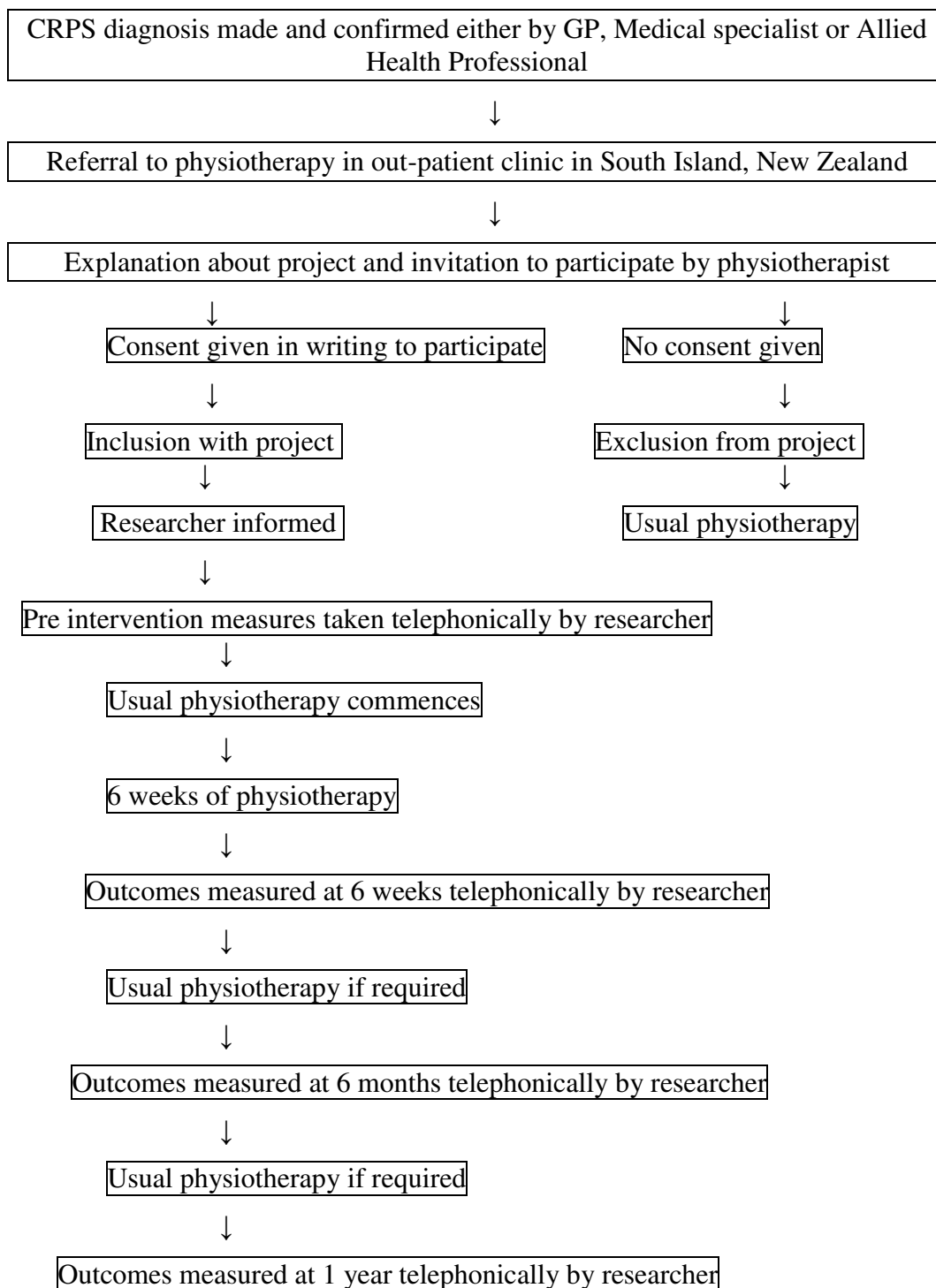
Exclusion criteria:

- Neuropathic pain that does not meet the CRPS criteria
- Blindness (sight is necessary for graded motor imagery)
- Any terminal co-morbid condition
- inability to answer questions, including age, cognitive impairment or language issues
- Voluntary withdrawal from the study

Analysis will not compare different outpatient physiotherapy departments or physiotherapists. Analysis compares only the type of intervention applied.

The flow chart for participation with this project is outlined in Figure 1.

Figure 1: Flow chart for participation in cohort longitudinal study of physiotherapy intervention for CRPS.



#### **4.2. Physiotherapy intervention**

Outpatient physiotherapy for CRPS in New Zealand is in private outpatient clinics and hospital physiotherapy outpatient departments. The physiotherapist involved with the patient will be asked to:

1. Explain the research objectives
2. Obtain consent.
3. Contact the researcher with the participants details for telephonic contact as well as listing the autonomic changes observed and reported
4. Send a copy of all clinical treatment notes to the researcher at 6 weeks post, 6 months post and 1 year post seeing the participant for details about the physiotherapy intervention given.

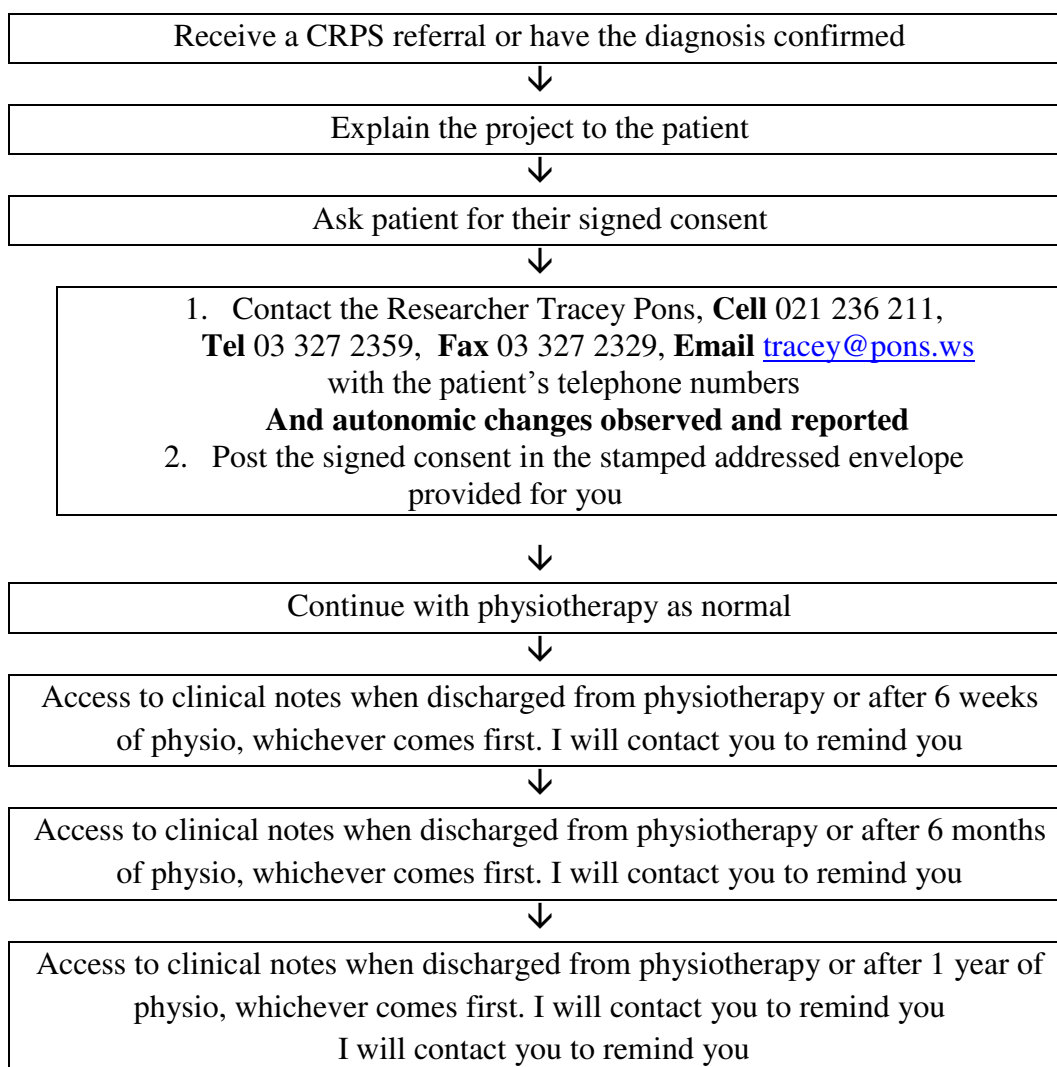
All treatment after one year will not be included in this research project.

Documentation of other intervention like nerve blocks or medication taken will be made by the researcher when interviewing the participant.

#### 4. 2.1. Physiotherapy flow chart for physiotherapist referral

The flow chart for physiotherapist referral is outlined in Figure 2.

Figure 2: Flow chart for participation in cohort longitudinal study of physiotherapy intervention for CRPS.



#### 4.4. Instruments

The quantitative tests outcome measures are as follows: the scores of pain experience on the Short form McGill Pain Questionnaire (MPQ-SF) [51, 52]; quality of life with World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2) [53], functional ability of upper limb CRPS with the Quick Disability of the Arm, Shoulder, Hand questionnaire (QuickDASH) [54-56], functional ability of the lower limb CRPS using the Foot Function Index (FFI) [57, 58] and satisfaction of care with the Deyo and Diehl Satisfaction (DDS) Questionnaire [59].

Demographic data will also be collected and will include the duration of time with CRPS diagnosis, length of time from first experience of pain to diagnosis, age, gender, and ethnicity as defined by Statistics New Zealand [60], frequency of physiotherapy intervention and adherence to intervention programme homework.

Quantitative tests will be taken by telephone interview:

- As physiotherapy intervention commences
- 6 weeks following commencing physiotherapy
- 6 months following commencing physiotherapy
- 1 year following commencing physiotherapy

Contact details will be necessary to obtain in order to complete the 6 month and 1 year post intervention outcome measurement. The participant will be contacted by telephone; an appointment will be arranged or the questionnaires answered at the time of the phone call.

Predictors for possible influences on the outcomes will be the Health Anxiety Index [61], Neuroticism scale of the Eysenck Personality Questionnaire, short form [62], Tampa scale for Kinesiophobia [63] , and the Ten item psychological distress Kessler (Kessler10) [64, 65] questionnaires. These predictors will only be administered once with the pre intervention measures.

Table 1 shows details about which questionnaires are used when and approximately how long each one takes to interview.

Table 2 shows details about measurement with Outcome instruments.

Table 3 shows the details about measurement with predictor instruments.

Table 1: Details about which questionnaires are used when and approximately how long each one takes to interview

<b>Interview schedule</b>	<b>Instrument</b>	<b>Approximate length of time to take</b>
As physiotherapy intervention commences	<u>Introduction</u>  <u>Baseline measures</u> MPQ-SF WHODAS 2 DASH or FFI (limb dependent)	1 min  2 min 4 min 1 min
6 weeks following commencing physiotherapy	<u>First predictor</u> TSK, HAI	2 min, 3min
6 weeks following commencing physiotherapy	<u>Introduction</u>  <u>Baseline measures</u> MPQ-SF WHODAS 2, section 4 only DASH or FFI (limb dependent)	1 min  2 min 3 min 1 min
6 weeks following commencing physiotherapy	<u>Satisfaction</u> DDS	1 min
6 weeks following commencing physiotherapy	<u>Adherence</u> Homework questions	2 min
6 weeks following commencing physiotherapy	<u>Second predictor</u> Kessler 10	2 min
6 months following commencing physiotherapy	<u>Introduction</u>  <u>Baseline measures</u> MPQ-SF WHODAS 2, section 4 only DASH or FFI (limb dependent)	1 min  2 min 3 min 1 min
6 months following commencing physiotherapy	<u>Satisfaction</u> DDS	1 min
6 months following commencing physiotherapy	<u>Adherence</u> Homework questions	2 min
6 months following commencing physiotherapy	<u>Third predictor</u> EPQ	2 min



1 year following commencing physiotherapy	<u>Introduction</u>	1 min
	<u>Baseline measures</u>	
	MPQ-SF	2 min
	WHODAS 2, section 4 only	3 min
	DASH or FFI (limb dependent)	1 min
	<u>Satisfaction</u>	
DDS	1 min	
<u>Adherence</u>		
Homework questions	1 min	
<u>Conclusion and thanks</u>		1 min

Table 2: Details of measurement with Outcome instrument

Name	Outcome Measures	Unit of measurement
MPQ-SF	a. Descriptive words for pain b. Numerical rating scale (NRS) c. Intensity of pain	a. Likert Scale + (n) words b. Likert Scale b. Likert Scale
WHODAS 2	a. Functional ability b. Pain experience	a. Likert scale b. Numbers of days
DASH	Upper limb functional ability	Likert scale
FFI	Lower limb functional ability	Likert scale
DDS	Satisfaction with physiotherapy	Likert scale
Homework	Adherence	Likert scale
	Frequency of adherence	Likert scale

Table 3: Details of measurement with predictor instrument

Predictor Measures	Unit of measurement
Time from first pain to diagnosis	Days
Time from diagnosis to first physiotherapy session	Days
TSK	Likert scale
HAI	Likert scale
Kessler 10	Likert scale
EPQ	Likert scale

#### **4.5. Intended Analysis**

Statistical analysis using Statistica ® will be used. The primary analysis will be for significance between pre and post outcome measures. Secondary analyses will compare variables and demographic data in categorical analysis and test for significance. Possible predictors and possible relationships between different types of physiotherapy intervention for outcome measures will be analysed. It is proposed that from the analysis a clinical model for the physiotherapy management of CRPS will be developed.

#### **4.6. Statistical power**

To detect for significance, a power  $1 - \beta$  (1-beta) of 0.8, and  $\alpha$  (alpha) of 0.05 will be used. To meet this significance, assuming a small effect for physiotherapy effectiveness of  $r = 0.2$ , a sample size of 153 participants [66] is required. In order to manage a potential dropout rate, a sample of 160 will be sought. If the effect of the intervention is found to be higher than anticipated as the project progresses; then less participants will be sought. Since this is an observational study, we estimate being able to recruit at least 100 participants in one year.

## **5. Ethical and cultural consideration**

The Ethical approval from the University is being sought. Since the project is a cohort, observational, outcome analysis of de-identified individuals, the National Health, Disability and Ethic committee has confirmed that this project does not require its review. The formal notification of this is in the appendix.

Participants will not be paid for their participation. A full written and verbal explanation about the project will be given to each participant, and again with the questionnaires. All participants will be asked for written consent to participate. This consent is for access to their clinical physiotherapy notes and telephone calls for outcomes measures from the researcher.

All participants will be given the option to withdraw at any stage from the project without giving an explanation. The Researcher has no commercial association or other relationship with outpatient physiotherapy departments or clinics in New Zealand that might result in a conflict of interest. This project is not anticipated to result in intellectual property, other than academic publication(s).

All participants' information is entered de-identified into the database as a numerical code. It will not be possible to identify any individual from any publication of the data. All clinical notes and outcomes measure records will be

stored in locked cabinets or electronically behind password protected servers so that anonymity is kept safe.

## **6. Timeline**

The project will be undertaken part-time.

July 2013: Formal enrolment with University

July 2013 - December 2013:

1. Ethical approval with National Ethics Committee
2. Formal arrangements with Physiotherapy Outpatient clinics to participate

January 2014-Dec 2017: Data collection

End 2014: International publication of literature search regarding predictors for CRPS outcomes

2015: International publication of initial findings

2016/7: International publication of outcomes

2018: Thesis submission

## **7. Resources**

The researcher has her own copy of Statistica® to analyse data. Costs for paper, printing, postage, phone calls and transport will be funded by the researcher or by small grants.

## **8. Discussion**

### **8.1. Strengths of this project**

There are many strengths of this cohort longitudinal study. They are firstly, the possibility for the development of an evidence based model for physiotherapy management of CRPS. Secondly, it is the first known longitudinal cohort of all physiotherapy interventions in the clinical setting for CRPS in the world.

Thirdly, this evaluation of clinical application provides current best-evidence of each intervention as well as its direction of effect. Fourthly, the project offers a unique window to determine what is actually being applied in the clinical setting. Fifthly, this project offers a unique view of the patient's perspective of their CRPS physiotherapy management.

Other strengths of the proposed project include its statistical power<sup>3</sup> so that error, though never possible to eliminate, is not likely to be significant.

Currently there is no physiotherapy model for the management of CRPS. A clinical model and protocol for the physiotherapy management of CRPS will be developed.

In the clinical field, the novel aspect of this project provides insight into the specific effect of different interventions towards the development of the model.

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<sup>3</sup> The high expected power is justified on the basis of the sample and effect size.

It is known by the author that physiotherapists are using a wide variety of interventions for the management of CRPS since there is currently no evidence based protocol.

## **8.2. Weaknesses of this project**

Clinical practice and research evidence do not always share everything in common with the interventions. The strict protocols that are essential to the scientific method can be difficult to apply in everyday clinical practice. In clinical practice a significant constraint is the adherence of the patient to the homework self-management strategies and exercises that are to be completed without supervision [67]. This is especially the case for CRPS where the benefit of pain relief associated with the self-management strategies and exercises are not necessarily immediately apparent. Instead, perseverance over a period of time brings about the pain relief that in turn assists with the motivation to continue. Although participants can be surveyed for their compliance, they may fake it. A further weakness is the impossibility of excluding participants from formal medical and other allied or alternative interventions that may be occurring concurrent with the physiotherapy intervention. In turn this is due to the nature of the insurance for accidents in New Zealand with the Accident Compensation Commission (ACC) often adopting a multi-treatment strategy to these cases.

Another weakness is the threat to the internal validity with the possibility that standard physiotherapy is interpreted differently by different clinical practitioners. Furthermore, it is difficult to determine to what extent harm might be occurring directly as a result of physiotherapy intervention. As discussed above, there is some evidence that even conventional physiotherapy intervention can be ineffective and harmful, although the consequences of such harm are generally limited to worsening of the pain rather than to physical injury. It should also be noted that the treatment strategies proposed in this project are widely used clinically (though their relative efficacy is unknown). In the normal course of clinical practice there are patients who do not get better.

### **8.3. Future research**

This proposed project provides a platform for future research for CRPS physiotherapy management in both the research and clinical fields. This is particularly with the specific effect of the commonly used intervention for CRPS management. There will potentially be many other unanswered questions from this project for CRPS outcomes and physiotherapy management:

- The effect of frequency of supervised physiotherapy and homework on CRPS outcomes
- The specific effects of different interventions that are shown to have similar outcomes

- How the physiotherapist and patient relationship affects CRPS outcomes
- Testing and validation of the model proposed to be developed

## **9. Conclusion**

Physiotherapy management for CRPS is regarded as essential despite the lack of robust evidence for physiotherapy interventions in outpatient clinics. This project will determine the outcomes of physiotherapy intervention for CRPS across the South Island, New Zealand. Validated and reliable outcome measures of the scores of pain experience will be determined by the MPQ-SF; quality of life with the WHODAS 2; the DASH for specific upper limb functioning CRPS; the FFI-R for specific lower limb functioning and the POSQ for patient satisfaction. Possible predictors for influences on the outcomes will be the HAI, Kessler-10, Tampa Scale for Kinesiophobia and Neuroticism scale of Eysenck personality questionnaire. Pre and post outcome measures will be measured after 6 weeks of the intervention; at 6 months and at 1 year. Significance: a power  $1-\beta$  of 0.8, and  $\alpha$  of 0.05 will be used; assuming an effect size of .2, a sample size of 153 (160 to include potential drop-out rate) participants will be sought. The potential weaknesses of the project are the internal validity with different therapists applying the intervention as well as the adherence of participants to attending their physiotherapy sessions and participating with the homework management. The potential strengths of the project are the development of an evidence based model for the physiotherapy



management of CRPS, the statistical evidence provided with the first cohort longitudinal clinical study, the novel aspects being researched, the evaluation of the efficacy of current clinical practice application for CRPS physiotherapy management and the possibility to evaluate the experience from the patient's perspective and explore the Maori narrative. The opportunities for future research from this project are potentially broad; the model for the physiotherapy management of CRPS that will be developed will be open for further scrutiny, testing and validation.

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